United States of America

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Therefore, this United States

Patent

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Katherine Kelly Vidal

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If the application for this patent was filed on or after June 8, 1995, the term of this patent begins on the date on which this patent issues and ends twenty years from the filing date of the application or, if the application contains a specific reference to an earlier filed application or applications under 35 U.S.C. 120, 121, 365(c), or 386(c), twenty years from the filing date of the earliest such application ("the twenty-year term"), subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b), and any extension as provided by 35 U.S.C. 154(b) or 156 or any disclaimer under 35 U.S.C. 253.

If this application was filed prior to June 8, 1995, the term of this patent begins on the date on which this patent issues and ends on the later of seventeen years from the date of the grant of this patent or the twenty-year term set forth above for patents resulting from applications filed on or after June 8, 1995, subject to the payment of maintenance fees as provided by 35 U.S.C. 41(b) and any extension as provided by 35 U.S.C. 156 or any disclaimer under 35 U.S.C. 253.

US012105089B2

(12) **United States Patent**
Shalek et al.

(10) **Patent No.: US 12,105,089 B2**
(45) **Date of Patent: Oct. 1, 2024**

(54) **CELL ATLAS OF THE HEALTHY AND ULCERATIVE COLITIS HUMAN COLON**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 871 days.

(21) Appl. No.: **16/632,018**

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§ 371 (c)(1),
(2) Date: **Jan. 17, 2020**

(87) PCT Pub. No.: **WO2019/018844**
PCT Pub. Date: **Jan. 24, 2019**

(65) **Prior Publication Data**

US 2021/0325387 A1 Oct. 21, 2021

Related U.S. Application Data

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(51) **Int. Cl.**
G01N 33/569 (2006.01)
C12Q 1/6883 (2018.01)
G01N 33/68 (2006.01)

(52) **U.S. Cl.**
CPC ***G01N 33/56966*** (2013.01); ***C12Q 1/6883*** (2013.01); ***G01N 33/6893*** (2013.01); *C12Q 2600/106* (2013.01); *C12Q 2600/158* (2013.01); *G01N 2800/065* (2013.01); *G01N 2800/52* (2013.01)

(58) **Field of Classification Search**
CPC G01N 33/56966; G01N 33/6893
See application file for complete search history.

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Primary Examiner — Kevin E Weddington

(74) *Attorney, Agent, or Firm* — F. Brent Nix, Esq.; Johnson, Marcou, Isaacs & Nix, LLC; Christopher D. Southgate, Esq.

(57) **ABSTRACT**

The present invention provides for a human cell atlas of the colon from healthy and diseased subjects. The atlas was obtained by single sequencing of about 117,000 cells. The present invention discloses novel markers for cell types. Moreover, genes associated with disease are identified in the colon and colon specific cell types. The invention provides for diagnostic assays based on gene markers and cell composition, as well as target cell types that express genes associated with disease. Finally, disclosed are novel cell types and methods of quantitating, detecting and isolating the cell types.

20 Claims, 70 Drawing Sheets

Specification includes a Sequence Listing.

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WO	2014/093595	A1		6/2014
WO	2014/093622	A2		6/2014
WO	2014/093635	A1		6/2014
WO	2014/093655	A2		6/2014
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WO	2014/093694	A1		6/2014
WO	2014/093701	A1		6/2014
WO	2014/093709	A1		6/2014
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WO	2014/093718	A1		6/2014
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WO	2014/204725	A1		12/2014
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WO	2018/035250	A1		2/2018
WO	2018/170333	A1		9/2018
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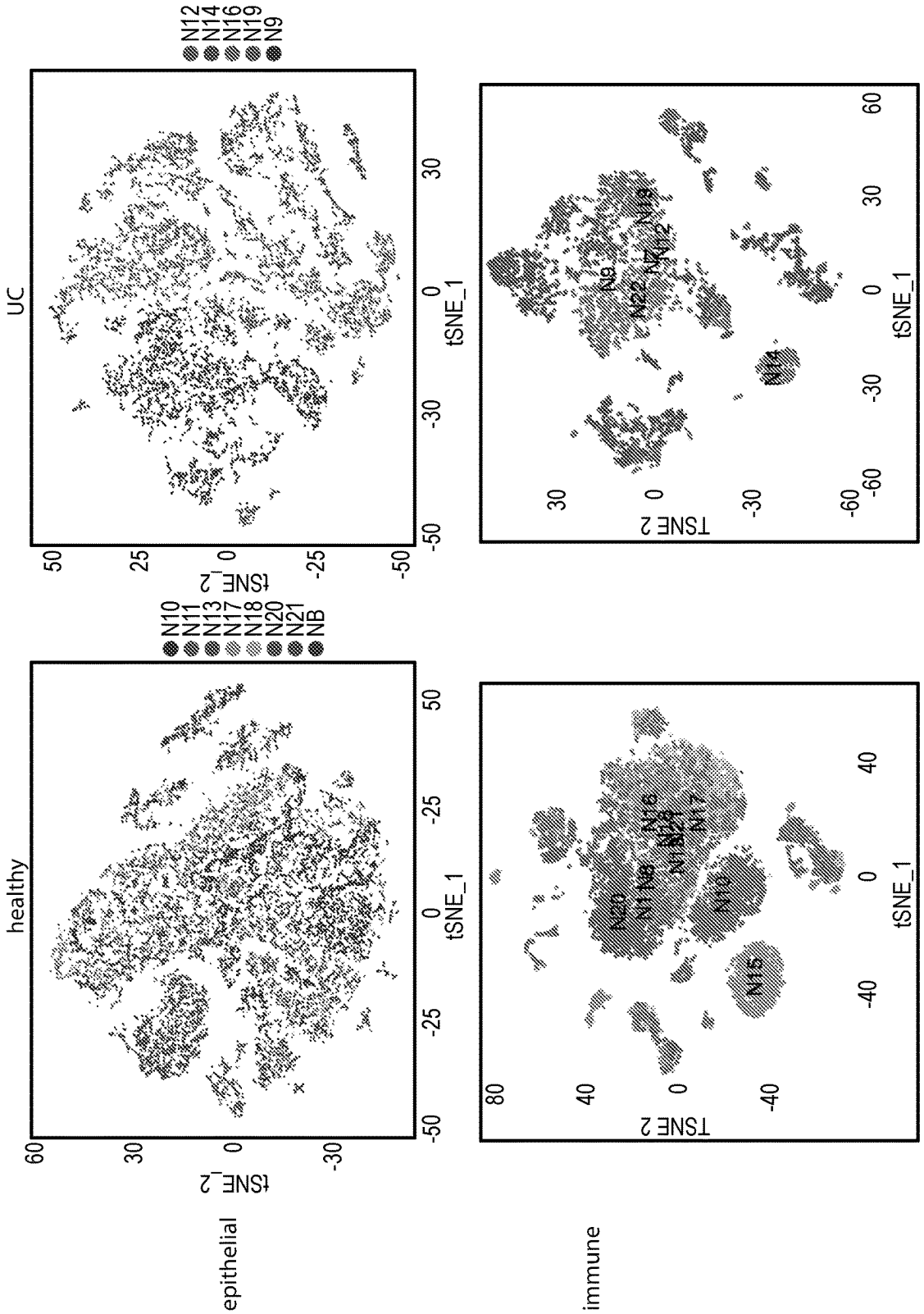

UC
healthy
epithelial
immune
tSNE_1
tSNE_2
TSNE 2
N10
N11
N13
N17
N18
N20
N21
NB
N12
N14
N16
N19
N9
N15

FIG. 1

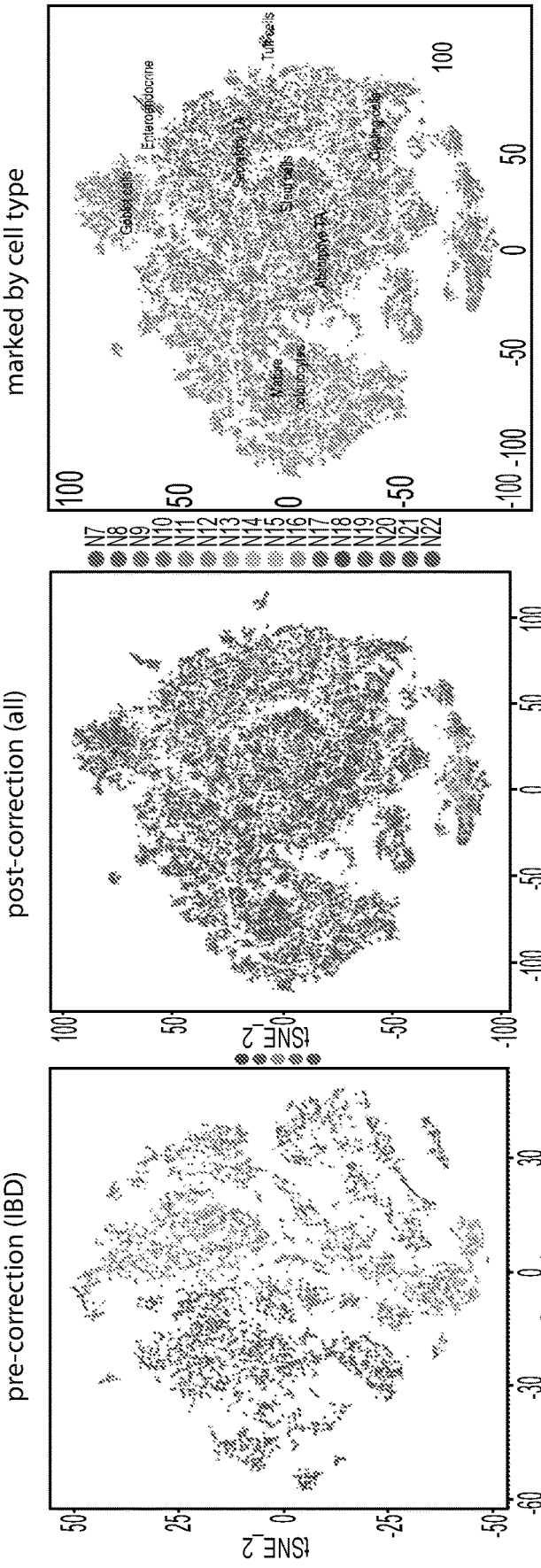

pre-correction (IBD)
post-correction (all)
marked by cell type
tSNE_1
tSNE_2
N7
N8
N9
N10
N11
N12
N13
N14
N15
N16
N17
N18
N19
N20
N21
N22
Goblet cells
Enteroendocrine
Tuft cells
Stem cells
Absorptive TA
Secretory TA
Colonocytes
Deep crypt cells

FIG. 2

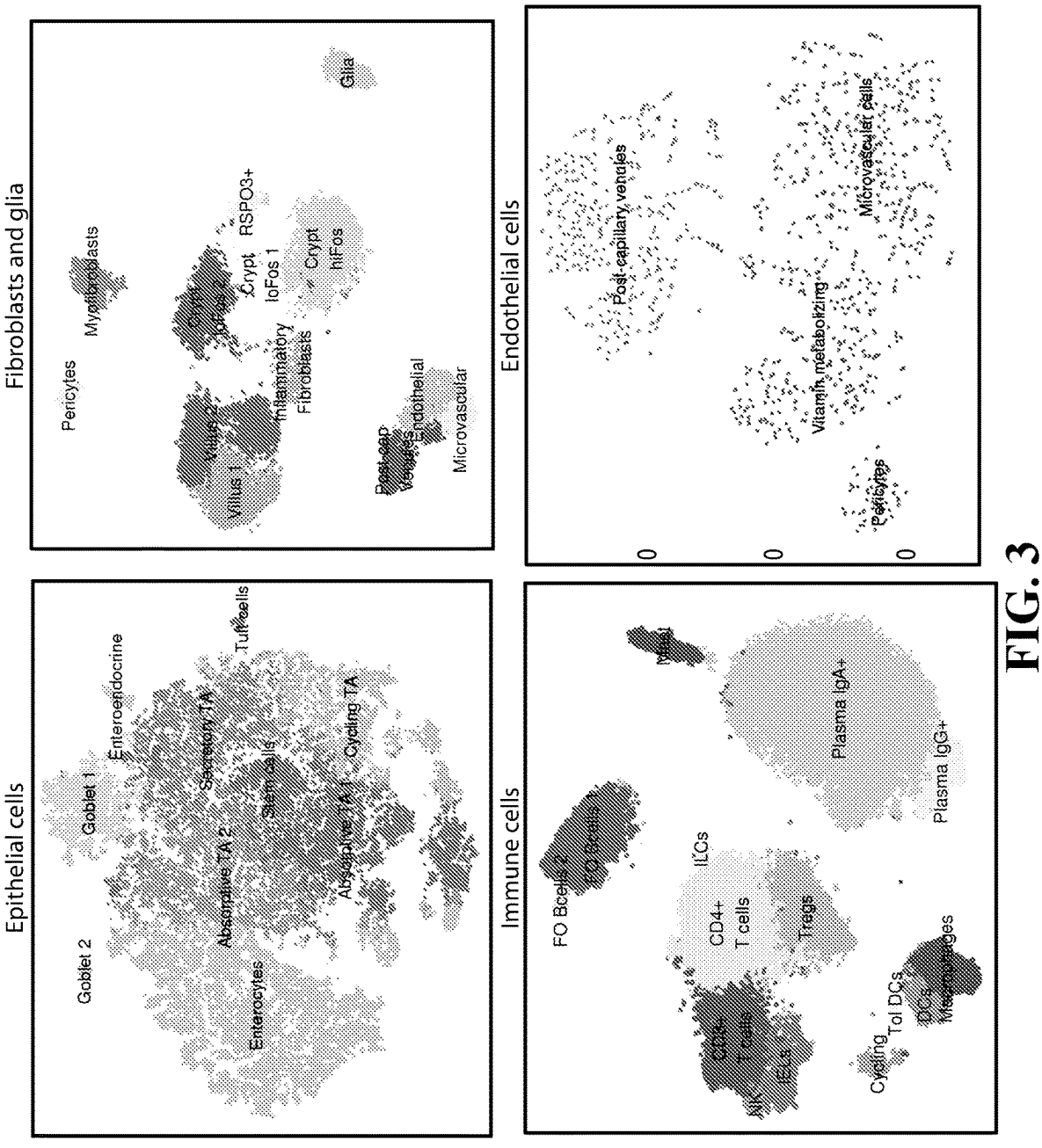

Fibroblasts and glia
Pericytes
Myofibroblasts
Villus 2
Villus 1
Crypt
IoFos 2
Crypt
IoFos 1
RSPO3+
Inflammatory
Fibroblasts
Crypt
hiFos
Glia
Post-cap
Venules
Endothelial
Microvascular
Epithelial cells
Goblet 2
Goblet 1
Enteroendocrine
Tuft cells
Secretory TA
Absorptive TA 2
Stem cells
Absorptive TA 1
Cycling TA
Enterocytes
Immune cells
FO Bcells 2
FO Bcells 1
Naive
Plasma IgA+
Plasma IgG+
ILCs
CD4+
T cells
Tregs
CD8+
T cells
IELs
NK
Cycling
Tol DCs
DCs
Macrophages
Endothelial cells
Post-capillary venules
Vitamin metabolizing
Microvascular cells
Pericytes
0
0
0

FIG. 3

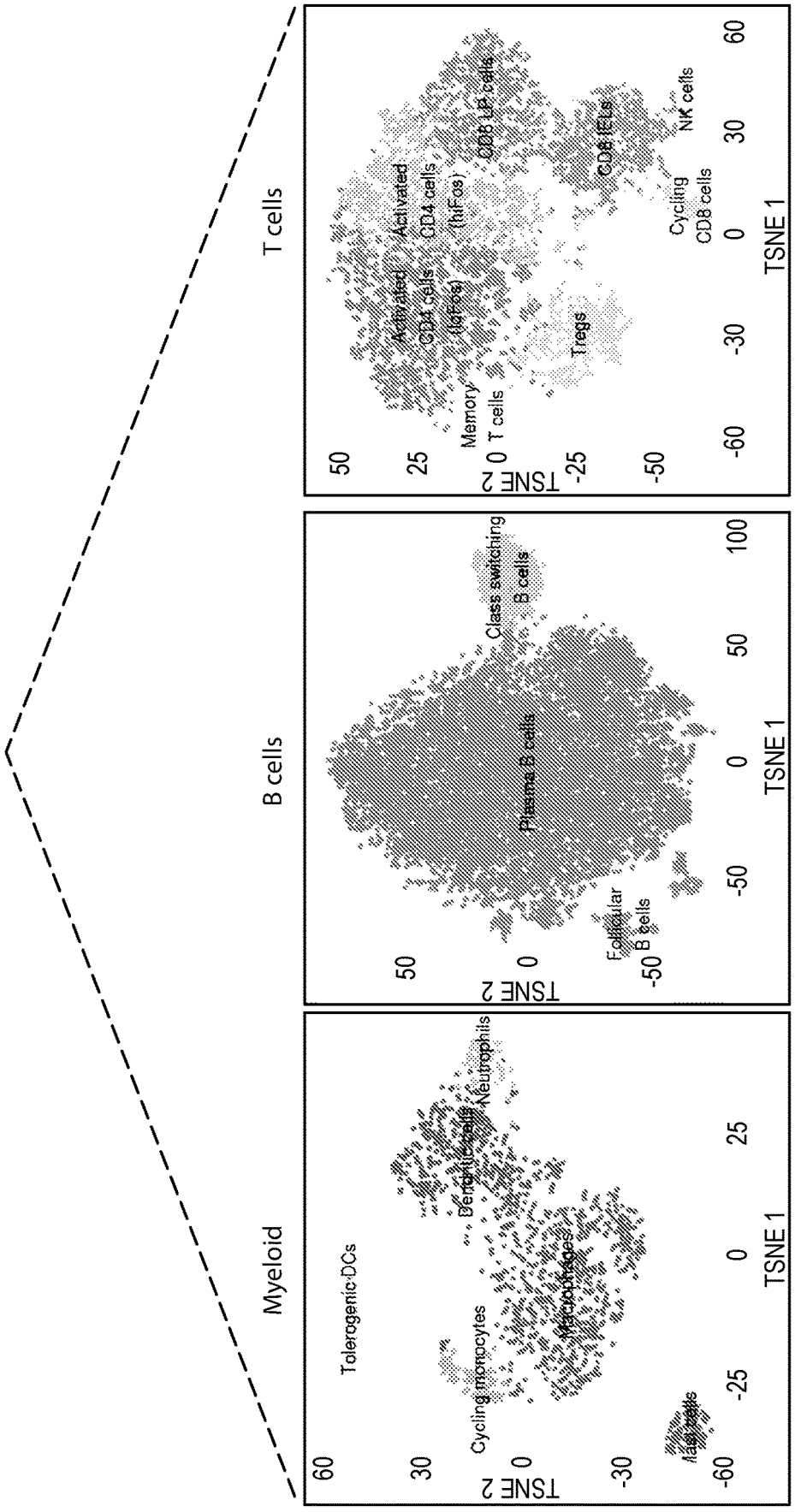

Myeloid
Tolerogenic DCs
Cycling monocytes
Neutrophils
TSNE 1
TSNE 2
B cells
Class switching B cells
Plasma B cells
Follicular B cells
TSNE 1
TSNE 2
T cells
Activated CD4 cells (IqFos)
Activated CD4 cells (hiFos)
Memory T cells
Tregs
CD8 LP cells
CD8 IELs
Cycling CD8 cells
NK cells
TSNE 1
TSNE 2

FIG. 4

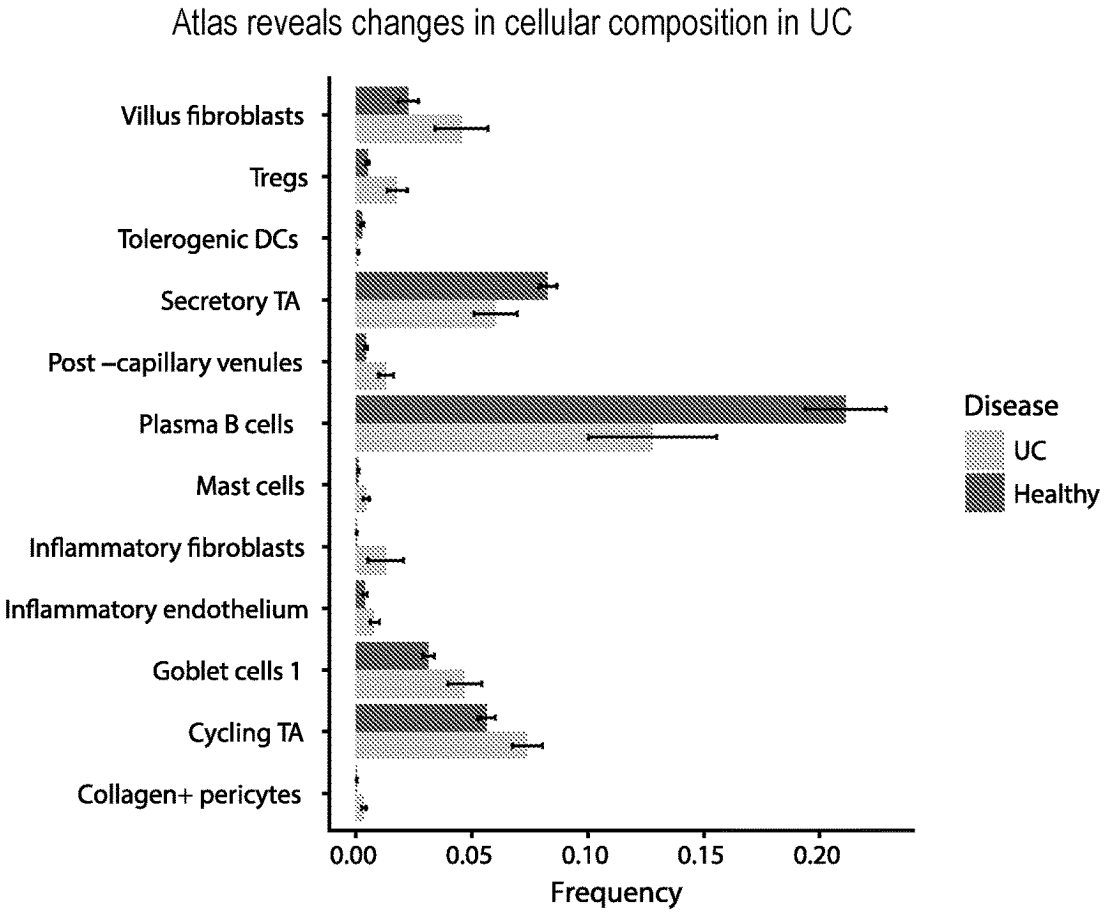

Atlas reveals changes in cellular composition in UC
Villus fibroblasts
Tregs
Tolerogenic DCs
Secretory TA
Post –capillary venules
Plasma B cells
Mast cells
Inflammatory fibroblasts
Inflammatory endothelium
Goblet cells 1
Cycling TA
Collagen+ pericytes
0.00
0.05
0.10
0.15
0.20
Frequency
Disease
UC
Healthy
All differences significant (p<=0.05; Mann-Whitney test)

FIG. 5

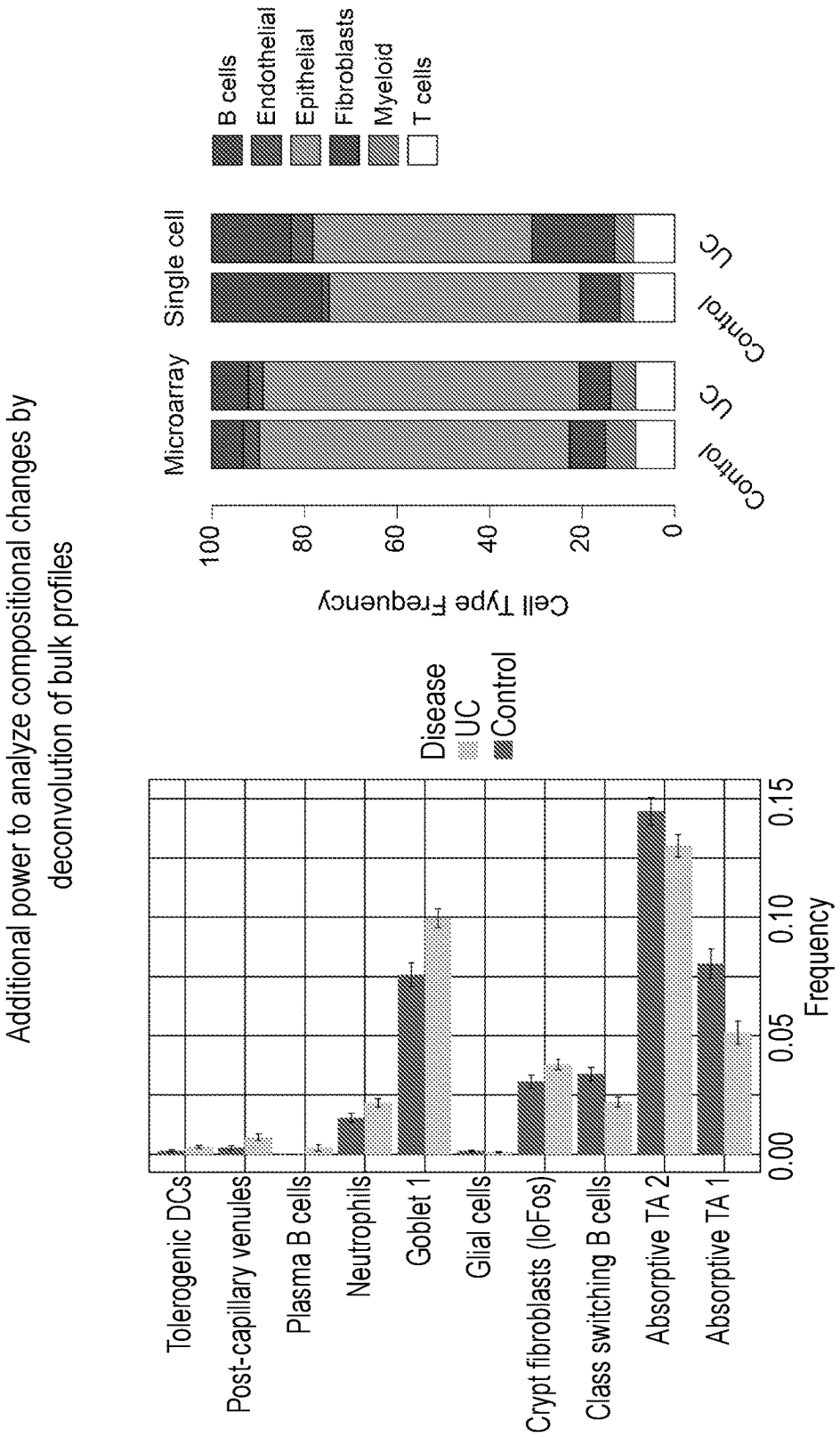

Additional power to analyze compositional changes by deconvolution of bulk profiles
Tolerogenic DCs
Post-capillary venules
Plasma B cells
Neutrophils
Goblet 1
Glial cells
Crypt fibroblasts (IoFos)
Class switching B cells
Absorptive TA 2
Absorptive TA 1
0.00
0.05
0.10
0.15
Frequency
Disease
UC
Control
Cell Type Frequency
100
80
60
40
20
0
Microarray
Single cell
Control
UC
Control
UC
B cells
Endothelial
Epithelial
Fibroblasts
Myeloid
T cells
Bulk data: Noble, C. L., et al. Gut (2008).

FIG. 6

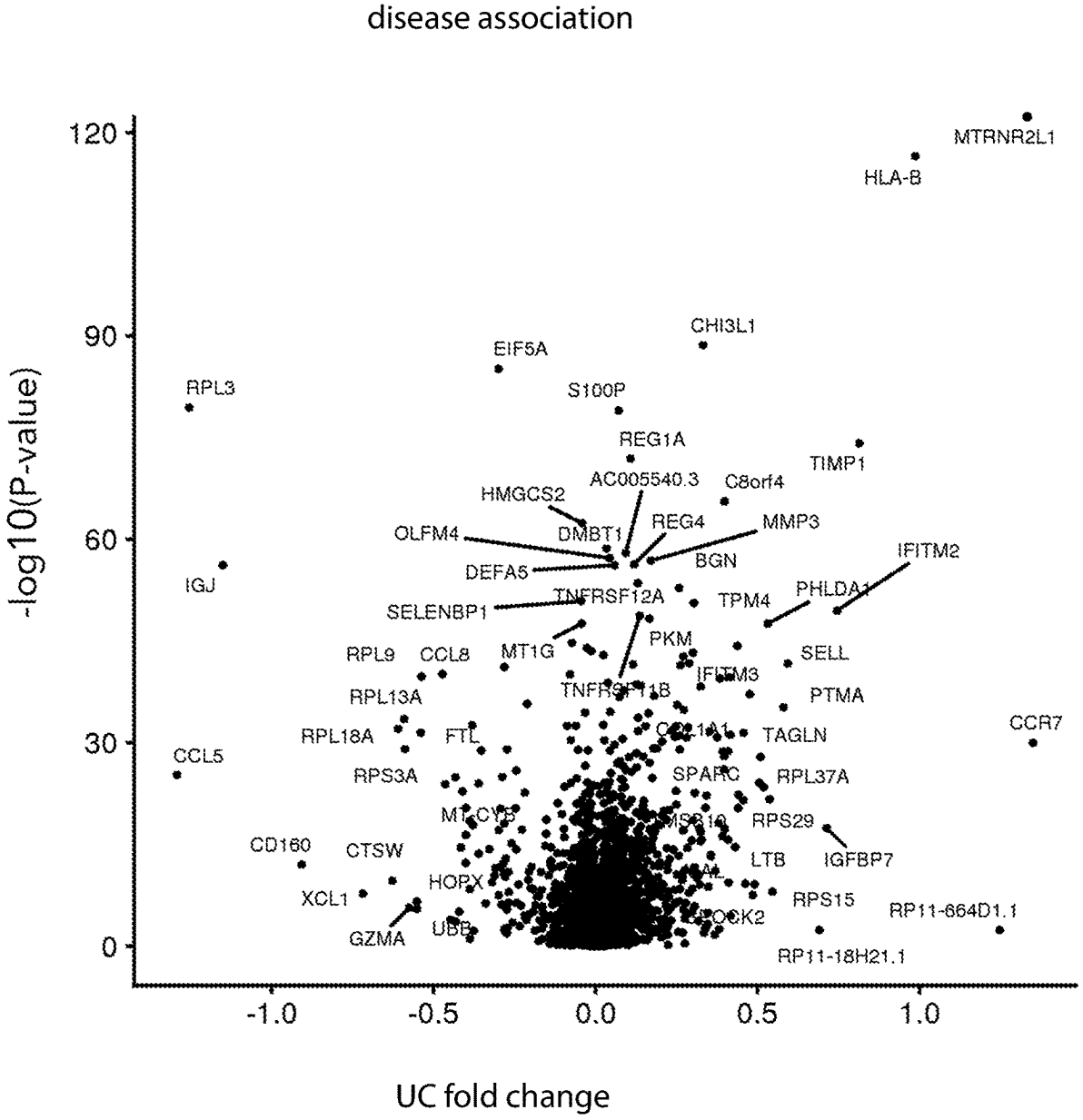

disease association
-log10(P-value)
120
90
60
30
0
-1.0
-0.5
0.0
0.5
1.0
UC fold change
MTRNR2L1
HLA-B
CHI3L1
EIF5A
RPL3
S100P
REG1A
TIMP1
AC005540.3
C8orf4
HMGCS2
OLFM4
DMBT1
REG4
MMP3
IFITM2
BGN
DEFA5
IGJ
TNFRSF12A
TPM4
PHLDA1
SELENBP1
PKM
RPL9
CCL8
MT1G
SELL
IFITM3
RPL13A
PTMA
CCR7
RPL18A
FTL
TAGLN
CCL5
RPS3A
SPARC
RPL37A
RPS29
CD160
CTSW
LTB
IGFBP7
HOPX
XCL1
RPS15
RP11-664D1.1
GZMA
UBB
RP11-18H21.1

FIG. 7

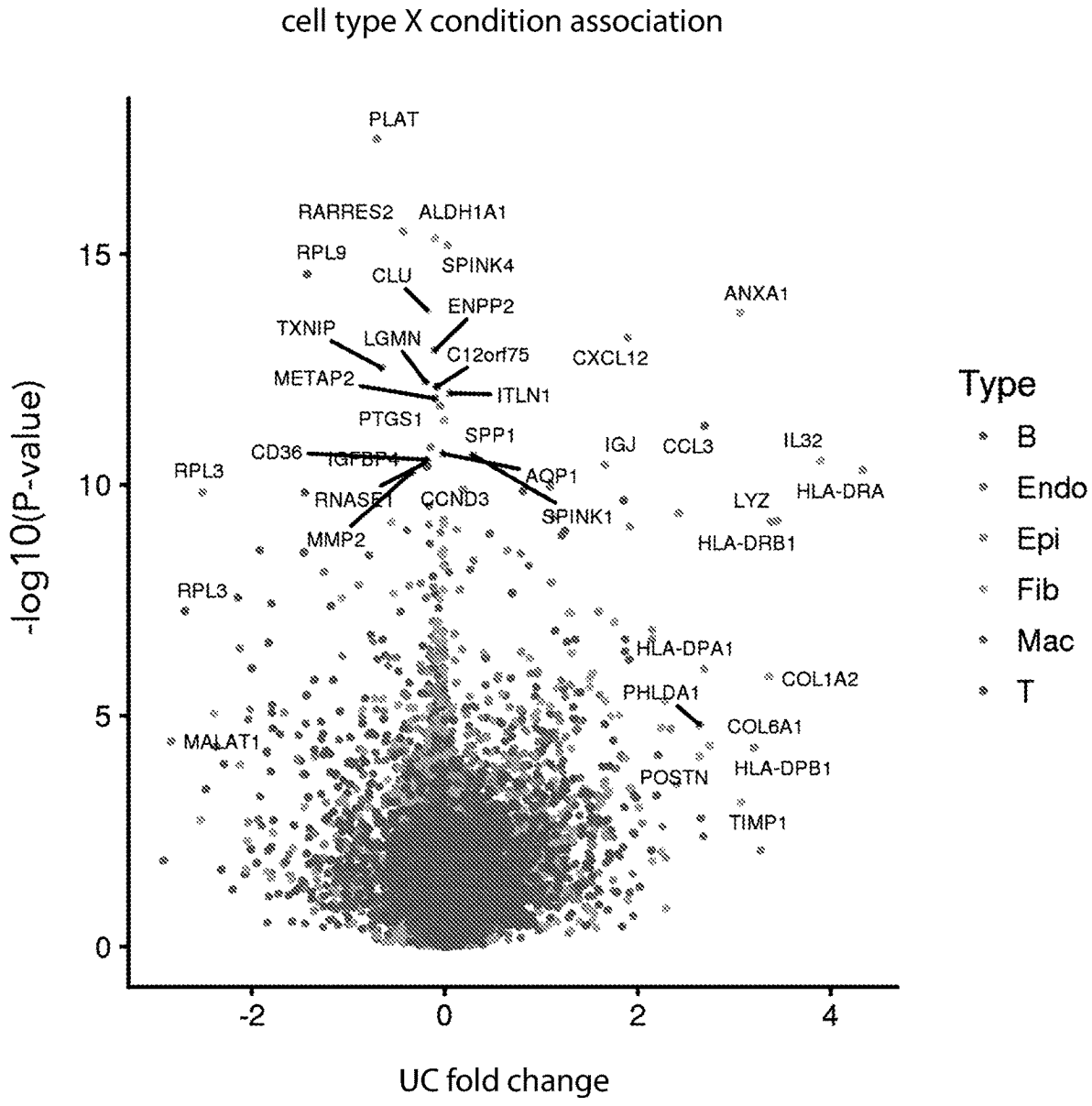

cell type X condition association
-log10(P-value)
UC fold change
15
10
5
0
-2
0
2
4
PLAT
RARRES2
ALDH1A1
RPL9
CLU
SPINK4
ENPP2
ANXA1
TXNIP
LGMN
C12orf75
CXCL12
METAP2
ITLN1
PTGS1
SPP1
CD36
IGFBP4
IGJ
CCL3
IL32
RPL3
AQP1
RNASE1
CCND3
LYZ
HLA-DRA
SPINK1
MMP2
HLA-DRB1
RPL3
HLA-DPA1
COL1A2
PHLDA1
COL6A1
MALAT1
HLA-DPB1
POSTN
TIMP1
Type
B
Endo
Epi
Fib
Mac
T

FIG. 8

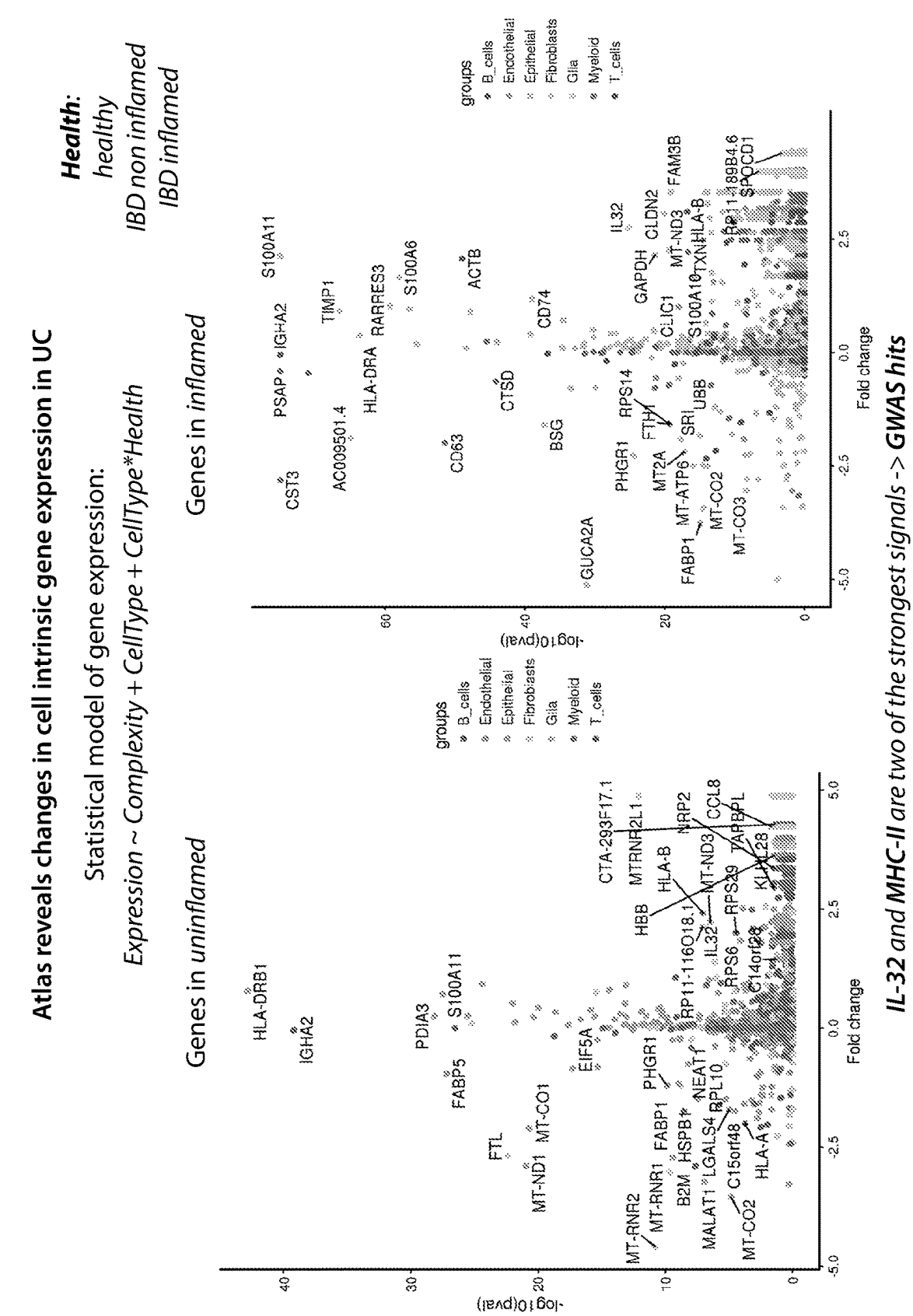


FIG. 9

IL-32 and MHC-II are two of the strongest signals -> GWAS hits

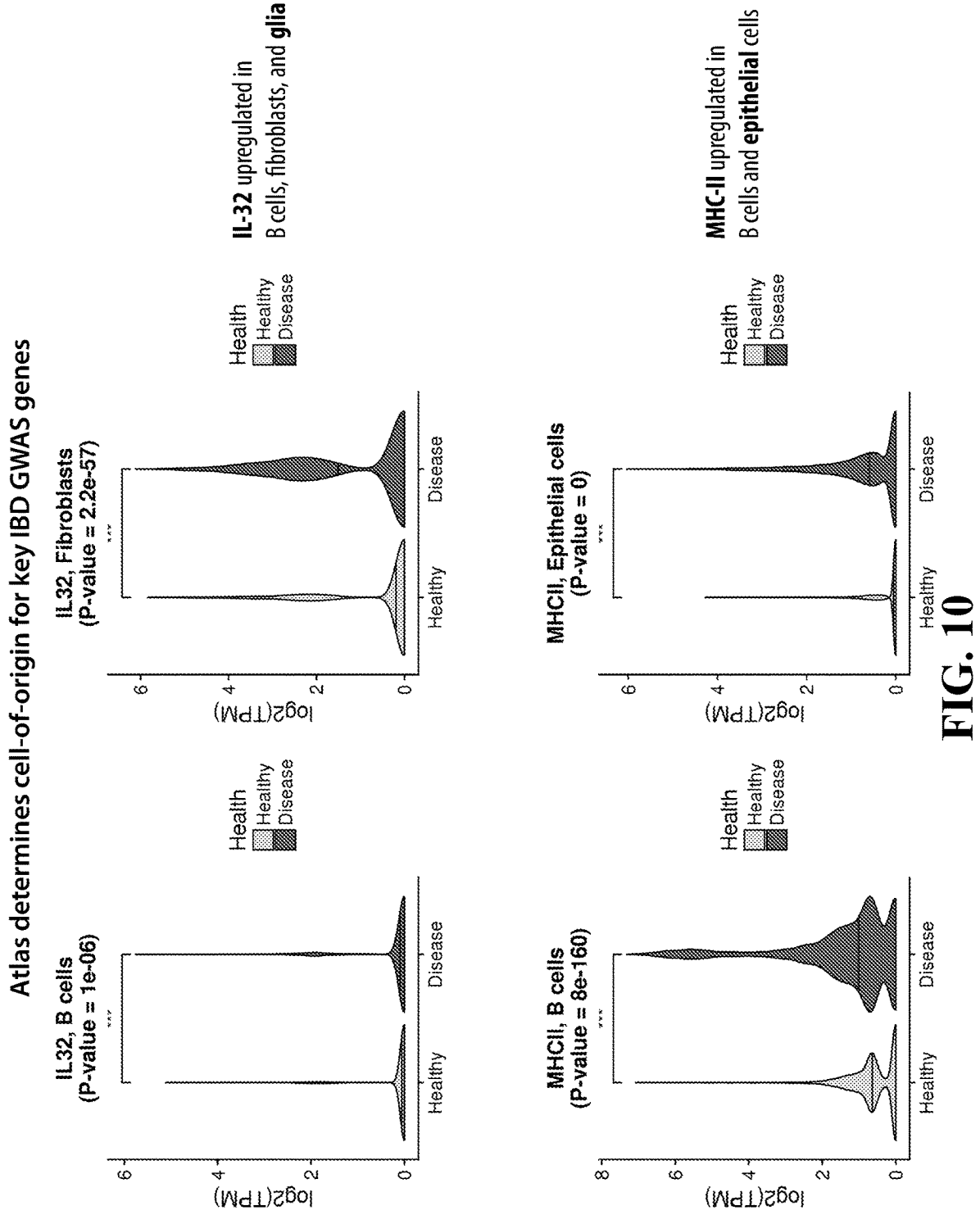

Atlas determines cell-of-origin for key IBD GWAS genes
IL32, B cells
(P-value = 1e-06)
IL32, Fibroblasts
(P-value = 2.2e-57)
MHCII, B cells
(P-value = 8e-160)
MHCII, Epithelial cells
(P-value = 0)
log2(TPM)
Healthy
Disease
Health
IL-32 upregulated in
B cells, fibroblasts, and glia
MHC-II upregulated in
B cells and epithelial cells

FIG. 10

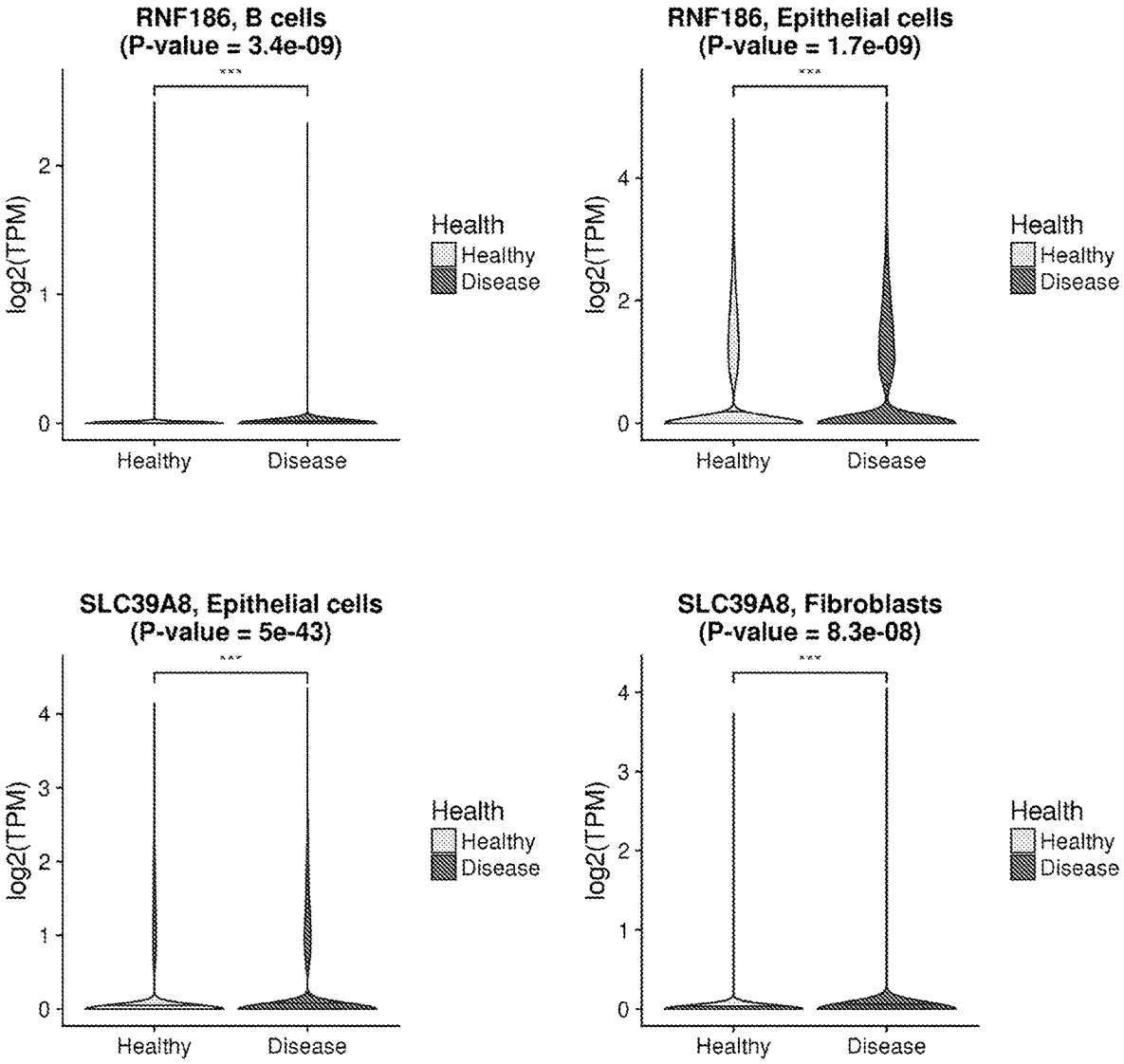

RNF186, B cells
(P-value = 3.4e-09)
RNF186, Epithelial cells
(P-value = 1.7e-09)
SLC39A8, Epithelial cells
(P-value = 5e-43)
SLC39A8, Fibroblasts
(P-value = 8.3e-08)
log2(TPM)
Health
Healthy
Disease
***

FIG. 11

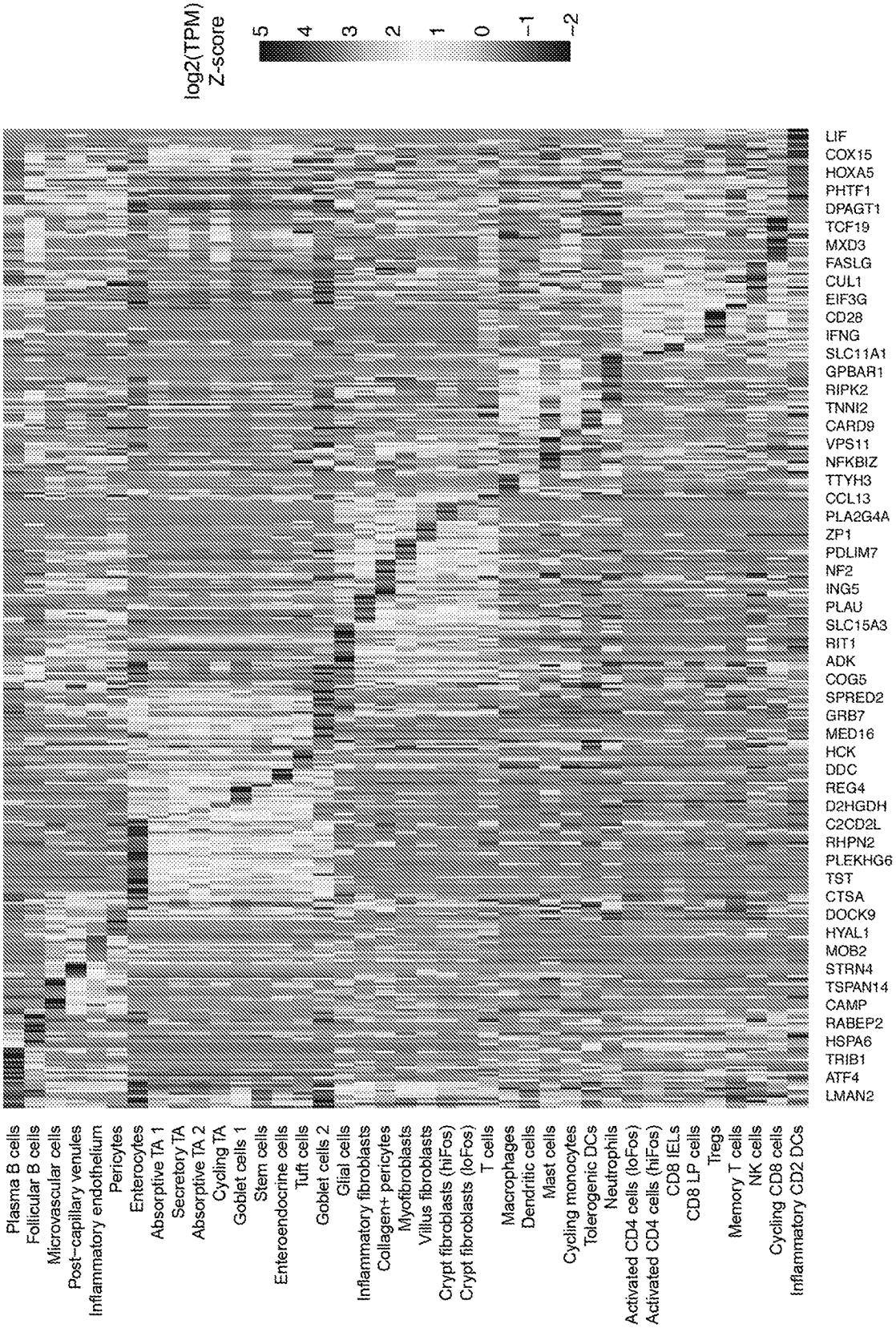

log2(TPM)
Z-score
5
4
3
2
1
0
−1
−2
LIF
COX15
HOXA5
PHTF1
DPAGT1
TCF19
MXD3
FASLG
CUL1
EIF3G
CD28
IFNG
SLC11A1
GPBAR1
RIPK2
TNNI2
CARD9
VPS11
NFKBIZ
TTYH3
CCL13
PLA2G4A
ZP1
PDLIM7
NF2
ING5
PLAU
SLC15A3
RIT1
ADK
COG5
SPRED2
GRB7
MED16
HCK
DDC
REG4
D2HGDH
C2CD2L
RHPN2
PLEKHG6
TST
CTSA
DOCK9
HYAL1
MOB2
STRN4
TSPAN14
CAMP
RABEP2
HSPA6
TRIB1
ATF4
LMAN2
Plasma B cells
Follicular B cells
Microvascular cells
Post−capillary venules
Inflammatory endothelium
Pericytes
Enterocytes
Absorptive TA 1
Secretory TA
Absorptive TA 2
Cycling TA
Goblet cells 1
Stem cells
Enteroendocrine cells
Tuft cells
Goblet cells 2
Glial cells
Inflammatory fibroblasts
Collagen+ pericytes
Myofibroblasts
Villus fibroblasts
Crypt fibroblasts (hiFos)
Crypt fibroblasts (loFos)
T cells
Macrophages
Dendritic cells
Mast cells
Cycling monocytes
Tolerogenic DCs
Neutrophils
Activated CD4 cells (loFos)
Activated CD4 cells (hiFos)
CD8 IELs
CD8 LP cells
Tregs
Memory T cells
NK cells
Cycling CD8 cells
Inflammatory CD2 DCs

FIG. 12

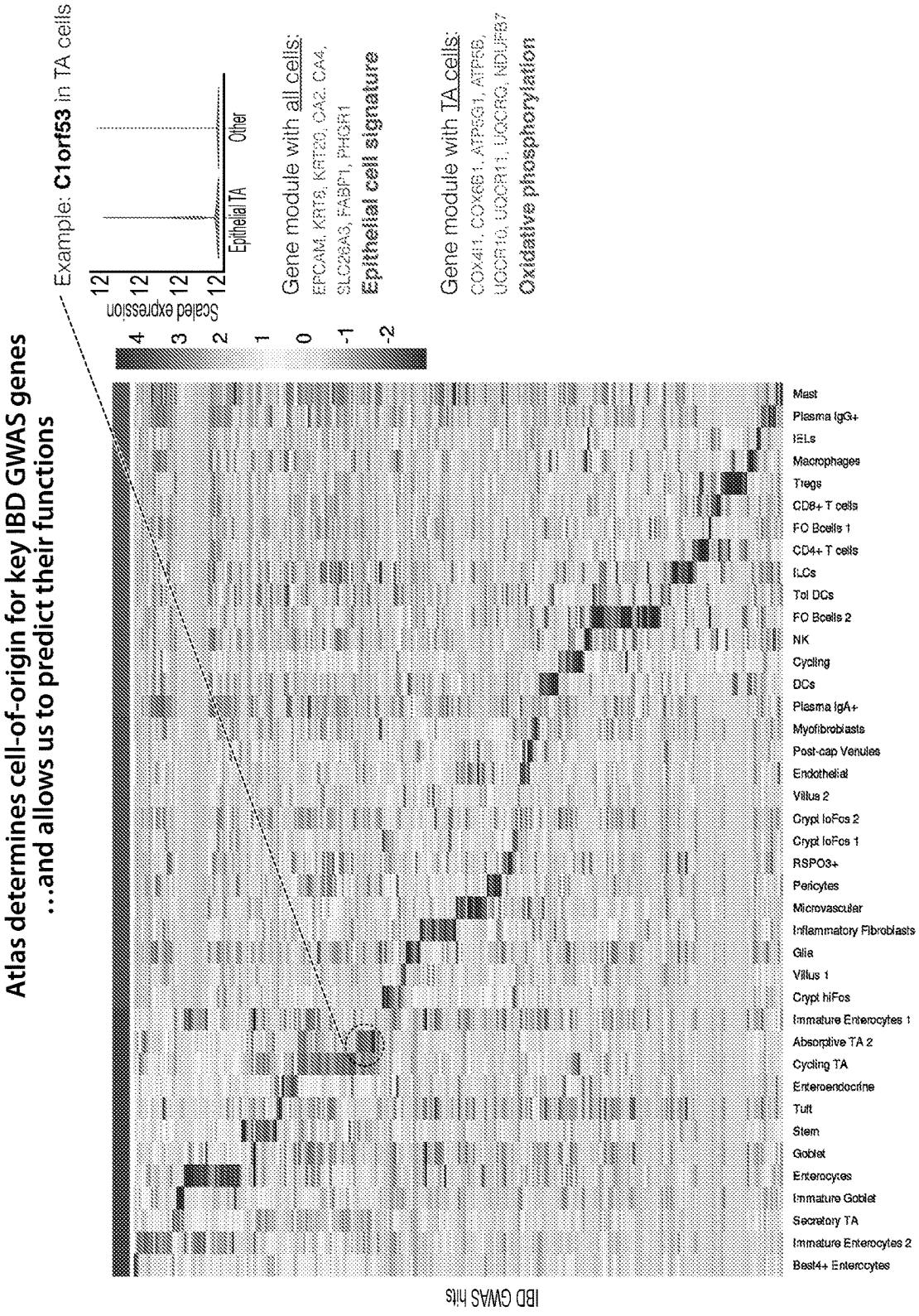

Atlas determines cell-of-origin for key IBD GWAS genes
...and allows us to predict their functions
Example: C1orf53 in TA cells
Scaled expression
12
12
12
12
Epithelial TA
Other
4
3
2
1
0
-1
-2
Gene module with all cells:
EPCAM, KRT8, KRT20, CA2, CA4, SLC26A3, FABP1, PHGR1
Epithelial cell signature
Gene module with TA cells:
COX411, COX6B1, ATP5G1, ATP5B, UQCR10, UQCR11, UQCRQ, NDUFB7
Oxidative phosphorylation
Mast
Plasma IgG+
IELs
Macrophages
Tregs
CD8+ T cells
FO Bcells 1
CD4+ T cells
ILCs
Tol DCs
FO Bcells 2
NK
Cycling
DCs
Plasma IgA+
Myofibroblasts
Post-cap Venules
Endothelial
Villus 2
Crypt loFos 2
Crypt loFos 1
RSPO3+
Pericytes
Microvascular
Inflammatory Fibroblasts
Glia
Villus 1
Crypt hiFos
Immature Enterocytes 1
Absorptive TA 2
Cycling TA
Enteroendocrine
Tuft
Stem
Goblet
Enterocytes
Immature Goblet
Secretory TA
Immature Enterocytes 2
Best4+ Enterocytes
IBD GWAS hits

FIG. 13

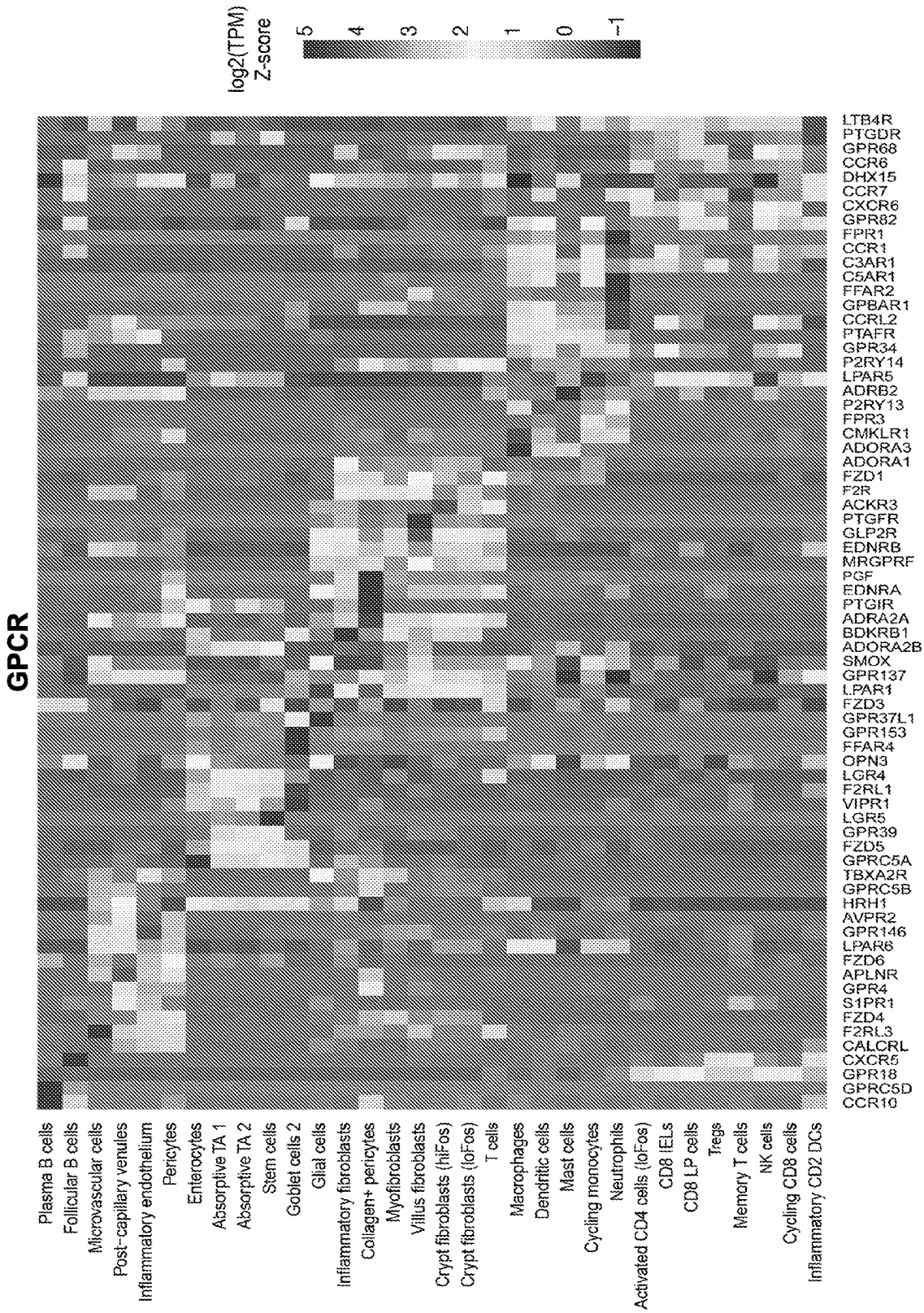

GPCR
log2(TPM)
Z-score
5
4
3
2
1
0
−1
LTB4R
PTGDR
GPR68
CCR6
DHX15
CCR7
CXCR6
GPR82
FPR1
CCR1
C3AR1
C5AR1
FFAR2
GPBAR1
CCRL2
PTAFR
GPR34
P2RY14
LPAR5
ADRB2
P2RY13
FPR3
CMKLR1
ADORA3
ADORA1
FZD1
F2R
ACKR3
PTGFR
GLP2R
EDNRB
MRGPRF
PGF
EDNRA
PTGIR
ADRA2A
BDKRB1
ADORA2B
SMOX
GPR137
LPAR1
FZD3
GPR37L1
GPR153
FFAR4
OPN3
LGR4
F2RL1
VIPR1
LGR5
GPR39
FZD5
GPRC5A
TBXA2R
GPRC5B
HRH1
AVPR2
GPR146
LPAR6
FZD6
APLNR
GPR4
S1PR1
FZD4
F2RL3
CALCRL
CXCR5
GPR18
GPRC5D
CCR10
Plasma B cells
Follicular B cells
Microvascular cells
Post−capillary venules
Inflammatory endothelium
Pericytes
Enterocytes
Absorptive TA 1
Absorptive TA 2
Stem cells
Goblet cells 2
Glial cells
Inflammatory fibroblasts
Collagen+ pericytes
Myofibroblasts
Villus fibroblasts
Crypt fibroblasts (hiFos)
Crypt fibroblasts (loFos)
T cells
Macrophages
Dendritic cells
Mast cells
Cycling monocytes
Neutrophils
Activated CD4 cells (loFos)
CD8 IELs
CD8 LP cells
Tregs
Memory T cells
NK cells
Cycling CD8 cells
Inflammatory CD2 DCs

FIG. 14

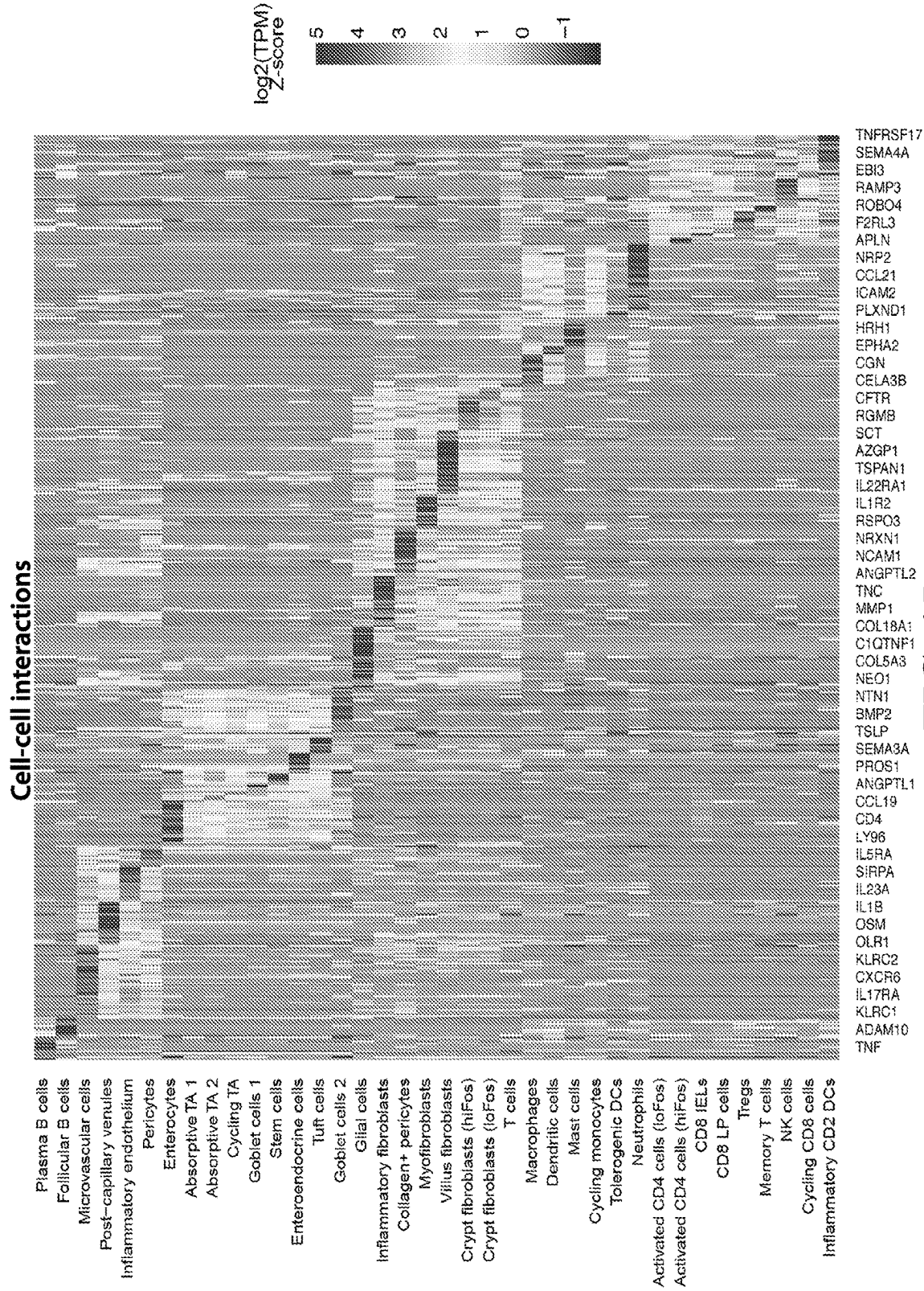

log2(TPM)
Z-score
5
4
3
2
1
0
−1
Cell-cell interactions
Plasma B cells
Follicular B cells
Microvascular cells
Post-capillary venules
Inflammatory endothelium
Pericytes
Enterocytes
Absorptive TA 1
Absorptive TA 2
Cycling TA
Goblet cells 1
Stem cells
Enteroendocrine cells
Tuft cells
Goblet cells 2
Glial cells
Inflammatory fibroblasts
Collagen+ pericytes
Myofibroblasts
Villus fibroblasts
Crypt fibroblasts (hiFos)
Crypt fibroblasts (loFos)
T cells
Macrophages
Dendritic cells
Mast cells
Cycling monocytes
Tolerogenic DCs
Neutrophils
Activated CD4 cells (loFos)
Activated CD4 cells (hiFos)
CD8 IELs
CD8 LP cells
Tregs
Memory T cells
NK cells
Cycling CD8 cells
Inflammatory CD2 DCs
TNFRSF17
SEMA4A
EBI3
RAMP3
ROBO4
F2RL3
APLN
NRP2
CCL21
ICAM2
PLXND1
HRH1
EPHA2
CGN
CELA3B
CFTR
RGMB
SCT
AZGP1
TSPAN1
IL22RA1
IL1R2
RSPO3
NRXN1
NCAM1
ANGPTL2
TNC
MMP1
COL18A1
C1QTNF1
COL5A3
NEO1
NTN1
BMP2
TSLP
SEMA3A
PROS1
ANGPTL1
CCL19
CD4
LY96
IL5RA
SIRPA
IL23A
IL1B
OSM
OLR1
KLRC2
CXCR6
IL17RA
KLRC1
ADAM10
TNF

FIG. 15

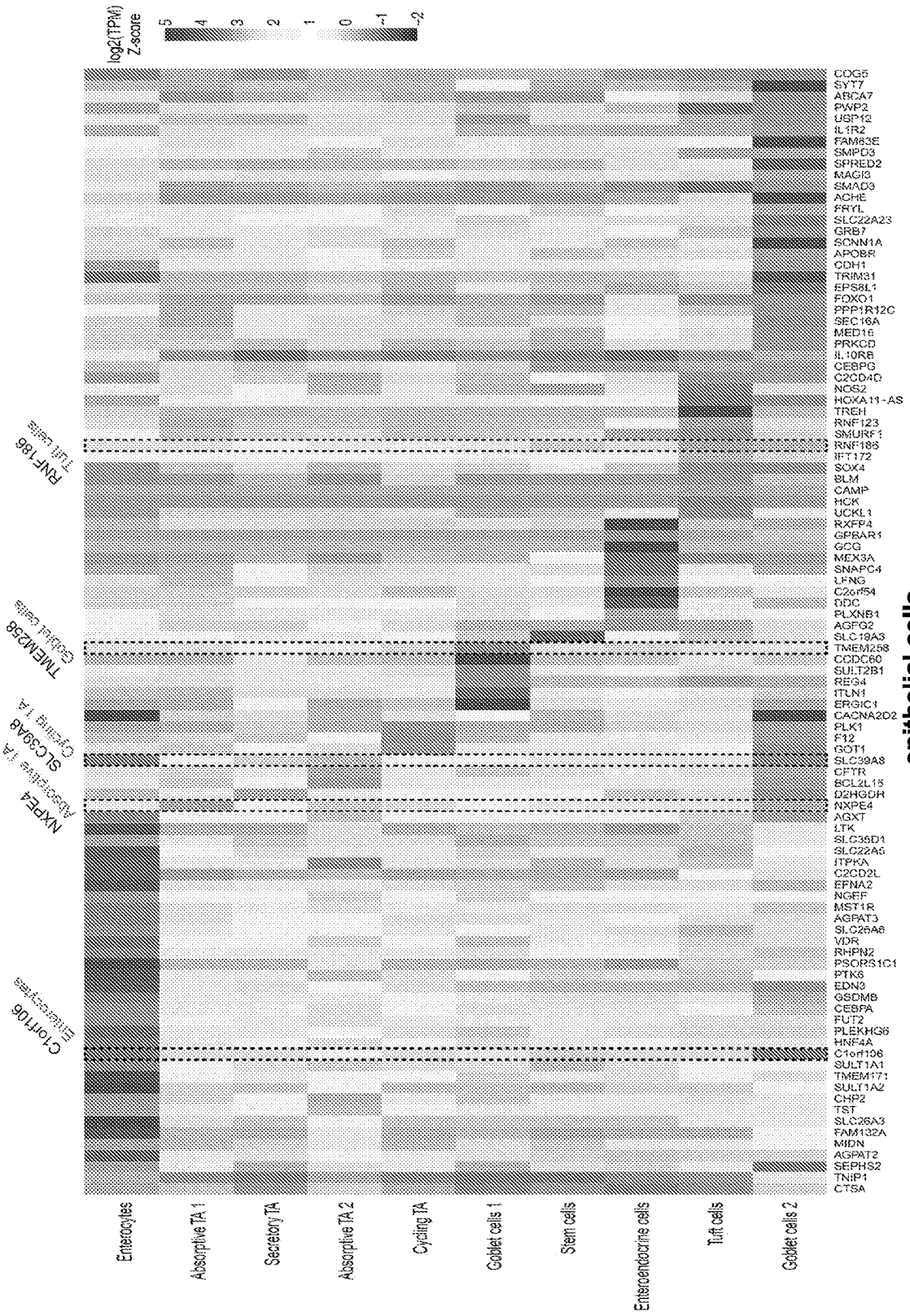

log2(TPM)
Z-score
5
4
3
2
1
0
−1
−2
COG5
SYT7
ABCA7
PWP2
USP12
IL1R2
FAM83E
SMPD3
SPRED2
MAGI3
SMAD3
ACHE
FRYL
SLC22A23
GRB7
SCNN1A
APOBR
CDH1
TRIM31
EPS8L1
FOXO1
PPP1R12C
SEC16A
MED16
PRKCD
IL10RB
CEBPG
C2CD4D
NOS2
HOXA11-AS
TREH
RNF123
SMURF1
RNF186
IFT172
SOX4
BLM
CAMP
HCK
UCKL1
RXFP4
GPBAR1
GCG
MEX3A
SNAPC4
IFNG
C2orf54
DDC
PLXNB1
AGFG2
SLC19A3
TMEM258
CCDC60
SULT2B1
REG4
ITLN1
ERGIC1
CACNA2D2
PLK1
F12
GOT1
SLC39A8
CFTR
BCL2L15
D2HGDH
NXPE4
AGXT
LTK
SLC35D1
SLC22A5
ITPKA
C2CD2L
EFNA2
NGFF
MST1R
AGPAT3
SLC26A6
VDR
RHPN2
PSORS1C1
PTK6
EDN3
GSDMB
CEBPA
FUT2
PLEKHG6
HNF4A
C1orf106
SULT1A1
TMEM171
SULT1A2
CHP2
TST
SLC26A3
FAM132A
MIDN
AGPAT2
SEPHS2
TNIP1
CTSA
RNF186
Tuft cells
TMEM258
Cycling cells
SLC39A8
Cycling TA
NXPE4
Absorptive TA
C1orf106
Enterocytes
Enterocytes
Absorptive TA 1
Secretory TA
Absorptive TA 2
Cycling TA
Goblet cells 1
Stem cells
Enteroendocrine cells
Tuft cells
Goblet cells 2
epithelial cells

FIG. 16

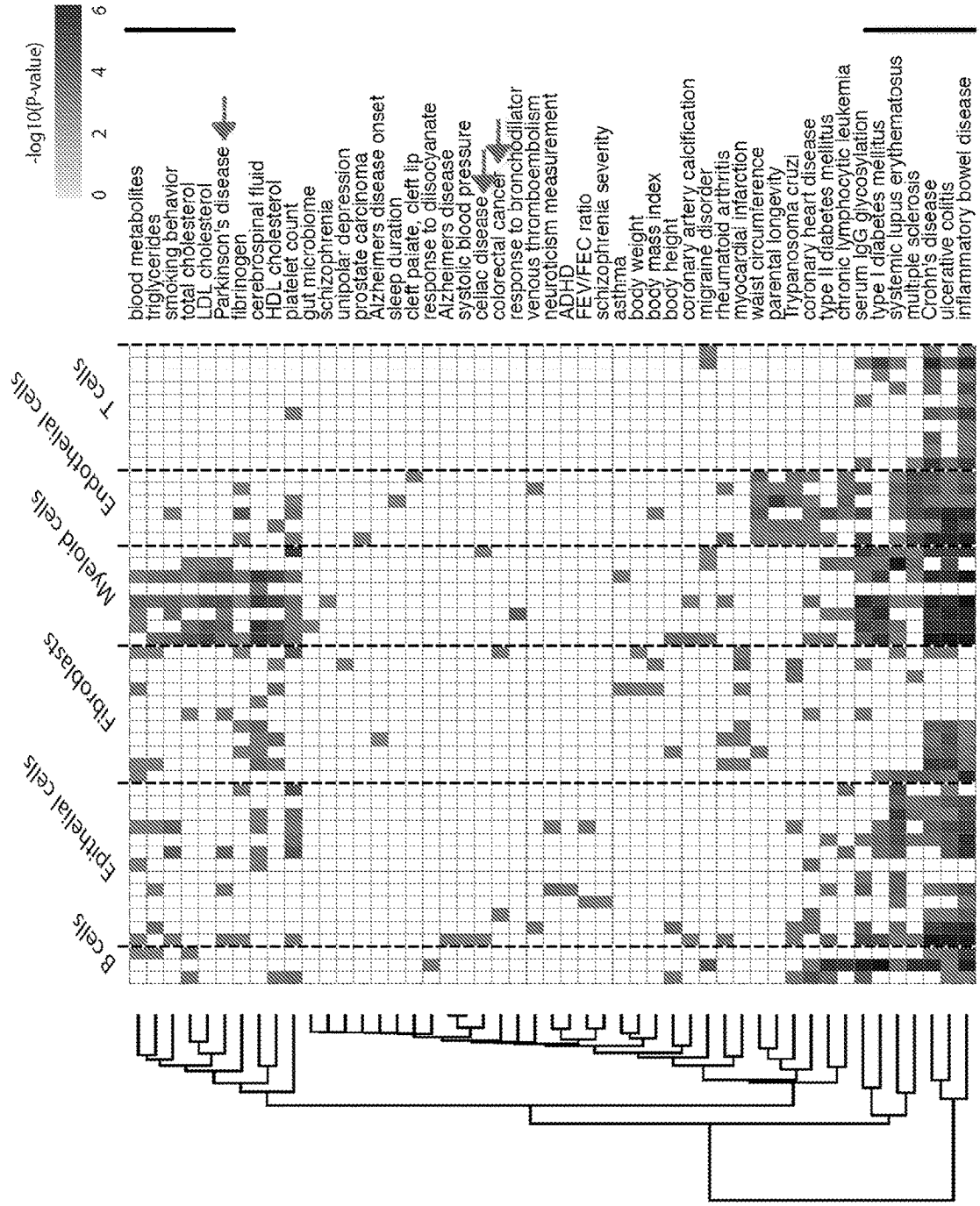

-log10(p-value)
0
2
4
6
B cells
Epithelial cells
Fibroblasts
Myeloid cells
Endothelial cells
T cells
blood metabolites
triglycerides
smoking behavior
total cholesterol
LDL cholesterol
Parkinson's disease
fibrinogen
cerebrospinal fluid
HDL cholesterol
platelet count
gut microbiome
schizophrenia
unipolar depression
prostate carcinoma
Alzheimers disease onset
sleep duration
cleft palate, cleft lip
response to diisocyanate
Alzheimers disease
systolic blood pressure
celiac disease
colorectal cancer
response to bronchodilator
venous thromboembolism
neuroticism measurement
ADHD
FEV/FEC ratio
schizophrenia severity
asthma
body weight
body mass index
body height
coronary artery calcification
migraine disorder
rheumatoid arthritis
myocardial infarction
waist circumference
parental longevity
Trypanosoma cruzi
coronary heart disease
type II diabetes mellitus
chronic lymphocytic leukemia
serum IgG glycosylation
type I diabetes mellitus
systemic lupus erythematosus
multiple sclerosis
Crohn's disease
ulcerative colitis
inflammatory bowel disease
enrichment of GWAS genes in each cell type; adjusted P<0.05

FIG. 17

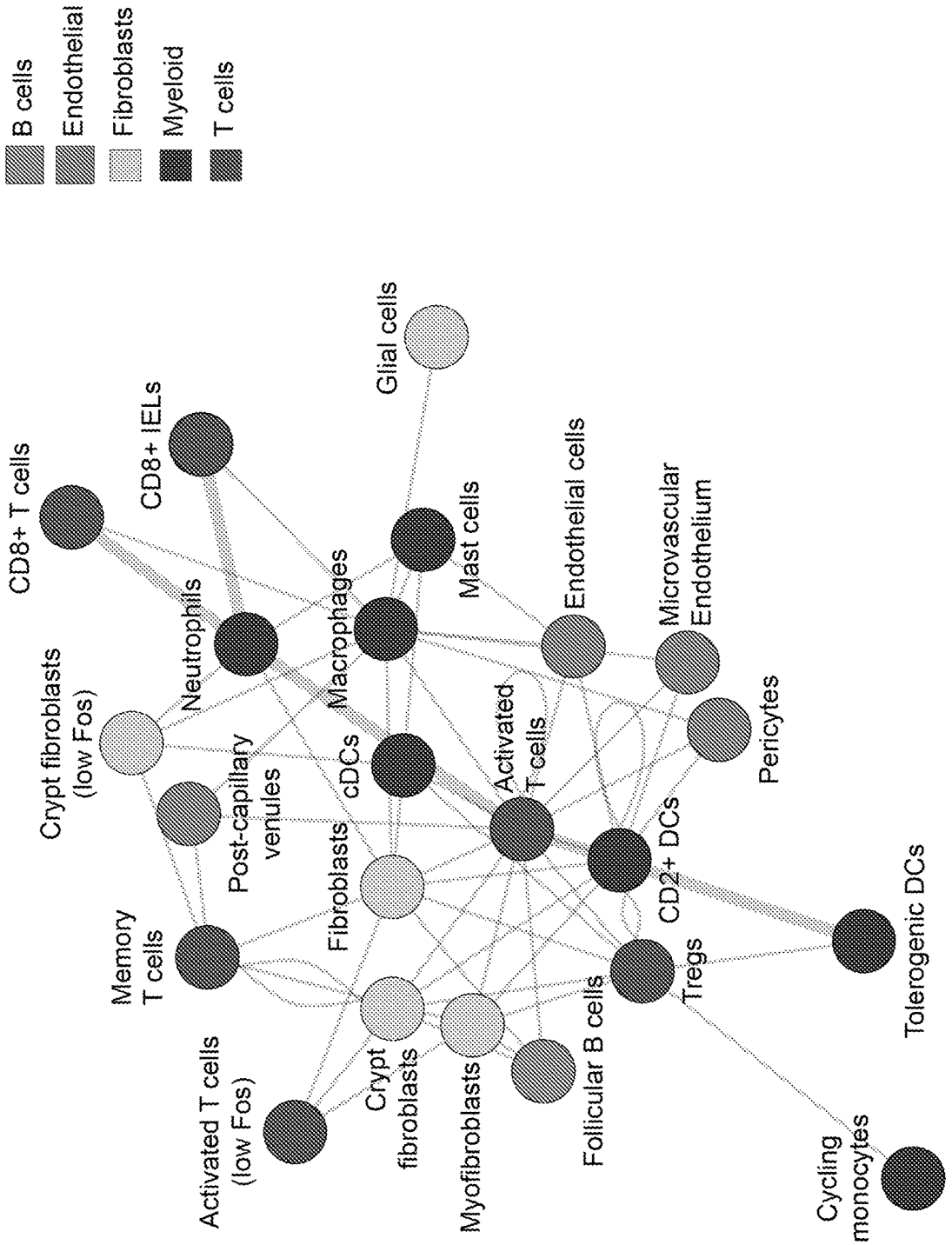

B cells
Endothelial
Fibroblasts
Myeloid
T cells
CD8+ T cells
CD8+ IELs
Glial cells
Crypt fibroblasts (low Fos)
Neutrophils
Macrophages
Mast cells
Endothelial cells
Microvascular Endothelium
Post-capillary venules
cDCs
Activated T cells
Pericytes
Memory T cells
Fibroblasts
CD2+ DCs
Tregs
Tolerogenic DCs
Activated T cells (low Fos)
Crypt fibroblasts
Myofibroblasts
Follicular B cells
Cycling monocytes

FIG. 18

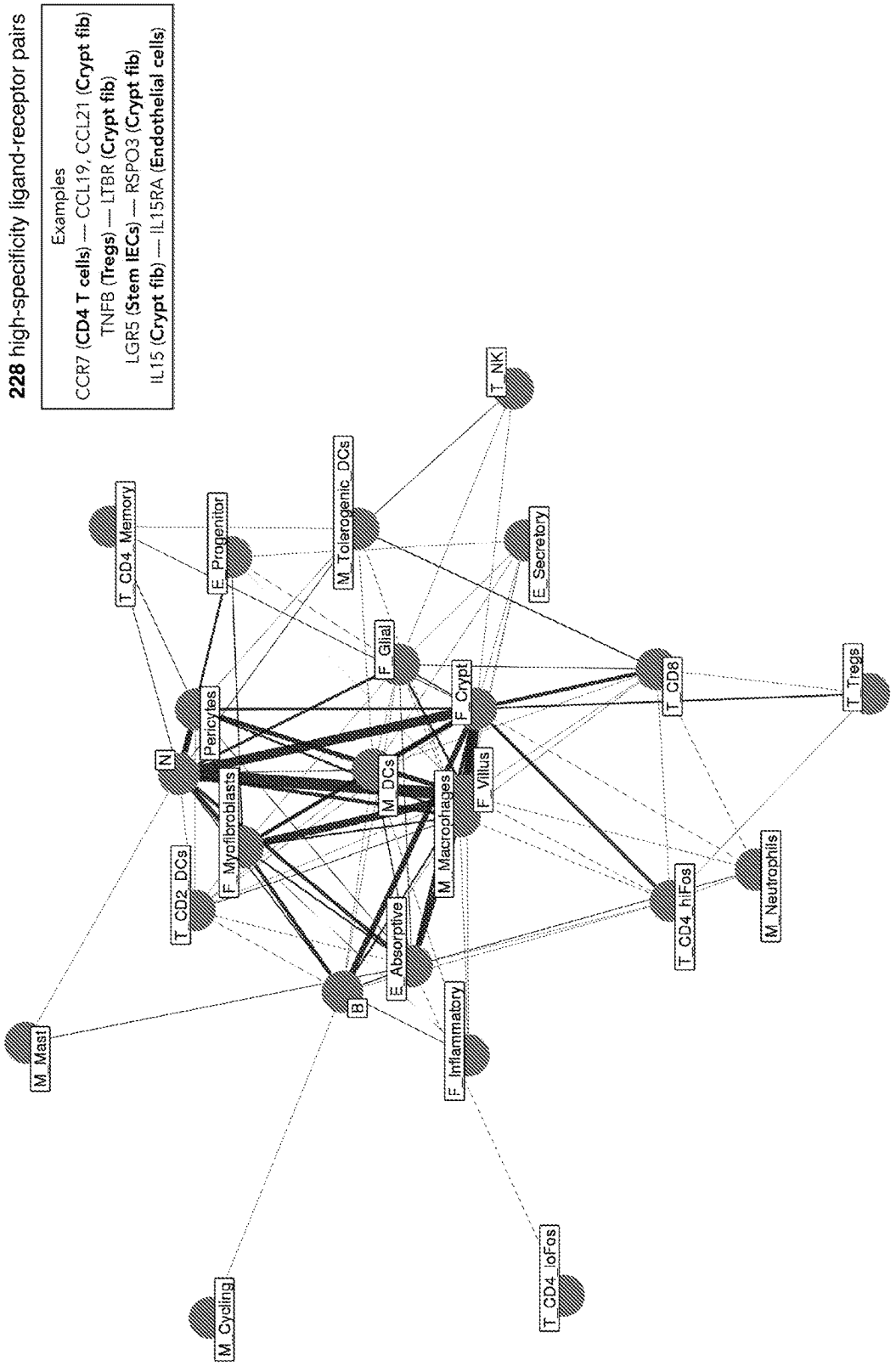

Atlas reveals potential cell-cell interactions in health
228 high-specificity ligand-receptor pairs
Examples
CCR7 (CD4 T cells) — CCL19, CCL21 (Crypt fib)
TNFB (Tregs) — LTBR (Crypt fib)
LGR5 (Stem IECs) — RSPO3 (Crypt fib)
IL15 (Crypt fib) — IL15RA (Endothelial cells)
M_Mast
M_Cycling
B
T_CD4_Memory
E_Progenitor
M_Tolerogenic_DCs
T_NK
E_Secretory
F_Glial
F_Crypt
T_CD8
T_Tregs
N
Pericytes
M_DCs
F_Villus
T_CD2_DCs
F_Myofibroblasts
M_Macrophages
E_Absorptive
T_CD4_hiFos
M_Neutrophils
F_Inflammatory
T_CD4_loFos

FIG. 19

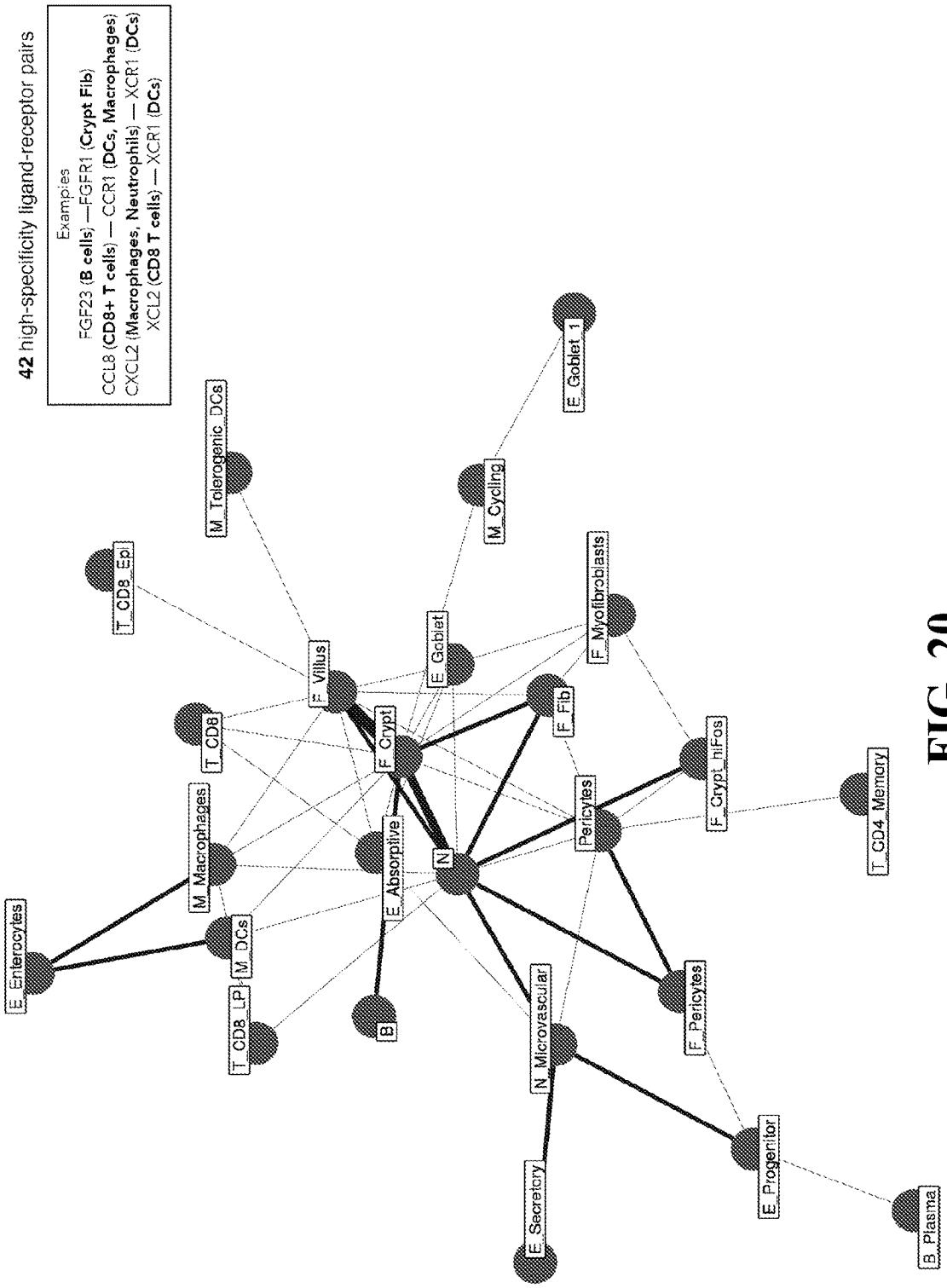

Atlas reveals perturbed cell-cell interactions in disease
42 high-specificity ligand-receptor pairs
Examples
FGF23 (B cells) —FGFR1 (Crypt Fib)
CCL8 (CD8+ T cells) — CCR1 (DCs, Macrophages)
CXCL2 (Macrophages, Neutrophils) — XCR1 (DCs)
XCL2 (CD8 T cells) — XCR1 (DCs)
E_Enterocytes
M_Macrophages
M_DCs
T_CD8_LP
T_CD8
T_CD8_Epi
M_Tolerogenic_DCs
F_Villus
F_Crypt
E_Absorptive
B
N
E_Goblet
M_Cycling
E_Goblet_1
F_Myofibroblasts
F_Fib
Pericytes
F_Crypt_hiFos
T_CD4_Memory
F_Pericytes
N_Microvascular
E_Secretory
E_Progenitor
B_Plasma

FIG. 20

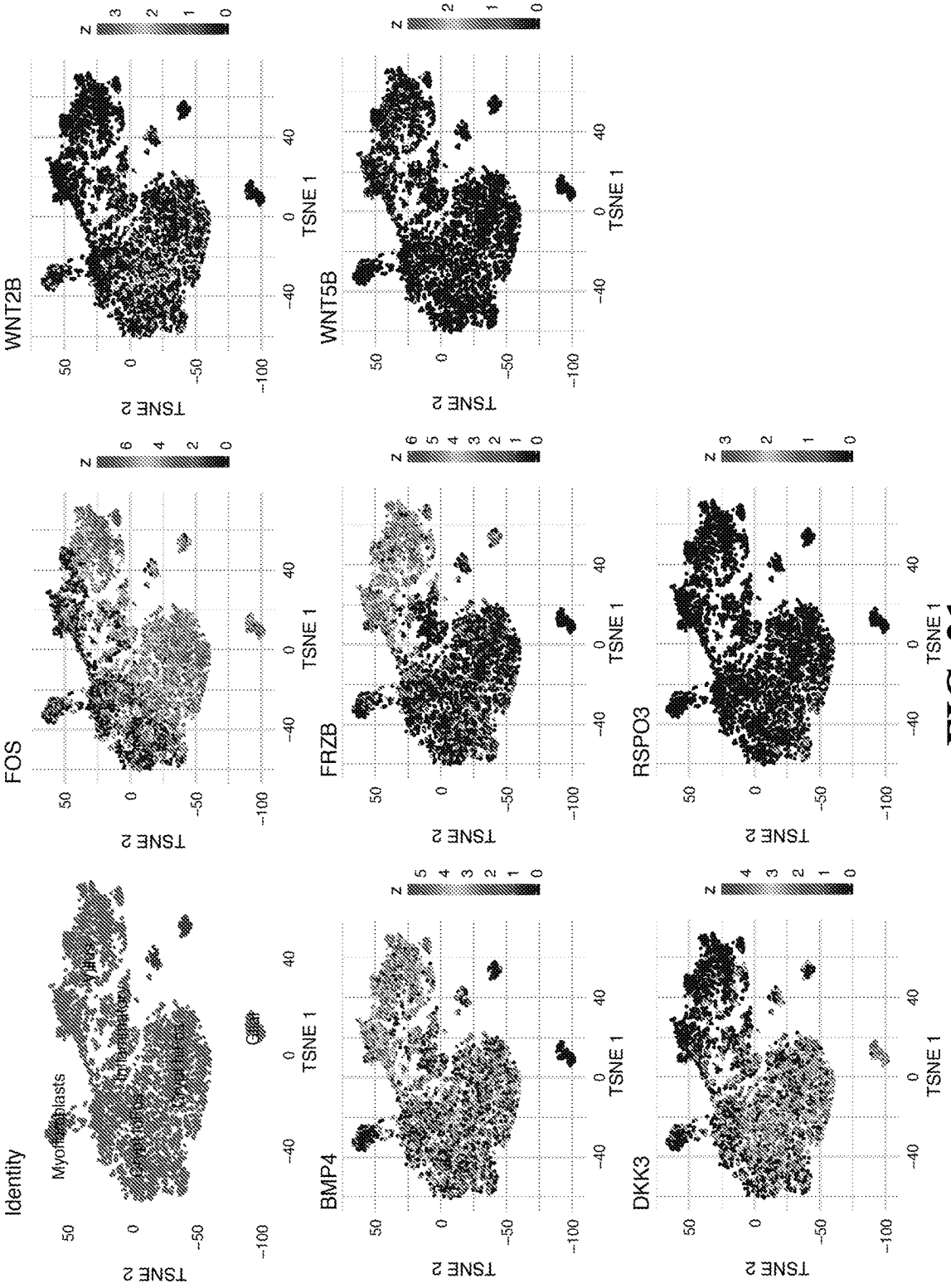

WNT2B
WNT5B
FOS
FRZB
RSPO3
Identity
BMP4
DKK3
TSNE 1
TSNE 2
Myofibroblasts
Glial

FIG. 21

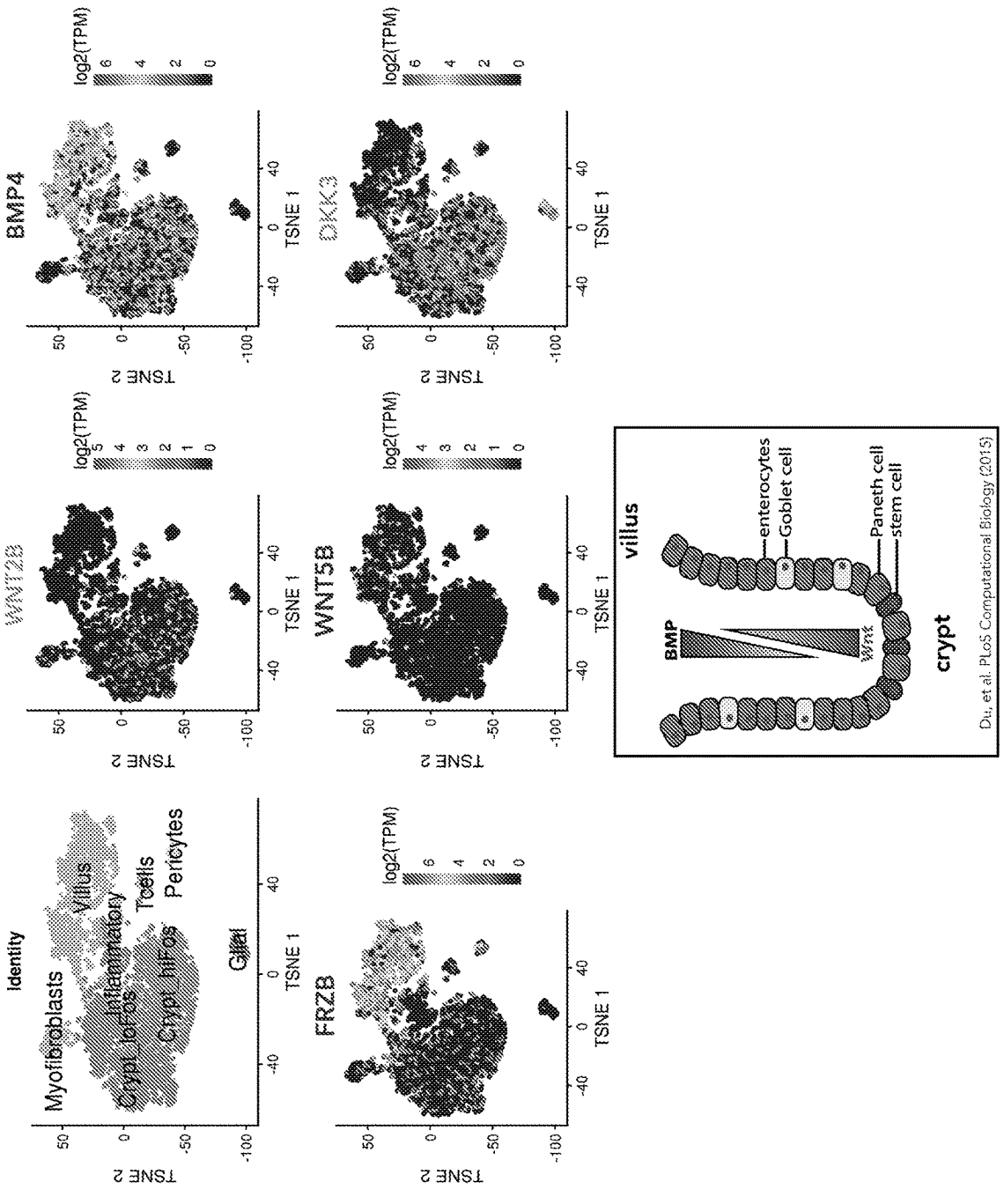

Identity
Myofibroblasts
Villus
Inflammatory
Crypt_loFos
Tcells
Crypt_hiFos
Pericytes
Glial
FRZB
WNT2B
WNT5B
BMP4
DKK3
log2(TPM)
TSNE 1
TSNE 2
villus
crypt
BMP
Wnt
enterocytes
Goblet cell
Paneth cell
stem cell
Du, et al. PLoS Computational Biology (2015)

FIG. 22

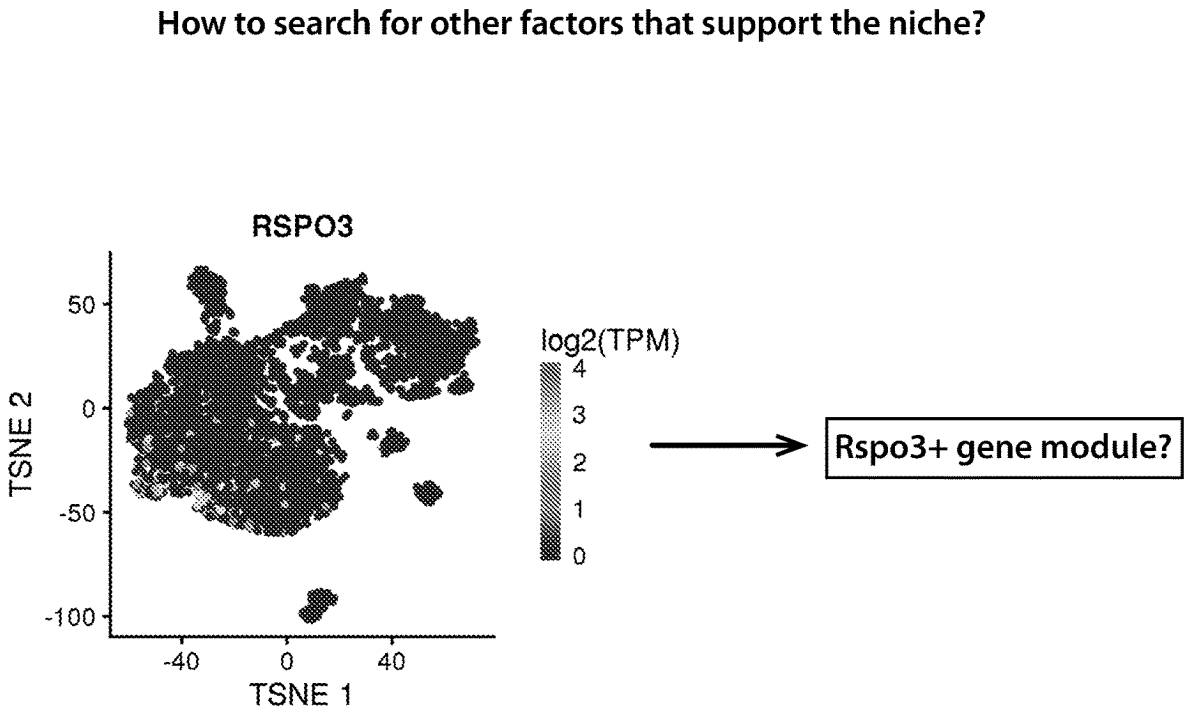

How to search for other factors that support the niche?
RSPO3
50
0
-50
-100
TSNE 2
-40
0
40
TSNE 1
log2(TPM)
4
3
2
1
0
Rspo3+ gene module?

FIG. 23

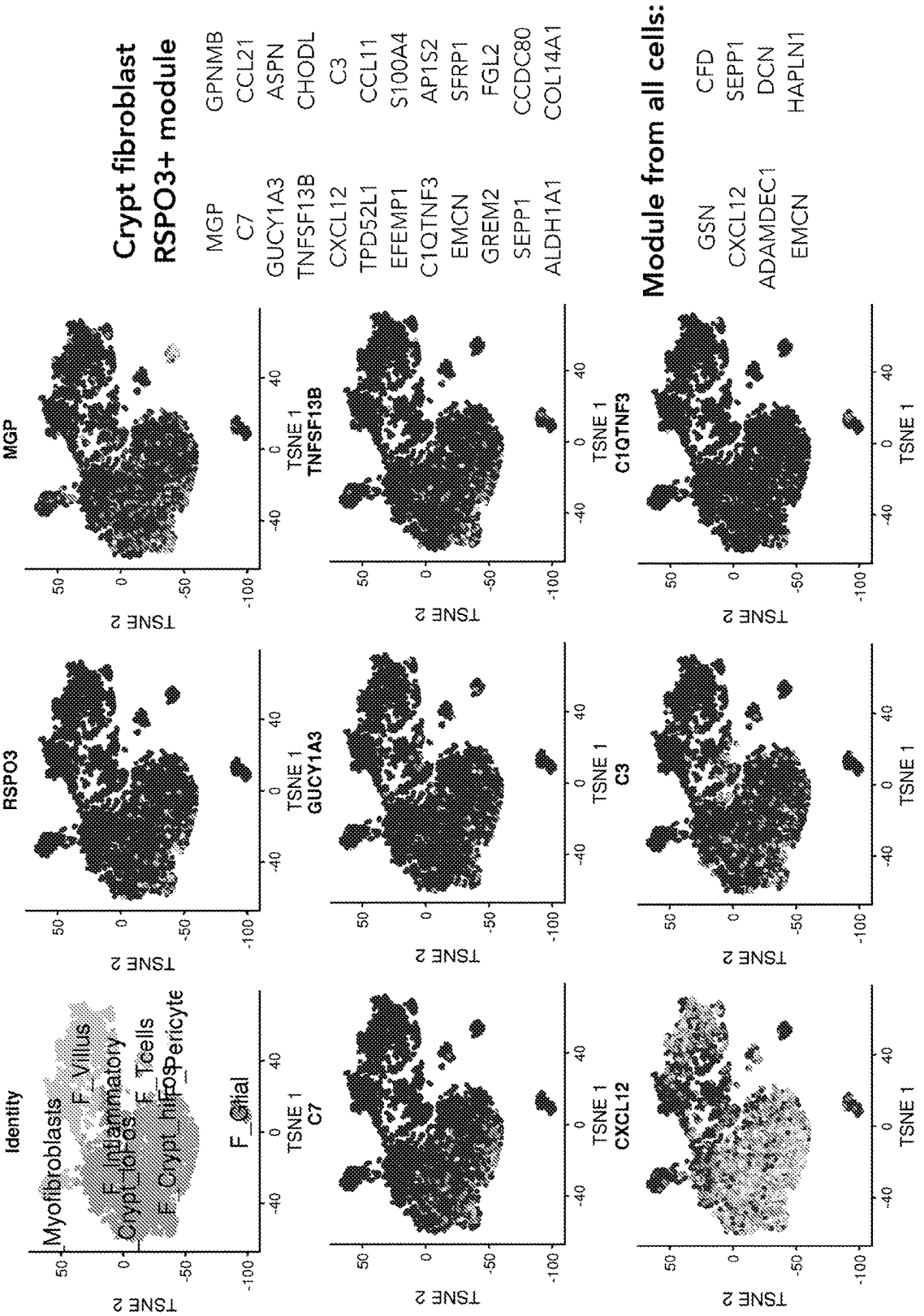

Identity
Myofibroblasts
F_Villus
F_Inflammatory
Crypt_cFos
F_Tcells
F_Crypt_hiFos
F_Pericyte
F_Glial
RSPO3
MGP
C7
GUCY1A3
TNFSF13B
CXCL12
C3
C1QTNF3
TSNE 1
TSNE 2
Crypt fibroblast RSPO3+ module
MGP GPNMB
C7 CCL21
GUCY1A3 ASPN
TNFSF13B CHODL
CXCL12 C3
TPD52L1 CCL11
EFEMP1 S100A4
C1QTNF3 AP1S2
EMCN SFRP1
GREM2 FGL2
SEPP1 CCDC80
ALDH1A1 COL14A1
Module from all cells:
GSN CFD
CXCL12 SEPP1
ADAMDEC1 DCN
EMCN HAPLN1

FIG. 24

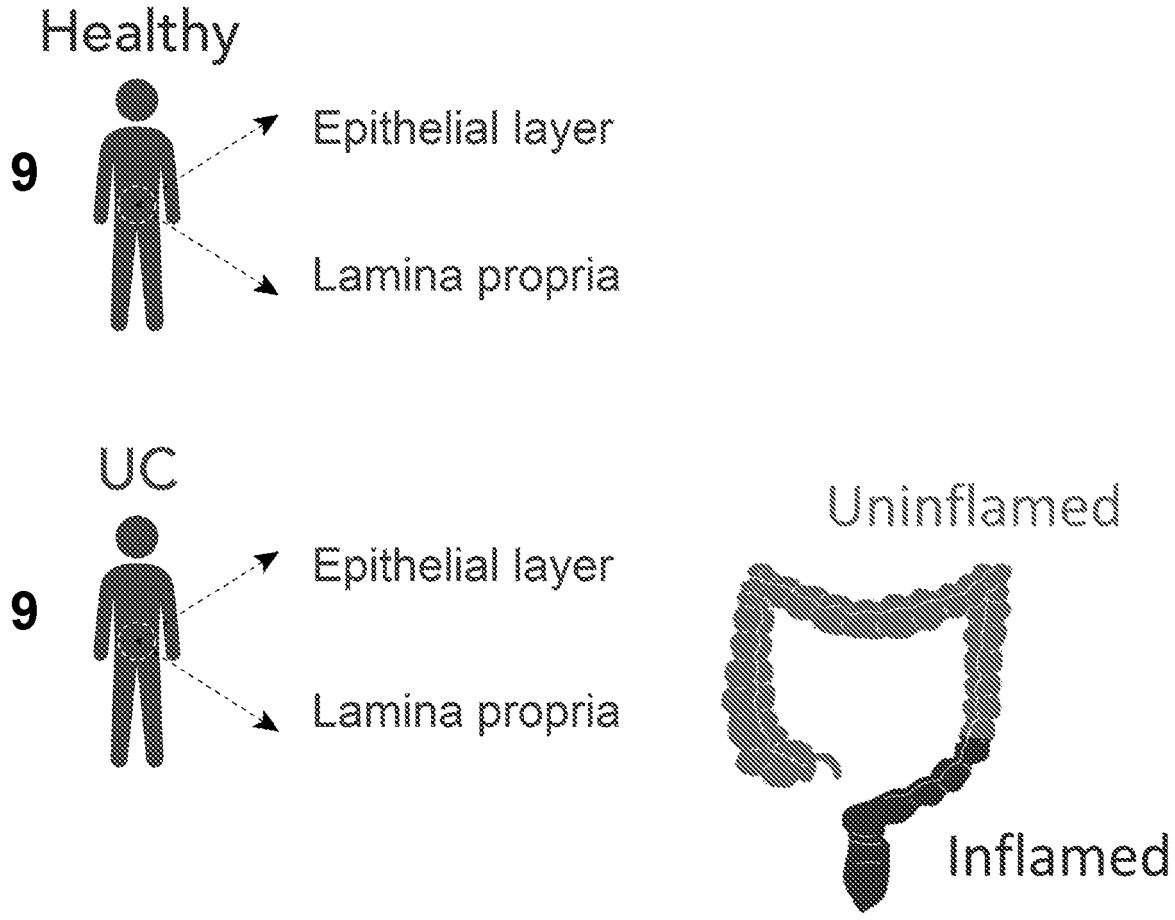

Healthy
9
Epithelial layer
Lamina propria
UC
9
Epithelial layer
Lamina propria
Uninflamed
Inflamed

FIG. 25

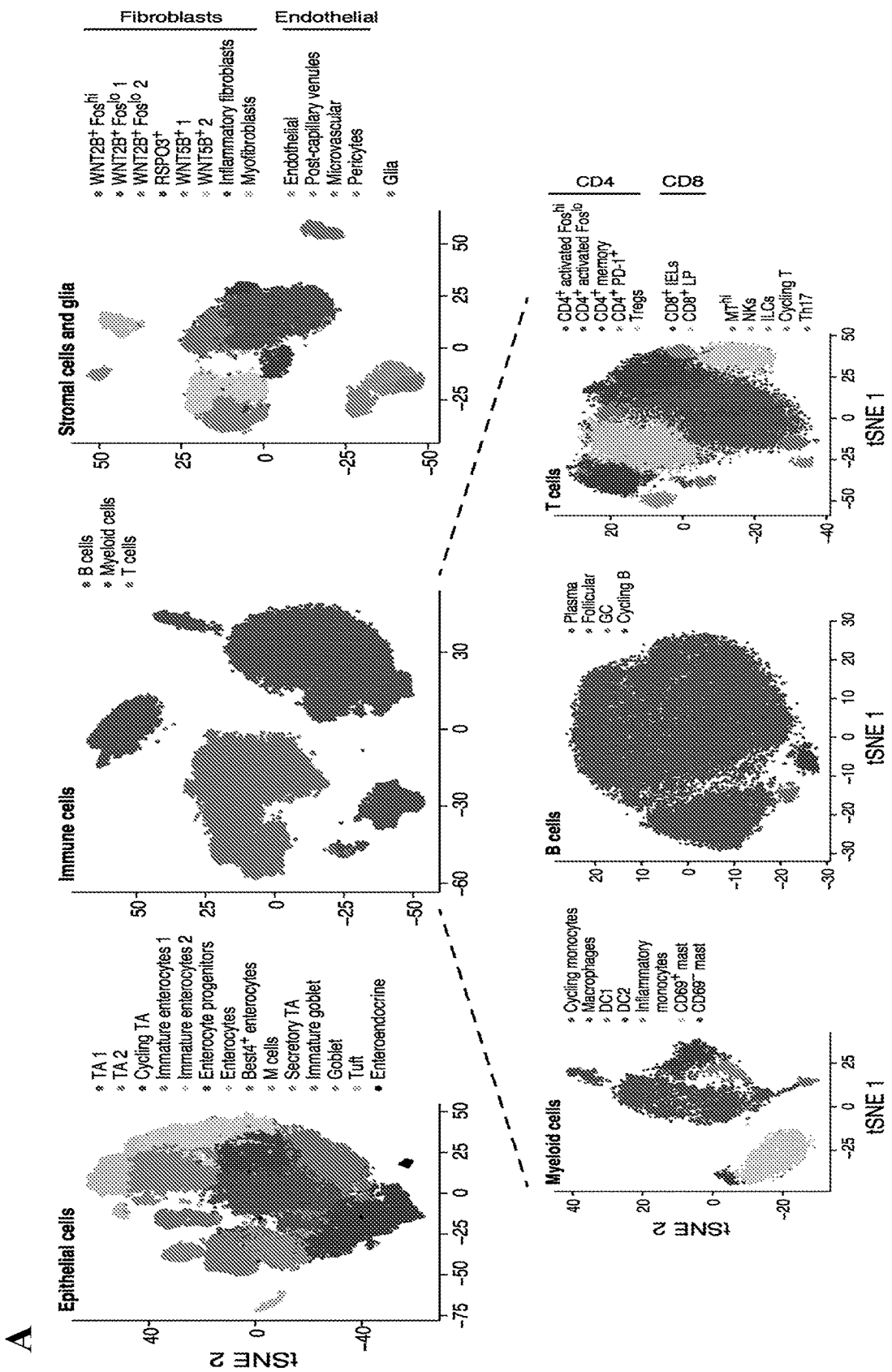

A
Epithelial cells
TA 1
TA 2
Cycling TA
Immature enterocytes 1
Immature enterocytes 2
Enterocyte progenitors
Enterocytes
Best4+ enterocytes
M cells
Secretory TA
Immature goblet
Goblet
Tuft
Enteroendocrine
tSNE 2
tSNE 1
Immune cells
B cells
Myeloid cells
T cells
Stromal cells and glia
Fibroblasts
Endothelial
WNT2B+ Fos^hi
WNT2B+ Fos^lo 1
WNT2B+ Fos^lo 2
RSPO3+
WNT5B+ 1
WNT5B+ 2
Inflammatory fibroblasts
Myofibroblasts
Endothelial
Post-capillary venules
Microvascular
Pericytes
Glia
Myeloid cells
Cycling monocytes
Macrophages
DC1
DC2
Inflammatory monocytes
CD69+ mast
CD69− mast
B cells
Plasma
Follicular
GC
Cycling B
T cells
CD4
CD8
CD4+ activated Fos^hi
CD4+ activated Fos^lo
CD4+ memory
CD4+ PD-1+
Tregs
CD8+ IELs
CD8+ LP
MT^hi
NKs
ILCs
Cycling T
Th17

FIG. 26A

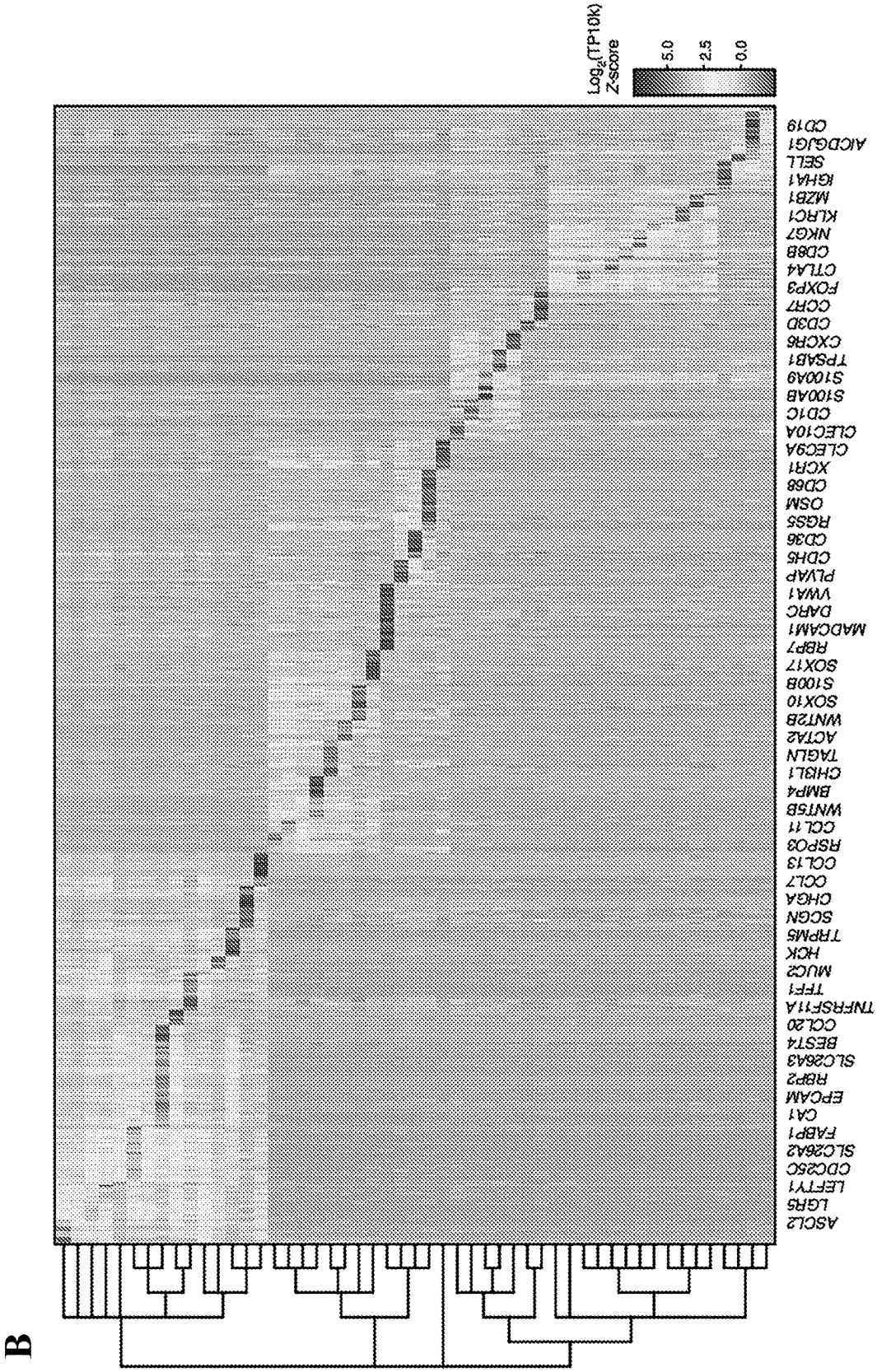
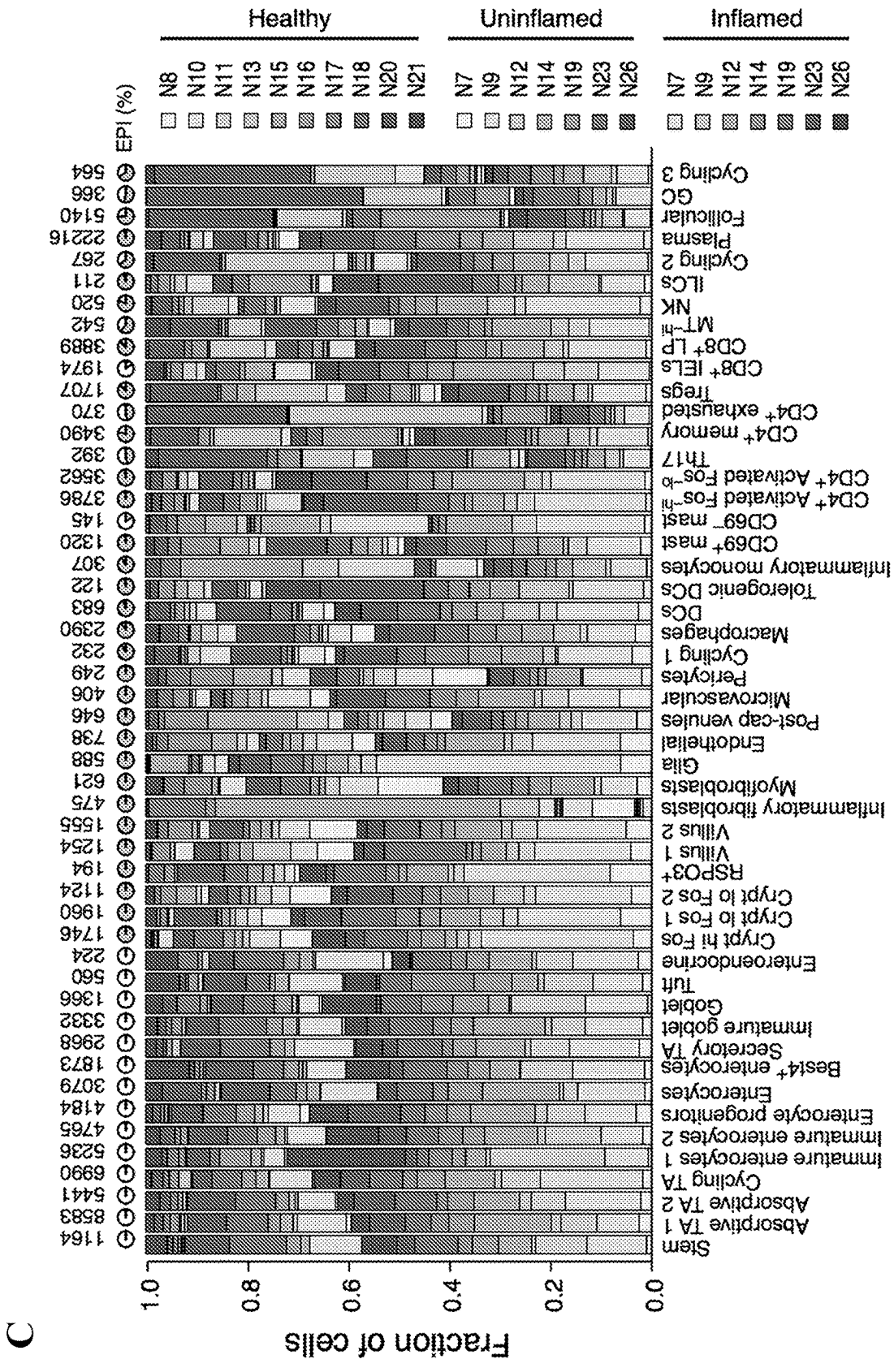

B
Log2(TP10K)
Z-score
5.0
2.5
0.0
CD19
AICDGJG1
SELL
IGHA1
MZB1
KLRC1
NKG7
CD8B
CTLA4
FOXP3
CCR7
CD3D
CXCR6
TPSAB1
S100A9
S100AB
CD1C
CLEC10A
CLEC9A
XCR1
CD68
OSM
RGS5
CD36
CDH5
PLVAP
VWA1
DARC
MADCAM1
RBP7
SOX17
S100B
SOX10
WNT2B
ACTA2
TAGLN
CHI3L1
BMP4
WNT5B
CCL11
RSPO3
CCL13
CCL7
CHGA
SCGN
TRPM5
HCK
MUC2
TFF1
TNFRSF11A
CCL20
BEST4
SLC26A3
RBP2
EPCAM
CA1
FABP1
SLC26A2
CDC25C
LEFTY1
LGR5
ASCL2

FIG. 26B


Healthy
Uninflamed
Inflamed
N8 N10 N11 N13 N15 N16 N17 N18 N20 N21
N7 N9 N12 N14 N19 N23 N26
N7 N9 N12 N14 N19 N23 N26
EPI (%)
Fraction of cells
1.0
0.8
0.6
0.4
0.2
0.0
Stem 1164
Absorptive TA 1 8583
Absorptive TA 2 5441
Cycling TA 6990
Immature enterocytes 1 5236
Immature enterocytes 2 4765
Enterocyte progenitors 4184
Enterocytes 3079
Best4+ enterocytes 1873
Secretory TA 2968
Immature goblet 3332
Goblet 1366
Tuft 560
Enteroendocrine 224
Crypt hi Fos 1746
Crypt lo Fos 1 1960
Crypt lo Fos 2 1124
RSPO3+ 194
Villus 1 1254
Villus 2 1555
Inflammatory fibroblasts 475
Myofibroblasts 621
Glia 588
Endothelial 738
Post-cap venules 646
Microvascular 406
Pericytes 249
Cycling 1 232
Macrophages 2390
DCs 683
Tolerogenic DCs 122
Inflammatory monocytes 307
CD69+ mast 1320
CD69− mast 145
CD4+ Activated Fos−hi 3786
CD4+ Activated Fos−lo 3562
Th17 392
CD4+ memory 3490
CD4+ exhausted 370
Tregs 1707
CD8+ IELs 1974
CD8+ LP 3889
MT−hi 542
NK 520
ILCs 211
Cycling 2 267
Plasma 22216
Follicular 5140
GC 366
Cycling 3 564

C

FIG. 26C

D

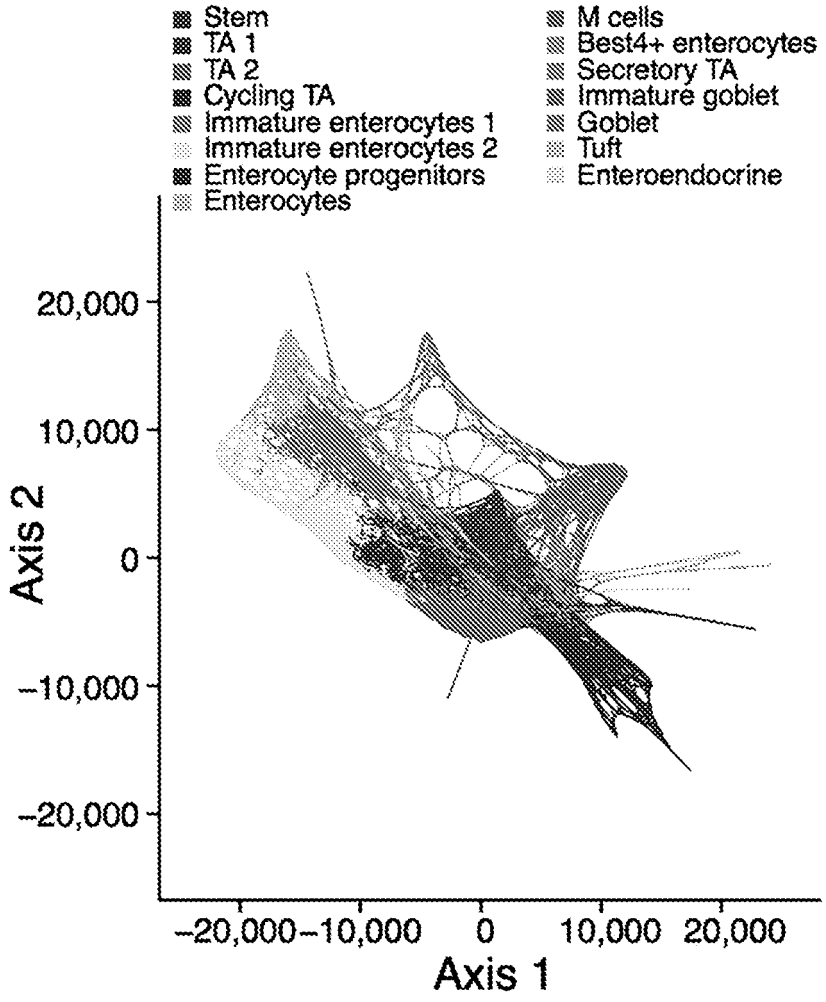
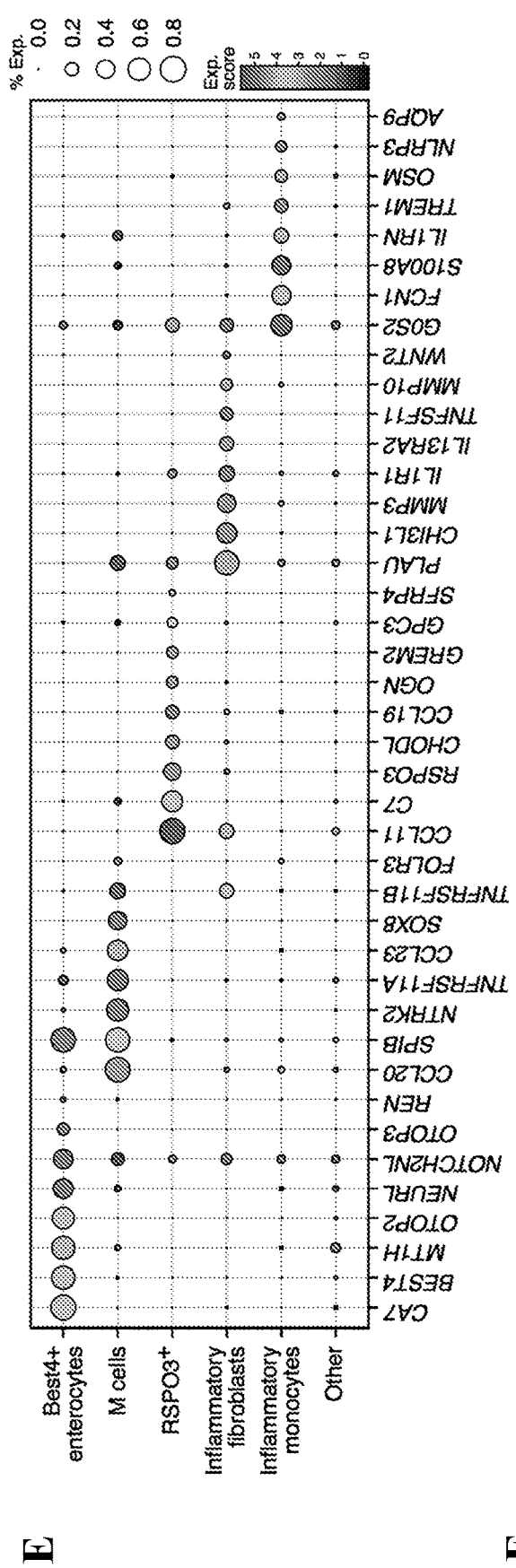

Stem
TA 1
TA 2
Cycling TA
Immature enterocytes 1
Immature enterocytes 2
Enterocyte progenitors
Enterocytes
M cells
Best4+ enterocytes
Secretory TA
Immature goblet
Goblet
Tuft
Enteroendocrine
20,000
10,000
0
−10,000
−20,000
Axis 2
−20,000 −10,000 0 10,000 20,000
Axis 1

FIG. 26D


E
% Exp.
0.0
0.2
0.4
0.6
0.8
Exp. score
5
4
3
2
1
0
CA7
BEST4
MT1H
OTOP2
NEURL
NOTCH2NL
OTOP3
REN
CCL20
SPIB
NTRK2
TNFRSF11A
CCL23
SOX8
TNFRSF11B
FOLR3
CCL11
C7
RSPO3
CHODL
CCL19
OGN
GREM2
GPC3
SFRP4
PLAU
CHI3L1
MMP3
IL1R1
IL13RA2
TNFSF11
MMP10
WNT2
G0S2
FCN1
S100A8
IL1RN
TREM1
OSM
NLRP3
ACP9
Best4+ enterocytes
M cells
RSPO3+
Inflammatory fibroblasts
Inflammatory monocytes
Other

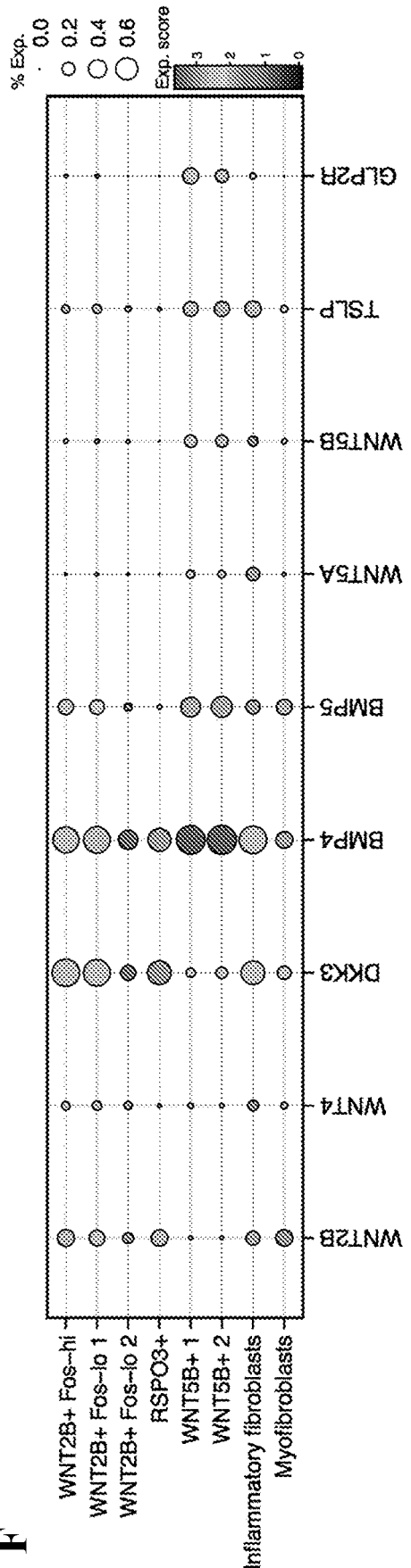

F
% Exp.
0.0
0.2
0.4
0.6
Exp. score
3
2
1
0
GLP2R
TSLP
WNT5B
WNT5A
BMP5
BMP4
DKK3
WNT4
WNT2B
WNT2B+ Fos−hi
WNT2B+ Fos−lo 1
WNT2B+ Fos−lo 2
RSPO3+
WNT5B+ 1
WNT5B+ 2
Inflammatory fibroblasts
Myofibroblasts

FIG. 26E-F

G

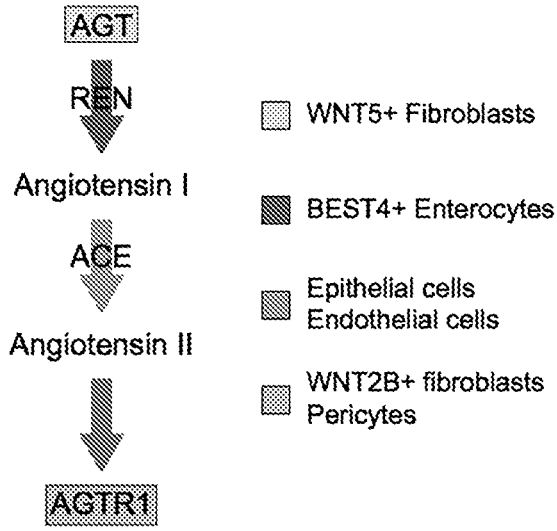

AGT
REN
Angiotensin I
ACE
Angiotensin II
AGTR1
WNT5+ Fibroblasts
BEST4+ Enterocytes
Epithelial cells
Endothelial cells
WNT2B+ fibroblasts
Pericytes

FIG. 26G

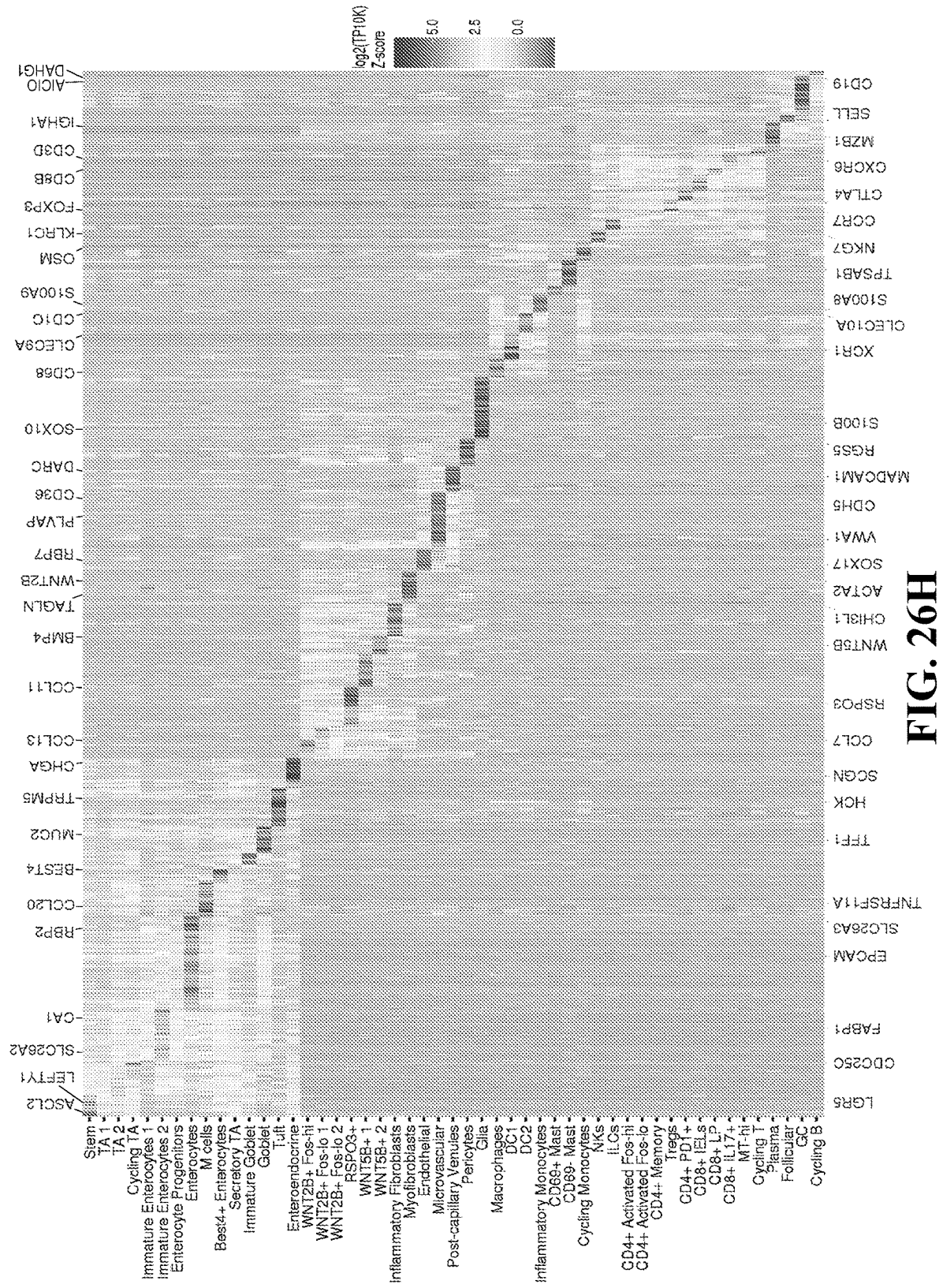

log2(TP10K)
Z-score
5.0
2.5
0.0
ASCL2
LEFTY1
SLC26A2
CA1
RBP2
CCL20
BEST4
MUC2
TRPM5
CHGA
CCL13
CCL11
BMP4
TAGLN
WNT2B
RBP7
PLVAP
CD36
DARC
SOX10
CD68
CLEC9A
CD1C
S100A9
OSM
KLRC1
FOXP3
CD8B
CD3D
IGHA1
AICIO
DAHG1
Stem
TA 1
TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
WNT2B+ Fos-hi
WNT2B+ Fos-lo 1
WNT2B+ Fos-lo 2
RSPO3+
WNT5B+ 1
WNT5B+ 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-capillary Venules
Pericytes
Glia
Macrophages
DC1
DC2
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling Monocytes
NKs
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ PD1+
CD8+ IELs
CD8+ LP
CD8+ IL17+
MT-hi
Cycling T
Plasma
Follicular
GC
Cycling B
LGR5
CDC25C
FABP1
EPCAM
SLC26A3
TNFRSF11A
TFF1
HCK
SCGN
CCL7
RSPO3
WNT5B
CHI3L1
ACTA2
SOX17
VWA1
CDH5
MADCAM1
RGS5
S100B
XCR1
CLEC10A
S100A8
TPSAB1
NKG7
CCR7
CTLA4
CXCR6
MZB1
SELL
CD19

FIG. 26H

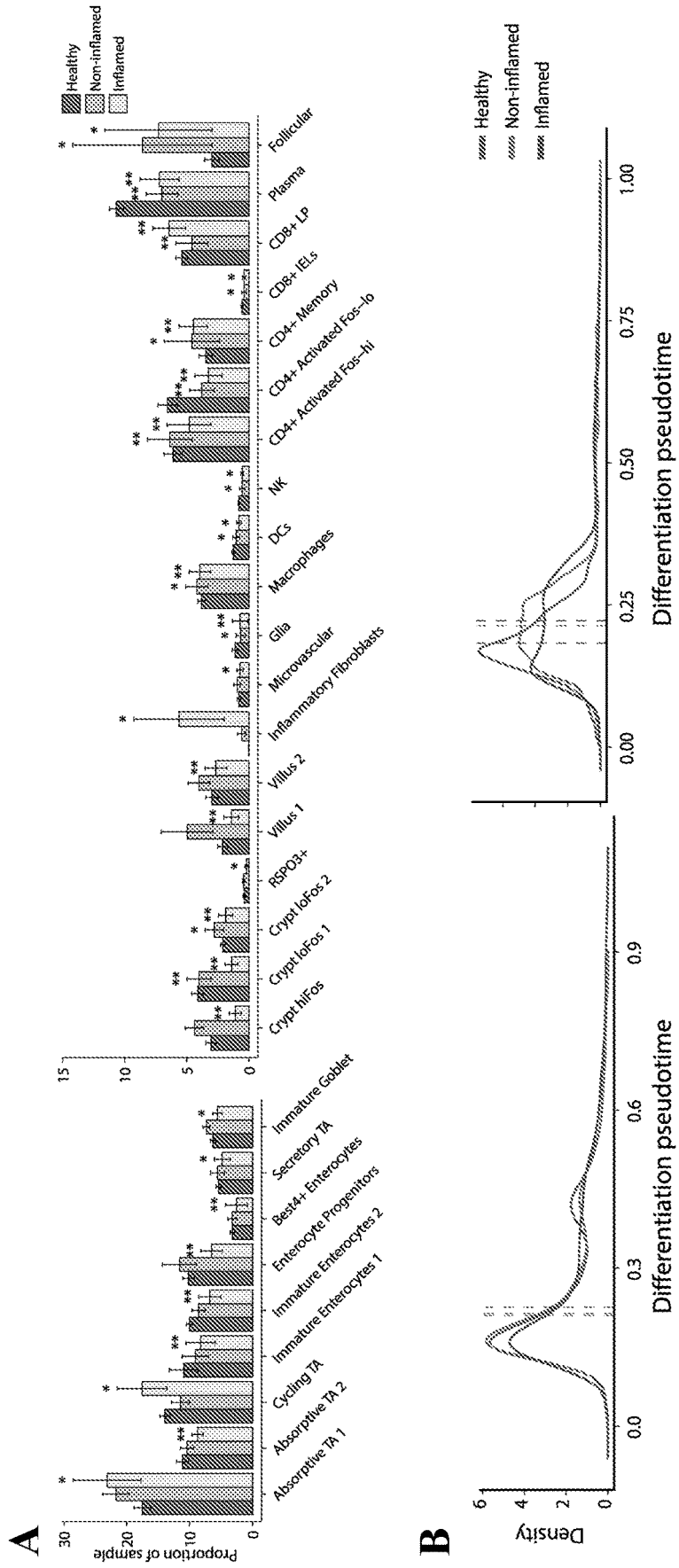

A
Proportion of sample
Healthy
Non-inflamed
Inflamed
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Best4+ Enterocytes
Secretory TA
Immature Goblet
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Microvascular
Glia
Macrophages
DCs
NK
CD4+ Activated Fos–hi
CD4+ Activated Fos–lo
CD4+ Memory
CD8+ IELs
CD8+ LP
Plasma
Follicular
B
Density
Healthy
Non-inflamed
Inflamed
Differentiation pseudotime
Differentiation pseudotime

FIG. 27A-B

C

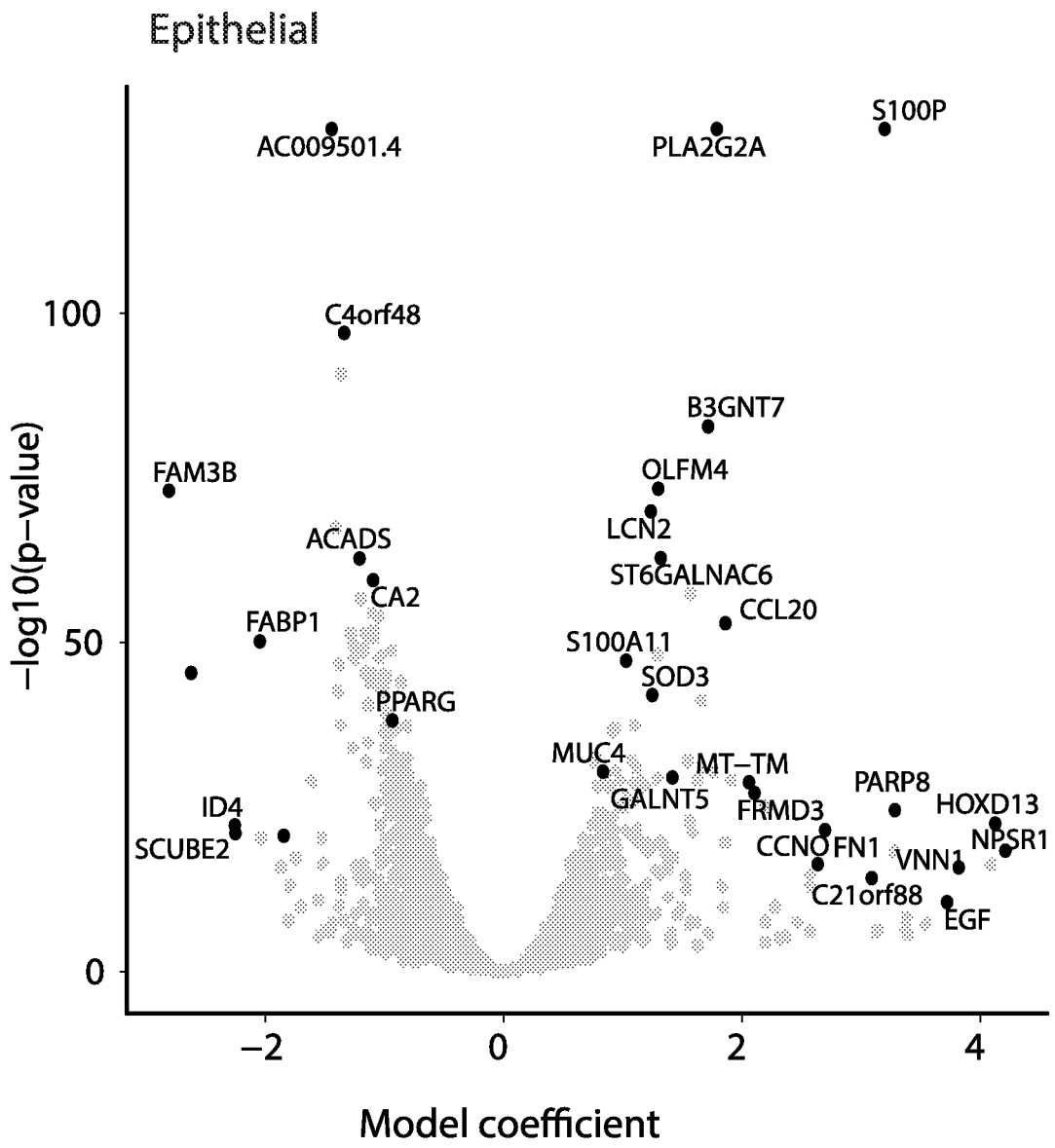

Epithelial
AC009501.4
PLA2G2A
S100P
C4orf48
B3GNT7
FAM3B
OLFM4
LCN2
ACADS
ST6GALNAC6
CA2
CCL20
FABP1
S100A11
SOD3
PPARG
MUC4
MT–TM
PARP8
GALNT5
FRMD3
HOXD13
ID4
SCUBE2
CCNO
FN1
VNN1
NPSR1
C21orf88
EGF
100
50
0
−log10(p−value)
−2
0
2
4
Model coefficient

FIG. 27C

D

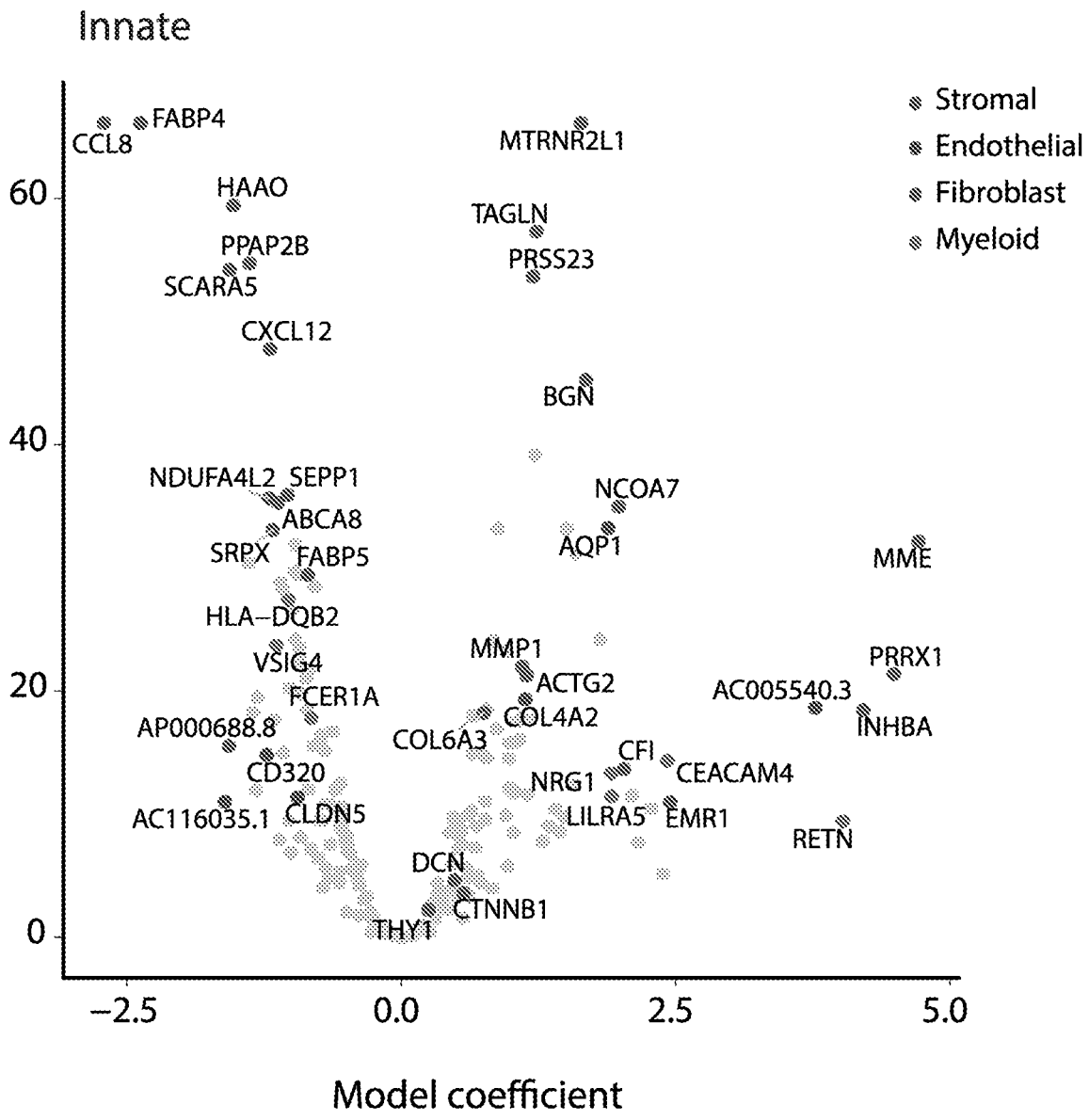

Innate
Stromal
Endothelial
Fibroblast
Myeloid
FABP4
CCL8
MTRNR2L1
HAAO
TAGLN
PPAP2B
PRSS23
SCARA5
CXCL12
BGN
NDUFA4L2
SEPP1
NCOA7
ABCA8
AQP1
SRPX
FABP5
MME
HLA−DQB2
MMP1
PRRX1
VSIG4
ACTG2
AC005540.3
FCER1A
COL4A2
INHBA
AP000688.8
COL6A3
CFI
CD320
NRG1
CEACAM4
AC116035.1
CLDN5
LILRA5
EMR1
RETN
DCN
CTNNB1
THY1
60
40
20
0
−2.5
0.0
2.5
5.0
Model coefficient

FIG. 27D

E

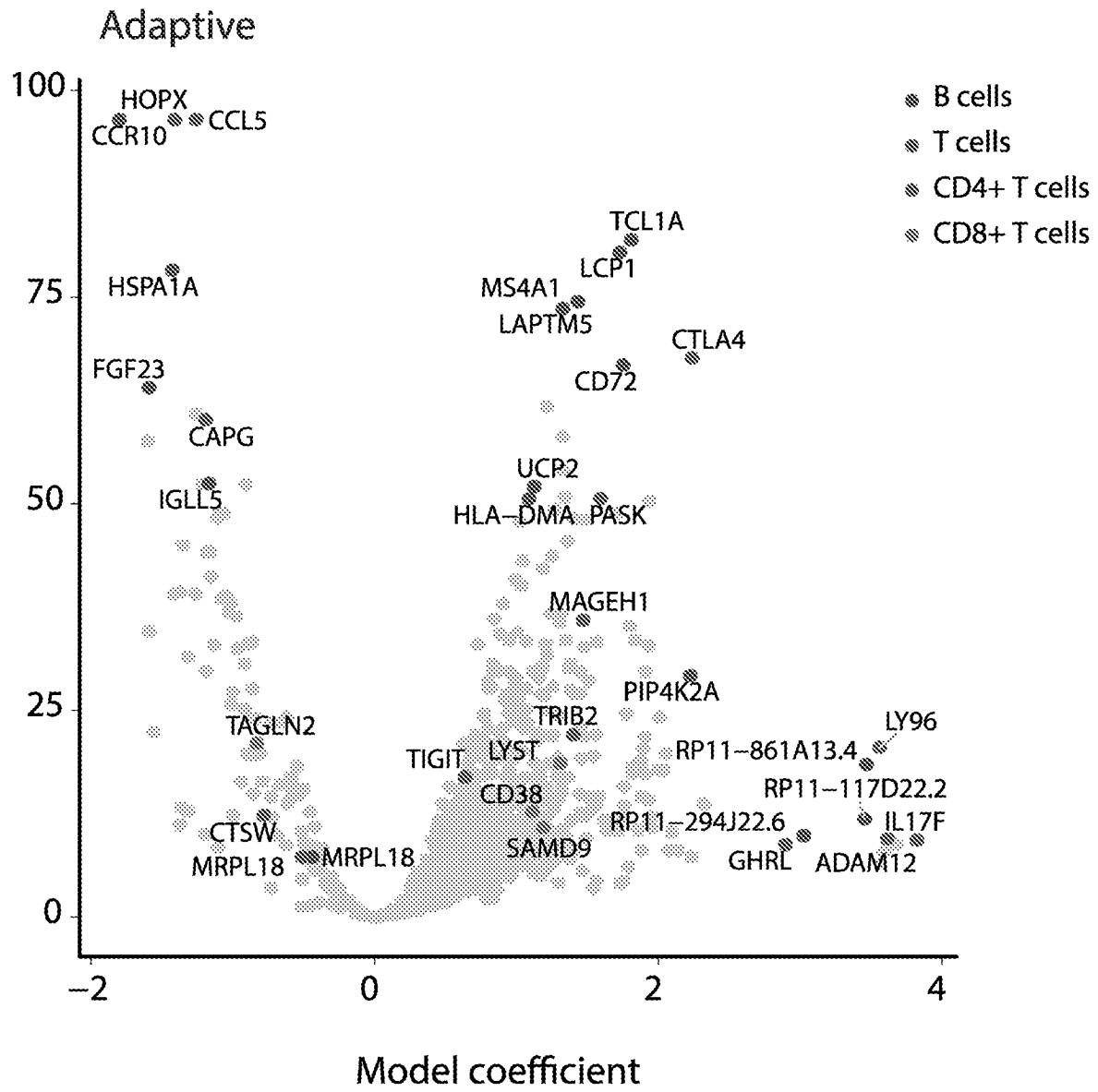

Adaptive
100
75
50
25
0
−2
0
2
4
Model coefficient
B cells
T cells
CD4+ T cells
CD8+ T cells
HOPX
CCR10
CCL5
HSPA1A
FGF23
CAPG
IGLL5
TAGLN2
CTSW
MRPL18
MRPL18
TCL1A
LCP1
MS4A1
LAPTM5
CTLA4
CD72
UCP2
HLA−DMA
PASK
MAGEH1
PIP4K2A
TRIB2
TIGIT
LYST
CD38
SAMD9
RP11−861A13.4
LY96
RP11−117D22.2
RP11−294J22.6
IL17F
GHRL
ADAM12

FIG. 27E

F

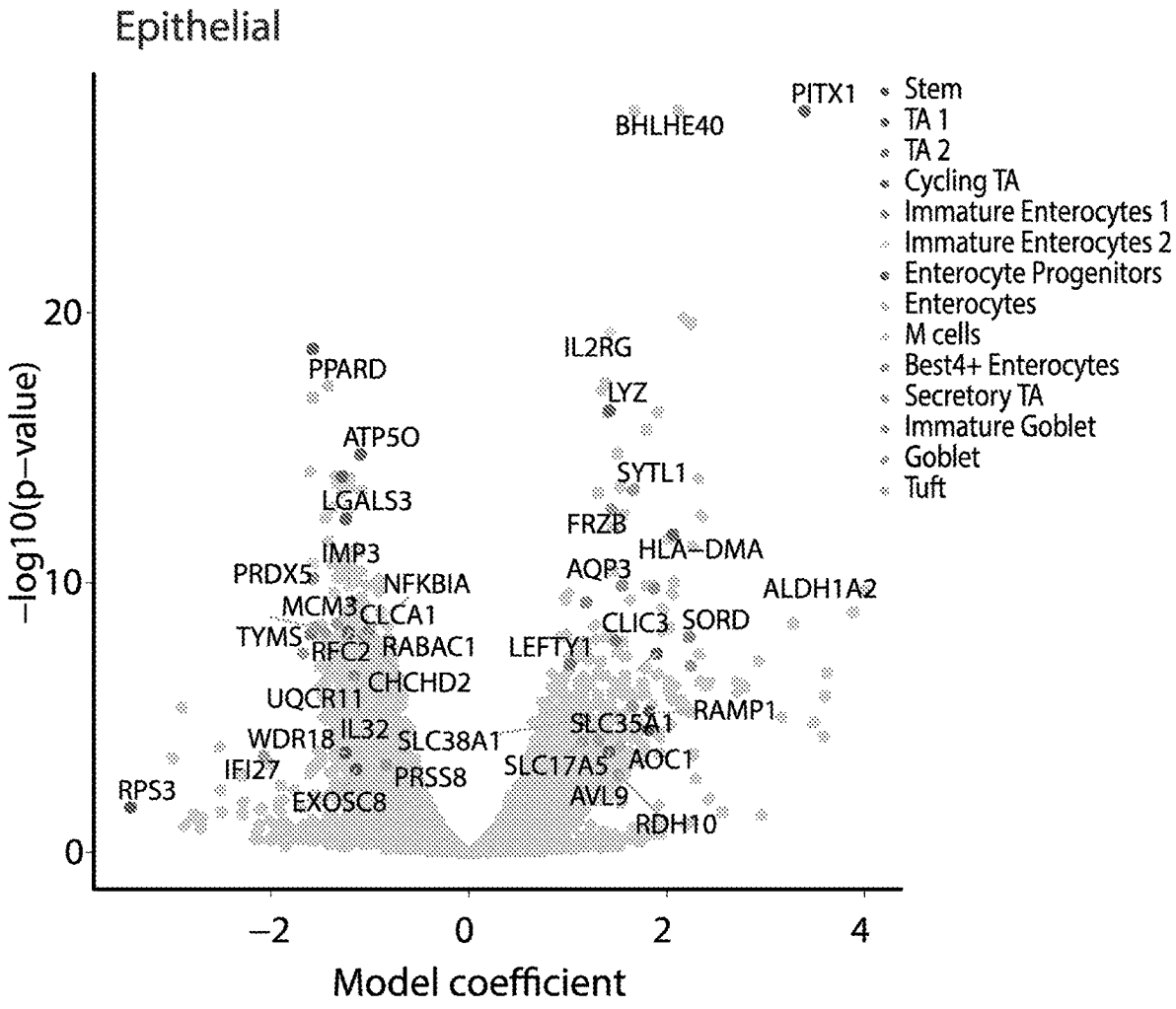

Epithelial
−log10(p−value)
20
10
0
−2
0
2
4
Model coefficient
PITX1
BHLHE40
IL2RG
LYZ
SYTL1
FRZB
HLA−DMA
AQP3
ALDH1A2
CLIC3
SORD
LEFTY1
RAMP1
SLC35A1
AOC1
SLC17A5
AVL9
RDH10
PPARD
ATP5O
LGALS3
IMP3
PRDX5
NFKBIA
MCM3
CLCA1
TYMS
RFC2
RABAC1
CHCHD2
UQCR11
IL32
WDR18
SLC38A1
IFI27
PRSS8
RPS3
EXOSC8
Stem
TA 1
TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft

FIG. 27F

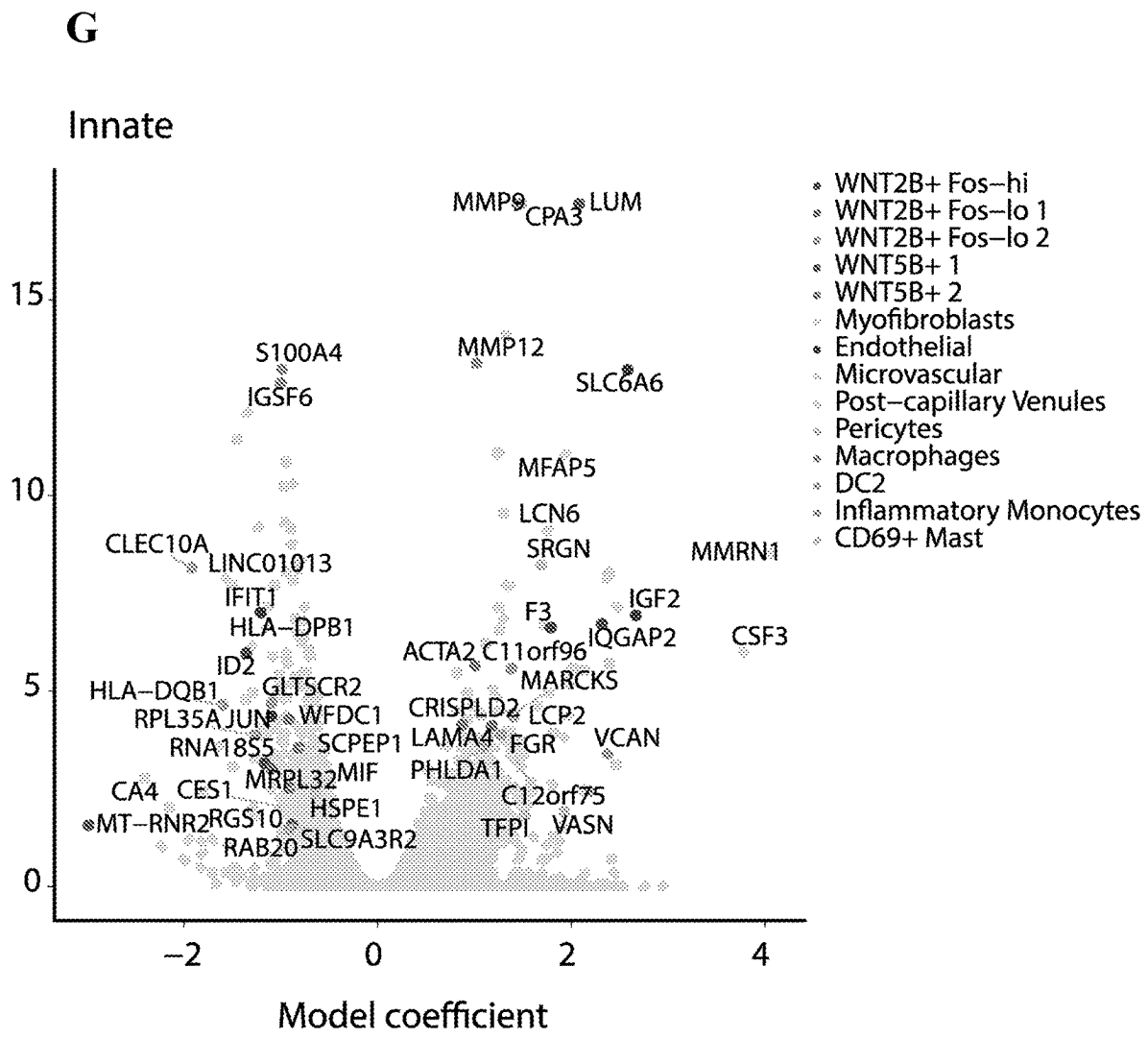

G
Innate
MMP9
CPA3
LUM
S100A4
MMP12
IGSF6
SLC6A6
MFAP5
LCN6
CLEC10A
LINC01013
SRGN
MMRN1
IFIT1
IGF2
F3
HLA−DPB1
IQGAP2
CSF3
ACTA2
C11orf96
ID2
MARCKS
HLA−DQB1
GLTSCR2
CRISPLD2
LCP2
RPL35A
JUN
WFDC1
LAMA4
FGR
VCAN
RNA18S5
SCPEP1
PHLDA1
MRPL32
MIF
CA4
CES1
C12orf75
HSPE1
MT−RNR2
RGS10
TFPI
VASN
RAB20
SLC9A3R2
15
10
5
0
−2
0
2
4
Model coefficient
WNT2B+ Fos−hi
WNT2B+ Fos−lo 1
WNT2B+ Fos−lo 2
WNT5B+ 1
WNT5B+ 2
Myofibroblasts
Endothelial
Microvascular
Post−capillary Venules
Pericytes
Macrophages
DC2
Inflammatory Monocytes
CD69+ Mast

FIG. 27G

H

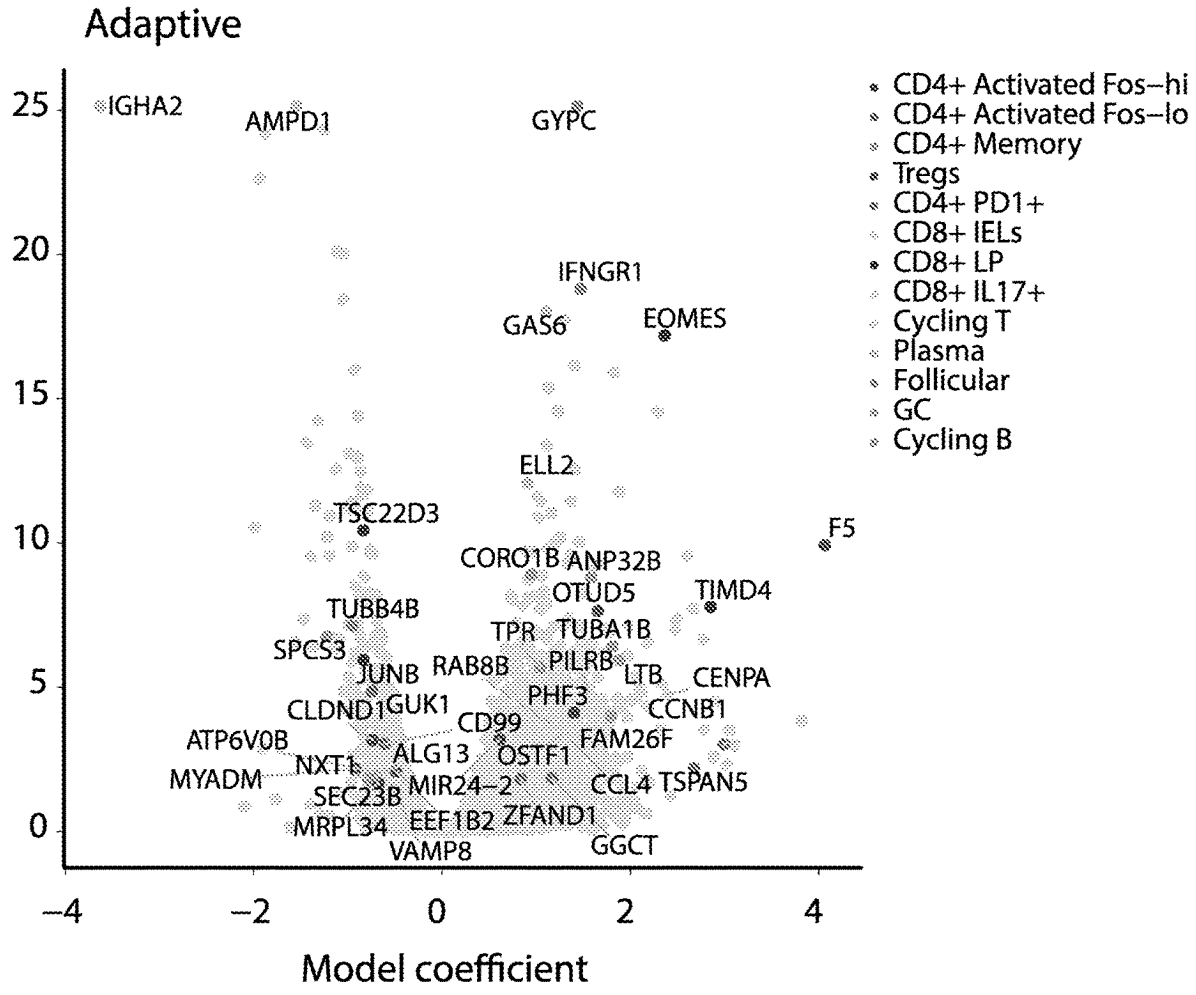

Adaptive
25
20
15
10
5
0
−4
−2
0
2
4
Model coefficient
IGHA2
AMPD1
GYPC
IFNGR1
GAS6
EOMES
ELL2
TSC22D3
F5
CORO1B
ANP32B
OTUD5
TIMD4
TUBB4B
TPR
TUBA1B
SPCS3
JUNB
RAB8B
PILRB
LTB
CENPA
PHF3
CLDND1
GUK1
CD99
CCNB1
ATP6V0B
FAM26F
NXT1
ALG13
OSTF1
MYADM
SEC23B
MIR24−2
CCL4
TSPAN5
MRPL34
EEF1B2
ZFAND1
VAMP8
GGCT
CD4+ Activated Fos−hi
CD4+ Activated Fos−lo
CD4+ Memory
Tregs
CD4+ PD1+
CD8+ IELs
CD8+ LP
CD8+ IL17+
Cycling T
Plasma
Follicular
GC
Cycling B

FIG. 27H

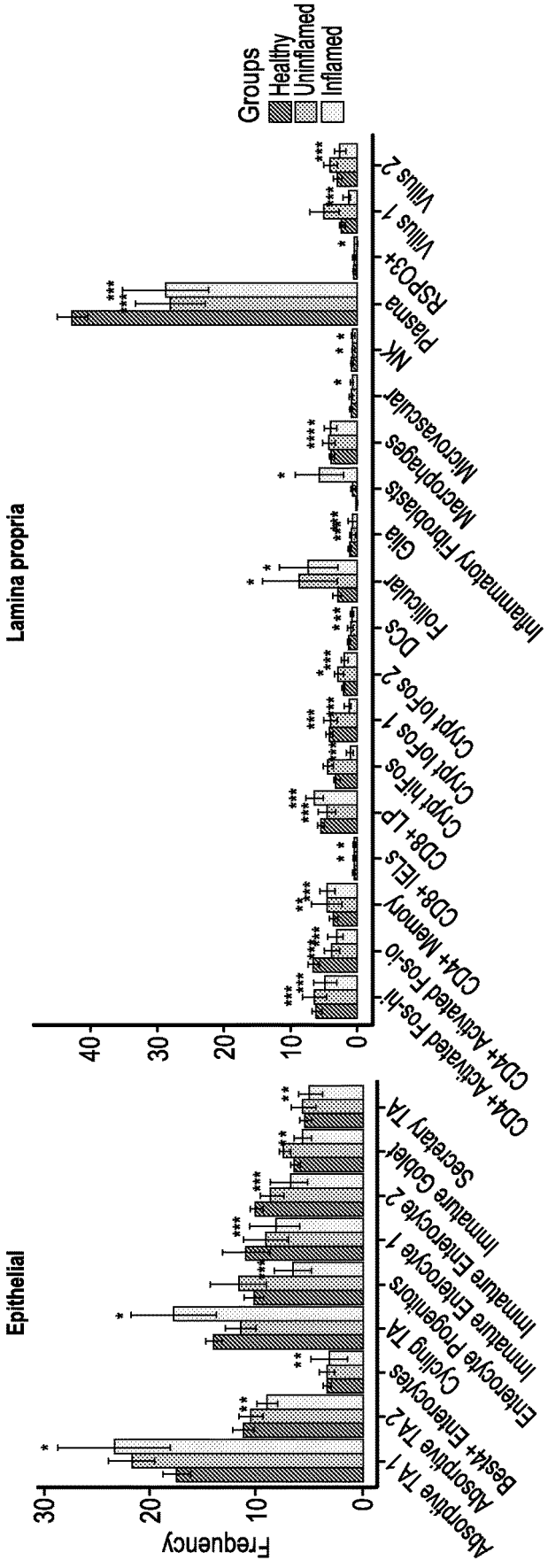

I
Epithelial
Lamina propria
Frequency
Groups
Healthy
Uninflamed
Inflamed
Absorptive TA 1
Absorptive TA 2
Best4+ Enterocytes
Cycling TA
Enterocyte Progenitors
Immature Enterocyte 1
Immature Enterocyte 2
Immature Goblet
Secretary TA
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
CD8+ IELs
CD8+ LP
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
DCs
Follicular
Glia
Inflammatory Fibroblasts
Macrophages
Microvascular
NK
Plasma
RSPO3+
Villus 1
Villus 2

FIG. 27I

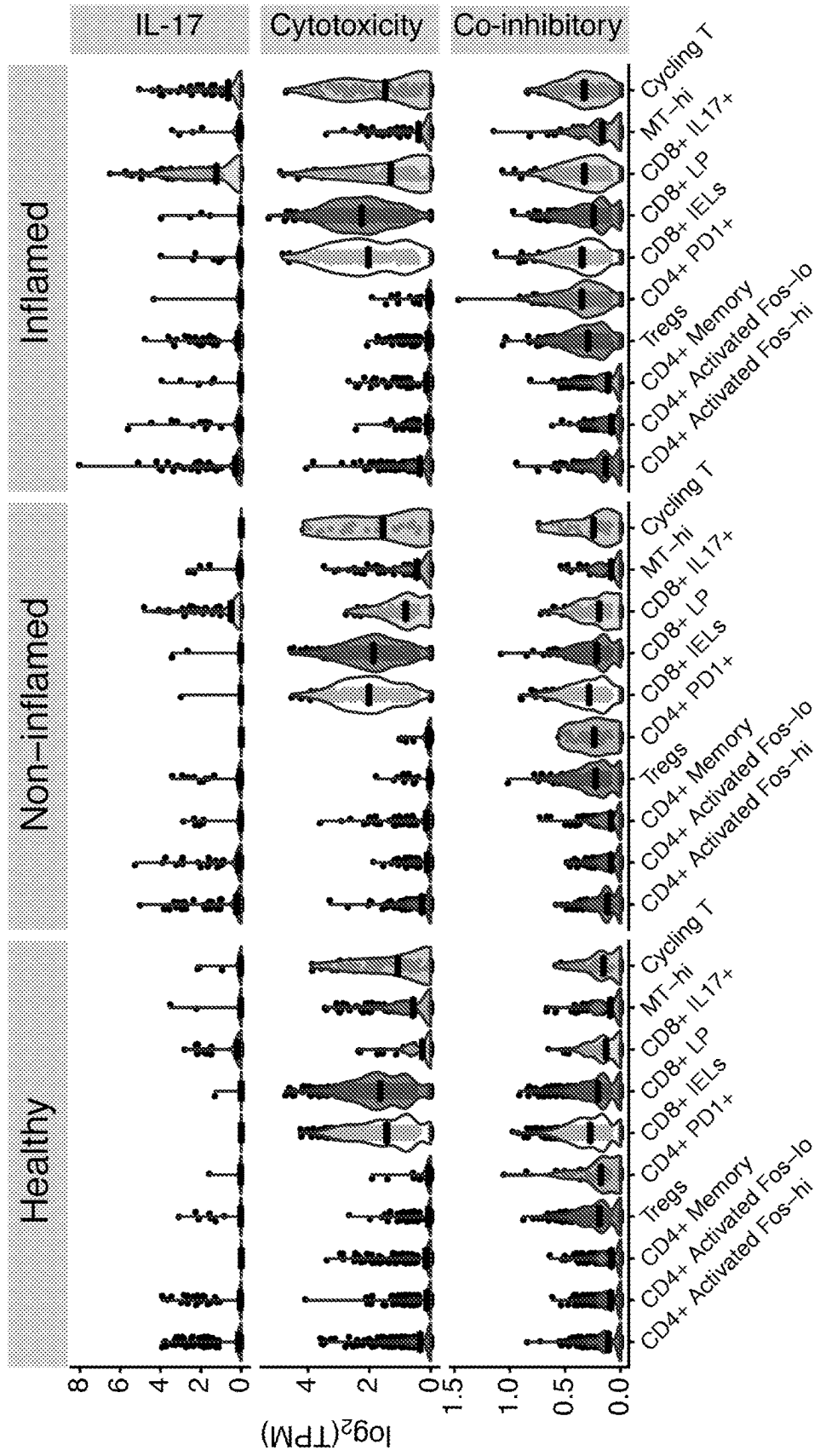

A
IL-17
Cytotoxicity
Co-inhibitory
Inflamed
Non–inflamed
Healthy
log2(TPM)
Cycling T
MT–hi
CD8+ IL17+
CD8+ LP
CD8+ IELs
CD4+ PD1+
Tregs
CD4+ Memory
CD4+ Activated Fos–lo
CD4+ Activated Fos–hi

FIG. 28A

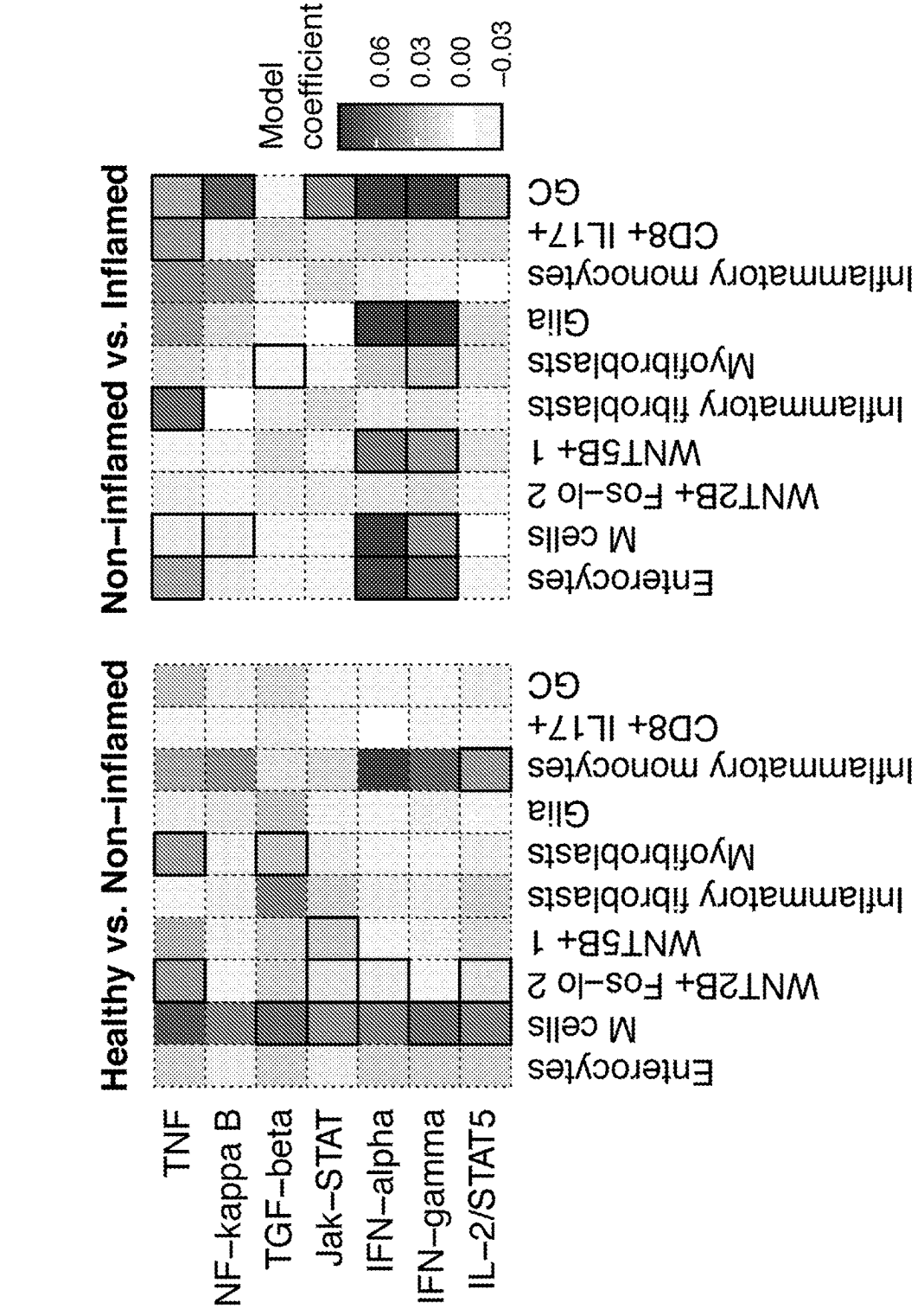

B
Healthy vs. Non−inflamed
Non−inflamed vs. Inflamed
Model coefficient
0.06
0.03
0.00
−0.03
TNF
NF−kappa B
TGF−beta
Jak−STAT
IFN−alpha
IFN−gamma
IL−2/STAT5
Enterocytes
M cells
WNT2B+ Fos−lo 2
WNT5B+ 1
Inflammatory fibroblasts
Myofibroblasts
Glia
Inflammatory monocytes
CD8+ IL17+
GC

FIG. 28B

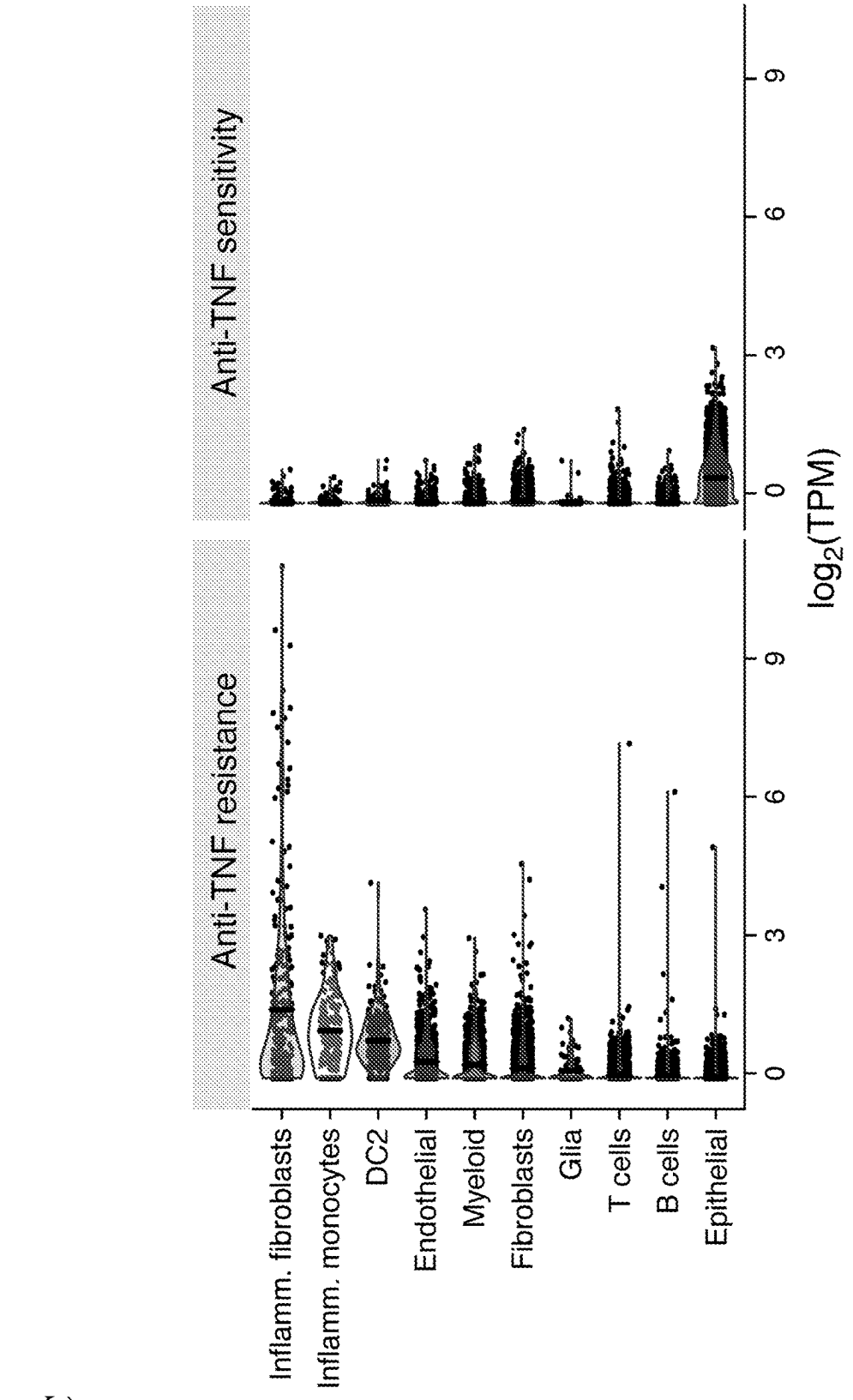

C
Anti-TNF resistance
Anti-TNF sensitivity
Inflamm. fibroblasts
Inflamm. monocytes
DC2
Endothelial
Myeloid
Fibroblasts
Glia
T cells
B cells
Epithelial
0
3
6
9
log2(TPM)

FIG. 28C

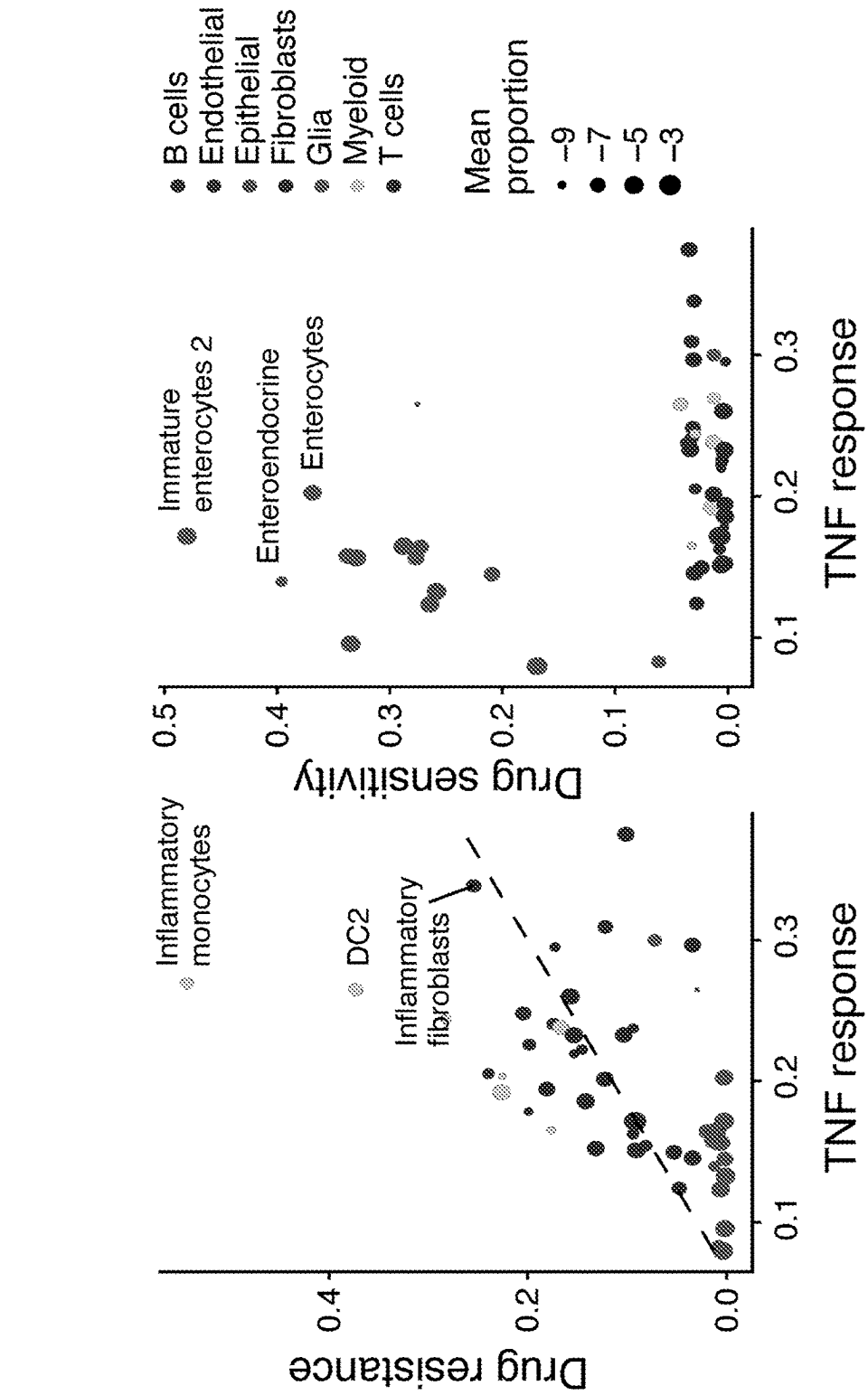

D
Drug resistance
0.4
0.2
0.0
0.1
0.2
0.3
TNF response
Inflammatory monocytes
DC2
Inflammatory fibroblasts
Drug sensitivity
0.5
0.4
0.3
0.2
0.1
0.0
Immature enterocytes 2
Enteroendocrine
Enterocytes
B cells
Endothelial
Epithelial
Fibroblasts
Glia
Myeloid
T cells
Mean proportion
−9
−7
−5
−3

FIG. 28D

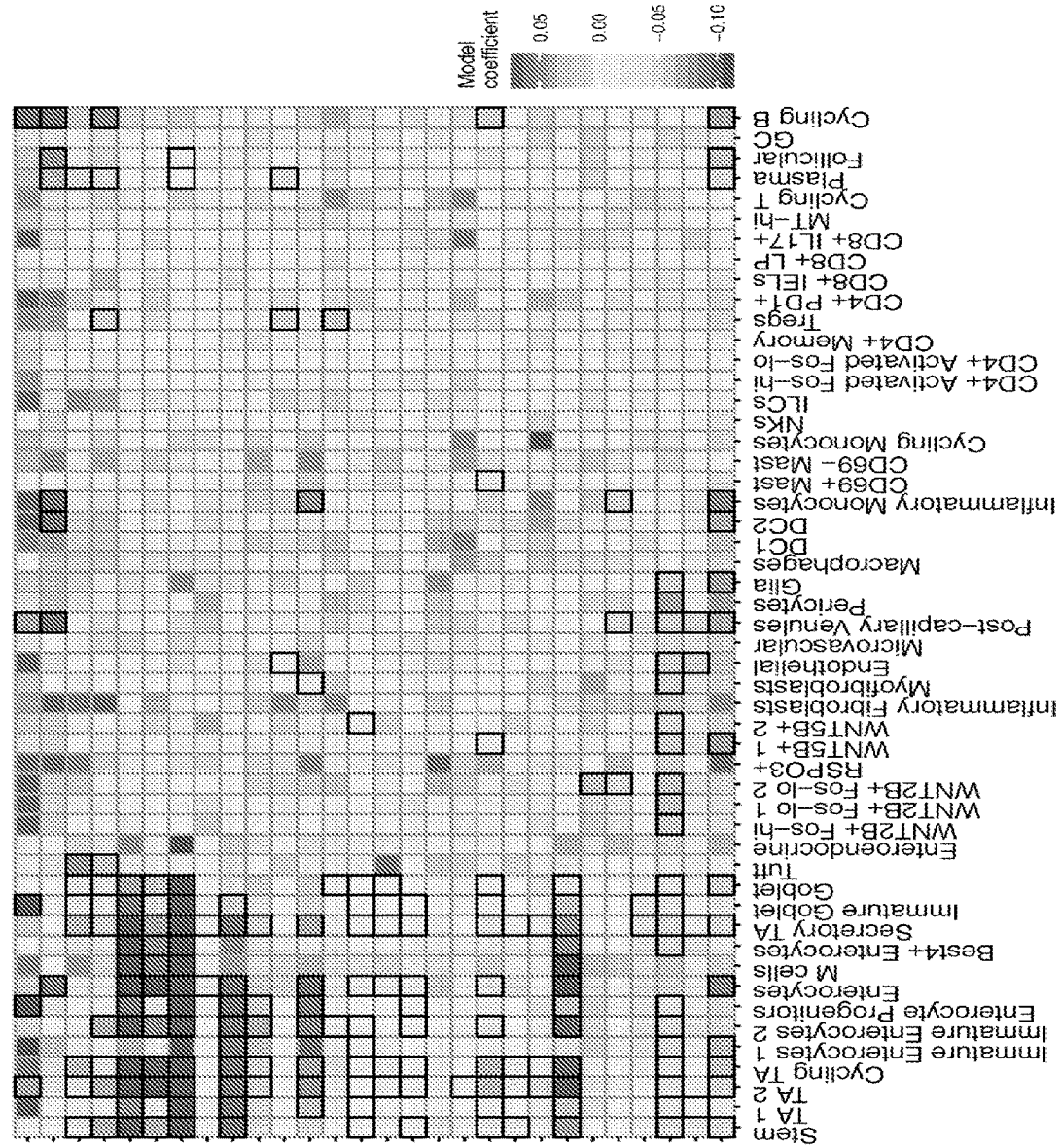

E
Oxidative phosphorylation
Glycolysis / Gluconeogenesis
Citrate cycle (TCA cycle)
Propanoate metabolism
Butanoate metabolism
Fatty acid degradation
Synthesis and degradation of ketone bodies
Primary bile acid biosynthesis
alpha-Linolenic acid metabolism
Alanine, aspartate and glutamate metabolism
Arginine and proline metabolism
Arginine biosynthesis
Cysteine and methionine metabolism
Glycine, serine and threonine metabolism
Histidine metabolism
Lysine degradation
Phenylalanine metabolism
Phenylalanine, tyrosine and tryptophan biosynthesis
Tryptophan metabolism
Tyrosine metabolism
Valine, leucine and isoleucine biosynthesis
Valine, leucine and isoleucine degradation
Apoptosis
Autophagy - animal
AMPK signaling pathway
PI3K-Akt signaling pathway
mTOR signaling pathway
HIF-1 signaling pathway
Stem
TA 1
TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
WNT2B+ Fos-hi
WNT2B+ Fos-lo 1
WNT2B+ Fos-lo 2
RSPO3+
WNT5B+ 1
WNT5B+ 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-capillary Venules
Pericytes
Glia
Macrophages
DC1
DC2
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling Monocytes
NKs
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ PD1+
CD8+ IELs
CD8+ LP
CD8+ IL17+
MT-hi
Cycling T
Plasma
Follicular
GC
Cycling B
Model coefficient
0.05
0.00
-0.05
-0.10

FIG. 28E

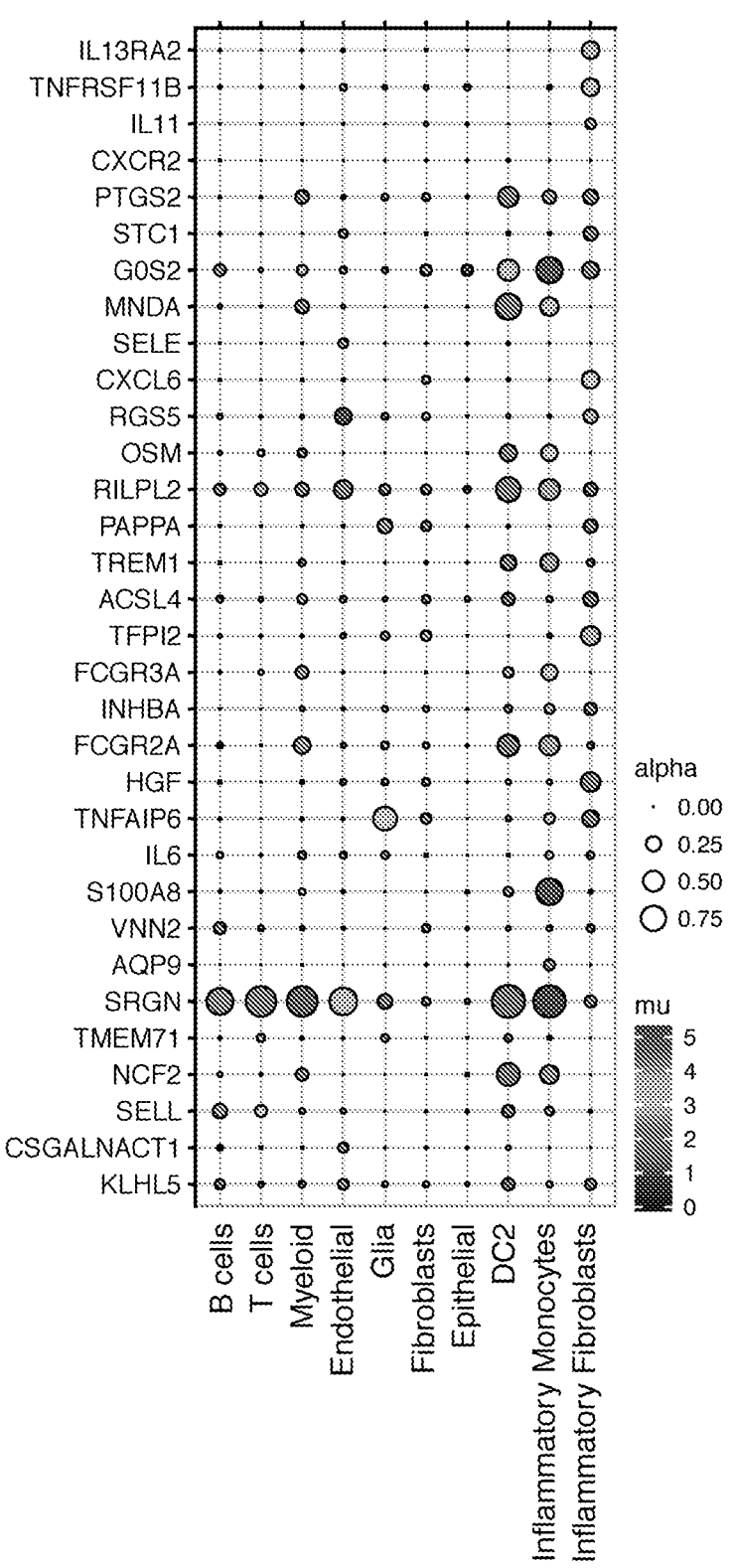

F
IL13RA2
TNFRSF11B
IL11
CXCR2
PTGS2
STC1
G0S2
MNDA
SELE
CXCL6
RGS5
OSM
RILPL2
PAPPA
TREM1
ACSL4
TFPI2
FCGR3A
INHBA
FCGR2A
HGF
TNFAIP6
IL6
S100A8
VNN2
AQP9
SRGN
TMEM71
NCF2
SELL
CSGALNACT1
KLHL5
B cells
T cells
Myeloid
Endothelial
Glia
Fibroblasts
Epithelial
DC2
Inflammatory Monocytes
Inflammatory Fibroblasts
alpha
0.00
0.25
0.50
0.75
mu
5
4
3
2
1
0

FIG. 28F

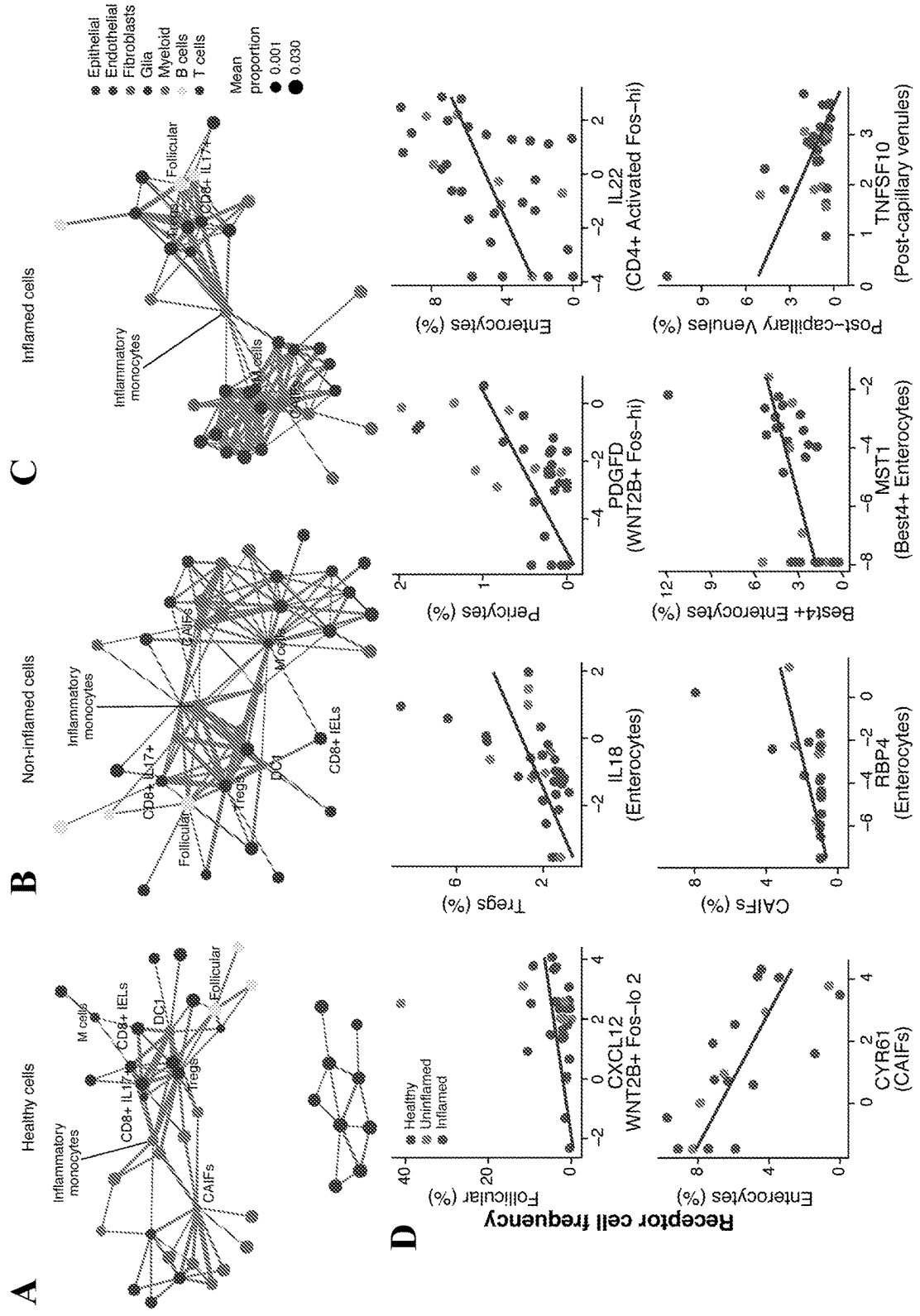

A
Healthy cells
Inflammatory monocytes
M cells
CD8+ IL17+
CD8+ IELs
DC1
Tregs
Follicular
CAIFs
B
Non-inflamed cells
Inflammatory monocytes
CD8+ IL17+
Follicular
CAIFs
Tregs
DC1
M cells
CD8+ IELs
C
Inflamed cells
Inflammatory monocytes
M cells
CAIFs
Follicular
CD8+ IL17+
Epithelial
Endothelial
Fibroblasts
Glia
Myeloid
B cells
T cells
Mean proportion
0.001
0.030
D
Receptor cell frequency
Healthy
Uninflamed
Inflamed
Follicular (%)
CXCL12
WNT2B+ Fos–lo 2
Enterocytes (%)
CYR61
(CAIFs)
Tregs (%)
IL18
(Enterocytes)
CAIFs (%)
RBP4
(Enterocytes)
Pericytes (%)
PDGFD
(WNT2B+ Fos–hi)
Best4+ Enterocytes (%)
MST1
(Best4+ Enterocytes)
Enterocytes (%)
IL22
(CD4+ Activated Fos–hi)
Post–capillary Venules (%)
TNFSF10
(Post-capillary venules)
Ligand <log2(TPM)>

FIG. 29A-D

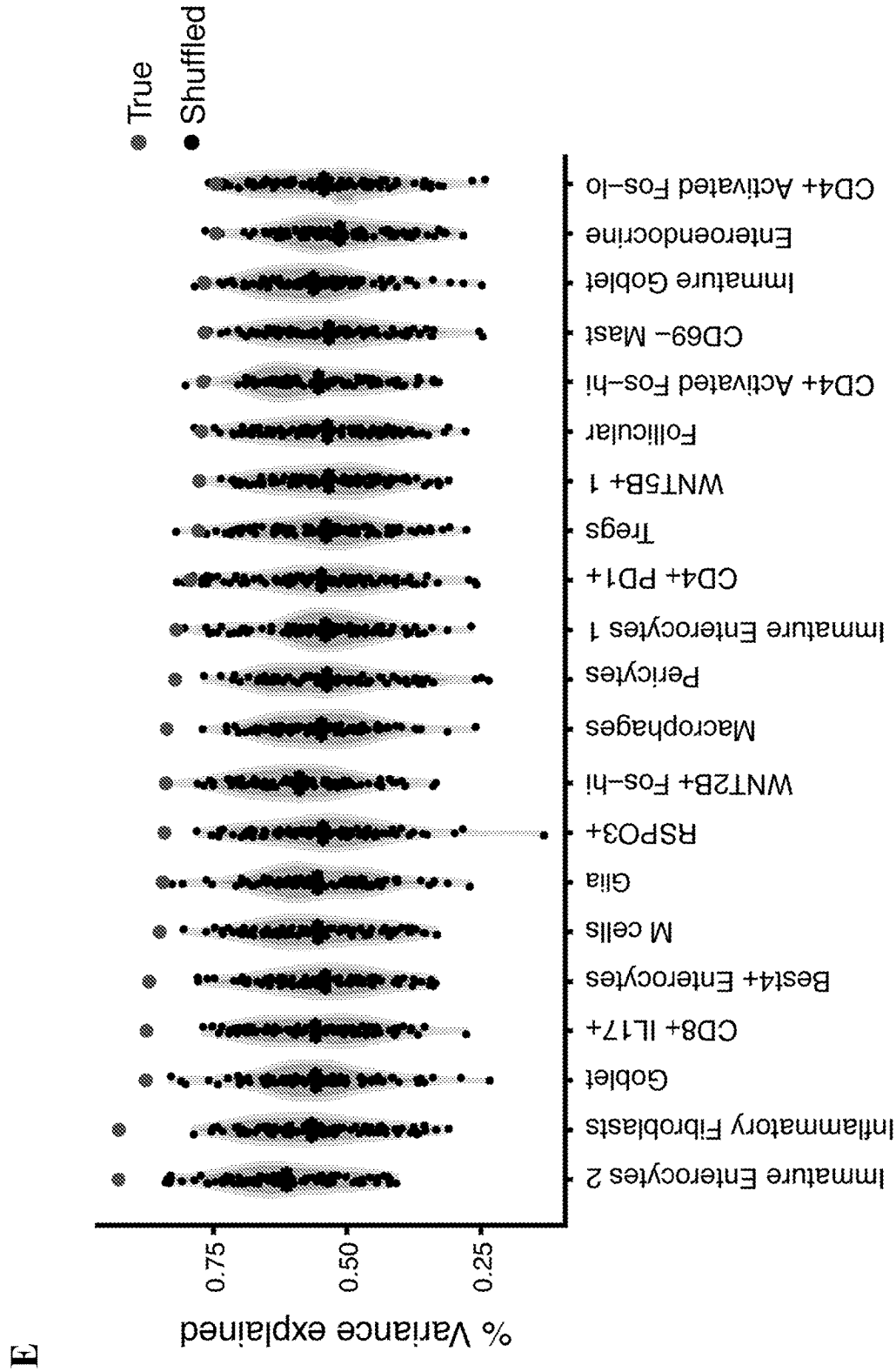

E
% Variance explained
0.75
0.50
0.25
True
Shuffled
Immature Enterocytes 2
Inflammatory Fibroblasts
Goblet
CD8+ IL17+
Best4+ Enterocytes
M cells
Glia
RSPO3+
WNT2B+ Fos-hi
Macrophages
Pericytes
Immature Enterocytes 1
CD4+ PD1+
Tregs
WNT5B+ 1
Follicular
CD4+ Activated Fos-hi
CD69- Mast
Immature Goblet
Enteroendocrine
CD4+ Activated Fos-lo

FIG. 29E

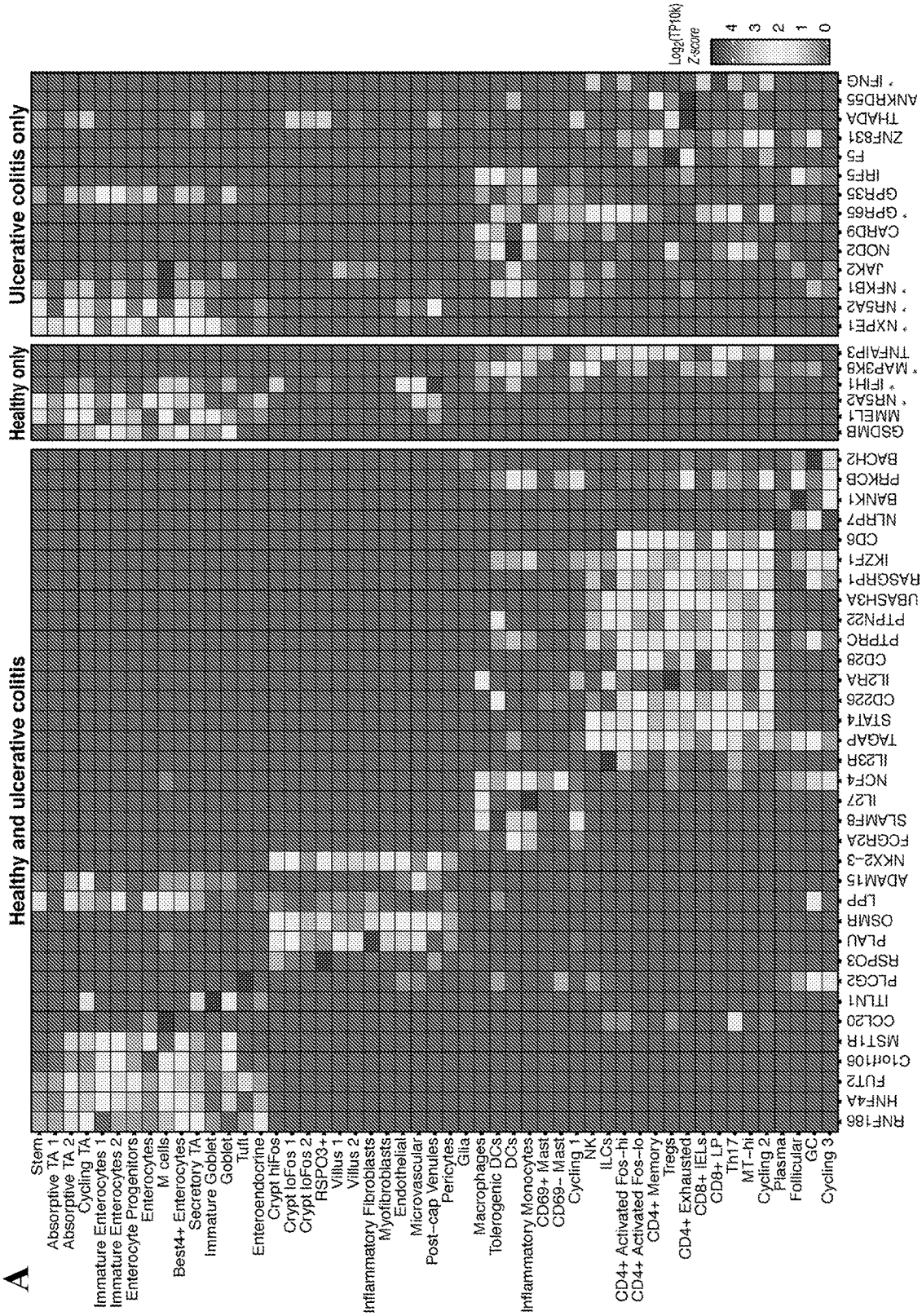

A
Healthy and ulcerative colitis
Healthy only
Ulcerative colitis only
Log2(TP10k)
Z-score
4
3
2
1
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
RNF186
HNF4A
FUT2
C10rf105
MST1R
CCL20
ITLN1
PLCG2
RSPO3
PLAU
OSMR
LPP
ADAM15
NKX2-3
FCGR2A
SLAMF8
IL27
NCF4
IL23R
TAGAP
STAT4
CD226
IL2RA
CD28
PTPRC
PTPN22
UBASH3A
RASGRP1
IKZF1
CD6
NLRP7
BANK1
PRKCB
BACH2
GSDMB
MMEL1
* NR5A2
* IFIH1
* MAP3K8
TNFAIP3
* NXPE1
* NR5A2
* NFKB1
JAK2
NOD2
CARD9
* GPR65
GPR35
IRF5
F5
ZNF831
THADA
ANKRD55
* IFNG

FIG. 30A

B

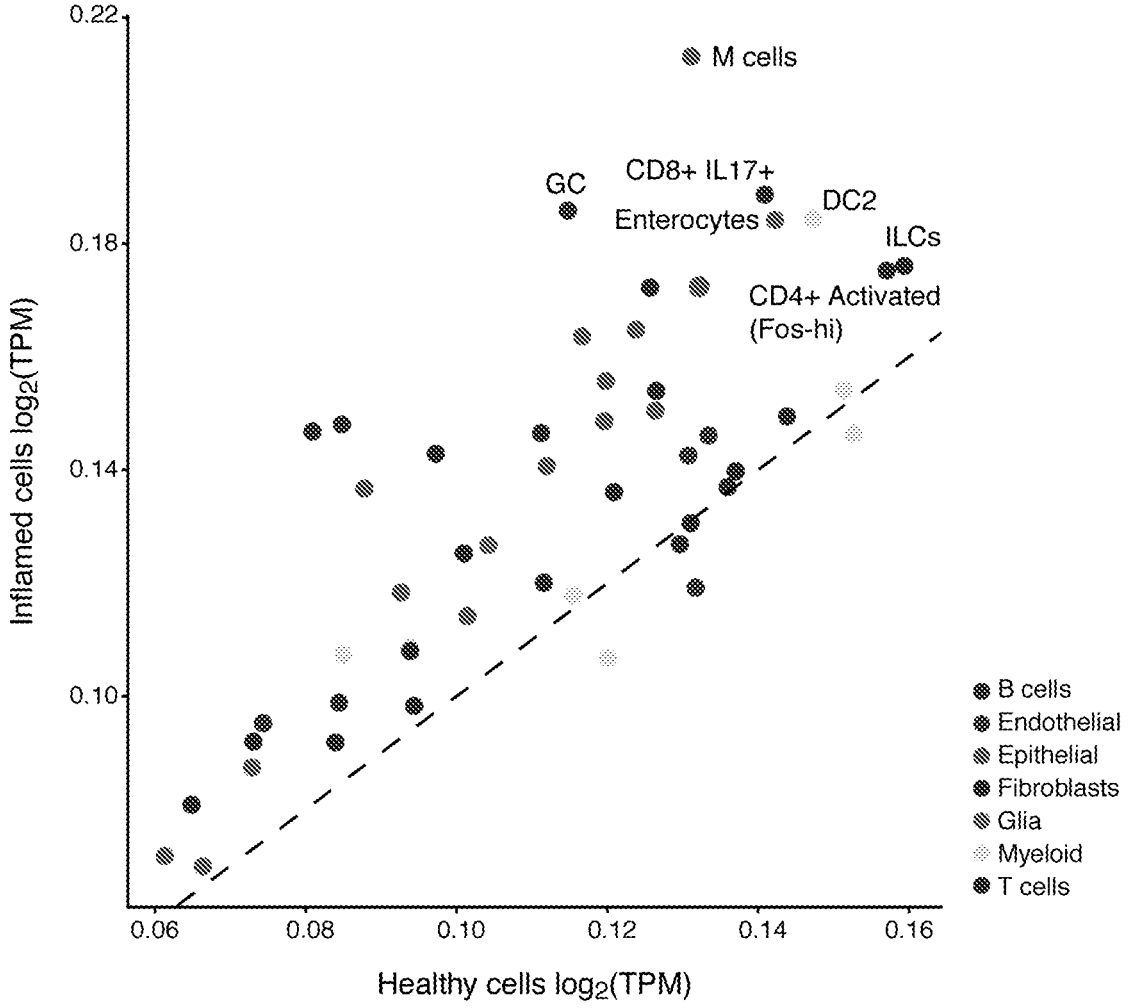

0.22
0.18
0.14
0.10
Inflamed cells log2(TPM)
0.06
0.08
0.10
0.12
0.14
0.16
Healthy cells log2(TPM)
M cells
GC
CD8+ IL17+
Enterocytes
DC2
ILCs
CD4+ Activated
(Fos-hi)
B cells
Endothelial
Epithelial
Fibroblasts
Glia
Myeloid
T cells

FIG. 30B

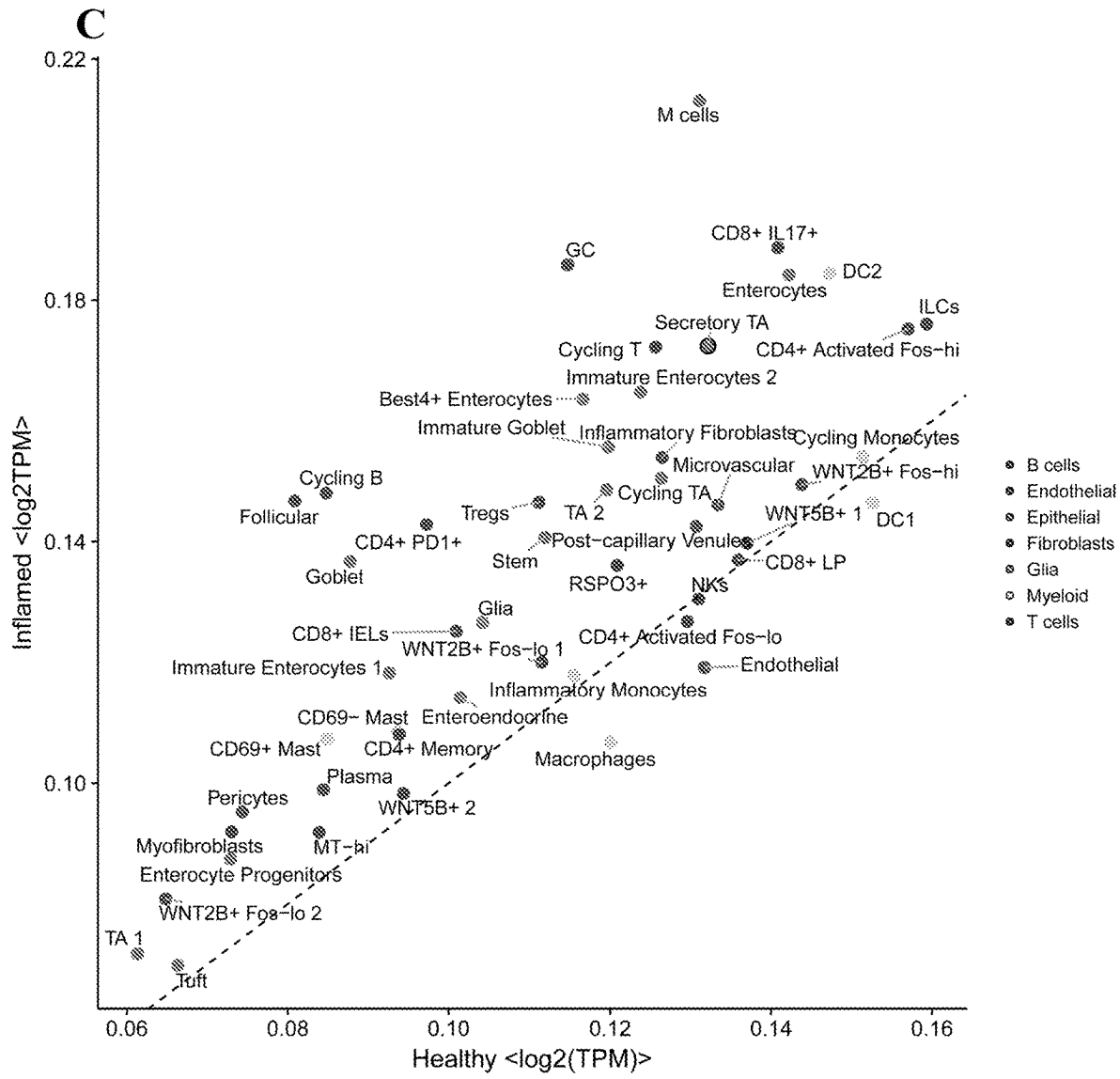

C
Inflamed <log2TPM>
Healthy <log2(TPM)>
0.22
0.18
0.14
0.10
0.06
0.08
0.10
0.12
0.14
0.16
M cells
CD8+ IL17+
GC
DC2
Enterocytes
ILCs
Secretory TA
Cycling T
CD4+ Activated Fos−hi
Immature Enterocytes 2
Best4+ Enterocytes
Immature Goblet
Inflammatory Fibroblasts
Cycling Monocytes
Microvascular
WNT2B+ Fos−hi
Cycling B
Cycling TA
Follicular
Tregs
TA 2
WNT5B+ 1
DC1
CD4+ PD1+
Post−capillary Venules
Stem
CD8+ LP
Goblet
RSPO3+
NKs
Glia
CD8+ IELs
WNT2B+ Fos−lo 1
CD4+ Activated Fos−lo
Immature Enterocytes 1
Endothelial
Inflammatory Monocytes
CD69− Mast
Enteroendocrine
CD69+ Mast
CD4+ Memory
Macrophages
Plasma
Pericytes
WNT5B+ 2
Myofibroblasts
MT−hi
Enterocyte Progenitors
WNT2B+ Fos−lo 2
TA 1
Tuft
B cells
Endothelial
Epithelial
Fibroblasts
Glia
Myeloid
T cells

FIG. 30C

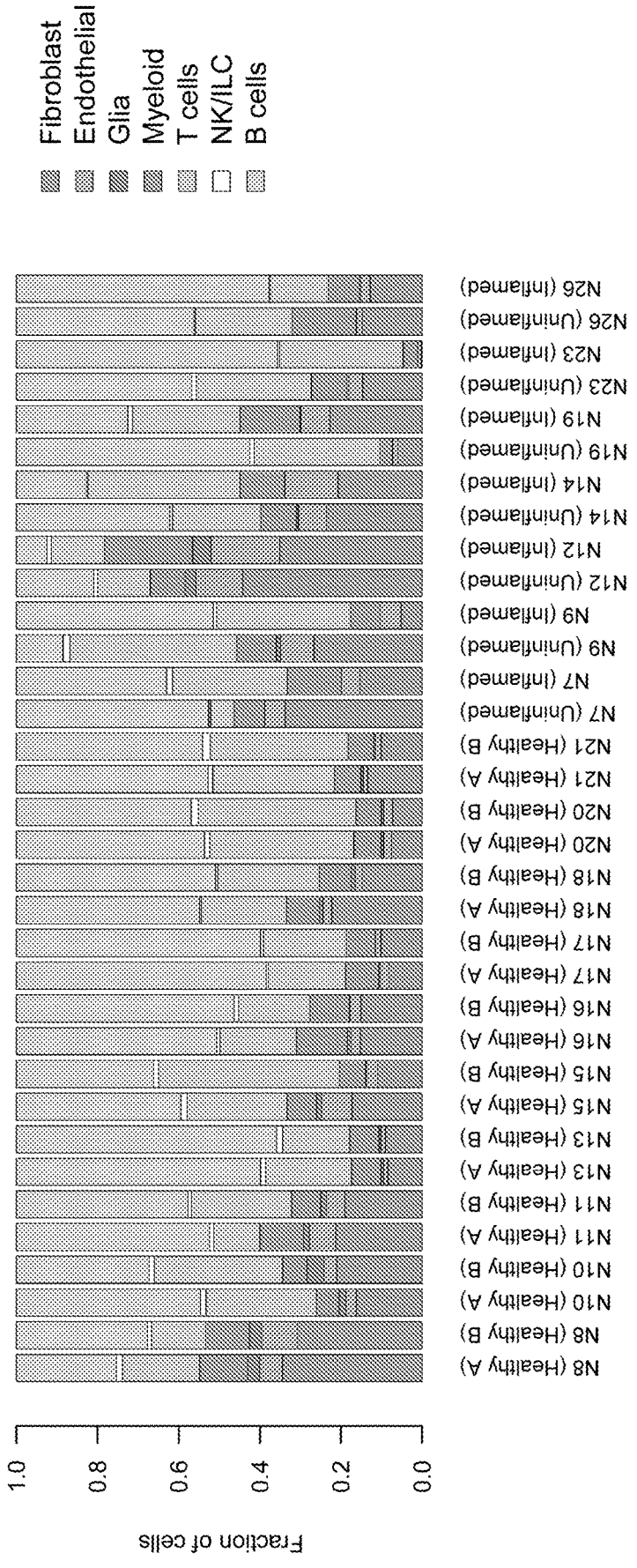

Fibroblast
Endothelial
Glia
Myeloid
T cells
NK/ILC
B cells
N8 (Healthy A)
N8 (Healthy B)
N10 (Healthy A)
N10 (Healthy B)
N11 (Healthy A)
N11 (Healthy B)
N13 (Healthy A)
N13 (Healthy B)
N15 (Healthy A)
N15 (Healthy B)
N16 (Healthy A)
N16 (Healthy B)
N17 (Healthy A)
N17 (Healthy B)
N18 (Healthy A)
N18 (Healthy B)
N20 (Healthy A)
N20 (Healthy B)
N21 (Healthy A)
N21 (Healthy B)
N7 (Uninflamed)
N7 (Inflamed)
N9 (Uninflamed)
N9 (Inflamed)
N12 (Uninflamed)
N12 (Inflamed)
N14 (Uninflamed)
N14 (Inflamed)
N19 (Uninflamed)
N19 (Inflamed)
N23 (Uninflamed)
N23 (Inflamed)
N26 (Uninflamed)
N26 (Inflamed)
1.0
0.8
0.6
0.4
0.2
0.0
Fraction of cells

FIG. 31

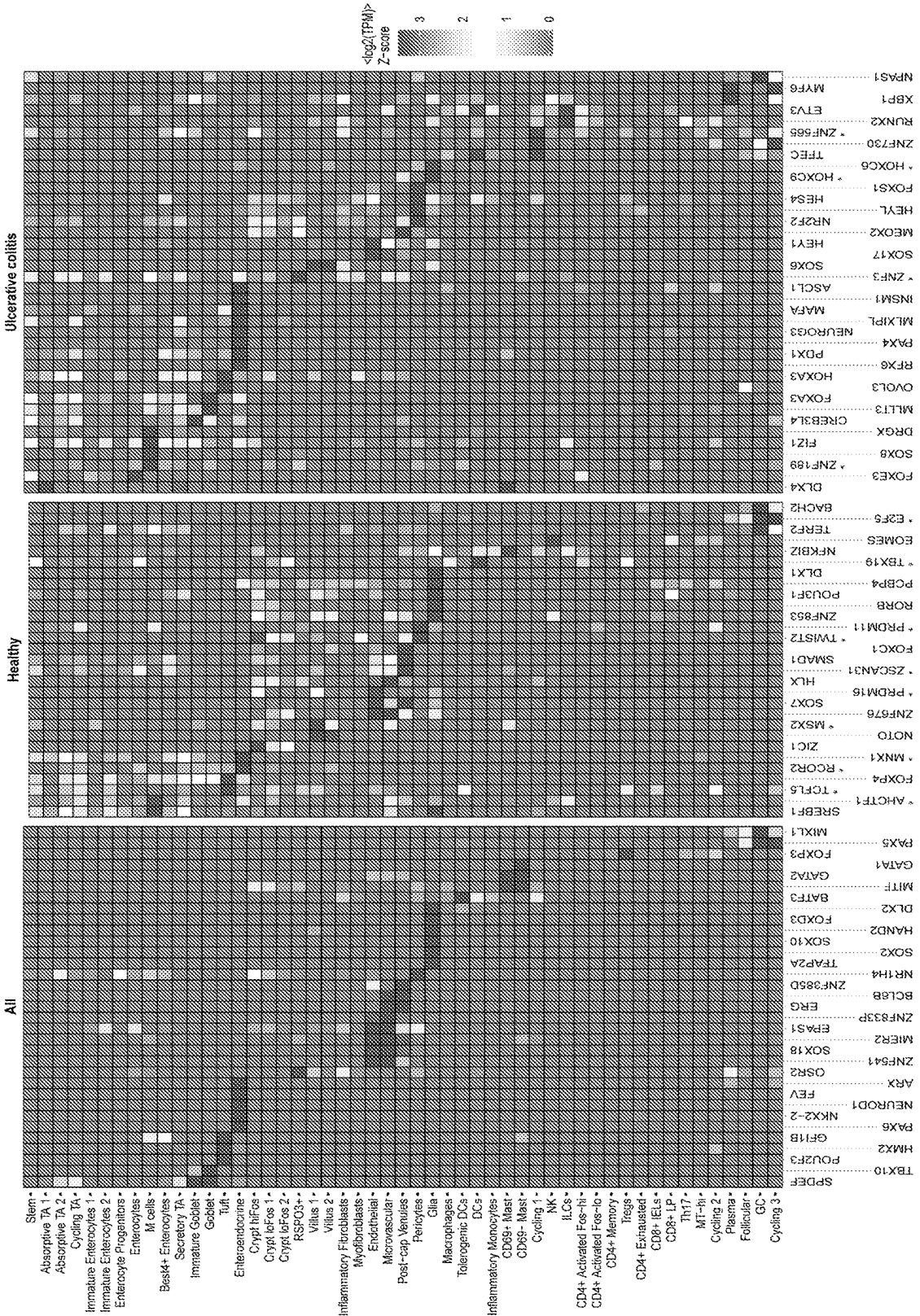

All
Healthy
Ulcerative colitis
<log2(TPM)>
Z-score
3
2
1
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
SPDEF
TBX10
HMX2
POU2F3
GFI1B
PAX6
NKX2-2
NEUROD1
FEV
ARX
OSR2
ZNF541
SOX18
MIER2
EPAS1
ZNF833P
ERG
BCL6B
ZNF385D
NR1H4
TFAP2A
SOX2
SOX10
HAND2
FOXD3
DLX2
BATF3
MITF
GATA2
GATA1
FOXP3
PAX5
MIXL1
SREBF1
TCF4
AHCTF1
RCOR2
FOXP4
MNX1
ZIC1
MSX2
NOTO
ZNF676
SOX7
PRDM16
HLX
ZSCAN31
SMAD1
FOXC1
TWIST2
PRDM11
ZNF853
RORB
POU3F1
PCBP4
DLX1
TBX19
NFKBIZ
EOMES
TERF2
E2F5
BACH2
DLX4
FOXE3
ZNF189
SOX9
FIZ1
DRGX
CREB3L4
MLLT3
FOXA3
OVOL3
HOXA3
RFX6
PDX1
PAX4
NEUROG3
MLXIPL
MAFA
INSM1
ASCL1
ZNF3
SOX6
SOX17
HEY1
MEOX2
NR2F2
HEYL
HES4
FOXS1
HOXC9
HOXC6
TFEC
ZNF730
ZNF565
RUNX2
ETV3
XBP1
MYF6
NPAS1

FIG. 32

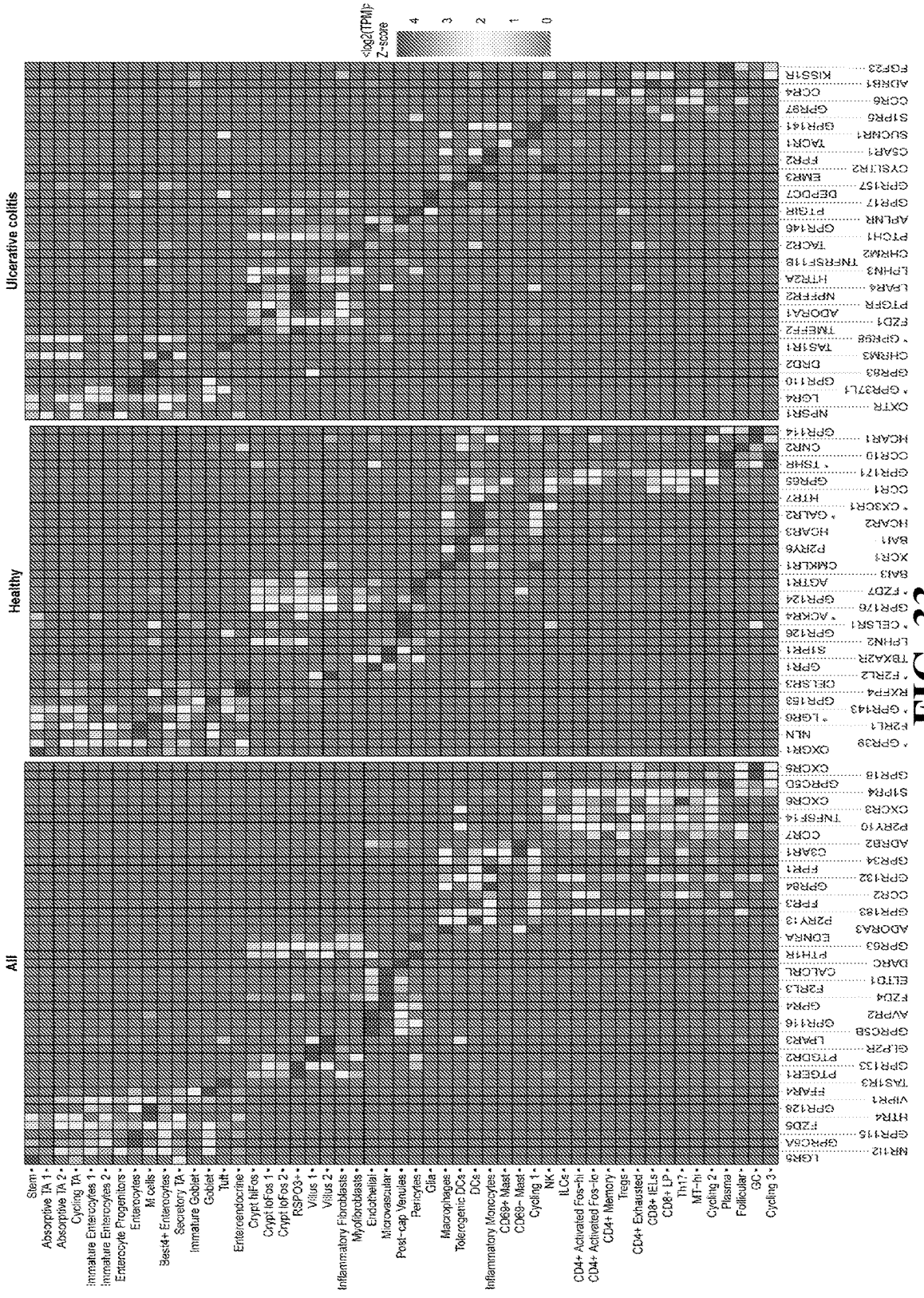

All
Healthy
Ulcerative colitis
log2(TPM)+
Z-score
4
3
2
1
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
NR1I2
GPR115
HTR4
VIPR1
TAS1R3
GPR133
GLP2R
GPRC5B
AVPR2
FZD4
ELTD1
DARC
GPR63
EDNRA
ADORA3
GPR183
CCR2
GPR132
GPR84
GPR34
ADRB2
P2RY10
CXCR3
S1PR4
GPR18
GPR39
F2RL1
GPR143
RXFP4
FZRL2
TBXA2R
S1PR1
LPHN2
CELSR1
GPR176
FZD7
BAI3
XCR1
HCAR2
CX3CR1
CCR1
GPR171
CCR10
HCAR1
GPR114
NPSR1
CXTR
GPR37L1
GPR83
CHRM3
GPR98
FZD1
PTGFR
LPAR4
LPHN3
CHRM2
PTCH1
APLNR
GPR17
GPR157
CYSLTR2
C5AR1
SUCNR1
S1PR5
CCR6
ADRB1
FGF23
FZD5
GPR128
FFAR4
PTGER1
PTGDR2
LPAR3
GPR116
GPR4
F2RL3
CALCRL
PTH1R
GPR63
EDNRA
P2RY13
FPR3
GPR84
FPR1
C3AR1
CCR7
TNFSF14
CXCR6
GPRC5D
CXCR6
CXCL8
NLN
LGR6
GPR183
CXCL8
GPR1
S1PR1
GPR126
ACKR4
GPR176
GPR124
AGTR1
CMKLR1
P2RY6
HCAR3
GALR2
HTR7
GPR65
TSHR
CNR2
GPR114
LGR6
GPR115
FZD5
GPR128
FFAR4
PTGER1
PTGDR2
LPAR3
GPR116
GPR4
F2RL3
CALCRL
PTH1R
EDNRA
P2RY13
FPR3
GPR84
FPR1
C3AR1
CCR7
TNFSF14
CXCR6
GPRC5D
CXCR6
NPSR1
LGR4
GPR110
DRD2
TAS1R1
TMEFF2
ADORA1
NPFFR2
HTR2A
TNFRSF11B
TACR2
GPR146
P1G1R
DEPDC7
EMR3
FPR2
TACR1
GPR141
GPR97
CCR4
KISS1R

FIG. 33

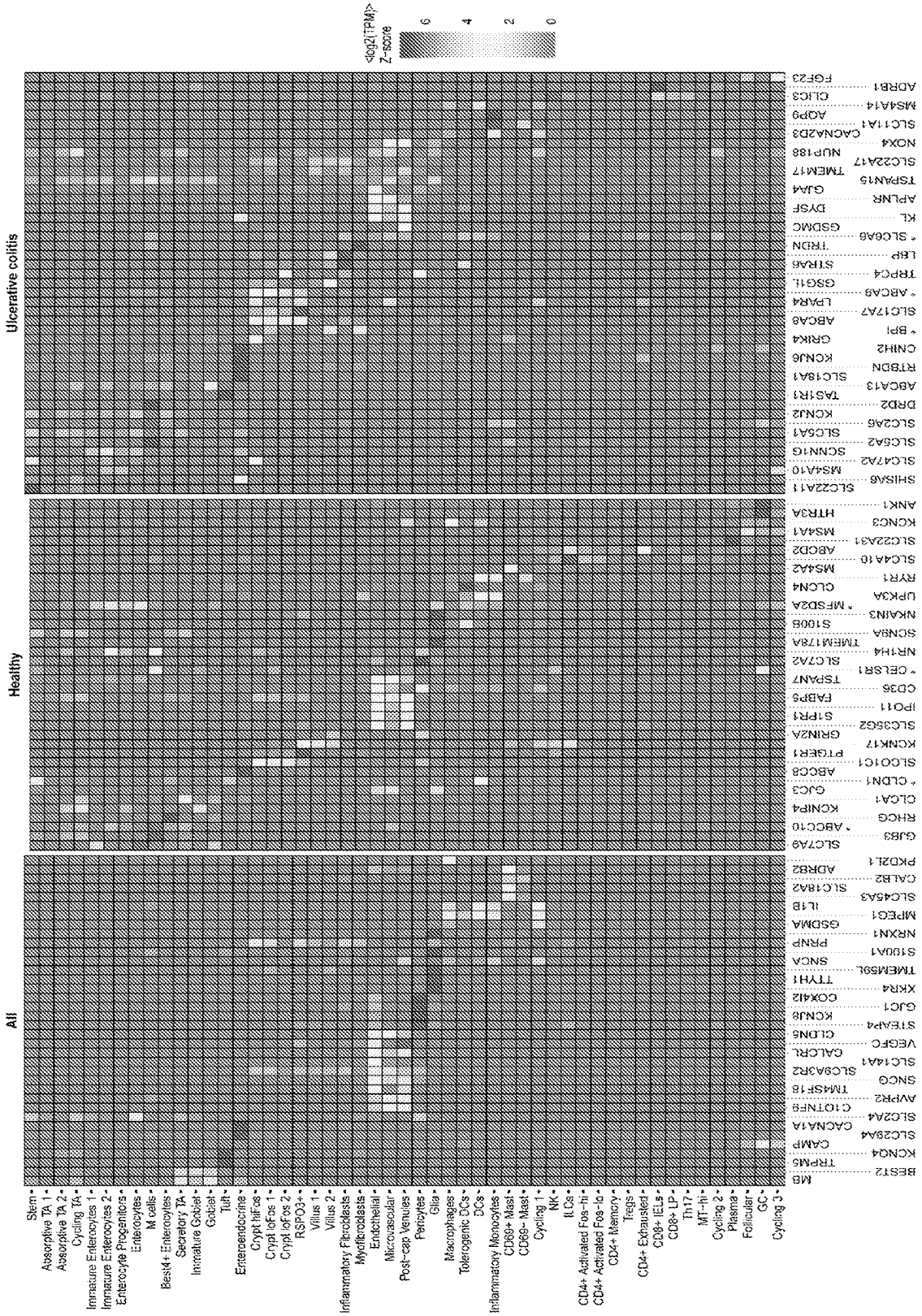

All
Healthy
Ulcerative colitis
<log2(TPM)>
Z-score
6
4
2
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
MB
BEST2
KCNQ4
SLC28A4
CACNA1A
SLC2A4
C10TNF8
AVPR2
TM4SF18
SLC9A3R2
SLC14A1
CALCRL
VEGFC
CLDN5
ST6AP4
KCNJ8
GJC1
COX4I2
KRT4
TTYH1
TMEM59L
SNCA
S100A1
PRNP
NRXN1
GSDMA
MPEG1
IL1B
SLC45A3
SLC18A2
CALB2
PKD2L1
ADRB2
GJB3
SLC7A9
RHCG
ABCC10
CLCA1
KCNIP4
CLDN1
GJC3
SLCO1C1
ABCC8
KCNK17
PTGER1
SLC35G2
GRIN2A
SPR1
IPO11
FABP6
CD36
TSPAN7
NR1H4
SLC7A2
CELSR1
SCN9A
TMEM178A
NKAIN3
S100B
UPK3A
MFSD2A
RYR1
CLCN4
SLC4A10
MS4A2
SLC22A31
ABCD2
KCNC3
MS4A1
ANK1
HTR3A
SHISA6
SLC22A11
SLC7A2
MS4A10
SLC5A2
SCNN1G
SLC2A6
SLC5A1
DRD2
KCNJ2
ABCA13
TAS1R1
RTBDN
SLC18A1
CNIH2
KCNJ6
BPI
GRIK4
SLC17A7
ABCA8
ABCA9
LPAR4
TRPC4
GSG1L
LBP
STRA6
SLC6A6
TRDN
KL
GSDMC
APLNR
DYSF
TSPAN15
GJA4
SLC22A17
TMEM17
NOX4
NUP188
SLC11A1
CACNA2D3
MS4A14
AQP9
ADRB1
CLIC3
FGF23

FIG. 34

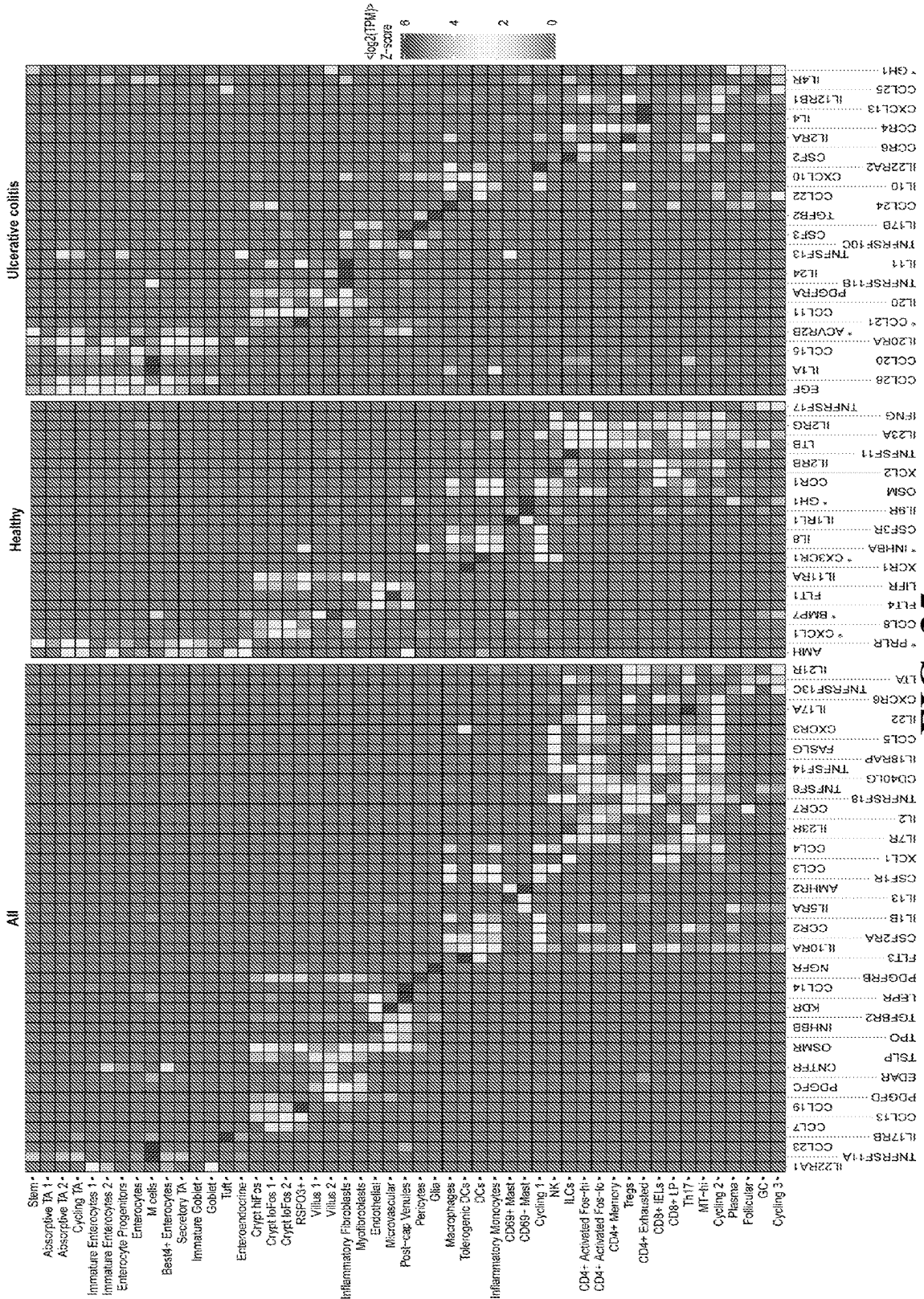

All
Healthy
Ulcerative colitis
<log2(TPM)>
Z-score
6
4
2
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
IL22RA1
TNFRSF11A
IL17RB
CCL23
CCL19
CCL7
PDGFC
CNTFR
EDAR
TSLP
OSMR
TPO
INHBB
TGFBR2
KDR
LEPR
PDGFRB
CCL14
NGFR
FLT3
IL10RA
CSF2RA
CCR2
IL1B
IL5RA
IL13
AMHR2
CSF1R
CCL3
XCL1
CCL4
IL7R
IL23R
IL2
CCR7
TNFRSF18
TNFSF8
CD40LG
TNFSF14
IL18RAP
FASLG
CCL5
CXCR3
IL22
IL17A
CXCR6
TNFRSF13C
LTA
IL2R
AMH
PRLR
CXCL1
CCL8
BMP7
FLT4
FLT1
LIFR
IL11RA
XCR1
CX3CR1
INHBA
IL6
CSF3R
IL1RL1
IL9R
GH1
OSM
CCR1
XCL2
IL2RB
TNFSF11
LTB
IL2RG
IL23A
IFNG
TNFRSF17
EGF
CCL28
IL1A
CCL20
CCL15
IL20RA
ACVR2B
CCL21
CCL11
IL20
PDGFRA
TNFRSF11B
IL24
IL11
TNFSF13
TNFRSF10C
CSF3
IL17B
TGFB2
CCL24
CCL22
IL10
CXCL10
IL22RA2
CSF2
CCR6
IL2RA
IL4
CCR4
CXCL13
IL12RB1
CCL25
IL4R
GH1

FIG. 35

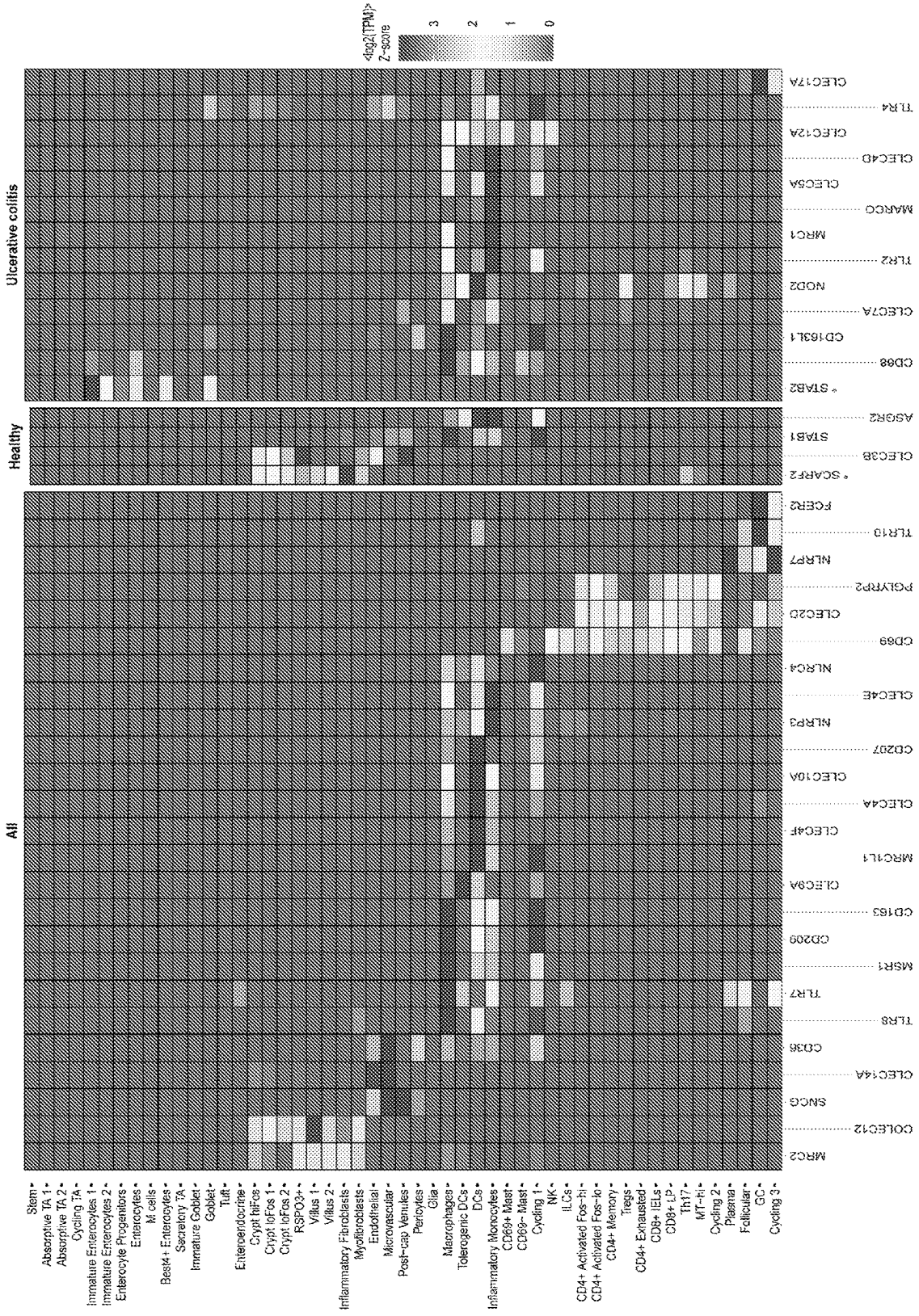

All
Healthy
Ulcerative colitis
<log2(TPM)>
Z-score
3
2
1
0
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
Cycling 1
NK
ILCs
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-Hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
MRC2
COLEC12
SNCG
CLEC14A
CD36
TLR8
TLR7
MSR1
CD209
CD163
CLEC9A
MRC1L1
CLEC4F
CLEC4A
CLEC10A
CD207
NLRP3
CLEC4E
NLRC4
CD89
CLEC2D
PGLYRP2
NLRP7
TLR10
FCER2
SCARF2
CLEC3B
STAB1
ASGR2
STAB2
CD68
CD163L1
CLEC7A
NOD2
TLR2
MRC1
MARCO
CLEC5A
CLEC4D
CLEC12A
TLR4
CLEC17A

FIG. 36

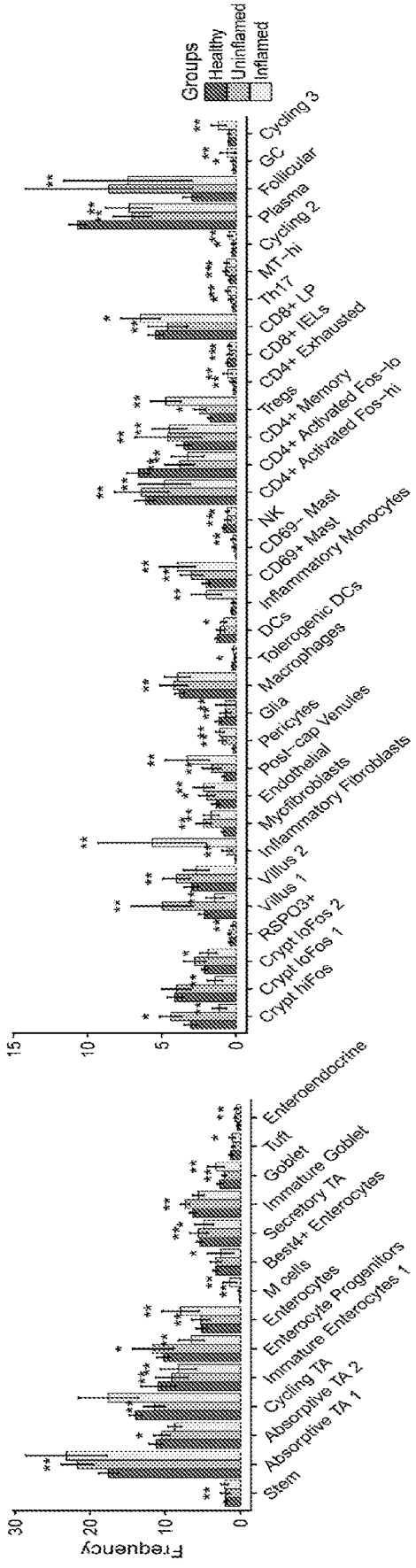

Groups
Healthy
Uninflamed
Inflamed
Frequency
0
5
10
15
20
30
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Post-cap Venules
Pericytes
Glia
Macrophages
Tolerogenic DCs
DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
NK
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
CD4+ Memory
Tregs
CD4+ Exhausted
CD8+ IELs
CD8+ LP
Th17
MT-hi
Cycling 2
Plasma
Follicular
GC
Cycling 3
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Enterocyte Progenitors
Enterocytes
M cells
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine

FIG. 37

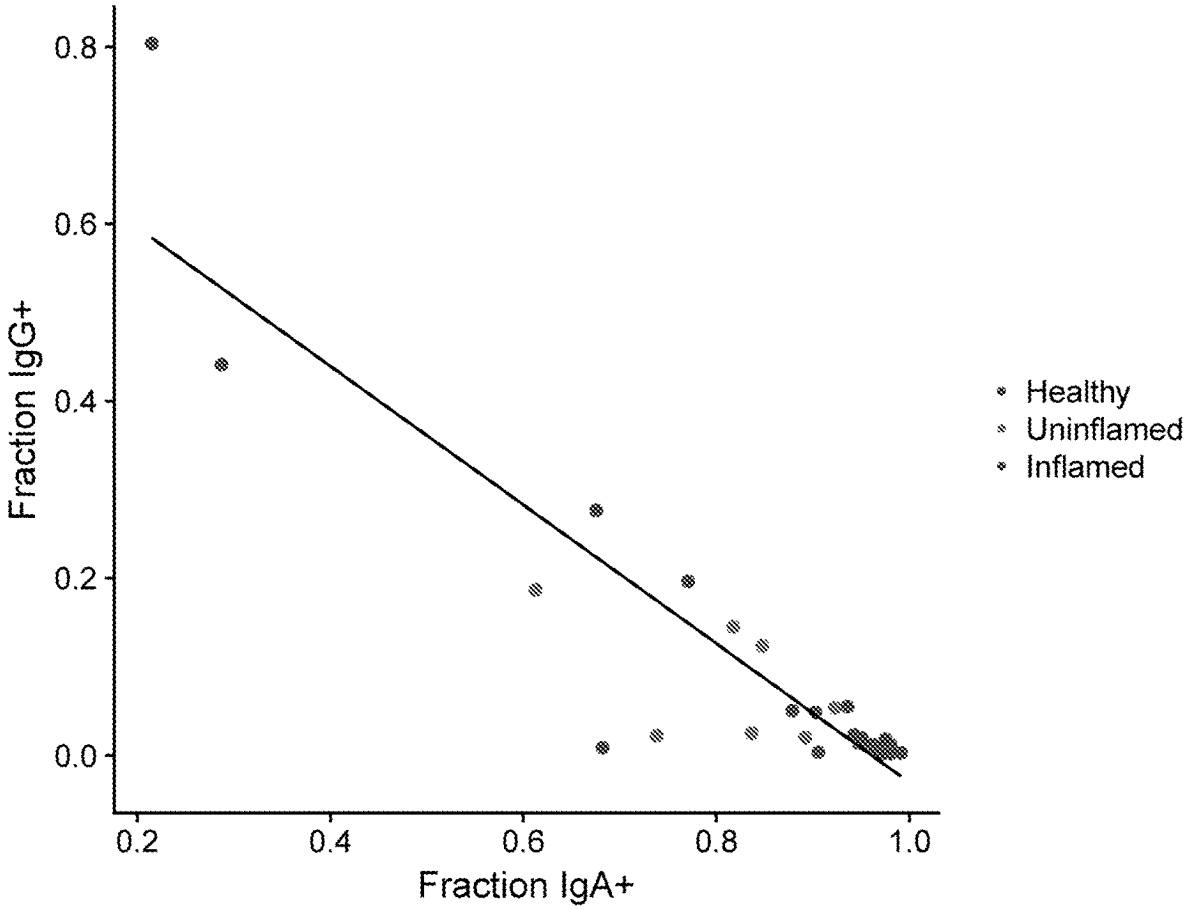

0.8
0.6
0.4
0.2
0.0
Fraction IgG+
0.2
0.4
0.6
0.8
1.0
Fraction IgA+
Healthy
Uninflamed
Inflamed

FIG. 38

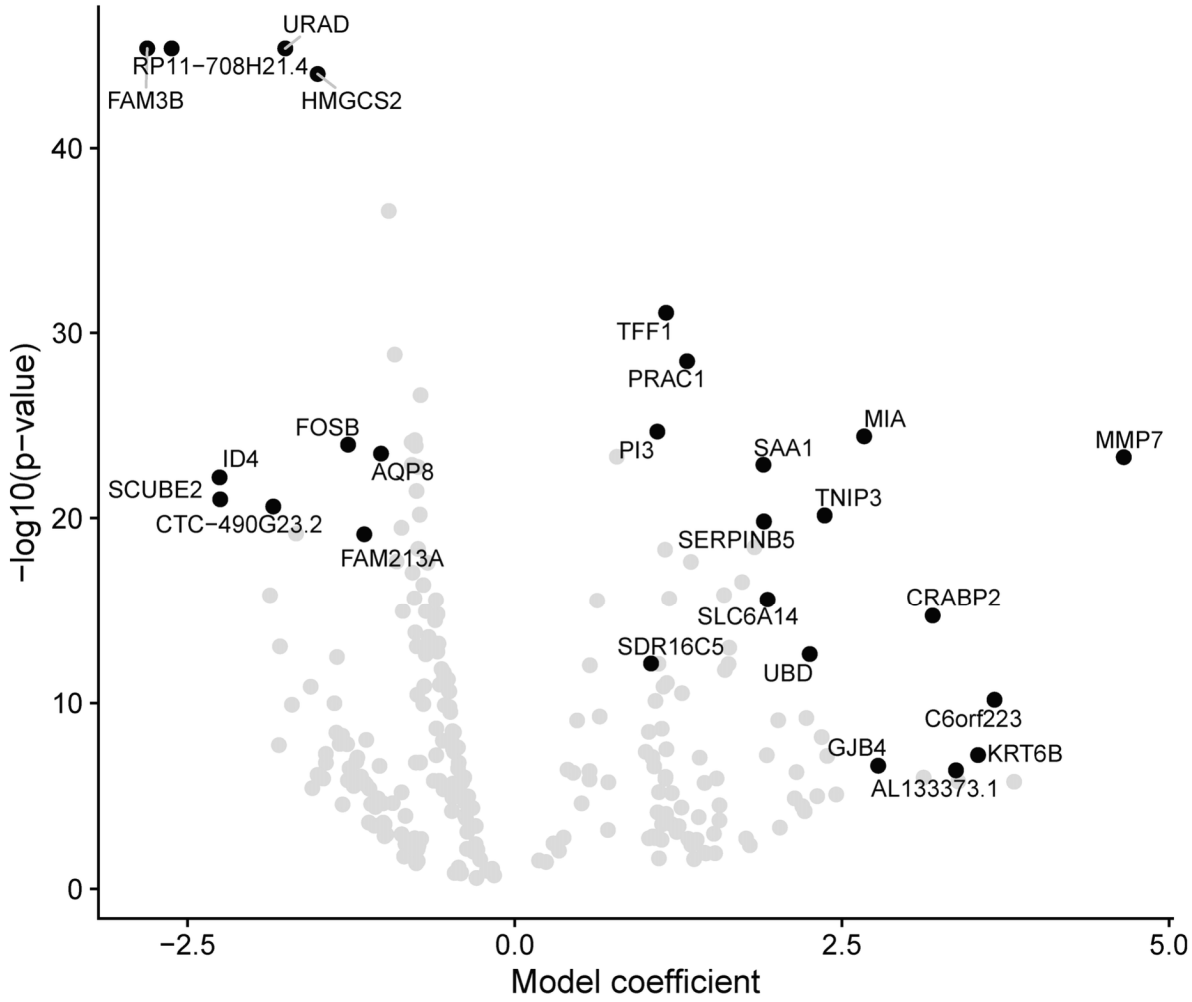

URAD
RP11−708H21.4
FAM3B
HMGCS2
TFF1
PRAC1
FOSB
PI3
SAA1
MIA
MMP7
ID4
AQP8
SCUBE2
TNIP3
CTC−490G23.2
SERPINB5
FAM213A
CRABP2
SLC6A14
SDR16C5
UBD
C6orf223
GJB4
KRT6B
AL133373.1
−log10(p−value)
40
30
20
10
0
−2.5
0.0
2.5
5.0
Model coefficient

FIG. 39A

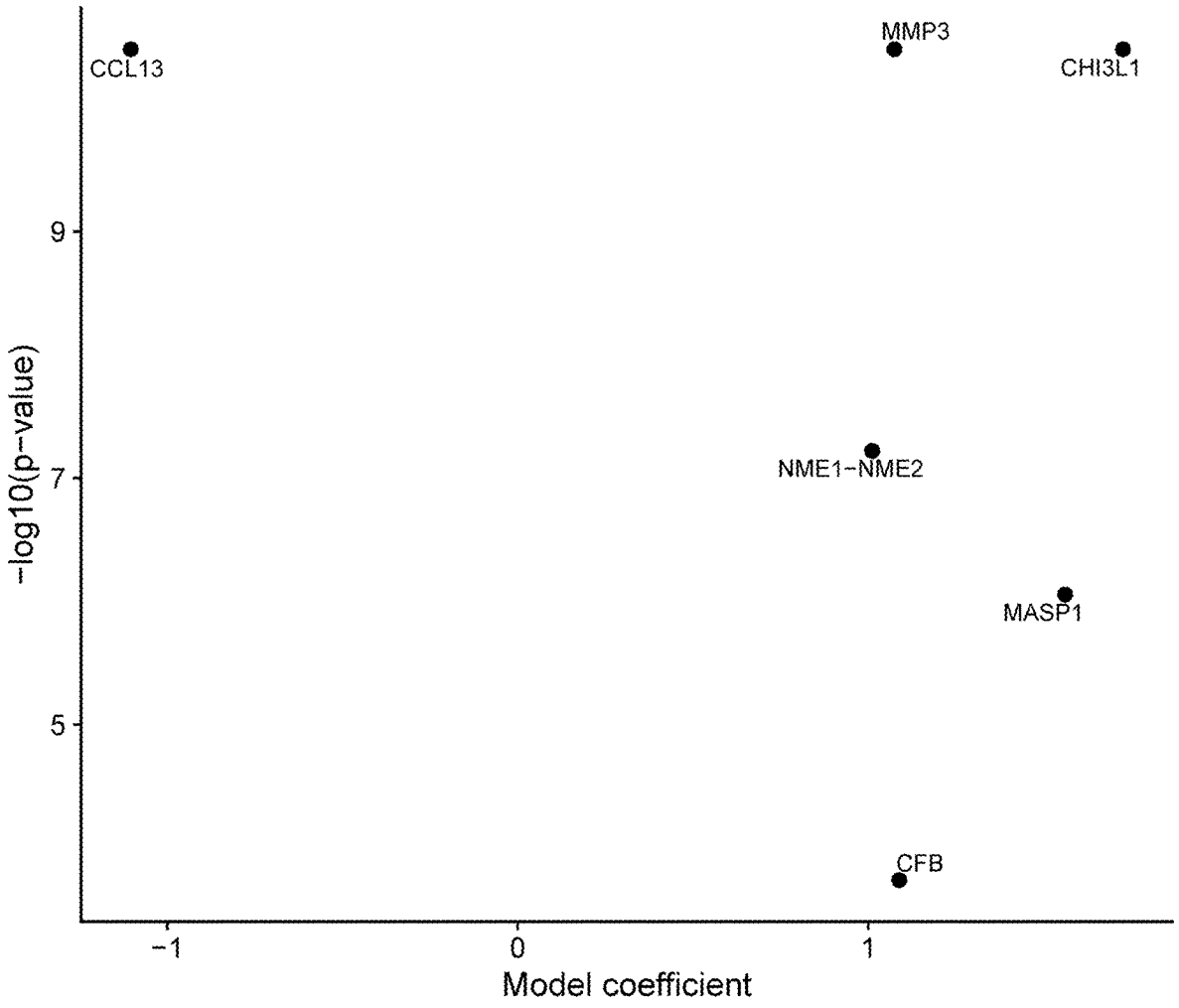

MMP3
CCL13
CHI3L1
9
−log10(p−value)
7
NME1−NME2
MASP1
5
CFB
−1
0
1
Model coefficient

FIG. 39B

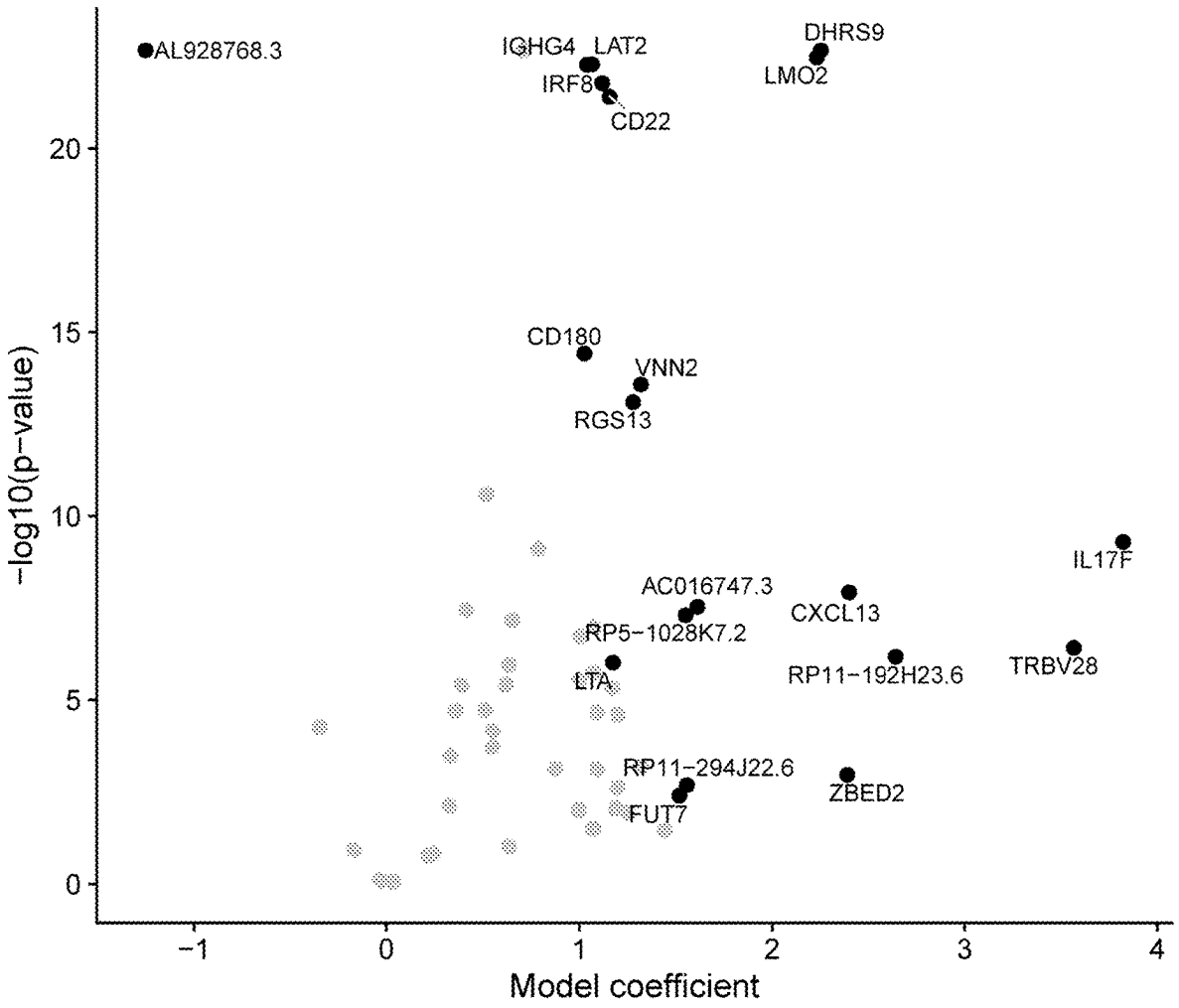

AL928768.3
IGHG4
LAT2
IRF8
CD22
DHRS9
LMO2
CD180
VNN2
RGS13
IL17F
AC016747.3
CXCL13
RP5−1028K7.2
LTA
RP11−192H23.6
TRBV28
RP11−294J22.6
ZBED2
FUT7
−log10(p−value)
Model coefficient
0
5
10
15
20
−1
0
1
2
3
4

FIG. 39C

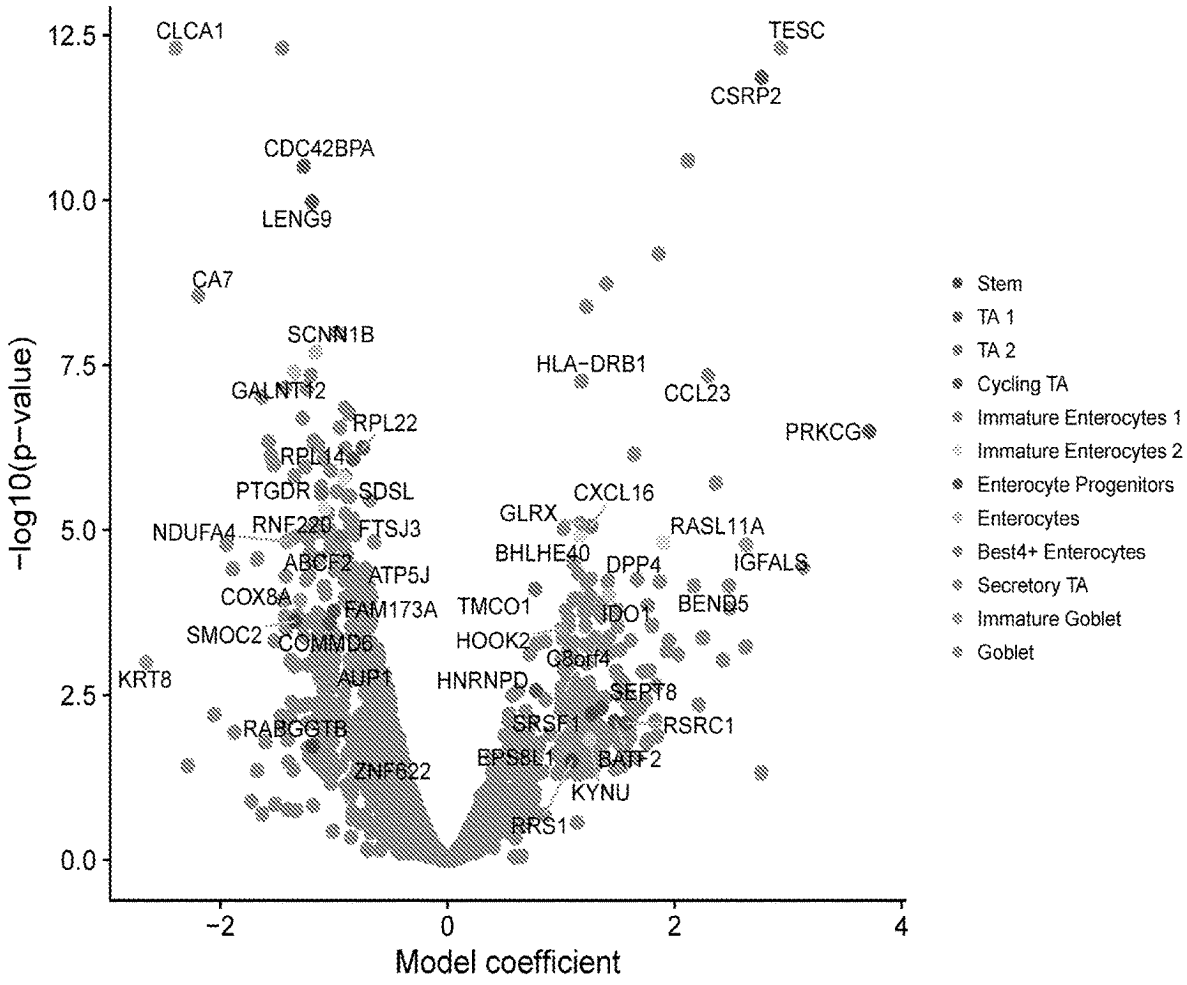

12.5
10.0
7.5
5.0
2.5
0.0
−log10(p−value)
−2
0
2
4
Model coefficient
CLCA1
TESC
CSRP2
CDC42BPA
LENG9
CA7
SCNN1B
HLA−DRB1
CCL23
GALNT12
PRKCG
RPL22
RPL14
PTGDR
SDSL
CXCL16
GLRX
RASL11A
NDUFA4
RNF220
FTSJ3
BHLHE40
DPP4
IGFALS
ABCF2
ATP5J
COX8A
FAM173A
TMCO1
IDO1
BEND5
SMOC2
COMMD6
HOOK2
C9orf4
KRT8
AUP1
HNRNPD
SEPT8
SRSF1
RSRC1
RABGGTB
BPSL1
BATF2
ZNF622
KYNU
RRS1
Stem
TA 1
TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet

FIG. 39D

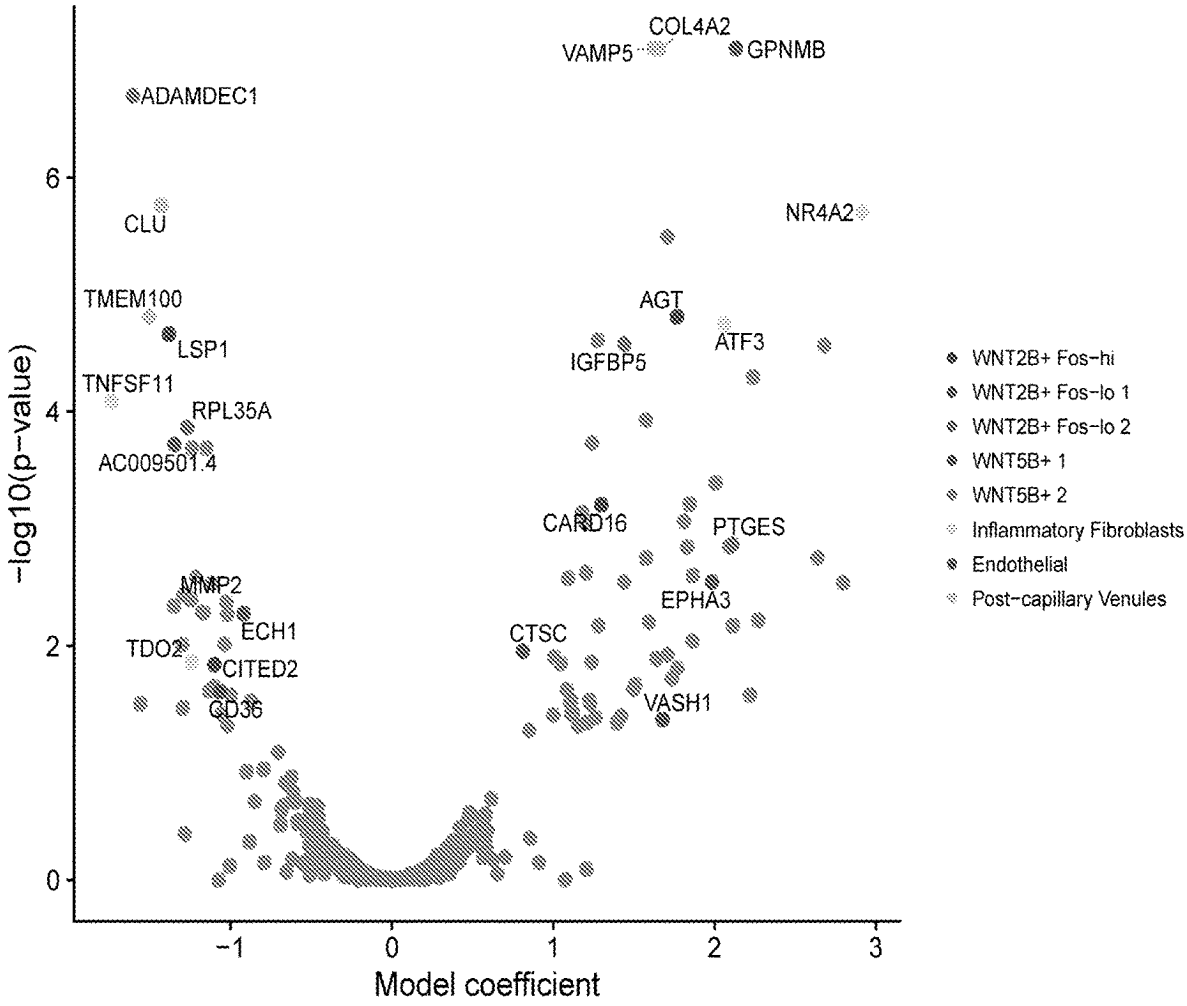

COL4A2
VAMP5
GPNMB
ADAMDEC1
CLU
NR4A2
TMEM100
AGT
LSP1
ATF3
IGFBP5
TNFSF11
RPL35A
AC009501.4
CARD16
PTGES
MMP2
EPHA3
ECH1
CTSC
TDO2
CITED2
CD36
VASH1
−log10(p−value)
Model coefficient
WNT2B+ Fos−hi
WNT2B+ Fos−lo 1
WNT2B+ Fos−lo 2
WNT5B+ 1
WNT5B+ 2
Inflammatory Fibroblasts
Endothelial
Post−capillary Venules

FIG. 39E

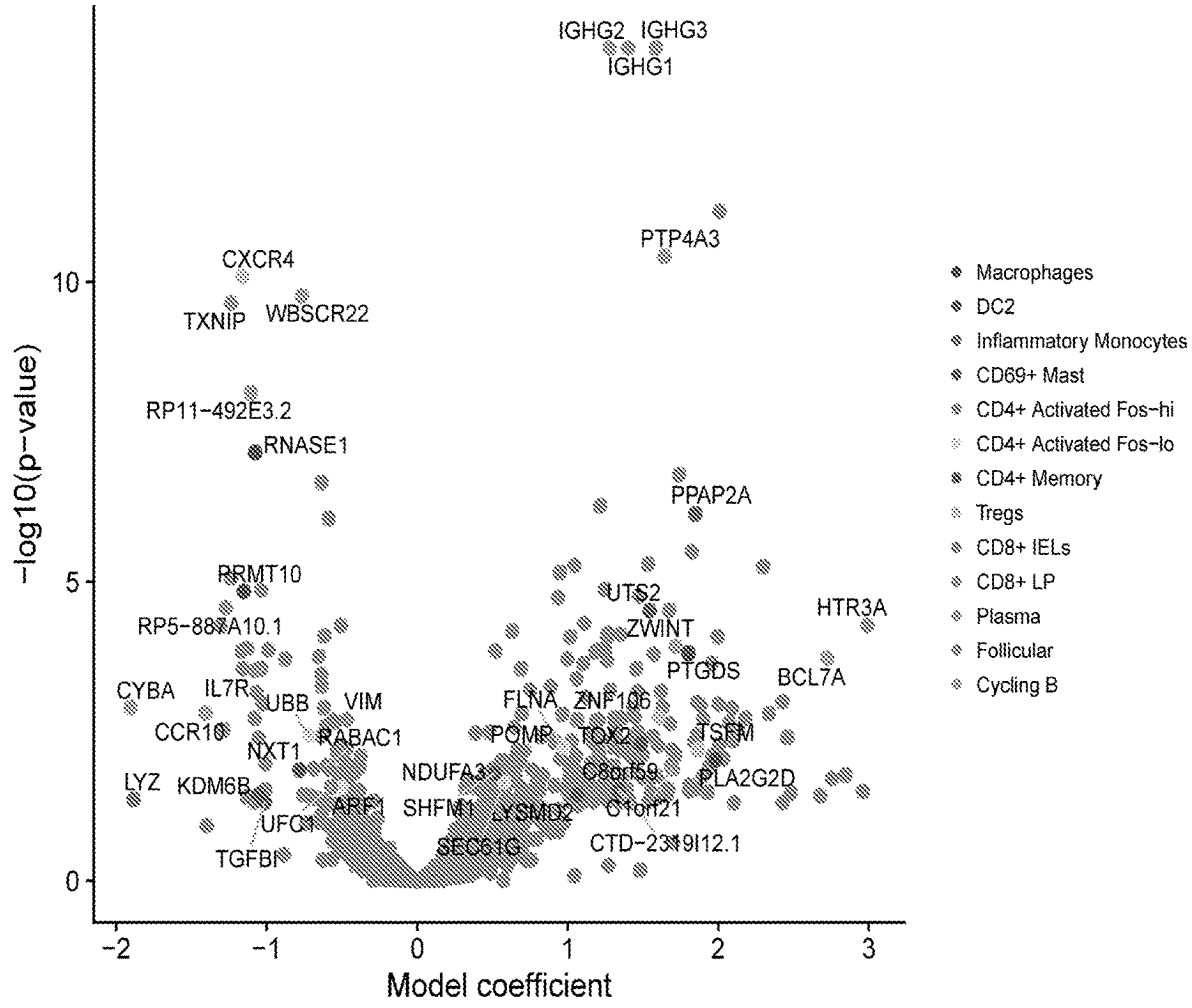

IGHG2
IGHG3
IGHG1
PTP4A3
CXCR4
TXNIP
WBSCR22
RP11-492E3.2
RNASE1
PPAP2A
RRMT10
RP5-887A10.1
UTS2
ZWINT
HTR3A
PTGDS
BCL7A
CYBA
IL7R
UBB
VIM
FLNA
ZNF106
CCR10
RABAC1
POMP
TOX2
TSFM
NXT1
NDUFA3
C8orf59
PLA2G2D
LYZ
KDM6B
ARF1
SHFM1
LYSMD2
C1orf21
UFC1
CTD-2319I12.1
SEC61G
TGFBI
10
5
0
−2
−1
0
1
2
3
−log10(p−value)
Model coefficient
Macrophages
DC2
Inflammatory Monocytes
CD69+ Mast
CD4+ Activated Fos−hi
CD4+ Activated Fos−lo
CD4+ Memory
Tregs
CD8+ IELs
CD8+ LP
Plasma
Follicular
Cycling B

FIG. 39F

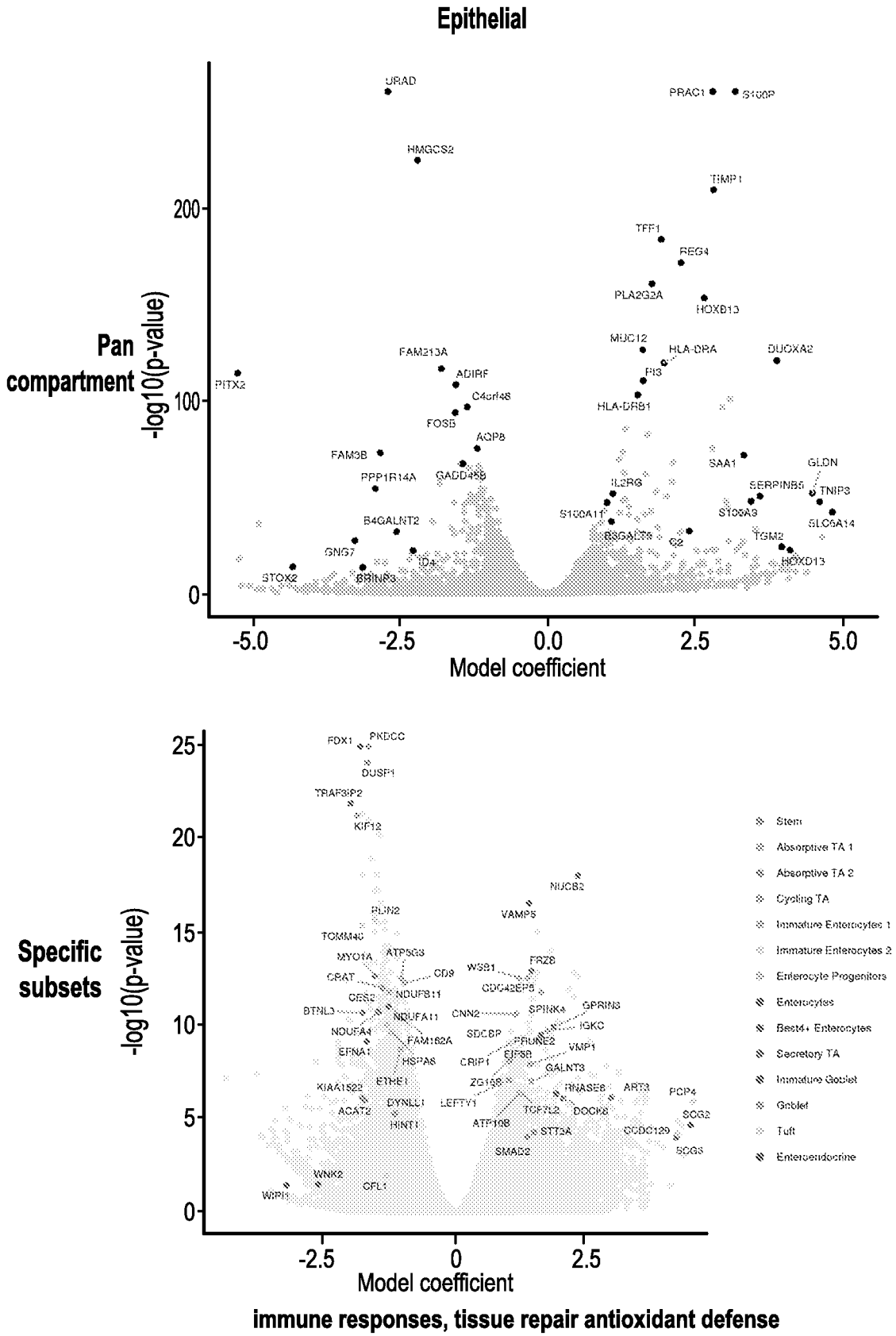

Epithelial
Pan compartment
-log10(p-value)
Model coefficient
URAD
PRAC1
S100P
HMGCS2
TIMP1
TFF1
REG4
PLA2G2A
HOXB13
MUC12
HLA-DRA
DUOXA2
PITX2
FAM213A
ADIRF
C4orf48
HLA-DRB1
FOSB
AQP8
FAM3B
SAA1
GLDN
PPP1R14A
GADD45B
IL2RG
SERPINB5
TNIP3
S100A11
S100A9
B4GALNT2
SLC6A14
TGM2
GNG7
ID4
HOXD13
STOX2
BRINP3
Specific subsets
-log10(p-value)
Model coefficient
FDX1
PKDCC
DUSP1
TRAF3IP2
KIF12
NUCB2
VAMP5
RUN2
TOMM40
MYO1A
ATP5G3
CRAT
CD9
WSB1
FRZ8
CES2
NDUFB11
CDC42EP5
BTNL3
NDUFA11
CNN2
SPINK4
GPRIN3
NDUFA4
SDCBP
IGKC
EFNA1
FAM162A
PRUNE2
VMP1
HSPA8
CRIP1
EIF5B
GALNT3
KIAA1522
ETHE1
ZG16B
RNASE6
ART3
PCP4
ACAT2
DYNLL1
LEFTY1
TCF7L2
DOCK8
SOG2
HINT1
ATP10B
STT3A
CCDC129
SCGS
SMAD2
WNK2
WIPI1
CFL1
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
Best4+ Enterocytes
Secretory TA
Immature Goblet
Goblet
Tuft
Enteroendocrine
immune responses, tissue repair antioxidant defense

FIG. 40A

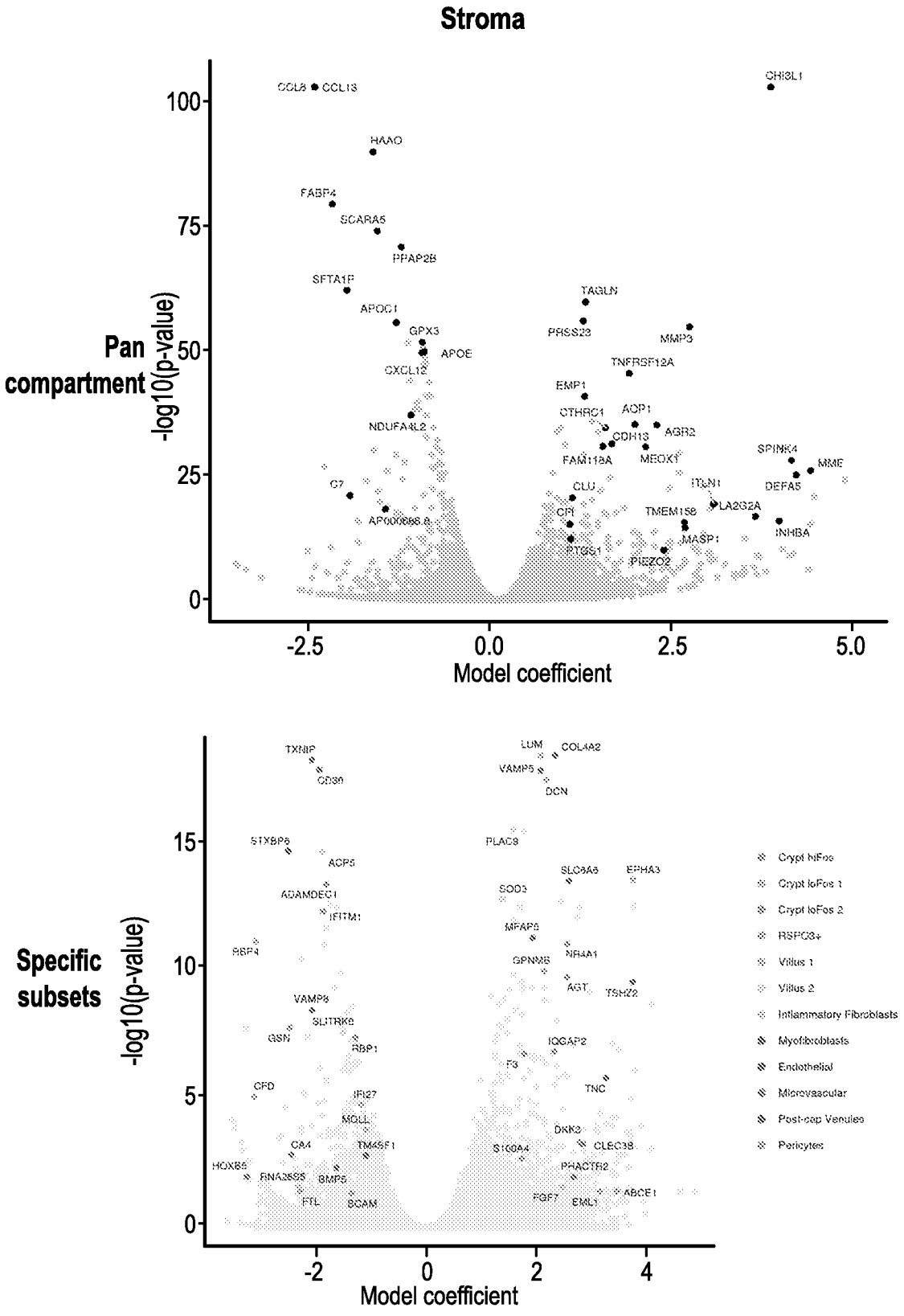
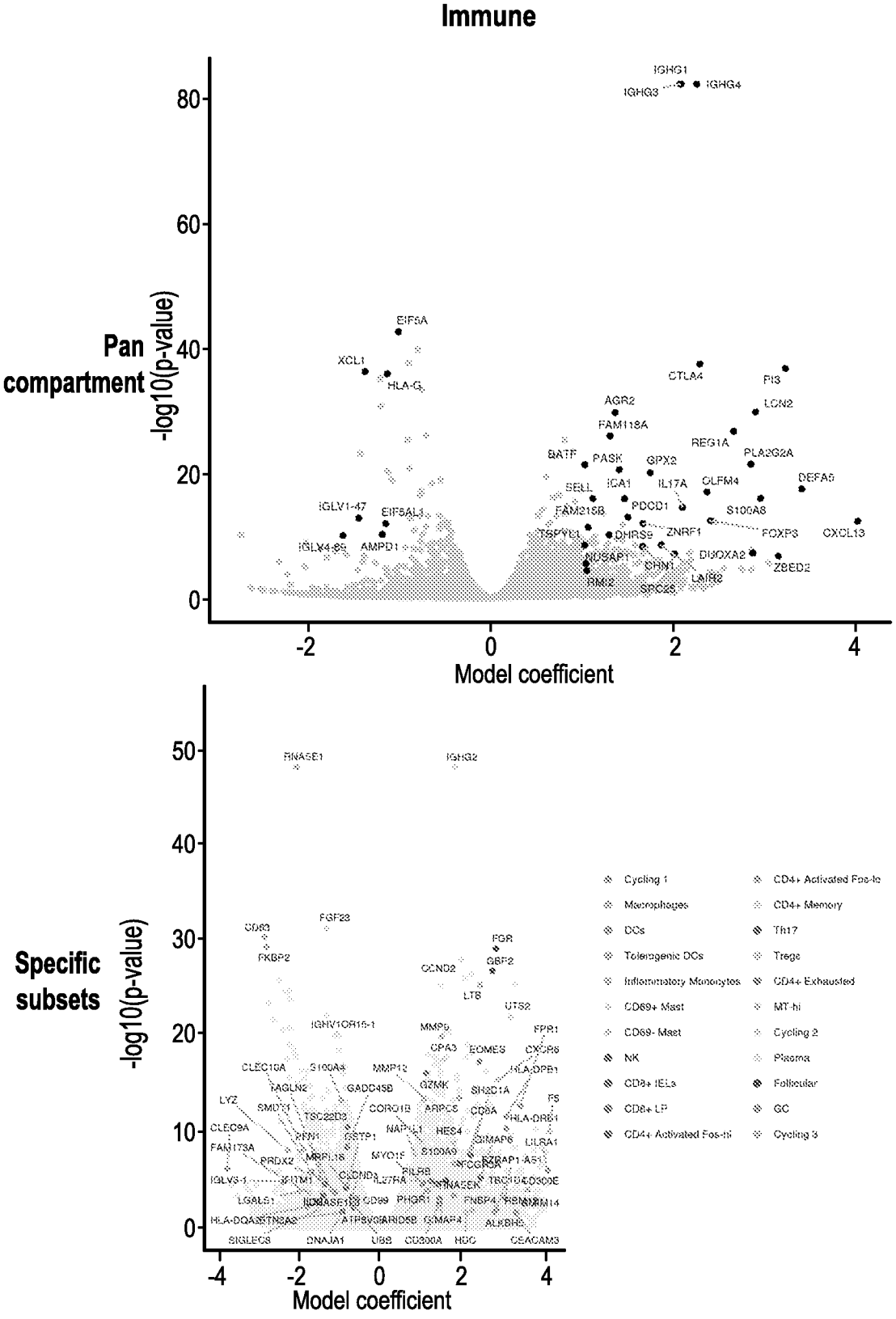

Stroma
Pan compartment
-log10(p-value)
Model coefficient
CCL8
CCL13
CHI3L1
HAAO
FABP4
SCARA5
PPAP2B
SFTA1P
APOC1
GPX3
APOE
CXCL12
NDUFA4L2
C7
AP000686.6
TAGLN
PRSS23
MMP3
TNFRSF12A
EMP1
CTHRC1
AOP1
CDH13
AGR2
FAM113A
MEOX1
SPINK4
MME
DEFA5
ITLN1
LA2G2A
CLU
CFI
TMEM158
MASP1
INHBA
PTGS1
PIEZO2
Specific subsets
TXNIP
CD36
LUM
COL4A2
VAMP5
DCN
STXBP6
ACP5
ADAMDEC1
IFITM1
RBP4
VAMP8
SLITRK6
GSN
RBP1
CFD
IFI27
MGLL
CA4
TM4SF1
HOXB5
RNA28S5
BMP5
FTL
SCAM
PLAC8
SLC9A6
EPHA3
SOD3
MFAP5
NR4A1
GPNMB
AGT
TSHZ2
IQGAP2
F3
TNC
DKK3
S100A4
CLEC3B
PHACTR2
FGF7
EML1
ABCE1
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Endothelial
Microvascular
Post-cap Venules
Pericytes
inflammatory cues, tissue repair, fibrosis, vascular expansion

FIG. 40B



Activation and inhibition of distinct arms of the immune response

FIG. 40C

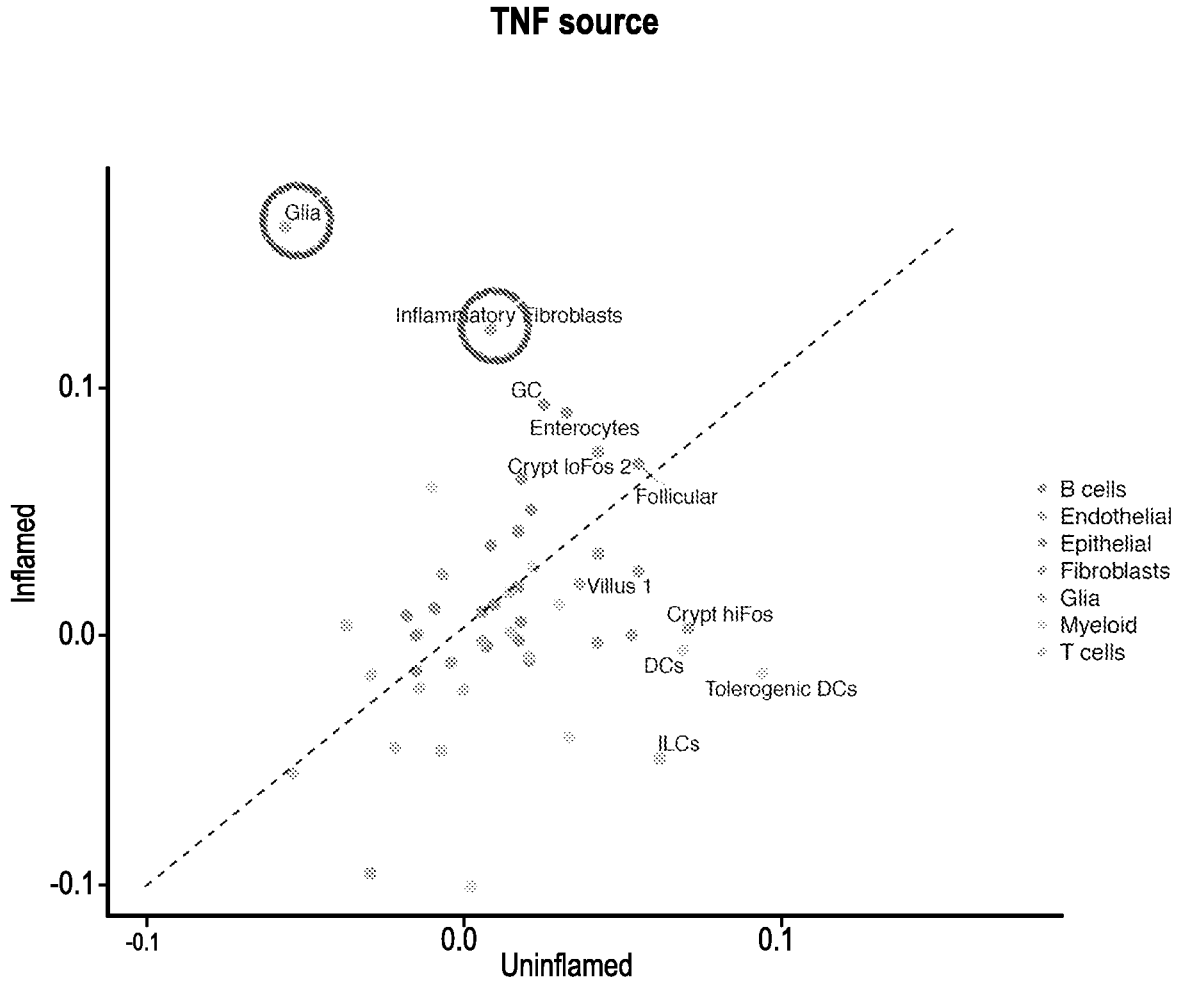

TNF source
Glia
Inflammatory Fibroblasts
GC
Enterocytes
Crypt loFos 2
Follicular
Villus 1
Crypt hiFos
DCs
Tolerogenic DCs
ILCs
0.1
0.0
-0.1
Inflamed
-0.1
0.0
0.1
Uninflamed
B cells
Endothelial
Epithelial
Fibroblasts
Glia
Myeloid
T cells

FIG. 41A

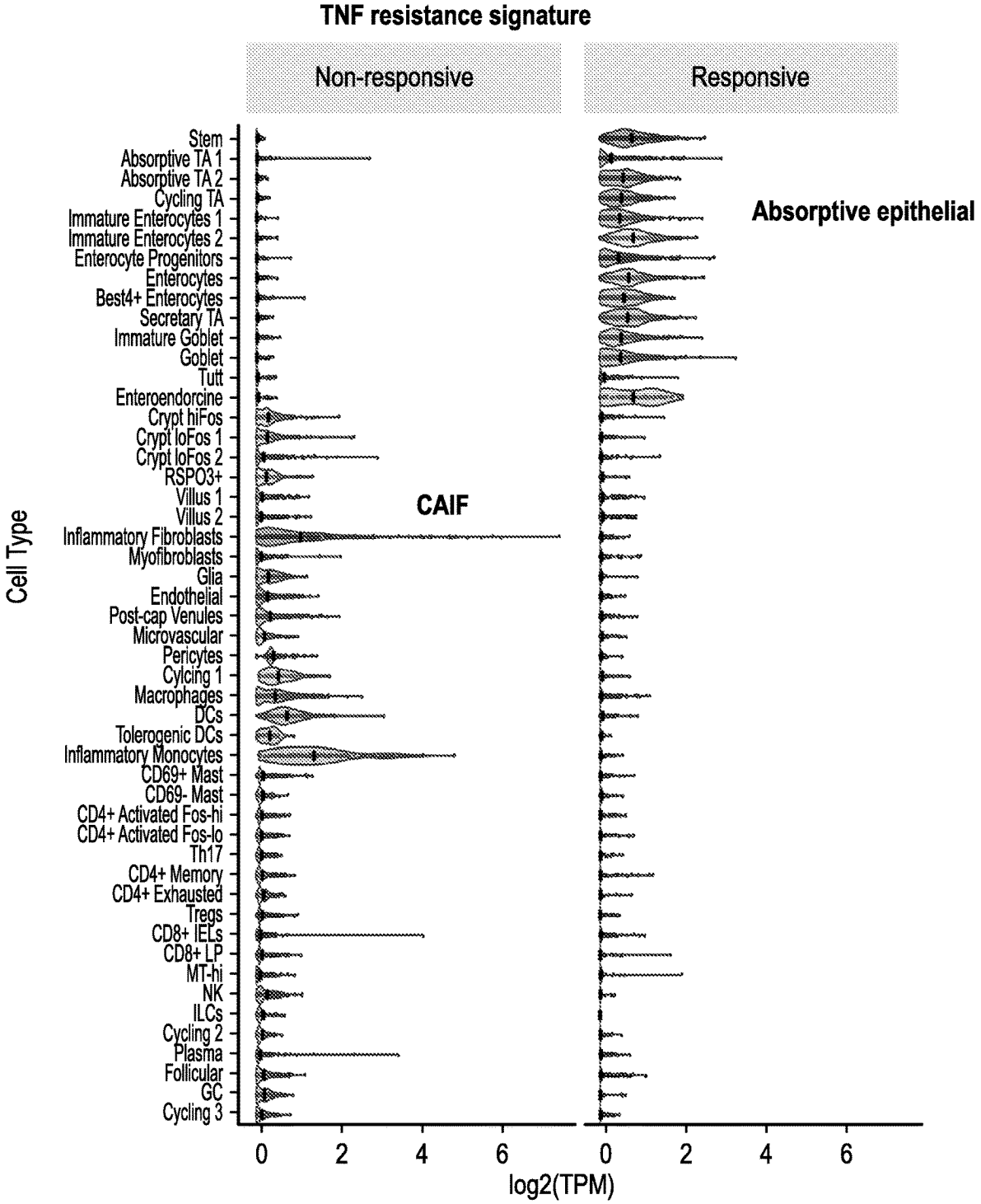

TNF resistance signature
Non-responsive
Responsive
Absorptive epithelial
CAIF
Cell Type
Stem
Absorptive TA 1
Absorptive TA 2
Cycling TA
Immature Enterocytes 1
Immature Enterocytes 2
Enterocyte Progenitors
Enterocytes
Best4+ Enterocytes
Secretary TA
Immature Goblet
Goblet
Tuft
Enteroendorcine
Crypt hiFos
Crypt loFos 1
Crypt loFos 2
RSPO3+
Villus 1
Villus 2
Inflammatory Fibroblasts
Myofibroblasts
Glia
Endothelial
Post-cap Venules
Microvascular
Pericytes
Cycling 1
Macrophages
DCs
Tolerogenic DCs
Inflammatory Monocytes
CD69+ Mast
CD69- Mast
CD4+ Activated Fos-hi
CD4+ Activated Fos-lo
Th17
CD4+ Memory
CD4+ Exhausted
Tregs
CD8+ IELs
CD8+ LP
MT-hi
NK
ILCs
Cycling 2
Plasma
Follicular
GC
Cycling 3
0
2
4
6
log2(TPM)

FIG. 41B

CELL ATLAS OF THE HEALTHY AND ULCERATIVE COLITIS HUMAN COLON

CROSS-REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Application Nos. 62/533,638, filed Jul. 17, 2017, 62/581,424, filed Nov. 3, 2017 and 62/692,541, filed Jun. 29, 2018. The entire contents of the above-identified applications are hereby fully incorporated herein by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

This invention was made with government support under Grant Nos. OD020839, AI089992, CA217377, AI039671, AI118672, HG006193 and CA202820 awarded by the National Institutes of Health. The government has certain rights in the invention.

REFERENCE TO AN ELECTRONIC SEQUENCE LISTING

The contents of the electronic sequence listing ("BROD-2203US_ST25.txt"; Size is 4,929 bytes and it was created on Nov. 23, 2020) is herein incorporated by reference in its entirety.

TECHNICAL FIELD

The subject matter disclosed herein is generally directed to a cell atlas of the human colon in healthy and disease states. The subject matter further relates to novel cell specific and disease specific markers.

BACKGROUND

Tissues function through the coordinated actions of diverse parenchymal, immune, and stromal cell types responding to local and distal cues. Breakdown in any cellular compartment can lead to disease, due to intrinsic cell dysfunction or through compensations by other cells to restore tissue homeostasis. This intricate interplay among cells makes it difficult to determine the causal cellular mechanisms that initiate or promote disease. In the past, measuring the contribution of each cellular compartment was hampered by the need to average bulk measurements across the entire tissue or to assess known cell subsets or selected genes a priori.

The small intestinal mucosa is a complex system. The mucosa comprises multiple cell types involved in absorption, defense, secretion and more. These cell types are rapidly renewed from intestinal stem cells. The types of cells, their differentiation, and signals controlling differentiation and activation are poorly understood. The small intestinal mucosa also possesses a large and active immune system, poised to detect antigens and bacteria at the mucosal surface and to drive appropriate responses of tolerance or an active immune response. Finally, there is complex luminal milieu which comprises a combination of diverse microbial species and their products as well as derivative products of the diet. It is increasingly clear that a functional balance between the epithelium and the constituents within the lumen plays a central role in both maintaining the normal mucosa and the pathophysiology of many gastrointestinal disorders. Many disorders, such as irritable bowel disease,

Crohn's disease, and food allergies, have proven difficult to treat. Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the colon and small intestine, principally including Crohn's disease and ulcerative colitis, with other forms of IBD representing far fewer cases (e.g., collagenous colitis, lymphocytic colitis, diversion colitis, Behçet's disease and indeterminate colitis). Pathologically, Crohn's disease affects the full thickness of the bowel wall (e.g., transmural lesions) and can affect any part of the gastrointestinal tract, while ulcerative colitis is restricted to the mucosa (epithelial lining) of the colon and rectum. Some of the genetic factors predisposing one to IBD are known, as explored in Daniel B. Graham and Ramnik J. Xavier "From Genetics of Inflammatory Bowel Disease Towards Mechanistic Insights" *Trends Immunol.* 2013 August; 34(8): 371-378 (incorporated herein). The manner in which these multiple factors interact remains unclear.

A case in point is ulcerative colitis (UC), a major subtype of Inflammatory Bowel Disease (IBD), where inflammation begins in the rectum and extends proximally in a contiguous fashion. Left-sided disease is characterized by a sharp demarcation between inflamed and non-inflamed segments. Explaining the geographical restriction of UC remains a challenge. While endoscopic examination followed by histological analysis are the current standard of care, they fail to capture key aspects of the disease, including immune cell activation states, cell-specific cytokine profiles, and disease-related features of stromal cells, and do not distinguish the pathways associated with chronic inflammation from attempts at disease restitution. Furthermore, several genes mapped by genome-wide association studies (GWAS) as associated with disease risk suggests a critical role for the intestinal barrier in preventing IBD, with defects in autophagy, ER stress, oxidative stress, cell death, IL23R/Th17 biology, immune tolerance, solute transport and perturbed innate and adaptive immune signaling [REF]. However, the cellular compartments and cell-cell interactions in which these GWAS genes and pathways act are often unknown.

Single-cell RNA-Seq (scRNA-Seq) can help advance our understanding of complex disease by comprehensively mapping the cell types and states in the tissue, distinguishing changes in cell-intrinsic expression programs from cell-extrinsic changes in cell frequencies, and predicting how these connect through cell-cell interactions. When comparing healthy and disease tissue, this may help determine with precision: which cell populations are disrupted in disease? Which cell-intrinsic programs are changed? What cell-cell interactions affect cell recruitment during inflammation and disease resolution? What are the cells-of-action of disease risk genes? and, What are the effects of current therapies and how might therapeutic resistance arise? Unlike bulk profiling, which averages across cell types, scRNA-Seq can readily distinguish between cell-intrinsic changes in expression program and cell-extrinsic changes in cell frequencies and cell-cell interactions. Unlike most in situ methods, which require prior knowledge of the genes and proteins of interest, scRNA-Seq can in principle do so systematically across all cells and programs in the tissue ecosystem, including those that may not yet be known to present in the tissue. This approach has been demonstrated for tumors (see, e.g., Tirosh, et al., Dissecting the multicellular ecosystem of metastatic melanoma by single-cell RNA-seq. Science 2016, 352, 189-196), but not yet for other complex immune mediated diseases, such as UC, where the window for disease onset, activity and resolution is measurable with endoscopic biopsies.

For example, Inflammatory bowel disease (IBD) is a chronic and debilitating disorder that affects millions of people worldwide. IBD is heterogeneous, comprising two main subtypes, Crohn's disease (CD) and ulcerative colitis (UC), which have different risk factors and clinical presentations. CD patients typically have discontinuous inflammation that extends deep into the mucosa throughout the gastrointestinal tract, while UC patients have continuous inflammation that is largely restricted to the mucosa of the large intestine. IBD is thought to arise from a maladaptive immune response to the gut Here, Applicants used intestinal biopsies microbiota in a genetically susceptible host. Genome-wide association studies (GWAS) have pinpointed hundreds of IBD-associated loci that explain ~10% of disease susceptibility. While linkage disequilibrium has precluded mapping most loci to single variants, fine-mapping studies have directly implicated several genes, including NOD2, IL23R, ATG16L1, and PTPN22. Functional analysis of these genes suggests a critical role for the intestinal barrier in preventing IBD, with defects in autophagy, immune signaling, and epithelial barrier function leading to elevated disease risk. However, the functional roles for most such genes are unknown and the ability of GWAS to detect causal variants exceeds our ability to generate functional insights into the disease.

SUMMARY

In certain example embodiments, the present invention provides for a human cell atlas of the colon for healthy and disease states and methods of use. This disclosure provides a rationale for modulating intestinal cell balance, function, differentiation and/or activity for the treatment of both IBD and other disorders.

In certain embodiments, the IBD is Crohn's disease or ulcerative colitis. In certain embodiments, the IBD is collagenous colitis, lymphocytic colitis, diversion colitis, Behçet's disease, or indeterminate colitis.

In one aspect, the present invention provides for a method of detecting inflammatory bowel disease (IBD) comprising measuring in a biological sample obtained from the gastrointestinal tract of a subject the frequency of one or more cell types selected from the group consisting of B cells, T cells, endothelial cells, epithelial cells, fibroblasts and myeloid cells compared to the total of all cell types in the sample, wherein IBD is detected when the frequency of one or more cell types is altered as compared to a healthy frequency. The one or more cell types may be selected from the group consisting of colitis-associated inflammatory fibroblasts (CAIFs), absorptive transit amplifying (TA) 1 cells, absorptive TA 2 cells, class switching B cells, crypt fibroblasts (loFos), glial cells, goblet 1 cells, neutrophils, plasma B cells, post-capillary venules and tolerogenic DCs.

In certain embodiments, the cell type may be detected by measuring one or markers for each cell type selected from Table 1 A-D, Table 9, Table 11 or Table 12. The top 250 markers for each cell type are listed in ranked order.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in a biological sample obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide selected from the group consisting of: MTRNR2L1, HLA-B, CHI3L1, EIF5A, RPL3, S100P, TIMP1, REG1A, C8orf4, HMGCS2, DMBT1, AC005540.3, OLFM4, IL13RA2, MMP3, REG4, IGJ, DEFA5, TNFRSF12A, BGN, SELENBP1, TPM4, IFITM2, TNFRSF11B, PKM, PHLDA1, MT1G, LGALS4, IGFBP5, URAD, ANXA2, HLA-DRA, PLA2G2A, PDPN, S100A11, SELL, SOD2, LDHA, SMDT1, CCL8, FCGRT, RPL9, CYR61, NNMT, LMNA, HIF1A, CD82, LINC00152, TAGLN2, IFITM3, EMP1, AKR1C1, CD63, FKBP1A, PTMA, COL6A3, REG3A, BACE2, C10orf99, CNN3, CEBPB, RPL13A, LCN2, HSPA1B, CKB, PHGR1, CD59, C11orf96, ANXA5, RPL18A, COL4A1, CTHRC1, PCOLCE, COL1A1, FTL, EMP3, GEM, COL4A2, PRSS23, S100A6, S100A3, CA1, REG1B, TNC, CCR7, MEOX1, FGF7, MMP1, RPS3A, THY1, RPS26, PKIB, CHP2, SERPINE1, TXNIP, COL6A1, RPS4Y1, PSME2, CAV1, ANGPTL2, TAGLN, TFF1, HGF, PDIA3, CDH13, ACADS, KDELR2, NOP10, SELM, HAPLN3, FABP4, PTGES, DSTN, CCL5, VAMP8, MT-ND1, SERPINH1, HYI, POLR2L, PPIB, HLA-DMA, TST, AQP1, SPARC, CA2, CCL13, MT-CYB, HLA-DPB1, SPINK1, AQP8, ATOX1, RPL37A, IER3, ENO1, MT1H, HSPA5, HSPA1A, ITM2C, SDC2, ID1, AMN, FABP6, PIGZ, COL8A1, DUOXA2, TPM2, CRIP2, HYAL2, CPXM1, NCOA7, RPS29, TMEM258, CLDN7, PHLDA2, TMSB10, F2R, PXMP2, SRM, CFB, NDUFA4L2, CBX3, NXPE4, ACAA2, NDRG2, KANSL1-AS1, KLF2, LAPTM4A, ITGA5, DHRS4, CDX2, PRKCDBP, RPL6, SOCS3, GPR160, PPDPF, SEPP1, TMEM141, ELP5, NRG1, SPON2, CXCL1, ID3, PTRF, CALR, TMEM165, HSP90B1, CLEC9A, INHBA, SPHK1, FABP1, LGALS2, PDLIM4, TMEM158, CKMT1A, TRMT112, CCDC3, HOXB13, MRGPRF, CALU, ACSF2, MMP10, VSIG2, RAMP1, MT1M, APOA4, TFPI2, FXYD3, MORF4L1, PEBP1, STAP2, NFKBIA, MT-CO3, DHRSl1, SPINT2, PRRX2, RCN3, EIF4A1, TUBB, TSHZ2, KRT8, ACTN1, VAMP5, RPL10, IL11, AGT, SERPINA1, SLC26A2, CLU, APOBEC3B, DNAJB1, THBS2, UBD, PIM3, PRKAR1A, IL32, IGFBP7, UGT2A3, HLA-DRB5, PPA1, CHCHD10, COL6A2, CD55, RNASET2, CTGF, MT-CO1, CTSK, C19orf10, SERPINE2, HSD17B12 and SAA1; or MTRNR2L1, HLA-B, RPL3, TIMP1, IGJ, IFITM2, CCR7, CCL5 and IGFBP7; or MTRNR2L1, HLA-B, RPL3, TIMP1, IGJ, IFITM2, CCR7, CCL5 and IGFBP7; or genes in Table 4, 6, 8, 13, 14 or 15, wherein the genes or polypeptides are differentially expressed in IBD as compared to a healthy gastrointestinal tract reference level. The expression of MTRNR2L1, HLA-B, TIMP1, CCR7, IFITM2, and IGFBP7 may be upregulated as compared to a healthy reference level and the expression of RPL3, IGJ and CCL5 may be downregulated as compared to a healthy reference level.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in B cells obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [Plasma_B_cells] G0S2, FABP1, TNFRSF18, PHGR1, AGR2, GAS6, RPL3, LMNA, TIMP1, SMOC1, HIST1H1C, HSP90AA1, TNFRSF4, HSPA1A, HSPA1B, CYP20A1, KRT19, CXCR4, DNAJB1, XBP1, GOLGA2 and CADM1; or [Class_switching_B_cells] TIMP1, RPL3, HSP90AA1, LMNA, ILVBL, CD69, CTHRC1, TNFRSF4, G0S2, PABPC4, ITM2C, AGR2, RPS3A, RNASE6, LGALS4, HLA-DMA, FXYD3, PTMA, TNFRSF18, RP11-16E12.2, H3F3B, KLF6, QPRT, TPM4 and SMOC1; or [Follicular_B_cells] C12orf75, METAP2, CCND3, HLA-DQB1, HLA-DRB5, RPS4Y1, TUBB2A, LCK, RMI2, SMARCB1, HLA-DPB1, TCEA1, MME, RPL9, SLBP, CD63, UBE2D3, A4GALT, PLD4, SIT1, PPP1CC, PAIP2, CCDC109B, DCAF12, SRSF3, HLA-DQA1, HLA-C, ISG20, HMGN1, HMCES, HNRNPC, HLA-DPA1, TUBB2B, HNRNPA3, CD27, EIF1AY, ITGAE, TPD52,

ECHS1, RAPiB, HLA-DQA2, GGA2, CHCHD10, ACTR3, HLA-DRA, SGPP1, PGAM1, DCK, TSG101, HNRNPM, LTB, CLIC4, LSM10, GDI2, RGS16, CAPG, SRSF2, ZFAND2A, RPL36, CBX3, AGR2, MRPL47, TRA2A, FBL, SELT, SUMO2, HADHB, DEF8, FGD2, LIMD2, PSIP1, RBBP7, BZW1, TSTD1, MTF2, IKZF1, RUVBL1, BACH2, PIM1, CHRAC1, EZR, MCM5, IGJ, COX6B1, PRPSAP2, TK1 and CCR7.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in endothelial cells obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [Microvascular_cells] PLAT, AQP1, CD9, HLA-A, HLA-DRA, EGLN3, LDHB, HLA-C, RBP5, CD99, PASK, S100A10, SERPINE1, CXCL12, JUN, ANXA2, TESC, IGJ, FOSB, LIMS1, HSPA1A, CALU, RCN3, S100A6, CST3, PRSS23, SEPP1, HSPA1B, WWTR1, RAMP1, GPX4, PSMB9, PSME2, CTGF, CD82, LGALS4, SNED1, TNFRSF4, IER3, VAMP8, ALDOA, HLA-B, TAP1, CD36, F2RL3, KDR, COL15A1 and PLAU; or [Post-capillary_venules] PTGS1, RAMP1, PDLIM1, HLA-A, OLFML3, PLAT, STXBP6, UBD, LY6E, TNFSF10, CD9, MGP, CPE, PSMB8, PHLDA1, EIF4A2, GIMAP7, TMEM100, CST3, HLA-C, RPL9, RPL10, LPCAT4, AQP1, GIMAP1, SRPX, MALAT1, RPL3, AGR2, PRSS23, COL4A3BP, EFEMP1, SNHG7, TUBA1B, PTGES, NFKBIZ, B2M, FTH1, C19orf66, CDKN3, RNF181, EEF1B2, MDK, CLIC1, TPTEP1, TFF3, S100A10, JUN, CRIP1 and MED24; or [Vitamin_metabolizing]PLAT, CXCL12, ENPP2, TXNIP, IGFBP4, CD36, ANXA2, OAZ2, CD320, AQP1, CTGF, RGS5, TGFBR2, RAMP1, CD9, C16orf80, CXCR4, CLDN5, STC1, GJA1, FAM213A, PLAU, HLA-E, PRKCDBP, RBP5, RPL9, SAT1, TNFSF10, S100A4, TSPAN7, AKRIC3, C8orf4, HLA-DPB1, SRP14, TNFRSF4, TIMP1, ANXA1, Clorf54, RND1, ANGPT2, EGR1, STAT3, SH3BP5, RPL29, CTNNBIP1, LSMD1, HLA-C, RBM17, GYPC, NDUFA7, IER2, COTL1, RPLP0, SDPR, IDI1, SLC6A6, RPL10A, MYL6, AQP3, NKX2-3, COASY and SOD2; or [Endothelial_pericytes] FAM222B, RP11-490M8.1, TWF2, ZNF205 and HYI.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in epithelial cells obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [Enterocytes] SPINK1, PLA2G2A, IL18, ATP1B3, MTRNR2L1, GSTP1, GPX2, CYBA, TAX1BP3, S100A14, NQO1, TSPAN3, NAALADL1, CTSA, RARRES3, OAS1, LGALS1, HMGCS2, PCK1, PRDX5, MUC1, TMEM37, KRTCAP3, MT2A, MX1 and S100A11; or [Tuft_cells] PTGS1, ESYT2, SHC1, HPGDS, HOOK1, BCKDK and RALGAPAl; or [Goblet_2] SPINK4, NUPR1, S100A14, BAIAP2L1, BDKRB1, MT-ND2, FAM3B, MUC13, TFF1, ANO9 and TUBB2A; or [Absorptive_TA_1] REG1A, CD74, RPL3, HLA-DRB1, MT2A, RPS3A, ARHGDIB, TIMP1, LIN7C, MTRNR2L1, KCNK6, RPL18A, TNFRSF12A and SEC11C; or [Secretory_TA] HLA-DRA, HLA-DRB1, RARRES2, ID3, HLA-DMA, UGT2B17, CD74, HLA-DRB5, REG1A, HLA-DPB1, HLA-DPA1 and GLBIL2; or [Absorptive_TA_2] AGR2, HLA-DRA, CD74, S100A11, HSPB1, SPINK1, HLA-DRB1, TIMP1, RARRES3, SELENBP1, GPX2, MUC12, ID3, ARHGDIB, REG1A, PLA2G2A, CEACAM5, IDH2, IGJ, RNASET2, BSG, PSMB9, ADIRF, LEFTYl, RARRES1, LYZ, MTRNR2L1, TFF1, RPS4Y1, SRSF6, CNPY2, GSTP1 and ATP1B3; or [Cycling_TA] RARRES2, ARHGDIB, IGJ, BST2, PKIG, PITX1, ETS2, HLA-DRA, TIMP1, MTRNR2L1, HRCT1, ZNF90, MUC12, AKR1B1, HLA-DPA1, VAMP7, S100P, NQO1, DEK, ABRACL, REG1A, ACAT1, DNAJB1, HLA-DRB1 and IGFBP4; or [Goblet_1] SPINK4, ITLN1, IGJ, AGR2, SDF2L1, TIMP1, PDLIM1, MUC2, LYZ, SELK, HMGCS2, SECllC, SSR4, DNAJA1, FKBP11, REG4, EZR, SELM, CISD1, SYTL1, PHLDA2 and CHPF.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in fibroblasts obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [Inflammatory_fibroblasts] COL1A2, GBP1, IFI27, DYNLT1, PKM, PHLDA1, DUSP1, CNOT4, CCL8, LAP3, ACP5, GSTT1, GALNT11, PSMB9, TNIP2, PSMB8, HAPLN3 and PERP; or [Fibroblast_pericytes] NET1; or [Myofibroblasts] PDLIM7, NBL1, C12orf75, PHLDA2, IGFBP5, PRSS23, TM4SF1, SQRDL, MRGPRF, RERG, MXRA8, RPS4Y1, EGR1, HOXD9, TDO2, DUSP1, LMNA, CYB5R3, DDAH2 and TFPI2; or [Villus_fibroblasts] MMP2, SRPX2, TNC, MMP1, S100A4, NSG1, EDNRB, AGT, TRPA1, CPE, VSTM2A, RBP4, TSHZ2, IL32, VASN, CRIP1, NR4A2, PCTP, PRSS23, MCL1, NDUFA4L2, ANXA1, TMSB4X, PDLIM1, IGFBP3, CEBPD, FOXF1, ACP1, CIS, FRZB, ECM1, DMKN, ID4, PDGFRA, GADD45B and SPARCL1; or [Crypt_fibroblasts_(hiFos)] TM4SF1, VASN, GSN, FGF7, PLAT, CLEC14A, IQGAP2, 11D3, FN1, SEPP1, TNXB, CCL13, TPBG, HSD17B2, STMN2, GPX3, VIM and TNFSF10; or [Crypt_fibroblasts_(loFos)] GPX3, NR4A1, CIS, TM4SF1, DUSP1, ID1, LGALS3BP, COL15A1, SERPINGI, TNFAIP6, CFD, ADAMDECI, MZT2B, MIF, EGR1, DKK3, NBEAL1, GSN, GGT5, FOXF1, RPL9 and CD74.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in macrophages obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of LGMN, RNASEI, AKR1B1, LGALS2, A2M, C15orf48, VMO1, SERPINF1, SPINT1, ACP5, TFF3, RNASET2, ENPP2, LGALS1, MMP9, CORO1A, CSTB, SELK, MT2A, FBP1, PLSCR1, FXYD5, NR1H3, UCHL3, SEPP1 and AGR2.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in T cells obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [T_cells] NUB1, CAV1, EIF2S1, COL6A1, POSTN, ALAS1 and RGCC; or [Activated_CD4_cells_loFos] S100A4, RPS29, TIMP1, RPL9, CFL1, VIM, ANXA1, PHLDA1, S100A11 and HLA-A; or [Activated_CD4_cells_hiFos] IGJ and ADSS; or [CD8_IELs] CCL3, CCL4, RPL10, RPL6, CD3E, MTRNR2L1, ARHGDIB, CD3G, RPL3, ITGB2, KLRB1, IFNG, RPL22, RPL18A and PTMA; or [CD8_LP_cells] RPL9, EMP3 and ARFRPI; or [Tregs] CD7, CD2, TIA1 and GRSF1; or [Memory_T_cells] RPL9, PFN1, IL32, ANXA1, S100A4, ARPCIB, KLRB1, RPL30, ANAPC5, GAPDH, B2M, RPS28, PSME2, AK5, SERF2, RILPL2, RPS29, TAGLN2, FXYD5, S100A11, ANXA5, S100A6, PNRC1, ARPC2 and ZFP36; or [Cycling_CD8_cells] ENTPD1, CD2, EIF5A, LCK, HAVCR2, ATP5L, KLRB1, CALR, MTPN, CENPA and MIF.

In another aspect, the present invention provides for a method of detecting IBD comprising measuring in cells obtained from the gastrointestinal tract of a subject the expression of a gene or polypeptide specific for the indicated cell type in brackets selected from the group consisting of: [Stem_cells] AQP1, RPL3, RPS4Y1, LYZ, LCN2, ID3, HLA-DRA, HLA-DRB1, HLA-DMA, HLA-DPA1, C2, NQO1, B2M, ARHGDIB, DNAJB1, RARRES2, MTRNR2L1, HLA-C, CD74, C19orf70, GSTT1, TESC, IFI27, PSME1, HMGCS2, HLA-DRB5, RPL6, UGT2B17, HLA-DPB1, PSMB9 and SCARB2; or [Enteroendocrine] RARRES2, HLA-DRA, SEC11C, MT2A, NIPSNAP1, OLFM4, DDC, MDK and CD82; or [Glial_cells] ALDH1A1, CLU, ANXA1, SPP1, IL32, CAPS, FIBIN, RPL3, RPL9, HLA-G, MRPS6, LINC00152, HOXC6, CDKN2A, TUBAIA, HLA-DQA2, SOCS3, SEPP1, IGJ, HLA-DRB5, KLC1, HLA-DRB1, NDUFB4, ENTPD2, SRGN, PMEPA1, HSPA1B, FKBPIA, GLIPR2, UBR4, UBB, COX7A1, LSM3, PRDX2 and NUPR1; or [Dendritic-_cells] CST3, MARCKSL1, CD52, PPA1, IGJ, SERPINBI, TYMP, STMN1, FCER1A, DNAJB1 and PRELIDI; or [Mast_cells], NFKBIZ, EGR3, ILIRL1, HLA-B, CAPG, EGR2, HLA-C, RPS4Y1, CTSW, EIF4G2 and ZEB2; or [Cycling_monocytes] TFF3, ATP2A3, GSDMD, EMP3, IL12RB1, PSMD11, ENPP2, ALOX5AP and AKl; or [Tolerogenic_DCs] TXN; or [Neutrophils] GBP1, FCGR2B, GSTO1, RPL30, TMEM176B, EMG1 and GDI2; or [NK_cells] ILF3, CALCOCO2 and CD47.

In certain embodiments, the cell type according to any embodiment herein may be obtained by sorting cells based on expression of one or markers for each cell type selected from Table 1 A-D, Table 9, Table 11 or Table 12. The sorting may be performed by deconvolution of bulk expression data in silico. Not being bound by a theory, the quantity of cells may be determined by cell specific markers and gene expression assigned to each cell. The biological sample according to any embodiment herein may be obtained by colonoscopy.

In another aspect, the present invention provides for a method of treating IBD comprising modulating the activity of one or more gastrointestinal tract cell types selected from the group consisting plasma B cells, class switching B cells, follicular B cells, microvascular cells, post-capillary venules, vitamin metabolizing, endothelial pericytes, enterocytes, tuft cells, goblet 2, absorptive TA 1, secretory TA, absorptive TA 2, cycling TA, goblet 1, stem cells, enteroendocrine, glial cells, inflammatory fibroblasts, fibroblast pericytes, myofibroblasts, villus fibroblasts, crypt fibroblasts (hiFos), crypt fibroblasts (loFos), T cells, macrophages, dendritic cells, mast cells, cycling monocytes, tolerogenic DCs, neutrophils, activated CD4 cells loFos, activated CD4 cells hiFos, CD8 IELs, CD8 LP cells, Tregs, memory T cells, NK cells and cycling CD8 cells. The one or more cell types may express one or more IBD GWAS genes selected from the group consisting of: IL32, MHCII, RNF186 and SLC39A8; or LMAN2, ATF4, TRIB1, HSPA6, RABEP2, CAMP, TSPAN14, STRN4, MOB2, HYAL1, DOCK9, CTSA, TST, PLEKHG6, RHPN2, C2CD2L, D2HGDH, REG4, DDC, HCK, MED16, GRB7, SPRED2, COG5, ADK, RIT1, SLC15A3, PLAU, ING5, NF2, PDLIM7, ZP1, PLA2G4A, CCL13, TTYH3, NFKBIZ, VPS 11, CARD9, TNNI2, RIPK2, GPBAR1, SLC11A1, IFNG, CD28, EIF3G, CUL1, FASLG, MXD3, TCF19, DPAGT1, PHTF1, HOXA5, COX15 and LIF; or [GPCR] CCR10, GPRC5D, GPR18, CXCR5, CALCRL, F2RL3, FZD4, SiPR1, GPR4, APLNR, FZD6, LPAR6, GPR146, AVPR2, HRH1, GPRC5B, TBXA2R, GPRC5A, FZD5, GPR39, LGR5, VIPR1, F2RL1, LGR4, OPN3, FFAR4, GPR153, GPR37L1, FZD3, LPAR1, GPR137, SMOX, ADORA2B, BDKRB1, PGF, ADRA2A, PTGIR, EDNRA, MRGPRF, F2R, EDNRB, GLP2R, PTGFR, ACKR3, FZD1, ADORA1, ADORA3, CMKLR1, FPR3, P2RY13, ADRB2, LPAR5, P2RY14, GPR34, PTAFR, CCRL2, GPBAR1, FFAR2, C5AR1, C3AR1, CCR1, FPR1, GPR82, CXCR6, CCR7, DHX15, CCR6, GPR68, PTGDR and LTB4R; or [cell-cell interaction] TNFRSF17, SEMA4A, EBI3, RAMP3, ROBO4, F2RL3, APLN, NRP2, CCL21, ICAM2, PLXND1, HRH1, EPHA2, CGN, CELA3B, CFTR, RGMB, SCT, AZGP1, TSPAN1, IL22RA1, ILIR2, RSPO3, NRXN1, NCAM1, ANGPTL2, TNC, MMP1, COL18A1, CIQTNF1, COL5A3, NEO1, NTN1, BMP2, TSLP, SEMA3A, PROS1, ANGPTL1, CCL19, CD4, LY96, IL5RA, SIRPA, IL23A, IL1B, OSM, OLR1, KLRC2, CXCR6, IL17RA, KLRC1, ADAM10 and TNF; or [epithelial cells] CTSA, TNIP1, SEPHS2, AGPAT2, MIDN, FAM132A, SLC26A3, CHP2, SULT1A2, TMEM171, SULT1A1, C1orf106, HNF4A, PLEKHG6, FUT2, CEBPA, GSDMB, EDN3, PTK6, PSORS1C1, RHPN2, VDR, SLC26A6, AGPAT3, MST1R, NGEF, EFNA2, C2CD2L, ITPKA, SLC22A5, SLC35D1, AGXT, NXPE4, SLC39A8, TMEM258, F12, D2HGDH, BCL2L15, CFTR, GOT1, PLK1, ERGIC1, ITLN1, REG4, SULT2B1, CCDC60, CACNA2D2, SLC19A3, AGFG2, PLXNB1, DDC, C2orf54, LFNG, SNAPC4, MEX3A, GCG, GPBAR1, RXFP4, UCKL1, HCK, CAMP, BLM, SOX4, IFT172, RNF186, SMURF1, RNF123, TREH, HOXA11-AS, NOS2, C2CD4D, CEBPG, IL10RB, PRKCD, MED16, SEC16A, PPP1R12C, FOXO1, EPS8L1, TRIM31, CDH1, APOBR, SCNNIA, GRB7, SLC22A23, FRYL, ACHE, SMAD3, MAGI3, SPRED2, SMPD3, FAM83E, IL1R2, USP12, PWP2, ABCA7, SYT7 and COG5. Thus, cells may be targeted that express GWAS genes.

In another aspect, the present invention provides for an isolated gastrointestinal tract cell characterized by expression of one or markers for a cell type selected from Table 1 A-D, Table 9, Table 11 or Table 12.

In another aspect, the present invention provides for a method for detecting or quantifying gastrointestinal tract cells in a biological sample of a subject, the method comprising detecting or quantifying in the biological sample gastrointestinal tract cells as defined in any embodiment herein. The gastrointestinal tract cell may be detected or quantified using one or more markers for a cell type selected from Table 1 A-D, Table 9, Table 11 or Table 12.

In another aspect, the present invention provides for a method of isolating a gastrointestinal tract cell from a biological sample of a subject, the method comprising isolating from the biological sample gastrointestinal tract cells as defined as defined in any embodiment herein. The gastrointestinal tract cell may be isolated using one or more surface markers for a cell type selected from Table 1 A-D, Table 9, Table 11 or Table 12.

In certain embodiments, the gastrointestinal tract cells may be isolated, detected or quantified using a technique selected from the group consisting of RT-PCR, RNA-seq, single cell RNA-seq, western blot, ELISA, flow cytometry, mass cytometry, fluorescence activated cell sorting, fluorescence microscopy, affinity separation, magnetic cell separation, microfluidic separation, and combinations thereof.

In another aspect, the present invention provides for a method of modulating the gastrointestinal tract cell composition comprising treating a subject with an agent capable of targeting intestinal stem cells to differentiate. The intestinal

stem cells may be targeted to differentiate into absorptive transit amplifying (TA) 1 cells, absorptive TA 2 cells or class switching B cells.

In another aspect, the present invention provides for a method of modulating the gastrointestinal tract cell composition or activity comprising treating a subject with an agent capable of targeting a receptor-ligand interaction. The receptor-ligand interaction may comprise: CCR7 and one or more of CCL19 and CCL21; TNFB and LTBR; LGR5 and RSPO3; IL15 and IL15RA; FGF23 and FGFR1; CCL8 and CCR1; CXCL2 and XCR1; or XCL2 and XCR1.

In certain embodiments, IBD comprises Crohn's disease or ulcerative colitis (UC).

In another aspect, the present invention provides for a method of detecting drug resistance in inflammatory bowel disease (IBD) comprising measuring in a biological sample obtained from the gastrointestinal tract of a subject the frequency of colitis-associated inflammatory fibroblasts (CAIFs) compared to the total of all cell types in the sample, wherein drug resistance is detected when the frequency of CAIFs is altered as compared to a healthy frequency. The drug resistance may be resistance to anti-TNF therapy. The cell type may be detected by measuring one or markers selected from the group consisting of MMP3, MMP10, PLAU, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11 and TNFRSF11B.

These and other aspects, objects, features, and advantages of the example embodiments will become apparent to those having ordinary skill in the art upon consideration of the following detailed description of illustrated example embodiments.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1**—illustrates that epithelial cells in UC patients partition by patient and healthy cells by cell type in tSNE plots.

FIG. **2**—illustrates that computational modeling can address batch effects in tSNE plots.

FIG. **3**—illustrates that the atlas uncovers almost all cell types and subtypes in the colon.

FIG. **4**—illustrates that the atlas uncovers almost all immune cell types and subtypes in the colon.

FIG. **5**—illustrates the changes in cellular composition in UC.

FIG. **6**—illustrates that the atlas can be used to analyze compositional changes by deconvolution of bulk profiles.

FIG. **7**—illustrates genes differentially expressed in UC.

FIG. **8**—illustrates cell type specific differential expression of genes in UC.

FIG. **9**—illustrates genes differentially expressed in uninflamed tissue and in inflamed tissue.

FIG. **10**—illustrates violin plots for key IBD GWAS in specific cell types present in healthy and disease colon.

FIG. **11**—illustrates violin plots for key IBD GWAS in specific cell types present in healthy and disease colon.

FIG. **12**—illustrates the cell-of-origin for key IBD GWAS genes.

FIG. **13**—illustrates the cell-of-origin for key IBD GWAS genes. Gene modules for all cells and TA cells are specific for an epithelial cell signature and oxidative phosphorylation signature.

FIG. **14**—illustrates the cell-of-origin for key IBD GWAS G-protein coupled receptor (GPCR) genes.

FIG. **15**—illustrates the cell-of-origin for key IBD GWAS cell-cell interaction or cell-cell communication genes.

FIG. **16**—illustrates the cell-of-origin for key IBD GWAS genes expressed in epithelial cells.

FIG. **17**—illustrates that the atlas can be used to determine the cell-of-origin for GWAS genes for other indications.

FIG. **18**—illustrates that the atlas can be used to determine cell-cell interaction mechanisms.

FIG. **19**—illustrates cell-cell interactions in the healthy gut.

FIG. **20**—illustrates cell-cell interactions in the diseased gut.

FIG. **21**—illustrates that the atlas can be used to determine fibroblasts that support the stem cell niche.

FIG. **22**—illustrates fibroblasts genes that support the stem cell niche (right) BMP expression and Wnt expression in the villus and crypt.

FIG. **23**—illustrates Rspo3 gene expression in the tSNE plot of FIG. **22**.

FIG. **24**—illustrates a Rspo3 gene-expression module and a module from all cells in the tSNE plot.

FIG. **25**—illustrates a diagram of the study design and sample collection.

FIG. **26**—Cell atlas of the human colon in health and disease. a. tSNE clustering by cell type. b. Heatmap showing expression of cell type specific markers. c. Barplot showing proportions of cell subsets across samples of the same type (health, uninflamed, inflamed). d. Plot showing distribution of cell types. e. Expression of novel markers in cell subsets. f. Expression of specific markers in cell subsets. g. Pathway showing that angiotensinogen is produced by WNT5B+ fibroblasts, renin by BEST4+ enterocytes, Angiotensin Converting Enzyme (ACE) by epithelial and endothelial cells, and the angiotensin receptor AGTR1 by WNT2B+ fibroblasts and pericytes. h. Heatmap showing expression of cell type specific markers.

FIG. **27**—Shifts in Cell Populations in UC. a. cell frequencies across samples. b. distribution of"pseudotime" values along each of the absorptive and secretory branches. c. general epithelial markers for inflamed cells. d. general innate immune markers for inflamed cells. e. general adaptive immune markers for inflamed cells. f. specific epithelial markers for inflamed cells. g. specific innate immune markers for inflamed cells. h. specific adaptive immune markers for inflamed cells. i. cell frequencies across samples. i. cell frequencies across samples.

FIG. **28**—Inflammatory pathways. a. Violin plots showing expression of IL-17, cytotoxicity, and co-inhibitory signatures in healthy, non-inflamed and inflamed samples. b. Heatmaps comparing cytokines between inflamed tissue, non-inflamed tissue and healthy tissue. c. Anti-TNF violin plots. Plot showing fold change of TNF signaling. d. TNF signature compared to the drug resistance signature and drug susceptibility signature in cell subsets. e. heatmap showing changes in the expression of pathways related to nutrient sensing, stress, and inflammation across all cell types. f. Expression of drug resistance signature genes in subsets.

FIG. **29**—Cell-Cell Network Rewiring and GWAS. a. Healthy cell-cell network. b. Non-inflamed cell-cell network c. Inflamed cell-cell network. d. shows ligand expression correlated with the frequency of the cells expressing its cognate receptor. e. LASSO regression analysis to predict the frequency of each cell subset using the expression levels of all cognate ligands of its receptors in other cells.

FIG. **30**—a. Heatmap of 53 IBD-associated GWAS genes onto the colon cell atlas. b,c. plot comparing GWAS expression in subsets for healthy and inflamed cells.

FIG. **31**—Barplots showing the fraction of cells in the samples.

FIG. **32**—Heatmap showing expression of transcription factors across all cells, healthy cells and UC cells.

FIG. **33**—Heatmap showing expression of G protein-coupled receptors (GPRC) across all cells, healthy cells and UC cells.

FIG. **34**—Heatmap showing expression of transporters across all cells, healthy cells and UC cells.

FIG. **35**—Heatmap showing expression of cytokines across all cells, healthy cells and UC cells.

FIG. **36**—Heatmap showing expression of pattern recognition receptors (PRR) across all cells, healthy cells and UC cells.

FIG. **37**—Univariate analysis (with Fisher's exact test) on each cell frequency.

FIG. **38**—illustrates IgG class switching in healthy and inflamed tissues.

FIG. **39**—a. Volcano plot showing general epithelial markers for uninflamed cells. b. Volcano plot showing general fibroblast markers for uninflamed cells. c. Volcano plot showing general immune markers for uninflamed cells. d. Volcano plot showing cell specific epithelial markers for uninflamed cells. e. Volcano plot showing cell specific fibroblast markers for uninflamed cells. f. Volcano plot showing cell specific immune markers for uninflamed cells.

FIG. **40**—Most cell intrinsic expression changes in UC are shared between inflamed and uninflamed regions. a. general pan compartment and subset specific epithelial markers for inflamed and uninflamed cells. b. general pan compartment and subset specific stroma markers for inflamed and uninflamed cells. c. general pan compartment and subset specific immune markers for inflamed and uninflamed cells.

FIG. **41**—A shift in TNF source to CAIF may underlie resistance to anti-TNF therapy. a. Plot showing fold change of TNF signaling. b. anti-TNF violin plots.

DETAILED DESCRIPTION OF THE EXAMPLE EMBODIMENTS

General Definitions

Unless defined otherwise, technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure pertains. Definitions of common terms and techniques in molecular biology may be found in Molecular Cloning: A Laboratory Manual, 2nd edition (1989) (Sambrook, Fritsch, and Maniatis); Molecular Cloning: A Laboratory Manual, 4th edition (2012) (Green and Sambrook); Current Protocols in Molecular Biology (1987) (F. M. Ausubel et al. eds.); the series Methods in Enzymology (Academic Press, Inc.): PCR 2: A Practical Approach (1995) (M. J. MacPherson, B. D. Hames, and G. R. Taylor eds.): Antibodies, A Laboratory Manual (1988) (Harlow and Lane, eds.): Antibodies A Laboratory Manual, 2nd edition 2013 (E. A. Greenfield ed.); Animal Cell Culture (1987) (R. I. Freshney, ed.); Benjamin Lewin, Genes IX, published by Jones and Bartlet, 2008 (ISBN 0763752223); Kendrew et al. (eds.), The Encyclopedia of Molecular Biology, published by Blackwell Science Ltd., 1994 (ISBN 0632021829); Robert A. Meyers (ed.), Molecular Biology and Biotechnology: a Comprehensive Desk Reference, published by VCH Publishers, Inc., 1995 (ISBN 9780471185710); Singleton et al., Dictionary of Microbiology and Molecular Biology 2nd ed., J. Wiley & Sons (New York, N.Y. 1994), March, Advanced Organic Chemistry Reactions, Mechanisms and Structure 4th ed., John Wiley & Sons (New York, N.Y. 1992); and Marten H. Hofker and Jan van Deursen, Transgenic Mouse Methods and Protocols, 2nd edition (2011).

As used herein, the singular forms "a", "an", and "the" include both singular and plural referents unless the context clearly dictates otherwise.

The term "optional" or "optionally" means that the subsequent described event, circumstance or substituent may or may not occur, and that the description includes instances where the event or circumstance occurs and instances where it does not.

The recitation of numerical ranges by endpoints includes all numbers and fractions subsumed within the respective ranges, as well as the recited endpoints.

The terms "about" or "approximately" as used herein when referring to a measurable value such as a parameter, an amount, a temporal duration, and the like, are meant to encompass variations of and from the specified value, such as variations of +/−10% or less, +/−5% or less, +/−1% or less, and +/−0.1% or less of and from the specified value, insofar such variations are appropriate to perform in the disclosed invention. It is to be understood that the value to which the modifier "about" or "approximately" refers is itself also specifically, and preferably, disclosed.

Reference throughout this specification to "one embodiment", "an embodiment," "an example embodiment," means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, appearances of the phrases "in one embodiment," "in an embodiment," or "an example embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment, but may. Furthermore, the particular features, structures or characteristics may be combined in any suitable manner, as would be apparent to a person skilled in the art from this disclosure, in one or more embodiments. Furthermore, while some embodiments described herein include some but not other features included in other embodiments, combinations of features of different embodiments are meant to be within the scope of the invention. For example, in the appended claims, any of the claimed embodiments can be used in any combination.

All publications, published patent documents, and patent applications cited in this application are indicative of the level of skill in the art(s) to which the application pertains. All publications, published patent documents, and patent applications cited herein are hereby incorporated by reference to the same extent as though each individual publication, published patent document, or patent application was specifically and individually indicated as being incorporated by reference.

Overview

Embodiments disclosed herein provide for a human cell atlas of the colon from healthy and diseased subjects. Applicants identified additional phenotypic markers for these cells in the lamina propria and addressed the role of these location-specific regulatory cells in the prevention and the resolution of intestinal inflammation in human UC. The atlas was obtained by single sequencing of about 117,819 cells. By sequencing single cells from biopsies that are routinely collected during the treatment of IBD, Applicants were able to generate complete molecular profiles of the disease within each patient at single cell resolution. This single cell census of the human colon during health and

disease revealed nearly all disease-relevant cell types, with the notable exception of neutrophils, and will serve as a foundational resource for the scientific community. Surprisingly, the analysis revealed new cell types and states in the colon, including a subset of chemosensory epithelial cells that may detect pH and contribute to sour taste perception in the colon, and several disease-specific cell subsets whose contributions to IBD were largely unknown, including M cells, CAIFs, inflammatory monocytes, and $CD8^{+}IL\text{-}17^{+}$ T cells. The analysis provides a framework for using sc-RNA-Seq to understand complex diseases: first, mapping cell types and cell states within healthy and diseased tissue, identifying changes in cell proportions with disease, and partitioning changes in gene expression into those that are shared by cell lineages or unique to cell subsets; then, integrating these analyses to understand how changes in gene expression propagate into changes in cell-cell interactions, identifying the "cell-of-action" for GWAS genes, and understanding the complex genetic risk factors for the disease.

The present invention discloses novel markers for cell types. Moreover, genes associated with disease are identified in the colon and colon specific cell types. The invention provides for diagnostic assays based on gene markers and cell composition, as well as target cell types that express genes associated with disease. The invention provides for modulating cell types and cell-cell interactions in the gut (e.g., for treating IBD). Finally, disclosed are novel cell types and methods of quantitating, detecting and isolating the cell types

Biomarkers and Signatures

The invention further relates to various biomarkers for quantitating, detecting or isolating gut cell subpopulations. The populations may be detected by detecting one or more biomarkers in a sample.

The term "biomarker" is widespread in the art and commonly broadly denotes a biological molecule, more particularly an endogenous biological molecule, and/or a detectable portion thereof, whose qualitative and/or quantitative evaluation in a tested object (e.g., in or on a cell, cell population, tissue, organ, or organism, e.g., in a biological sample of a subject) is predictive or informative with respect to one or more aspects of the tested object's phenotype and/or genotype. The terms "marker" and "biomarker" may be used interchangeably throughout this specification. Biomarkers as intended herein may be nucleic acid-based or peptide-, polypeptide- and/or protein-based. For example, a marker may be comprised of peptide(s), polypeptide(s) and/or protein(s) encoded by a given gene, or of detectable portions thereof. Further, whereas the term "nucleic acid" generally encompasses DNA, RNA and DNA/RNA hybrid molecules, in the context of markers the term may typically refer to heterogeneous nuclear RNA (hnRNA), pre-mRNA, messenger RNA (mRNA), or complementary DNA (cDNA), or detectable portions thereof. Such nucleic acid species are particularly useful as markers, since they contain qualitative and/or quantitative information about the expression of the gene. Particularly preferably, a nucleic acid-based marker may encompass mRNA of a given gene, or cDNA made of the mRNA, or detectable portions thereof. Any such nucleic acid(s), peptide(s), polypeptide(s) and/or protein(s) encoded by or produced from a given gene are encompassed by the term "gene product(s)".

Preferably, markers as intended herein may be extracellular or cell surface markers, as methods to measure extracellular or cell surface marker(s) need not disturb the integrity of the cell membrane and may not require fixation/permeabilization of the cells.

Unless otherwise apparent from the context, reference herein to any marker, such as a peptide, polypeptide, protein, or nucleic acid, may generally also encompass modified forms of said marker, such as bearing post-expression modifications including, for example, phosphorylation, glycosylation, lipidation, methylation, cysteinylation, sulphonation, glutathionylation, acetylation, oxidation of methionine to methionine sulphoxide or methionine sulphone, and the like.

The term "peptide" as used throughout this specification preferably refers to a polypeptide as used herein consisting essentially of 50 amino acids or less, e.g., 45 amino acids or less, preferably 40 amino acids or less, e.g., 35 amino acids or less, more preferably 30 amino acids or less, e.g., 25 or less, 20 or less, 15 or less, 10 or less or 5 or less amino acids.

The term "polypeptide" as used throughout this specification generally encompasses polymeric chains of amino acid residues linked by peptide bonds. Hence, insofar a protein is only composed of a single polypeptide chain, the terms "protein" and "polypeptide" may be used interchangeably herein to denote such a protein. The term is not limited to any minimum length of the polypeptide chain. The term may encompass naturally, recombinantly, semi-synthetically or synthetically produced polypeptides. The term also encompasses polypeptides that carry one or more co- or post-expression-type modifications of the polypeptide chain, such as, without limitation, glycosylation, acetylation, phosphorylation, sulfonation, methylation, ubiquitination, signal peptide removal, N-terminal Met removal, conversion of pro-enzymes or pre-hormones into active forms, etc. The term further also includes polypeptide variants or mutants which carry amino acid sequence variations vis-à-vis a corresponding native polypeptide, such as, e.g., amino acid deletions, additions and/or substitutions. The term contemplates both full-length polypeptides and polypeptide parts or fragments, e.g., naturally-occurring polypeptide parts that ensue from processing of such full-length polypeptides.

The term "protein" as used throughout this specification generally encompasses macromolecules comprising one or more polypeptide chains, i.e., polymeric chains of amino acid residues linked by peptide bonds. The term may encompass naturally, recombinantly, semi-synthetically or synthetically produced proteins. The term also encompasses proteins that carry one or more co- or post-expression-type modifications of the polypeptide chain(s), such as, without limitation, glycosylation, acetylation, phosphorylation, sulfonation, methylation, ubiquitination, signal peptide removal, N-terminal Met removal, conversion of pro-enzymes or pre-hormones into active forms, etc. The term further also includes protein variants or mutants which carry amino acid sequence variations vis-à-vis a corresponding native protein, such as, e.g., amino acid deletions, additions and/or substitutions. The term contemplates both full-length proteins and protein parts or fragments, e.g., naturally-occurring protein parts that ensue from processing of such full-length proteins.

The reference to any marker, including any peptide, polypeptide, protein, or nucleic acid, corresponds to the marker commonly known under the respective designations in the art. The terms encompass such markers of any organism where found, and particularly of animals, preferably warm-blooded animals, more preferably vertebrates, yet more preferably mammals, including humans and non-human mammals, still more preferably of humans.

The terms particularly encompass such markers, including any peptides, polypeptides, proteins, or nucleic acids, with a native sequence, i.e., ones of which the primary sequence is the same as that of the markers found in or derived from nature. A skilled person understands that native sequences may differ between different species due to genetic divergence between such species. Moreover, native sequences may differ between or within different individuals of the same species due to normal genetic diversity (variation) within a given species. Also, native sequences may differ between or even within different individuals of the same species due to somatic mutations, or post-transcriptional or post-translational modifications. Any such variants or isoforms of markers are intended herein. Accordingly, all sequences of markers found in or derived from nature are considered "native". The terms encompass the markers when forming a part of a living organism, organ, tissue or cell, when forming a part of a biological sample, as well as when at least partly isolated from such sources. The terms also encompass markers when produced by recombinant or synthetic means.

In certain embodiments, markers, including any peptides, polypeptides, proteins, or nucleic acids, may be human, i.e., their primary sequence may be the same as a corresponding primary sequence of or present in a naturally occurring human markers. Hence, the qualifier "human" in this connection relates to the primary sequence of the respective markers, rather than to their origin or source. For example, such markers may be present in or isolated from samples of human subjects or may be obtained by other means (e.g., by recombinant expression, cell-free transcription or translation, or non-biological nucleic acid or peptide synthesis).

The reference herein to any marker, including any peptide, polypeptide, protein, or nucleic acid, also encompasses fragments thereof. Hence, the reference herein to measuring (or measuring the quantity of) any one marker may encompass measuring the marker and/or measuring one or more fragments thereof.

For example, any marker and/or one or more fragments thereof may be measured collectively, such that the measured quantity corresponds to the sum amounts of the collectively measured species. In another example, any marker and/or one or more fragments thereof may be measured each individually. The terms encompass fragments arising by any mechanism, in vivo and/or in vitro, such as, without limitation, by alternative transcription or translation, exo- and/or endo-proteolysis, exo- and/or endo-nucleolysis, or degradation of the peptide, polypeptide, protein, or nucleic acid, such as, for example, by physical, chemical and/or enzymatic proteolysis or nucleolysis.

The term "fragment" as used throughout this specification with reference to a peptide, polypeptide, or protein generally denotes a portion of the peptide, polypeptide, or protein, such as typically an N- and/or C-terminally truncated form of the peptide, polypeptide, or protein. Preferably, a fragment may comprise at least about 30%, e.g., at least about 50% or at least about 70%, preferably at least about 80%, e.g., at least about 85%, more preferably at least about 90%, and yet more preferably at least about 95% or even about 99% of the amino acid sequence length of said peptide, polypeptide, or protein. For example, insofar not exceeding the length of the full-length peptide, polypeptide, or protein, a fragment may include a sequence of ≥5 consecutive amino acids, or ≥10 consecutive amino acids, or ≥20 consecutive amino acids, or ≥30 consecutive amino acids, e.g., ≥40 consecutive amino acids, such as for example ≥50 consecutive amino acids, e.g., ≥60, ≥70, ≥80, ≥90, ≥100, ≥200, ≥300, ≥400, ≥500 or ≥600 consecutive amino acids of the corresponding full-length peptide, polypeptide, or protein.

The term "fragment" as used throughout this specification with reference to a nucleic acid (polynucleotide) generally denotes a 5'- and/or 3'-truncated form of a nucleic acid. Preferably, a fragment may comprise at least about 30%, e.g., at least about 50% or at least about 70%, preferably at least about 80%, e.g., at least about 85%, more preferably at least about 90%, and yet more preferably at least about 95% or even about 99% of the nucleic acid sequence length of said nucleic acid. For example, insofar not exceeding the length of the full-length nucleic acid, a fragment may include a sequence of ≥5 consecutive nucleotides, or ≥10 consecutive nucleotides, or ≥20 consecutive nucleotides, or ≥30 consecutive nucleotides, e.g., ≥40 consecutive nucleotides, such as for example ≥50 consecutive nucleotides, e.g., ≥60, ≥70, ≥80, ≥90, ≥100, ≥200, ≥300, ≥400, ≥500 or ≥600 consecutive nucleotides of the corresponding full-length nucleic acid.

Cells such as immune cells as disclosed herein may in the context of the present specification be said to "comprise the expression" or conversely to "not express" one or more markers, such as one or more genes or gene products; or be described as "positive" or conversely as "negative" for one or more markers, such as one or more genes or gene products; or be said to "comprise" a defined "gene or gene product signature".

Such terms are commonplace and well-understood by the skilled person when characterizing cell phenotypes. By means of additional guidance, when a cell is said to be positive for or to express or comprise expression of a given marker, such as a given gene or gene product, a skilled person would conclude the presence or evidence of a distinct signal for the marker when carrying out a measurement capable of detecting or quantifying the marker in or on the cell. Suitably, the presence or evidence of the distinct signal for the marker would be concluded based on a comparison of the measurement result obtained for the cell to a result of the same measurement carried out for a negative control (for example, a cell known to not express the marker) and/or a positive control (for example, a cell known to express the marker). Where the measurement method allows for a quantitative assessment of the marker, a positive cell may generate a signal for the marker that is at least 1.5-fold higher than a signal generated for the marker by a negative control cell or than an average signal generated for the marker by a population of negative control cells, e.g., at least 2-fold, at least 4-fold, at least 10-fold, at least 20-fold, at least 30-fold, at least 40-fold, at least 50-fold higher or even higher. Further, a positive cell may generate a signal for the marker that is 3.0 or more standard deviations, e.g., 3.5 or more, 4.0 or more, 4.5 or more, or 5.0 or more standard deviations, higher than an average signal generated for the marker by a population of negative control cells.

The present invention is also directed to signatures and uses thereof. As used herein a "signature" may encompass any gene or genes, protein or proteins, or epigenetic element(s) whose expression profile or whose occurrence is associated with a specific cell type, subtype, or cell state of a specific cell type or subtype within a population of cells (e.g., tumor infiltrating lymphocytes). In certain embodiments, the expression of the $CD8^+$ TIL signatures are dependent on epigenetic modification of the genes or regulatory elements associated with the genes. Thus, in certain embodiments, use of signature genes includes epigenetic modifications that may be detected or modulated. For ease of discussion, when discussing gene expression, any gene or

genes, protein or proteins, or epigenetic element(s) may be substituted. Reference to a gene name throughout the specification encompasses the human gene, mouse gene and all other orthologues as known in the art in other organisms. As used herein, the terms "signature", "expression profile", or "expression program" may be used interchangeably. It is to be understood that also when referring to proteins (e.g. differentially expressed proteins), such may fall within the definition of "gene" signature. Levels of expression or activity or prevalence may be compared between different cells in order to characterize or identify for instance signatures specific for cell (sub)populations. Increased or decreased expression or activity of signature genes may be compared between different cells in order to characterize or identify for instance specific cell (sub)populations. The detection of a signature in single cells may be used to identify and quantitate for instance specific cell (sub)populations. A signature may include a gene or genes, protein or proteins, or epigenetic element(s) whose expression or occurrence is specific to a cell (sub)population, such that expression or occurrence is exclusive to the cell (sub) population. A gene signature as used herein, may thus refer to any set of up- and down-regulated genes that are representative of a cell type or subtype. A gene signature as used herein, may also refer to any set of up- and down-regulated genes between different cells or cell (sub)populations derived from a gene-expression profile. For example, a gene signature may comprise a list of genes differentially expressed in a distinction of interest.

The signature as defined herein (being it a gene signature, protein signature or other genetic or epigenetic signature) can be used to indicate the presence of a cell type, a subtype of the cell type, the state of the microenvironment of a population of cells, a particular cell type population or subpopulation, and/or the overall status of the entire cell (sub)population. Furthermore, the signature may be indicative of cells within a population of cells in vivo. The signature may also be used to suggest for instance particular therapies, or to follow up treatment, or to suggest ways to modulate immune systems. The signatures of the present invention may be discovered by analysis of expression profiles of single-cells within a population of cells from isolated samples (e.g. tumor samples), thus allowing the discovery of novel cell subtypes or cell states that were previously invisible or unrecognized. The presence of subtypes or cell states may be determined by subtype specific or cell state specific signatures. The presence of these specific cell (sub)types or cell states may be determined by applying the signature genes to bulk sequencing data in a sample. Not being bound by a theory the signatures of the present invention may be microenvironment specific, such as their expression in a particular spatio-temporal context. Not being bound by a theory, signatures as discussed herein are specific to a particular pathological context. Not being bound by a theory, a combination of cell subtypes having a particular signature may indicate an outcome. Not being bound by a theory, the signatures can be used to deconvolute the network of cells present in a particular pathological condition. Not being bound by a theory the presence of specific cells and cell subtypes are indicative of a particular response to treatment, such as including increased or decreased susceptibility to treatment. The signature may indicate the presence of one particular cell type.

The signature according to certain embodiments of the present invention may comprise or consist of one or more genes, proteins and/or epigenetic elements, such as for instance 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of two or more genes, proteins and/or epigenetic elements, such as for instance 2, 3, 4, 5, 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of three or more genes, proteins and/or epigenetic elements, such as for instance 3, 4, 5, 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of four or more genes, proteins and/or epigenetic elements, such as for instance 4, 5, 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of five or more genes, proteins and/or epigenetic elements, such as for instance 5, 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of six or more genes, proteins and/or epigenetic elements, such as for instance 6, 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of seven or more genes, proteins and/or epigenetic elements, such as for instance 7, 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of eight or more genes, proteins and/or epigenetic elements, such as for instance 8, 9, 10 or more. In certain embodiments, the signature may comprise or consist of nine or more genes, proteins and/or epigenetic elements, such as for instance 9, 10 or more. In certain embodiments, the signature may comprise or consist of ten or more genes, proteins and/or epigenetic elements, such as for instance 10, 11, 12, 13, 14, 15, or more. It is to be understood that a signature according to the invention may for instance also include genes or proteins as well as epigenetic elements combined.

In certain embodiments, a signature is characterized as being specific for a particular cell or cell (sub)population state if it is upregulated or only present, detected or detectable in that particular cell or cell (sub)population state (e.g., disease or healthy), or alternatively is downregulated or only absent, or undetectable in that particular cell or cell (sub) population state. In this context, a signature consists of one or more differentially expressed genes/proteins or differential epigenetic elements when comparing different cells or cell (sub)populations, including comparing different gut cell or gut cell (sub)populations, as well as comparing gut cell or gut cell (sub)populations with healthy or disease (sub) populations. It is to be understood that "differentially expressed" genes/proteins include genes/proteins which are up- or down-regulated as well as genes/proteins which are turned on or off. When referring to up- or down-regulation, in certain embodiments, such up- or down-regulation is preferably at least two-fold, such as two-fold, three-fold, four-fold, five-fold, or more, such as for instance at least ten-fold, at least 20-fold, at least 30-fold, at least 40-fold, at least 50-fold, or more. Alternatively, or in addition, differential expression may be determined based on common statistical tests, as is known in the art.

As discussed herein, differentially expressed genes/proteins, or differential epigenetic elements may be differentially expressed on a single cell level, or may be differentially expressed on a cell population level. Preferably, the differentially expressed genes/proteins or epigenetic elements as discussed herein, such as constituting the gene signatures as discussed herein, when as to the cell population or subpopulation level, refer to genes that are differentially expressed in all or substantially all cells of the population or subpopulation (such as at least 80%, preferably at least 90%, such as at least 95% of the individual cells). This allows one to define a particular subpopulation of immune cells. As referred to herein, a "subpopulation" of cells preferably refers to a particular subset of cells of a particular cell type which can be distinguished or are uniquely identifiable and

set apart from other cells of this cell type. The cell subpopulation may be phenotypically characterized, and is preferably characterized by the signature as discussed herein. A cell (sub)population as referred to herein may constitute of a (sub)population of cells of a particular cell type characterized by a specific cell state.

When referring to induction, or alternatively suppression of a particular signature, preferable is meant induction or alternatively suppression (or upregulation or downregulation) of at least one gene/protein and/or epigenetic element of the signature, such as for instance at least two, at least three, at least four, at least five, at least six, or all genes/proteins and/or epigenetic elements of the signature.

Various aspects and embodiments of the invention may involve analyzing gene signatures, protein signature, and/or other genetic or epigenetic signature based on single cell analyses (e.g. single cell RNA sequencing) or alternatively based on cell population analyses, as is defined herein elsewhere.

In certain example embodiments, the signature genes may be used to deconvolute the network of cells present in a tumor based on comparing them to data from bulk analysis of a tumor sample. In certain example embodiments, the presence of specific immune cells and immune cell subtypes may be indicative of tumor growth, invasiveness and/or resistance to treatment. In one example embodiment, detection of one or more signature genes may indicate the presence of a particular cell type or cell types. In certain example embodiments, the presence of immune cell types within a tumor may indicate that the tumor will be sensitive to a treatment (e.g., checkpoint blockade therapy). In one embodiment, the signature genes of the present invention are applied to bulk sequencing data from a tumor sample obtained from a subject, such that information relating to disease outcome and personalized treatments is determined.

Detection of Gut Cell Sub-Populations

In one embodiment, the method comprises detecting or quantifying gut cells in a biological sample obtained from the gastrointestinal tract (e.g., colon, intestine). A marker, for example a gene or gene product, for example a peptide, polypeptide, protein, or nucleic acid, or a group of two or more markers, is "detected" or "measured" in a tested object (e.g., in or on a cell, cell population, tissue, organ, or organism, e.g., in a biological sample of a subject) when the presence or absence and/or quantity of said marker or said group of markers is detected or determined in the tested object, preferably substantially to the exclusion of other molecules and analytes, e.g., other genes or gene products.

The terms "increased" or "increase" or "upregulated" or "upregulate" as used herein generally mean an increase by a statically significant amount. For avoidance of doubt, "increased" means a statistically significant increase of at least 10% as compared to a reference level, including an increase of at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100% or more, including, for example at least 2-fold, at least 3-fold, at least 4-fold, at least 5-fold, at least 10-fold increase or greater as compared to a reference level, as that term is defined herein.

The term "reduced" or "reduce" or "decrease" or "decreased" or "downregulate" or "downregulated" as used herein generally means a decrease by a statistically significant amount relative to a reference. For avoidance of doubt, "reduced" means statistically significant decrease of at least 10% as compared to a reference level, for example a decrease by at least 20%, at least 30%, at least 40%, at least 50%, or at least 60%, or at least 70%, or at least 80%, at least 90% or more, up to and including a 100% decrease (i.e., absent level as compared to a reference sample), or any decrease between 10-100% as compared to a reference level, as that.

The terms "sample" or "biological sample" as used throughout this specification include any biological specimen obtained from a subject. Particularly useful samples are those known to comprise, or expected or predicted to comprise gut cells as taught herein. Preferably, a sample may be readily obtainable by minimally invasive methods, such as blood collection or tissue biopsy, allowing the removal/isolation/provision of the sample from the subject (e.g., colonoscopy).

The terms "quantity", "amount" and "level" are synonymous and generally well-understood in the art. The terms as used throughout this specification may particularly refer to an absolute quantification of a marker in a tested object (e.g., in or on a cell, cell population, tissue, organ, or organism, e.g., in a biological sample of a subject), or to a relative quantification of a marker in a tested object, i.e., relative to another value such as relative to a reference value, or to a range of values indicating a base-line of the marker. Such values or ranges may be obtained as conventionally known.

An absolute quantity of a marker may be advantageously expressed as weight or as molar amount, or more commonly as a concentration, e.g., weight per volume or mol per volume. A relative quantity of a marker may be advantageously expressed as an increase or decrease or as a fold-increase or fold-decrease relative to said another value, such as relative to a reference value. Performing a relative comparison between first and second variables (e.g., first and second quantities) may but need not require determining first the absolute values of said first and second variables. For example, a measurement method may produce quantifiable readouts (such as, e.g., signal intensities) for said first and second variables, wherein said readouts are a function of the value of said variables, and wherein said readouts may be directly compared to produce a relative value for the first variable vs. the second variable, without the actual need to first convert the readouts to absolute values of the respective variables.

Reference values may be established according to known procedures previously employed for other cell populations, biomarkers and gene or gene product signatures. For example, a reference value may be established in an individual or a population of individuals characterized by a particular diagnosis, prediction and/or prognosis of said disease or condition (i.e., for whom said diagnosis, prediction and/or prognosis of the disease or condition holds true). Such population may comprise without limitation 2 or more, 10 or more, 100 or more, or even several hundred or more individuals.

A "deviation" of a first value from a second value may generally encompass any direction (e.g., increase: first value>second value; or decrease: first value<second value) and any extent of alteration.

For example, a deviation may encompass a decrease in a first value by, without limitation, at least about 10% (about 0.9-fold or less), or by at least about 20% (about 0.8-fold or less), or by at least about 30% (about 0.7-fold or less), or by at least about 40% (about 0.6-fold or less), or by at least about 50% (about 0.5-fold or less), or by at least about 60% (about 0.4-fold or less), or by at least about 70% (about 0.3-fold or less), or by at least about 80% (about 0.2-fold or less), or by at least about 90% (about 0.1-fold or less), relative to a second value with which a comparison is being made.

For example, a deviation may encompass an increase of a first value by, without limitation, at least about 10% (about 1.1-fold or more), or by at least about 20% (about 1.2-fold or more), or by at least about 30% (about 1.3-fold or more), or by at least about 40% (about 1.4-fold or more), or by at least about 50% (about 1.5-fold or more), or by at least about 60% (about 1.6-fold or more), or by at least about 70% (about 1.7-fold or more), or by at least about 80% (about 1.8-fold or more), or by at least about 90% (about 1.9-fold or more), or by at least about 100% (about 2-fold or more), or by at least about 150% (about 2.5-fold or more), or by at least about 200% (about 3-fold or more), or by at least about 500% (about 6-fold or more), or by at least about 700% (about 8-fold or more), or like, relative to a second value with which a comparison is being made.

Preferably, a deviation may refer to a statistically significant observed alteration. For example, a deviation may refer to an observed alteration which falls outside of error margins of reference values in a given population (as expressed, for example, by standard deviation or standard error, or by a predetermined multiple thereof, e.g., ±1×SD or ±2×SD or ±3×SD, or ±1×SE or ±2×SE or ±3×SE). Deviation may also refer to a value falling outside of a reference range defined by values in a given population (for example, outside of a range which comprises ≥40%, ≥50%, ≥60%, ≥70%, ≥75% or 80% or ≥85% or 90% or ≥95% or even 100% of values in said population).

In a further embodiment, a deviation may be concluded if an observed alteration is beyond a given threshold or cut-off. Such threshold or cut-off may be selected as generally known in the art to provide for a chosen sensitivity and/or specificity of the prediction methods, e.g., sensitivity and/or specificity of at least 50%, or at least 60%, or at least 70%, or at least 80%, or at least 85%, or at least 90%, or at least 95%.

For example, receiver-operating characteristic (ROC) curve analysis can be used to select an optimal cut-off value of the quantity of a given immune cell population, biomarker or gene or gene product signatures, for clinical use of the present diagnostic tests, based on acceptable sensitivity and specificity, or related performance measures which are well-known per se, such as positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR−), Youden index, or similar.

The terms "diagnosis" and "monitoring" are commonplace and well-understood in medical practice. By means of further explanation and without limitation the term "diagnosis" generally refers to the process or act of recognizing, deciding on or concluding on a disease or condition in a subject on the basis of symptoms and signs and/or from results of various diagnostic procedures (such as, for example, from knowing the presence, absence and/or quantity of one or more biomarkers characteristic of the diagnosed disease or condition).

The term "monitoring" generally refers to the follow-up of a disease or a condition in a subject for any changes which may occur over time.

The terms "prognosing" or "prognosis" generally refer to an anticipation on the progression of a disease or condition and the prospect (e.g., the probability, duration, and/or extent) of recovery. A good prognosis of the diseases or conditions taught herein may generally encompass anticipation of a satisfactory partial or complete recovery from the diseases or conditions, preferably within an acceptable time period. A good prognosis of such may more commonly encompass anticipation of not further worsening or aggravating of such, preferably within a given time period. A poor prognosis of the diseases or conditions as taught herein may generally encompass anticipation of a substandard recovery and/or unsatisfactorily slow recovery, or to substantially no recovery or even further worsening of such.

The terms also encompass prediction of a disease. The terms "predicting" or "prediction" generally refer to an advance declaration, indication or foretelling of a disease or condition in a subject not (yet) having said disease or condition. For example, a prediction of a disease or condition in a subject may indicate a probability, chance or risk that the subject will develop said disease or condition, for example within a certain time period or by a certain age. Said probability, chance or risk may be indicated inter alia as an absolute value, range or statistics, or may be indicated relative to a suitable control subject or subject population (such as, e.g., relative to a general, normal or healthy subject or subject population). Hence, the probability, chance or risk that a subject will develop a disease or condition may be advantageously indicated as increased or decreased, or as fold-increased or fold-decreased relative to a suitable control subject or subject population. As used herein, the term "prediction" of the conditions or diseases as taught herein in a subject may also particularly mean that the subject has a 'positive' prediction of such, i.e., that the subject is at risk of having such (e.g., the risk is significantly increased vis-à-vis a control subject or subject population). The term "prediction of no" diseases or conditions as taught herein as described herein in a subject may particularly mean that the subject has a 'negative' prediction of such, i.e., that the subject's risk of having such is not significantly increased vis-à-vis a control subject or subject population.

Methods of Detection and Isolation of Cell Types Using Biomarkers

In certain embodiments, the gut cell types may be detected, quantified or isolated using a technique selected from the group consisting of flow cytometry, mass cytometry, fluorescence activated cell sorting (FACS), fluorescence microscopy, affinity separation, magnetic cell separation, microfluidic separation, RNA-seq (e.g., bulk or single cell), quantitative PCR, MERFISH (multiplex (in situ) RNA FISH) and combinations thereof. The technique may employ one or more agents capable of specifically binding to one or more gene products expressed or not expressed by the gut cells, preferably on the cell surface of the gut cells. The one or more agents may be one or more antibodies. Other methods including absorbance assays and colorimetric assays are known in the art and may be used herein.

Depending on factors that can be evaluated and decided on by a skilled person, such as, inter alia, the type of a marker (e.g., peptide, polypeptide, protein, or nucleic acid), the type of the tested object (e.g., a cell, cell population, tissue, organ, or organism, e.g., the type of biological sample of a subject, e.g., whole blood, plasma, serum, tissue biopsy), the expected abundance of the marker in the tested object, the type, robustness, sensitivity and/or specificity of the detection method used to detect the marker, etc., the marker may be measured directly in the tested object, or the tested object may be subjected to one or more processing steps aimed at achieving an adequate measurement of the marker.

In other example embodiments, detection of a marker may include immunological assay methods, wherein the ability of an assay to separate, detect and/or quantify a marker (such as, preferably, peptide, polypeptide, or protein) is conferred by specific binding between a separable, detectable and/or quantifiable immunological binding agent (anti-

body) and the marker. Immunological assay methods include without limitation immunohistochemistry, immunocytochemistry, flow cytometry, mass cytometry, fluorescence activated cell sorting (FACS), fluorescence microscopy, fluorescence based cell sorting using microfluidic systems, immunoaffinity adsorption based techniques such as affinity chromatography, magnetic particle separation, magnetic activated cell sorting or bead based cell sorting using microfluidic systems, enzyme-linked immunosorbent assay (ELISA) and ELISPOT based techniques, radioimmunoassay (RIA), Western blot, etc.

In certain example embodiments, detection of a marker or signature may include biochemical assay methods, including inter alia assays of enzymatic activity, membrane channel activity, substance-binding activity, gene regulatory activity, or cell signaling activity of a marker, e.g., peptide, polypeptide, protein, or nucleic acid.

In other example embodiments, detection of a marker may include mass spectrometry analysis methods. Generally, any mass spectrometric (MS) techniques that are capable of obtaining precise information on the mass of peptides, and preferably also on fragmentation and/or (partial) amino acid sequence of selected peptides (e.g., in tandem mass spectrometry, MS/MS; or in post source decay, TOF MS), may be useful herein for separation, detection and/or quantification of markers (such as, preferably, peptides, polypeptides, or proteins). Suitable peptide MS and MS/MS techniques and systems are well-known per se (see, e.g., Methods in Molecular Biology, vol. 146: "Mass Spectrometry of Proteins and Peptides", by Chapman, ed., Humana Press 2000, ISBN 089603609x; Biemann 1990. Methods Enzymol 193: 455-79; or Methods in Enzymology, vol. 402: "Biological Mass Spectrometry", by Burlingame, ed., Academic Press 2005, ISBN 9780121828073) and may be used herein. MS arrangements, instruments and systems suitable for biomarker peptide analysis may include, without limitation, matrix-assisted laser desorption/ionisation time-of-flight (MALDI-TOF) MS; MALDI-TOF post-source-decay (PSD); MALDI-TOF/TOF; surface-enhanced laser desorption/ionization time-of-flight mass spectrometry (SELDI-TOF) MS; electrospray ionization mass spectrometry (ESI-MS); ESI-MS/MS; ESI-MS/(MS)n (n is an integer greater than zero); ESI 3D or linear (2D) ion trap MS; ESI triple quadrupole MS; ESI quadrupole orthogonal TOF (Q-TOF); ESI Fourier transform MS systems; desorption/ionization on silicon (DIOS); secondary ion mass spectrometry (SIMS); atmospheric pressure chemical ionization mass spectrometry (APCI-MS); APCI-MS/MS; APCI-(MS)n; atmospheric pressure photoionization mass spectrometry (APPI-MS); APPI-MS/MS; and APPI-(MS)n. Peptide ion fragmentation in tandem MS (MS/MS) arrangements may be achieved using manners established in the art, such as, e.g., collision induced dissociation (CID). Detection and quantification of markers by mass spectrometry may involve multiple reaction monitoring (MRM), such as described among others by Kuhn et al. 2004 (Proteomics 4: 1175-86). MS peptide analysis methods may be advantageously combined with upstream peptide or protein separation or fractionation methods, such as for example with the chromatographic and other methods.

In other example embodiments, detection of a marker may include chromatography methods. In a one example embodiment, chromatography refers to a process in which a mixture of substances (analytes) carried by a moving stream of liquid or gas ("mobile phase") is separated into components as a result of differential distribution of the analytes, as they flow around or over a stationary liquid or solid phase ("stationary phase"), between said mobile phase and said stationary phase. The stationary phase may be usually a finely divided solid, a sheet of filter material, or a thin film of a liquid on the surface of a solid, or the like. Chromatography may be columnar. While particulars of chromatography are well known in the art, for further guidance see, e.g., Meyer M., 1998, ISBN: 047198373X, and "Practical HPLC Methodology and Applications", Bidlingmeyer, B. A., John Wiley & Sons Inc., 1993. Exemplary types of chromatography include, without limitation, high-performance liquid chromatography (HPLC), normal phase HPLC (NP-HPLC), reversed phase HPLC (RP-HPLC), ion exchange chromatography (IEC), such as cation or anion exchange chromatography, hydrophilic interaction chromatography (HILIC), hydrophobic interaction chromatography (HIC), size exclusion chromatography (SEC) including gel filtration chromatography or gel permeation chromatography, chromatofocusing, affinity chromatography such as immunoaffinity, immobilised metal affinity chromatography, and the like.

In certain embodiments, further techniques for separating, detecting and/or quantifying markers may be used in conjunction with any of the above described detection methods. Such methods include, without limitation, chemical extraction partitioning, isoelectric focusing (IEF) including capillary isoelectric focusing (CIEF), capillary isotachophoresis (CITP), capillary electrochromatography (CEC), and the like, one-dimensional polyacrylamide gel electrophoresis (PAGE), two-dimensional polyacrylamide gel electrophoresis (2D-PAGE), capillary gel electrophoresis (CGE), capillary zone electrophoresis (CZE), micellar electrokinetic chromatography (MEKC), free flow electrophoresis (FFE), etc.

In certain examples, such methods may include separating, detecting and/or quantifying markers at the nucleic acid level, more particularly RNA level, e.g., at the level of hnRNA, pre-mRNA, mRNA, or cDNA. Standard quantitative RNA or cDNA measurement tools known in the art may be used. Non-limiting examples include hybridization-based analysis, microarray expression analysis, digital gene-expression profiling (DGE), RNA-in-situ hybridization (RISH), Northern-blot analysis and the like; PCR, RT-PCR, RT-qPCR, end-point PCR, digital PCR or the like; supported oligonucleotide detection, pyrosequencing, polony cyclic sequencing by synthesis, simultaneous bi-directional sequencing, single-molecule sequencing, single molecule real time sequencing, true single molecule sequencing, hybridization-assisted nanopore sequencing, sequencing by synthesis, single-cell RNA sequencing (sc-RNA seq), or the like. By means of an example, methods to profile the RNA content of large numbers of individual cells have been recently developed.

In certain embodiments, the invention involves plate based single cell RNA sequencing (see, e.g., Picelli, S. et al., 2014, "Full-length RNA-seq from single cells using Smart-seq2" Nature protocols 9, 171-181, doi:10.1038/nprot.2014.006).

In certain embodiments, special microfluidic devices have been developed to encapsulate each cell in an individual drop, associate the RNA of each cell with a 'cell barcode' unique to that cell/drop, measure the expression level of each RNA with sequencing, and then use the cell barcodes to determine which cell each RNA molecule came from. In certain embodiments, single cells are segregated. In these regards, reference is made to Macosko et al., 2015, "Highly Parallel Genome-wide Expression Profiling of Individual Cells Using Nanoliter Droplets" Cell 161, 1202-1214; Inter-

national patent application number PCT/US2015/049178, published as WO2016/040476 on Mar. 17, 2016; Klein et al., 2015, "Droplet Barcoding for Single-Cell Transcriptomics Applied to Embryonic Stem Cells" Cell 161, 1187-1201; International patent application number PCT/US2016/027734, published as WO2016168584A1 on Oct. 20, 2016; Zheng, et al., 2016, "Haplotyping germline and cancer genomes with high-throughput linked-read sequencing" Nature Biotechnology 34, 303-311; Zheng, et al., 2017, "Massively parallel digital transcriptional profiling of single cells" Nat. Commun. 8, 14049 doi: 10.1038/ncomms14049; International patent publication number WO2014210353A2; Zilionis, et al., 2017, "Single-cell barcoding and sequencing using droplet microfluidics" Nat Protoc. January; 12(1):44-73; Cao et al., 2017, "Comprehensive single cell transcriptional profiling of a multicellular organism by combinatorial indexing" bioRxiv preprint first posted online Feb. 2, 2017, doi: dx.doi.org/10.1101/104844; Rosenberg et al., 2017, "Scaling single cell transcriptomics through split pool barcoding" bioRxiv preprint first posted online Feb. 2, 2017, doi: dx.doi.org/10.1101/105163; Vitak, et al., "Sequencing thousands of single-cell genomes with combinatorial indexing" Nature Methods, 14(3):302-308, 2017; Cao, et al., Comprehensive single-cell transcriptional profiling of a multicellular organism. Science, 357(6352): 661-667, 2017; and Gierahn et al., "Seq-Well: portable, low-cost RNA sequencing of single cells at high throughput" Nature Methods 14, 395-398 (2017), all the contents and disclosure of each of which are herein incorporated by reference in their entirety.

In certain embodiments, the invention involves single nucleus RNA sequencing. In this regard reference is made to Swiech et al., 2014, "In vivo interrogation of gene function in the mammalian brain using CRISPR-Cas9" Nature Biotechnology Vol. 33, pp. 102-106; Habib et al., 2016, "Div-Seq: Single-nucleus RNA-Seq reveals dynamics of rare adult newborn neurons" Science, Vol. 353, Issue 6302, pp. 925-928; Habib et al., 2017, "Massively parallel single-nucleus RNA-seq with DroNc-seq" Nat Methods. 2017 October; 14(10):955-958; and International patent application number PCT/US2016/059239, published as WO2017164936 on Sep. 28, 2017, which are herein incorporated by reference in their entirety.

The terms "isolating" or "purifying" as used throughout this specification with reference to a particular component of a composition or mixture (e.g., the tested object such as the biological sample) encompass processes or techniques whereby such component is separated from one or more or (substantially) all other components of the composition or mixture (e.g., the tested object such as the biological sample). The terms do not require absolute purity. Instead, isolating or purifying the component will produce a discrete environment in which the abundance of the component relative to one or more or all other components is greater than in the starting composition or mixture (e.g., the tested object such as the biological sample). A discrete environment may denote a single medium, such as for example a single solution, dispersion, gel, precipitate, etc. Isolating or purifying the specified cells from the tested object such as the biological sample may increase the abundance of the specified cells relative to all other cells comprised in the tested object such as the biological sample, or relative to other cells of a select subset of the cells comprised in the tested object such as the biological sample, e.g., relative to other white blood cells, peripheral blood mononuclear cells, immune cells, antigen presenting cells, or dendritic cells comprised in the tested object such as the biological sample. By means of example, isolating or purifying the specified cells from the tested object such as the biological sample may yield a cell population, in which the specified cells constitute at least 40% (by number) of all cells of said cell population, for example, at least 45%, preferably at least 50%, at least 55%, more preferably at least 60%, at least 65%, still more preferably at least 70%, at least 75%, even more preferably at least 80%, at least 85%, and yet more preferably at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or even 100% of all cells of said cell population.

The method may allow to detect or conclude the presence or absence of the specified cells in a tested object (e.g., in a cell population, tissue, organ, organism, or in a biological sample of a subject). The method may also allow to quantify the specified cells in a tested object (e.g., in a cell population, tissue, organ, organism, or in a biological sample of a subject). The quantity of the specified cells in the tested object such as the biological sample may be suitably expressed for example as the number (count) of the specified immune cells per standard unit of volume (e.g., ml, µl or nl) or weight (e.g., g or mg or ng) of the tested object such as the biological sample. The quantity of the specified cells in the tested object such as the biological sample may also be suitably expressed as a percentage or fraction (by number) of all cells comprised in the tested object such as the biological sample, or as a percentage or fraction (by number) of a select subset of the cells comprised in the tested object such as the biological sample, e.g., as a percentage or fraction (by number) of white blood cells, peripheral blood mononuclear cells, immune cells, antigen presenting cells, or dendritic cells comprised in the tested object such as the biological sample. The quantity of the specified cells in the tested object such as the biological sample may also be suitably represented by an absolute or relative quantity of a suitable surrogate analyte, such as a peptide, polypeptide, protein, or nucleic acid expressed or comprised by the specified cells.

Where a marker is detected in or on a cell, the cell may be conventionally denoted as positive ($^{+}$) or negative (–) for the marker. Semi-quantitative denotations of marker expression in cells are also commonplace in the art, such as particularly in flow cytometry quantifications, for example, "dim" vs. "bright", or "low" vs. "medium"/"intermediate" vs. "high", or "–" vs. "$^{+}$" vs. "$^{++}$", commonly controlled in flow cytometry quantifications by setting of the gates. Where a marker is quantified in or on a cell, absolute quantity of the marker may also be expressed for example as the number of molecules of the marker comprised by the cell.

Where a marker is detected and/or quantified on a single cell level in a cell population, the quantity of the marker may also be expressed as a percentage or fraction (by number) of cells comprised in said population that are positive for said marker, or as percentages or fractions (by number) of cells comprised in said population that are "dim" or "bright", or that are "low" or "medium"/"intermediate" or "high", or that are "–" or "$^{+}$" or "$^{++}$". By means of an example, a sizeable proportion of the tested cells of the cell population may be positive for the marker, e.g., at least about 20%, at least about 40%, at least about 50%, at least about 60%, at least about 70%, at least about 80%, at least about 90%, at least about 95%, or up to 100%.

Use of Specific Binding Agents

In certain embodiments, the aforementioned methods and techniques may employ agent(s) capable of specifically binding to one or more gene products, e.g., peptides, polypeptides, proteins, or nucleic acids, expressed or not

expressed by the immune cells as taught herein. In certain preferred embodiments, such one or more gene products, e.g., peptides, polypeptides, or proteins, may be expressed on the cell surface of the immune cells (i.e., cell surface markers, e.g., transmembrane peptides, polypeptides or proteins, or secreted peptides, polypeptides or proteins which remain associated with the cell surface). Hence, further disclosed are binding agents capable of specifically binding to markers, such as genes or gene products, e.g., peptides, polypeptides, proteins, or nucleic acids as taught herein. Binding agents as intended throughout this specification may include inter alia antibodies, aptamers, spiegelmers (L-aptamers), photoaptamers, protein, peptides, peptidomimetics, nucleic acids such as oligonucleotides (e.g., hybridization probes or amplification or sequencing primers and primer pairs), small molecules, or combinations thereof.

The term "aptamer" refers to single-stranded or double-stranded oligo-DNA, oligo-RNA or oligo-DNA/RNA or any analogue thereof that specifically binds to a target molecule such as a peptide. Advantageously, aptamers display fairly high specificity and affinity (e.g., KA in the order 1×109 M−1) for their targets. Aptamer production is described inter alia in U.S. Pat. No. 5,270,163; Ellington & Szostak 1990 (Nature 346: 818-822); Tuerk & Gold 1990 (Science 249: 505-510); or "Me Aptamer Handbook: Functional Oligonucleotides and Their Applications", by Klussmann, ed., Wiley-VCH 2006, ISBN 3527310592, incorporated by reference herein. The term "photoaptamer" refers to an aptamer that contains one or more photoreactive functional groups that can covalently bind to or crosslink with a target molecule. The term "spiegelmer" refers to an aptamer which includes L-DNA, L-RNA, or other left-handed nucleotide derivatives or nucleotide-like molecules. Aptamers containing left-handed nucleotides are resistant to degradation by naturally occurring enzymes, which normally act on substrates containing right-handed nucleotides. The term "peptidomimetic" refers to a non-peptide agent that is a topological analogue of a corresponding peptide. Methods of rationally designing peptidomimetics of peptides are known in the art. For example, the rational design of three peptidomimetics based on the sulphated 8-mer peptide CCK26-33, and of two peptidomimetics based on the 11-mer peptide Substance P, and related peptidomimetic design principles, are described in Horwell 1995 (Trends Biotechnol 13: 132-134).

Binding agents may be in various forms, e.g., lyophilised, free in solution, or immobilised on a solid phase. They may be, e.g., provided in a multi-well plate or as an array or microarray, or they may be packaged separately, individually, or in combination.

The term "specifically bind" as used throughout this specification means that an agent (denoted herein also as "specific-binding agent") binds to one or more desired molecules or analytes (e.g., peptides, polypeptides, proteins, or nucleic acids) substantially to the exclusion of other molecules which are random or unrelated, and optionally substantially to the exclusion of other molecules that are structurally related. The term "specifically bind" does not necessarily require that an agent binds exclusively to its intended target(s). For example, an agent may be said to specifically bind to target(s) of interest if its affinity for such intended target(s) under the conditions of binding is at least about 2-fold greater, preferably at least about 5-fold greater, more preferably at least about 10-fold greater, yet more preferably at least about 25-fold greater, still more preferably at least about 50-fold greater, and even more preferably at least about 100-fold, or at least about 1000-fold, or at least about 104-fold, or at least about 105-fold, or at least about 106-fold or more greater, than its affinity for a non-target molecule, such as for a suitable control molecule (e.g., bovine serum albumin, casein).

Preferably, the specific binding agent may bind to its intended target(s) with affinity constant (KA) of such binding KA≥1×106 M−1, more preferably KA≥1×107 M−1, yet more preferably KA≥1×108 M−1, even more preferably KA≥1×109 M−1, and still more preferably KA≥1×1010 M−1 or KA≥1×1011 M−1 or KA≥1×1012 M−1, wherein KA=[SBA_T]/[SBA][T], SBA denotes the specific-binding agent, T denotes the intended target. Determination of KA can be carried out by methods known in the art, such as for example, using equilibrium dialysis and Scatchard plot analysis.

In certain embodiments, the one or more binding agents may be one or more antibodies. As used herein, the term "antibody" is used in its broadest sense and generally refers to any immunologic binding agent. The term specifically encompasses intact monoclonal antibodies, polyclonal antibodies, multivalent (e.g., 2-, 3- or more-valent) and/or multi-specific antibodies (e.g., bi- or more-specific antibodies) formed from at least two intact antibodies, and antibody fragments insofar they exhibit the desired biological activity (particularly, ability to specifically bind an antigen of interest, i.e., antigen-binding fragments), as well as multivalent and/or multi-specific composites of such fragments. The term "antibody" is not only inclusive of antibodies generated by methods comprising immunization, but also includes any polypeptide, e.g., a recombinantly expressed polypeptide, which is made to encompass at least one complementarity-determining region (CDR) capable of specifically binding to an epitope on an antigen of interest. Hence, the term applies to such molecules regardless whether they are produced in vitro or in vivo. Antibodies also encompasses chimeric, humanized and fully humanized antibodies.

An antibody may be any of IgA, IgD, IgE, IgG and IgM classes, and preferably IgG class antibody. An antibody may be a polyclonal antibody, e.g., an antiserum or immunoglobulins purified there from (e.g., affinity-purified). An antibody may be a monoclonal antibody or a mixture of monoclonal antibodies. Monoclonal antibodies can target a particular antigen or a particular epitope within an antigen with greater selectivity and reproducibility. By means of example and not limitation, monoclonal antibodies may be made by the hybridoma method first described by Kohler et al. 1975 (Nature 256: 495), or may be made by recombinant DNA methods (e.g., as in U.S. Pat. No. 4,816,567). Monoclonal antibodies may also be isolated from phage antibody libraries using techniques as described by Clackson et al. 1991 (Nature 352: 624-628) and Marks et al. 1991 (J Mol Biol 222: 581-597), for example.

Antibody binding agents may be antibody fragments. "Antibody fragments" comprise a portion of an intact antibody, comprising the antigen-binding or variable region thereof. Examples of antibody fragments include Fab, Fab', F(ab')2, Fv and scFv fragments, single domain (sd) Fv, such as VH domains, VL domains and VHH domains; diabodies; linear antibodies; single-chain antibody molecules, in particular heavy-chain antibodies; and multivalent and/or multispecific antibodies formed from antibody fragment(s), e.g., dibodies, tribodies, and multibodies. The above designations Fab, Fab', F(ab')2, Fv, scFv etc. are intended to have their art-established meaning.

The term antibody includes antibodies originating from or comprising one or more portions derived from any animal species, preferably vertebrate species, including, e.g., birds

and mammals. Without limitation, the antibodies may be chicken, turkey, goose, duck, guinea fowl, quail or pheasant. Also without limitation, the antibodies may be human, murine (e.g., mouse, rat, etc.), donkey, rabbit, goat, sheep, guinea pig, camel (e.g., *Camelus bactrianus* and *Camelus dromedarius*), llama (e.g., *Lama pacos, Lama glama* or *Lama vicugna*) or horse.

A skilled person will understand that an antibody can include one or more amino acid deletions, additions and/or substitutions (e.g., conservative substitutions), insofar such alterations preserve its binding of the respective antigen. An antibody may also include one or more native or artificial modifications of its constituent amino acid residues (e.g., glycosylation, etc.).

Methods of producing polyclonal and monoclonal antibodies as well as fragments thereof are well known in the art, as are methods to produce recombinant antibodies or fragments thereof (see for example, Harlow and Lane, "Antibodies: A Laboratory Manual", Cold Spring Harbour Laboratory, New York, 1988; Harlow and Lane, "Using Antibodies: A Laboratory Manual", Cold Spring Harbour Laboratory, New York, 1999, ISBN 0879695447; "Monoclonal Antibodies: A Manual of Techniques", by Zola, ed., CRC Press 1987, ISBN 0849364760; "Monoclonal Antibodies: A Practical Approach", by Dean & Shepherd, eds., Oxford University Press 2000, ISBN 0199637229; Methods in Molecular Biology, vol. 248: "Antibody Engineering: Methods and Protocols", Lo, ed., Humana Press 2004, ISBN 1588290921).

As used herein, a "blocking" antibody or an antibody "antagonist" is one which inhibits or reduces biological activity of the antigen(s) it binds. In certain embodiments, the blocking antibodies or antagonist antibodies or portions thereof described herein completely inhibit the biological activity of the antigen(s).

Antibodies may act as agonists or antagonists of the recognized polypeptides. For example, the present invention includes antibodies which disrupt receptor/ligand interactions either partially or fully. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or of one of its down-stream substrates by immunoprecipitation followed by western blot analysis. In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex. Likewise, encompassed by the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides disclosed herein. The antibody agonists and antagonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Pat. No. 5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16): 3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. III (Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautard et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4): 755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996).

The antibodies as defined for the present invention include derivatives that are modified, i.e., by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphorylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

Simple binding assays can be used to screen for or detect agents that bind to a target protein, or disrupt the interaction between proteins (e.g., a receptor and a ligand). Because certain targets of the present invention are transmembrane proteins, assays that use the soluble forms of these proteins rather than full-length protein can be used, in some embodiments. Soluble forms include, for example, those lacking the transmembrane domain and/or those comprising the IgV domain or fragments thereof which retain their ability to bind their cognate binding partners. Further, agents that inhibit or enhance protein interactions for use in the compositions and methods described herein, can include recombinant peptido-mimetics.

Detection methods useful in screening assays include antibody-based methods, detection of a reporter moiety, detection of cytokines as described herein, and detection of a gene signature as described herein.

Another variation of assays to determine binding of a receptor protein to a ligand protein is through the use of affinity biosensor methods. Such methods may be based on the piezoelectric effect, electrochemistry, or optical methods, such as ellipsometry, optical wave guidance, and surface plasmon resonance (SPR).

The term "antibody-like protein scaffolds" or "engineered protein scaffolds" broadly encompasses proteinaceous non-immunoglobulin specific-binding agents, typically obtained by combinatorial engineering (such as site-directed random mutagenesis in combination with phage display or other molecular selection techniques). Usually, such scaffolds are derived from robust and small soluble monomeric proteins (such as Kunitz inhibitors or lipocalins) or from a stably folded extra-membrane domain of a cell surface receptor (such as protein A, fibronectin or the ankyrin repeat).

Such scaffolds have been extensively reviewed in Binz et al. (Engineering novel binding proteins from nonimmunoglobulin domains. Nat Biotechnol 2005, 23:1257-1268), Gebauer and Skerra (Engineered protein scaffolds as next-

generation antibody therapeutics. Curr Opin Chem Biol. 2009, 13:245-55), Gill and Damle (Biopharmaceutical drug discovery using novel protein scaffolds. Curr Opin Biotechnol 2006, 17:653-658), Skerra (Engineered protein scaffolds for molecular recognition. J Mol Recognit 2000, 13:167-187), and Skerra (Alternative non-antibody scaffolds for molecular recognition. Curr Opin Biotechnol 2007, 18:295-304), and include without limitation affibodies, based on the Z-domain of staphylococcal protein A, a three-helix bundle of 58 residues providing an interface on two of its alpha-helices (Nygren, Alternative binding proteins: Affibody binding proteins developed from a small three-helix bundle scaffold. FEBS J 2008, 275:2668-2676); engineered Kunitz domains based on a small (ca. 58 residues) and robust, disulphide-crosslinked serine protease inhibitor, typically of human origin (e.g. LACI-D1), which can be engineered for different protease specificities (Nixon and Wood, Engineered protein inhibitors of proteases. Curr Opin Drug Discov Dev 2006, 9:261-268); monobodies or adnectins based on the 10th extracellular domain of human fibronectin III (10Fn3), which adopts an Ig-like beta-sandwich fold (94 residues) with 2-3 exposed loops, but lacks the central disulphide bridge (Koide and Koide, Monobodies: antibody mimics based on the scaffold of the fibronectin type III domain. Methods Mol Biol 2007, 352:95-109); anticalins derived from the lipocalins, a diverse family of eight-stranded beta-barrel proteins (ca. 180 residues) that naturally form binding sites for small ligands by means of four structurally variable loops at the open end, which are abundant in humans, insects, and many other organisms (Skerra, Alternative binding proteins: Anticalins-harnessing the structural plasticity of the lipocalin ligand pocket to engineer novel binding activities. FEBS J 2008, 275:2677-2683); DARPins, designed ankyrin repeat domains (166 residues), which provide a rigid interface arising from typically three repeated beta-turns (Stumpp et al., DARPins: a new generation of protein therapeutics. Drug Discov Today 2008, 13:695-701); avimers (multimerized LDLR-A module) (Silverman et al., Multivalent avimer proteins evolved by exon shuffling of a family of human receptor domains. Nat Biotechnol 2005, 23:1556-1561); and cysteine-rich knottin peptides (Kolmar, Alternative binding proteins: biological activity and therapeutic potential of cystine-knot miniproteins. FEBS J 2008, 275:2684-2690).

Nucleic acid binding agents, such as oligonucleotide binding agents, are typically at least partly antisense to a target nucleic acid of interest. The term "antisense" generally refers to an agent (e.g., an oligonucleotide) configured to specifically anneal with (hybridise to) a given sequence in a target nucleic acid, such as for example in a target DNA, hnRNA, pre-mRNA or mRNA, and typically comprises, consist essentially of or consist of a nucleic acid sequence that is complementary or substantially complementary to said target nucleic acid sequence. Antisense agents suitable for use herein, such as hybridisation probes or amplification or sequencing primers and primer pairs may typically be capable of annealing with (hybridizing to) the respective target nucleic acid sequences at high stringency conditions, and capable of hybridising specifically to the target under physiological conditions. The terms "complementary" or "complementarity" as used throughout this specification with reference to nucleic acids, refer to the normal binding of single-stranded nucleic acids under permissive salt (ionic strength) and temperature conditions by base pairing, preferably Watson-Crick base pairing. By means of example, complementary Watson-Crick base pairing occurs between the bases A and T, A and U or G and C. For example, the sequence 5'-A-G-U-3' is complementary to sequence 5'-A-C-U-3'.

The reference to oligonucleotides may in particular but without limitation include hybridization probes and/or amplification primers and/or sequencing primers, etc., as commonly used in nucleic acid detection technologies.

Binding agents as discussed herein may suitably comprise a detectable label. The term "label" refers to any atom, molecule, moiety or biomolecule that may be used to provide a detectable and preferably quantifiable read-out or property, and that may be attached to or made part of an entity of interest, such as a binding agent. Labels may be suitably detectable by for example mass spectrometric, spectroscopic, optical, colourimetric, magnetic, photochemical, biochemical, immunochemical or chemical means. Labels include without limitation dyes; radiolabels such as ^{32}P, ^{33}P, ^{35}S, ^{125}I, ^{131}I; electron-dense reagents; enzymes (e.g., horse-radish peroxidase or alkaline phosphatase as commonly used in immunoassays); binding moieties such as biotin-streptavidin; haptens such as digoxigenin; luminogenic, phosphorescent or fluorogenic moieties; mass tags; and fluorescent dyes alone or in combination with moieties that may suppress or shift emission spectra by fluorescence resonance energy transfer (FRET).

In some embodiments, binding agents may be provided with a tag that permits detection with another agent (e.g., with a probe binding partner). Such tags may be, for example, biotin, streptavidin, his-tag, myc tag, maltose, maltose binding protein or any other kind of tag known in the art that has a binding partner. Example of associations which may be utilised in the probe:binding partner arrangement may be any, and includes, for example biotin:streptavidin, his-tag:metal ion (e.g., $Ni2^{+}$), maltose:maltose binding protein, etc.

The marker-binding agent conjugate may be associated with or attached to a detection agent to facilitate detection. Examples of detection agents include, but are not limited to, luminescent labels; colourimetric labels, such as dyes; fluorescent labels; or chemical labels, such as electroactive agents (e.g., ferrocyanide); enzymes; radioactive labels; or radiofrequency labels. The detection agent may be a particle. Examples of such particles include, but are not limited to, colloidal gold particles; colloidal sulphur particles; colloidal selenium particles; colloidal barium sulfate particles; colloidal iron sulfate particles; metal iodate particles; silver halide particles; silica particles; colloidal metal (hydrous) oxide particles; colloidal metal sulfide particles; colloidal lead selenide particles; colloidal cadmium selenide particles; colloidal metal phosphate particles; colloidal metal ferrite particles; any of the above-mentioned colloidal particles coated with organic or inorganic layers; protein or peptide molecules; liposomes; or organic polymer latex particles, such as polystyrene latex beads. Preferable particles may be colloidal gold particles.

In certain embodiments, the one or more binding agents are configured for use in a technique selected from the group consisting of flow cytometry, fluorescence activated cell sorting, mass cytometry, fluorescence microscopy, affinity separation, magnetic cell separation, microfluidic separation, and combinations thereof.

Identifying Modulators

A further aspect of the invention relates to a method for identifying an agent capable of modulating one or more phenotypic aspects of a gut cell or gut cell population as disclosed herein, comprising: a) applying a candidate agent to the cell or cell population; b) detecting modulation of one

or more phenotypic aspects of the cell or cell population by the candidate agent, thereby identifying the agent.

The term "modulate" broadly denotes a qualitative and/or quantitative alteration, change or variation in that which is being modulated. Where modulation can be assessed quantitatively—for example, where modulation comprises or consists of a change in a quantifiable variable such as a quantifiable property of a cell or where a quantifiable variable provides a suitable surrogate for the modulation—modulation specifically encompasses both increase (e.g., activation) or decrease (e.g., inhibition) in the measured variable. The term encompasses any extent of such modulation, e.g., any extent of such increase or decrease, and may more particularly refer to statistically significant increase or decrease in the measured variable. By means of example, modulation may encompass an increase in the value of the measured variable by at least about 10%, e.g., by at least about 20%, preferably by at least about 30%, e.g., by at least about 40%, more preferably by at least about 50%, e.g., by at least about 75%, even more preferably by at least about 100%, e.g., by at least about 150%, 200%, 250%, 300%, 400% or by at least about 500%, compared to a reference situation without said modulation; or modulation may encompass a decrease or reduction in the value of the measured variable by at least about 10%, e.g., by at least about 20%, by at least about 30%, e.g., by at least about 40%, by at least about 50%, e.g., by at least about 60%, by at least about 70%, e.g., by at least about 80%, by at least about 90%, e.g., by at least about 95%, such as by at least about 96%, 97%, 98%, 99% or even by 100%, compared to a reference situation without said modulation. Preferably, modulation may be specific or selective, hence, one or more desired phenotypic aspects of a gut cell or gut cell population may be modulated without substantially altering other (unintended, undesired) phenotypic aspect(s).

The term "agent" broadly encompasses any condition, substance or agent capable of modulating one or more phenotypic aspects of an gut cell or gut cell population as disclosed herein. Such conditions, substances or agents may be of physical, chemical, biochemical and/or biological nature. The term "candidate agent" refers to any condition, substance or agent that is being examined for the ability to modulate one or more phenotypic aspects of an gut cell or gut cell population as disclosed herein in a method comprising applying the candidate agent to the gut cell or gut cell population (e.g., exposing the gut cell or gut cell population to the candidate agent or contacting the gut cell or gut cell population with the candidate agent) and observing whether the desired modulation takes place.

Agents may include any potential class of biologically active conditions, substances or agents, such as for instance antibodies, proteins, peptides, nucleic acids, oligonucleotides, small molecules, or combinations thereof.

By means of example but without limitation, agents can include low molecular weight compounds, but may also be larger compounds, or any organic or inorganic molecule effective in the given situation, including modified and unmodified nucleic acids such as antisense nucleic acids, RNAi, such as siRNA or shRNA, CRISPR/Cas systems, peptides, peptidomimetics, receptors, ligands, and antibodies, aptamers, polypeptides, nucleic acid analogues or variants thereof. Examples include an oligomer of nucleic acids, amino acids, or carbohydrates including without limitation proteins, oligonucleotides, ribozymes, DNAzymes, glycoproteins, siRNAs, lipoproteins, aptamers, and modifications and combinations thereof. Agents can be selected from a group comprising: chemicals; small molecules; nucleic acid sequences; nucleic acid analogues; proteins; peptides; aptamers; antibodies; or fragments thereof. A nucleic acid sequence can be RNA or DNA, and can be single or double stranded, and can be selected from a group comprising; nucleic acid encoding a protein of interest, oligonucleotides, nucleic acid analogues, for example peptide-nucleic acid (PNA), pseudo-complementary PNA (pc-PNA), locked nucleic acid (LNA), modified RNA (mod-RNA), single guide RNA etc. Such nucleic acid sequences include, for example, but are not limited to, nucleic acid sequence encoding proteins, for example that act as transcriptional repressors, antisense molecules, ribozymes, small inhibitory nucleic acid sequences, for example but are not limited to RNAi, shRNAi, siRNA, micro RNAi (mRNAi), antisense oligonucleotides, CRISPR guide RNA, for example that target a CRISPR enzyme to a specific DNA target sequence etc. A protein and/or peptide or fragment thereof can be any protein of interest, for example, but are not limited to: mutated proteins; therapeutic proteins and truncated proteins, wherein the protein is normally absent or expressed at lower levels in the cell. Proteins can also be selected from a group comprising; mutated proteins, genetically engineered proteins, peptides, synthetic peptides, recombinant proteins, chimeric proteins, antibodies, midibodies, minibodies, triabodies, humanized proteins, humanized antibodies, chimeric antibodies, modified proteins and fragments thereof. Alternatively, the agent can be intracellular within the cell as a result of introduction of a nucleic acid sequence into the cell and its transcription resulting in the production of the nucleic acid and/or protein modulator of a gene within the cell. In some embodiments, the agent is any chemical, entity or moiety, including without limitation synthetic and naturally-occurring non-proteinaceous entities. In certain embodiments, the agent is a small molecule having a chemical moiety. Agents can be known to have a desired activity and/or property, or can be selected from a library of diverse compounds.

In certain embodiments, an agent may be a hormone, a cytokine, a lymphokine, a growth factor, a chemokine, a cell surface receptor ligand such as a cell surface receptor agonist or antagonist, or a mitogen.

Non-limiting examples of hormones include growth hormone (GH), adrenocorticotropic hormone (ACTH), dehydroepiandrosterone (DHEA), cortisol, epinephrine, thyroid hormone, estrogen, progesterone, testosterone, or combinations thereof.

Non-limiting examples of cytokines include lymphokines (e.g., interferon-γ, IL-2, IL-3, IL-4, IL-6, granulocyte-macrophage colony-stimulating factor (GM-CSF), interferon-γ, leukocyte migration inhibitory factors (T-LIF, B-LIF), lymphotoxin-alpha, macrophage-activating factor (MAF), macrophage migration-inhibitory factor (MIF), neuroleukin, immunologic suppressor factors, transfer factors, or combinations thereof), monokines (e.g., IL-1, TNF-alpha, interferon-α, interferon-β, colony stimulating factors, e.g., CSF2, CSF3, macrophage CSF or GM-CSF, or combinations thereof), chemokines (e.g., beta-thromboglobulin, C chemokines, CC chemokines, CXC chemokines, CX3C chemokines, macrophage inflammatory protein (MIP), or combinations thereof), interleukins (e.g., IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-17, IL-18, IL-19, IL-20, IL-21, IL-22, IL-23, IL-24, IL-25, IL-26, IL-27, IL-28, IL-29, IL-30, IL-31, IL-32, IL-33, IL-34, IL-35, IL-36, or combinations thereof), and several related signalling molecules,

such as tumour necrosis factor (TNF) and interferons (e.g., interferon-α, interferon-β, interferon-γ, interferon-k, or combinations thereof).

Non-limiting examples of growth factors include those of fibroblast growth factor (FGF) family, bone morphogenic protein (BMP) family, platelet derived growth factor (PDGF) family, transforming growth factor beta (TGFbeta) family, nerve growth factor (NGF) family, epidermal growth factor (EGF) family, insulin related growth factor (IGF) family, hepatocyte growth factor (HGF) family, hematopoietic growth factors (HeGFs), platelet-derived endothelial cell growth factor (PD-ECGF), angiopoietin, vascular endothelial growth factor (VEGF) family, glucocorticoids, or combinations thereof.

Non-limiting examples of mitogens include phytohaemagglutinin (PHA), concanavalin A (conA), lipopolysaccharide (LPS), pokeweed mitogen (PWM), phorbol ester such as phorbol myristate acetate (PMA) with or without ionomycin, or combinations thereof.

Non-limiting examples of cell surface receptors the ligands of which may act as agents include Toll-like receptors (TLRs) (e.g., TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, TLR11, TLR12 or TLR13), CD80, CD86, CD40, CCR7, or C-type lectin receptors.

In certain embodiments, the present invention provides for gene signature screening. The concept of signature screening was introduced by Stegmaier et al. (Gene expression-based high-throughput screening (GE-HTS) and application to leukemia differentiation. Nature Genet. 36, 257-263 (2004)), who realized that if a gene-expression signature was the proxy for a phenotype of interest, it could be used to find small molecules that effect that phenotype without knowledge of a validated drug target. The signatures of the present invention may be used to screen for drugs that induce or reduce the signature in epithelial, stromal, glia, or immune cells as described herein. The signature may be used for GE-HTS. In certain embodiments, pharmacological screens may be used to identify drugs that selectively activate gut cells. Not being bound by a theory, activation or inactivation of gut cells may have a therapeutic effect. Not being bound by a theory modulating a signature associated with disease may provide a therapeutic effect.

The Connectivity Map (cmap) is a collection of genome-wide transcriptional expression data from cultured human cells treated with bioactive small molecules and simple pattern-matching algorithms that together enable the discovery of functional connections between drugs, genes and diseases through the transitory feature of common gene-expression changes (see, Lamb et al., The Connectivity Map: Using Gene-Expression Signatures to Connect Small Molecules, Genes, and Disease. Science 29 Sep. 2006: Vol. 313, Issue 5795, pp. 1929-1935, DOI: 10.1126/science.1132939; and Lamb, J., The Connectivity Map: a new tool for biomedical research. Nature Reviews Cancer January 2007: Vol. 7, pp. 54-60). In certain embodiments, Cmap can be used to screen for small molecules capable of modulating a signature of the present invention in silico.

Particular screening applications of this invention relate to the testing of pharmaceutical compounds in drug research. The reader is referred generally to the standard textbook In vitro Methods in Pharmaceutical Research, Academic Press, 1997, and U.S. Pat. No. 5,030,015. In certain aspects of this invention, the culture of the invention is used to grow and differentiate a cachectic target cell to play the role of test cells for standard drug screening and toxicity assays. Assessment of the activity of candidate pharmaceutical compounds generally involves combining the target cell (e.g., a myocyte, an adipocyte, a cardiomyocyte or a hepatocyte) with the candidate compound, determining any change in the morphology, marker phenotype, or metabolic activity of the cells that is attributable to the candidate compound (compared with untreated cells or cells treated with an inert compound, such as vehicle), and then correlating the effect of the candidate compound with the observed change. The screening may be done because the candidate compound is designed to have a pharmacological effect on the target cell, or because a candidate compound may have unintended side effects on the target cell. Alternatively, libraries can be screened without any predetermined expectations in hopes of identifying compounds with desired effects.

Cytotoxicity can be determined in the first instance by the effect on cell viability and morphology. In certain embodiments, toxicity may be assessed by observation of vital staining techniques, ELISA assays, immunohistochemistry, and the like or by analyzing the cellular content of the culture, e.g., by total cell counts, and differential cell counts or by metabolic markers such as MTT and XTT.

Additional further uses of the culture of the invention include, but are not limited to, its use in research e.g., to elucidate mechanisms leading to the identification of novel targets for therapies, and to generate genotype-specific cells for disease modeling, including the generation of new therapies customized to different genotypes. Such customization can reduce adverse drug effects and help identify therapies appropriate to the patient's genotype.

In certain embodiments, the present invention provides method for high-throughput screening. "High-throughput screening" (HTS) refers to a process that uses a combination of modern robotics, data processing and control software, liquid handling devices, and/or sensitive detectors, to efficiently process a large amount of (e.g., thousands, hundreds of thousands, or millions of) samples in biochemical, genetic or pharmacological experiments, either in parallel or in sequence, within a reasonably short period of time (e.g., days). Preferably, the process is amenable to automation, such as robotic simultaneous handling of 96 samples, 384 samples, 1536 samples or more. A typical HTS robot tests up to 100,000 to a few hundred thousand compounds per day. The samples are often in small volumes, such as no more than 1 mL, 500 μl, 200 μl, 100 μl, 50 μl or less. Through this process, one can rapidly identify active compounds, small molecules, antibodies, proteins or polynucleotides which modulate a particular biomolecular/genetic pathway. The results of these experiments provide starting points for further drug design and for understanding the interaction or role of a particular biochemical process in biology. Thus "high-throughput screening" as used herein does not include handling large quantities of radioactive materials, slow and complicated operator-dependent screening steps, and/or prohibitively expensive reagent costs, etc.

Genetic Modifying Agents

In certain embodiments, the one or more modulating agents may be a genetic modifying agent. The genetic modifying agent may comprise a CRISPR system, a zinc finger nuclease system, a TALEN, or a meganuclease.

In general, a CRISPR-Cas or CRISPR system as used in herein and in documents, such as WO 2014/093622 (PCT/US2013/074667), refers collectively to transcripts and other elements involved in the expression of or directing the activity of CRISPR-associated ("Cas") genes, including sequences encoding a Cas gene, a tracr (trans-activating CRISPR) sequence (e.g. tracrRNA or an active partial tracrRNA), a tracr-mate sequence (encompassing a "direct repeat" and a tracrRNA-processed partial direct repeat in the

context of an endogenous CRISPR system), a guide sequence (also referred to as a "spacer" in the context of an endogenous CRISPR system), or "RNA(s)" as that term is herein used (e.g., RNA(s) to guide Cas, such as Cas9, e.g. CRISPR RNA and transactivating (tracr) RNA or a single guide RNA (sgRNA)(chimeric RNA)) or other sequences and transcripts from a CRISPR locus. In general, a CRISPR system is characterized by elements that promote the formation of a CRISPR complex at the site of a target sequence (also referred to as a protospacer in the context of an endogenous CRISPR system). See, e.g, Shmakov et al. (2015) "Discovery and Functional Characterization of Diverse Class 2 CRISPR-Cas Systems", Molecular Cell, DOI: dx.doi.org/10.1016/j.molcel.2015.10.008.

In certain embodiments, a protospacer adjacent motif (PAM) or PAM-like motif directs binding of the effector protein complex as disclosed herein to the target locus of interest. In some embodiments, the PAM may be a 5' PAM (i.e., located upstream of the 5' end of the protospacer). In other embodiments, the PAM may be a 3' PAM (i.e., located downstream of the 5' end of the protospacer). The term "PAM" may be used interchangeably with the term "PFS" or "protospacer flanking site" or "protospacer flanking sequence".

In a preferred embodiment, the CRISPR effector protein may recognize a 3' PAM. In certain embodiments, the CRISPR effector protein may recognize a 3' PAM which is 5'H, wherein H is A, C or U.

In the context of formation of a CRISPR complex, "target sequence" refers to a sequence to which a guide sequence is designed to have complementarity, where hybridization between a target sequence and a guide sequence promotes the formation of a CRISPR complex. A target sequence may comprise RNA polynucleotides. The term "target RNA" refers to a RNA polynucleotide being or comprising the target sequence. In other words, the target RNA may be a RNA polynucleotide or a part of a RNA polynucleotide to which a part of the gRNA, i.e. the guide sequence, is designed to have complementarity and to which the effector function mediated by the complex comprising CRISPR effector protein and a gRNA is to be directed. In some embodiments, a target sequence is located in the nucleus or cytoplasm of a cell.

In certain example embodiments, the CRISPR effector protein may be delivered using a nucleic acid molecule encoding the CRISPR effector protein. The nucleic acid molecule encoding a CRISPR effector protein, may advantageously be a codon optimized CRISPR effector protein. An example of a codon optimized sequence, is in this instance a sequence optimized for expression in eukaryote, e.g., humans (i.e. being optimized for expression in humans), or for another eukaryote, animal or mammal as herein discussed; see, e.g., SaCas9 human codon optimized sequence in WO 2014/093622 (PCT/US2013/074667). Whilst this is preferred, it will be appreciated that other examples are possible and codon optimization for a host species other than human, or for codon optimization for specific organs is known. In some embodiments, an enzyme coding sequence encoding a CRISPR effector protein is a codon optimized for expression in particular cells, such as eukaryotic cells. The eukaryotic cells may be those of or derived from a particular organism, such as a plant or a mammal, including but not limited to human, or non-human eukaryote or animal or mammal as herein discussed, e.g., mouse, rat, rabbit, dog, livestock, or non-human mammal or primate. In some embodiments, processes for modifying the germ line genetic identity of human beings and/or processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal, and also animals resulting from such processes, may be excluded. In general, codon optimization refers to a process of modifying a nucleic acid sequence for enhanced expression in the host cells of interest by replacing at least one codon (e.g. about or more than about 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, or more codons) of the native sequence with codons that are more frequently or most frequently used in the genes of that host cell while maintaining the native amino acid sequence. Various species exhibit particular bias for certain codons of a particular amino acid. Codon bias (differences in codon usage between organisms) often correlates with the efficiency of translation of messenger RNA (mRNA), which is in turn believed to be dependent on, among other things, the properties of the codons being translated and the availability of particular transfer RNA (tRNA) molecules. The predominance of selected tRNAs in a cell is generally a reflection of the codons used most frequently in peptide synthesis. Accordingly, genes can be tailored for optimal gene expression in a given organism based on codon optimization. Codon usage tables are readily available, for example, at the "Codon Usage Database" available at kazusa.or.jp/codon/and these tables can be adapted in a number of ways. See Nakamura, Y., et al. "Codon usage tabulated from the international DNA sequence databases: status for the year 2000" Nucl. Acids Res. 28:292 (2000). Computer algorithms for codon optimizing a particular sequence for expression in a particular host cell are also available, such as Gene Forge (Aptagen; Jacobus, PA), are also available. In some embodiments, one or more codons (e.g. 1, 2, 3, 4, 5, 10, 15, 20, 25, 50, or more, or all codons) in a sequence encoding a Cas correspond to the most frequently used codon for a particular amino acid.

In certain embodiments, the methods as described herein may comprise providing a Cas transgenic cell in which one or more nucleic acids encoding one or more guide RNAs are provided or introduced operably connected in the cell with a regulatory element comprising a promoter of one or more gene of interest. As used herein, the term "Cas transgenic cell" refers to a cell, such as a eukaryotic cell, in which a Cas gene has been genomically integrated. The nature, type, or origin of the cell are not particularly limiting according to the present invention. Also the way the Cas transgene is introduced in the cell may vary and can be any method as is known in the art. In certain embodiments, the Cas transgenic cell is obtained by introducing the Cas transgene in an isolated cell. In certain other embodiments, the Cas transgenic cell is obtained by isolating cells from a Cas transgenic organism. By means of example, and without limitation, the Cas transgenic cell as referred to herein may be derived from a Cas transgenic eukaryote, such as a Cas knock-in eukaryote. Reference is made to WO 2014/093622 (PCT/US13/74667), incorporated herein by reference. Methods of US Patent Publication Nos. 20120017290 and 20110265198 assigned to Sangamo BioSciences, Inc. directed to targeting the Rosa locus may be modified to utilize the CRISPR Cas system of the present invention. Methods of US Patent Publication No. 20130236946 assigned to Cellectis directed to targeting the Rosa locus may also be modified to utilize the CRISPR Cas system of the present invention. By means of further example reference is made to Platt et. al. (Cell; 159(2):440-455 (2014)), describing a Cas9 knock-in mouse, which is incorporated herein by reference. The Cas transgene can further comprise a Lox-Stop-polyA-Lox(LSL) cassette thereby rendering Cas expression inducible by Cre recombinase. Alternatively, the Cas transgenic cell may be

obtained by introducing the Cas transgene in an isolated cell. Delivery systems for transgenes are well known in the art. By means of example, the Cas transgene may be delivered in for instance eukaryotic cell by means of vector (e.g., AAV, adenovirus, lentivirus) and/or particle and/or nanoparticle delivery, as also described herein elsewhere.

It will be understood by the skilled person that the cell, such as the Cas transgenic cell, as referred to herein may comprise further genomic alterations besides having an integrated Cas gene or the mutations arising from the sequence specific action of Cas when complexed with RNA capable of guiding Cas to a target locus.

In certain aspects the invention involves vectors, e.g. for delivering or introducing in a cell Cas and/or RNA capable of guiding Cas to a target locus (i.e. guide RNA), but also for propagating these components (e.g. in prokaryotic cells). A used herein, a "vector" is a tool that allows or facilitates the transfer of an entity from one environment to another. It is a replicon, such as a plasmid, phage, or cosmid, into which another DNA segment may be inserted so as to bring about the replication of the inserted segment. Generally, a vector is capable of replication when associated with the proper control elements. In general, the term "vector" refers to a nucleic acid molecule capable of transporting another nucleic acid to which it has been linked. Vectors include, but are not limited to, nucleic acid molecules that are single-stranded, double-stranded, or partially double-stranded; nucleic acid molecules that comprise one or more free ends, no free ends (e.g. circular); nucleic acid molecules that comprise DNA, RNA, or both; and other varieties of polynucleotides known in the art. One type of vector is a "plasmid," which refers to a circular double stranded DNA loop into which additional DNA segments can be inserted, such as by standard molecular cloning techniques. Another type of vector is a viral vector, wherein virally-derived DNA or RNA sequences are present in the vector for packaging into a virus (e.g. retroviruses, replication defective retroviruses, adenoviruses, replication defective adenoviruses, and adeno-associated viruses (AAVs)). Viral vectors also include polynucleotides carried by a virus for transfection into a host cell. Certain vectors are capable of autonomous replication in a host cell into which they are introduced (e.g. bacterial vectors having a bacterial origin of replication and episomal mammalian vectors). Other vectors (e.g., non-episomal mammalian vectors) are integrated into the genome of a host cell upon introduction into the host cell, and thereby are replicated along with the host genome. Moreover, certain vectors are capable of directing the expression of genes to which they are operatively-linked. Such vectors are referred to herein as "expression vectors." Common expression vectors of utility in recombinant DNA techniques are often in the form of plasmids.

Recombinant expression vectors can comprise a nucleic acid of the invention in a form suitable for expression of the nucleic acid in a host cell, which means that the recombinant expression vectors include one or more regulatory elements, which may be selected on the basis of the host cells to be used for expression, that is operatively-linked to the nucleic acid sequence to be expressed. Within a recombinant expression vector, "operably linked" is intended to mean that the nucleotide sequence of interest is linked to the regulatory element(s) in a manner that allows for expression of the nucleotide sequence (e.g. in an in vitro transcription/translation system or in a host cell when the vector is introduced into the host cell). With regards to recombination and cloning methods, mention is made of U.S. patent application Ser. No. 10/815,730, published Sep. 2, 2004 as US 2004-0171156 A1, the contents of which are herein incorporated by reference in their entirety. Thus, the embodiments disclosed herein may also comprise transgenic cells comprising the CRISPR effector system. In certain example embodiments, the transgenic cell may function as an individual discrete volume. In other words samples comprising a masking construct may be delivered to a cell, for example in a suitable delivery vesicle and if the target is present in the delivery vesicle the CRISPR effector is activated and a detectable signal generated.

The vector(s) can include the regulatory element(s), e.g., promoter(s). The vector(s) can comprise Cas encoding sequences, and/or a single, but possibly also can comprise at least 3 or 8 or 16 or 32 or 48 or 50 guide RNA(s) (e.g., sgRNAs) encoding sequences, such as 1-2, 1-3, 1-4 1-5, 3-6, 3-7, 3-8, 3-9, 3-10, 3-8, 3-16, 3-30, 3-32, 3-48, 3-50 RNA(s) (e.g., sgRNAs). In a single vector there can be a promoter for each RNA (e.g., sgRNA), advantageously when there are up to about 16 RNA(s); and, when a single vector provides for more than 16 RNA(s), one or more promoter(s) can drive expression of more than one of the RNA(s), e.g., when there are 32 RNA(s), each promoter can drive expression of two RNA(s), and when there are 48 RNA(s), each promoter can drive expression of three RNA(s). By simple arithmetic and well established cloning protocols and the teachings in this disclosure one skilled in the art can readily practice the invention as to the RNA(s) for a suitable exemplary vector such as AAV, and a suitable promoter such as the U6 promoter. For example, the packaging limit of AAV is ~4.7 kb. The length of a single U6-gRNA (plus restriction sites for cloning) is 361 bp. Therefore, the skilled person can readily fit about 12-16, e.g., 13 U6-gRNA cassettes in a single vector. This can be assembled by any suitable means, such as a golden gate strategy used for TALE assembly (genome-engineering.org/taleffectors/). The skilled person can also use a tandem guide strategy to increase the number of U6-gRNAs by approximately 1.5 times, e.g., to increase from 12-16, e.g., 13 to approximately 18-24, e.g., about 19 U6-gRNAs. Therefore, one skilled in the art can readily reach approximately 18-24, e.g., about 19 promoter-RNAs, e.g., U6-gRNAs in a single vector, e.g., an AAV vector. A further means for increasing the number of promoters and RNAs in a vector is to use a single promoter (e.g., U6) to express an array of RNAs separated by cleavable sequences. And an even further means for increasing the number of promoter-RNAs in a vector, is to express an array of promoter-RNAs separated by cleavable sequences in the intron of a coding sequence or gene; and, in this instance it is advantageous to use a polymerase II promoter, which can have increased expression and enable the transcription of long RNA in a tissue specific manner. (see, e.g., nar.oxfordjournals.org/content/34/7/e53.short and nature.com/mt/journal/v16/n9/abs/mt2008144a.html). In an advantageous embodiment, AAV may package U6 tandem gRNA targeting up to about 50 genes. Accordingly, from the knowledge in the art and the teachings in this disclosure the skilled person can readily make and use vector(s), e.g., a single vector, expressing multiple RNAs or guides under the control or operatively or functionally linked to one or more promoters-especially as to the numbers of RNAs or guides discussed herein, without any undue experimentation.

The guide RNA(s) encoding sequences and/or Cas encoding sequences, can be functionally or operatively linked to regulatory element(s) and hence the regulatory element(s) drive expression. The promoter(s) can be constitutive promoter(s) and/or conditional promoter(s) and/or inducible promoter(s) and/or tissue specific promoter(s). The promoter

can be selected from the group consisting of RNA polymerases, pol I, pol II, pol III, T7, U6, H1, retroviral Rous sarcoma virus (RSV) LTR promoter, the cytomegalovirus (CMV) promoter, the SV40 promoter, the dihydrofolate reductase promoter, the β-actin promoter, the phosphoglycerol kinase (PGK) promoter, and the EF1α promoter. An advantageous promoter is the promoter is U6.

Additional effectors for use according to the invention can be identified by their proximity to cas1 genes, for example, though not limited to, within the region 20 kb from the start of the cas1 gene and 20 kb from the end of the cas1 gene. In certain embodiments, the effector protein comprises at least one HEPN domain and at least 500 amino acids, and wherein the C2c2 effector protein is naturally present in a prokaryotic genome within 20 kb upstream or downstream of a Cas gene or a CRISPR array. Non-limiting examples of Cas proteins include Cas1, CasiB, Cas2, Cas3, Cas4, Cas5, Cas6, Cas7, Cas8, Cas9 (also known as Csn1 and Csx12), Cas10, Csy1, Csy2, Csy3, Cse1, Cse2, Csc1, Csc2, Csa5, Csn2, Csm2, Csm3, Csm4, Csm5, Csm6, Cmr1, Cmr3, Cmr4, Cmr5, Cmr6, Csb1, Csb2, Csb3, Csx17, Csx14, Csx10, Csx16, CsaX, Csx3, Csx1, Csx15, Csf1, Csf2, Csf3, Csf4, homologues thereof, or modified versions thereof. In certain example embodiments, the C2c2 effector protein is naturally present in a prokaryotic genome within 20 kb upstream or downstream of a Cas 1 gene. The terms "orthologue" (also referred to as "ortholog" herein) and "homologue" (also referred to as "homolog" herein) are well known in the art. By means of further guidance, a "homologue" of a protein as used herein is a protein of the same species which performs the same or a similar function as the protein it is a homologue of. Homologous proteins may but need not be structurally related, or are only partially structurally related. An "orthologue" of a protein as used herein is a protein of a different species which performs the same or a similar function as the protein it is an orthologue of. Orthologous proteins may but need not be structurally related, or are only partially structurally related.

Guide Molecules

The methods described herein may be used to screen inhibition of CRISPR systems employing different types of guide molecules. As used herein, the term "guide sequence" and "guide molecule" in the context of a CRISPR-Cas system, comprises any polynucleotide sequence having sufficient complementarity with a target nucleic acid sequence to hybridize with the target nucleic acid sequence and direct sequence-specific binding of a nucleic acid-targeting complex to the target nucleic acid sequence. The guide sequences made using the methods disclosed herein may be a full-length guide sequence, a truncated guide sequence, a full-length sgRNA sequence, a truncated sgRNA sequence, or an E+F sgRNA sequence. In some embodiments, the degree of complementarity of the guide sequence to a given target sequence, when optimally aligned using a suitable alignment algorithm, is about or more than about 50%, 60%, 75%, 80%, 85%, 90%, 95%, 97.5%, 99%, or more. In certain example embodiments, the guide molecule comprises a guide sequence that may be designed to have at least one mismatch with the target sequence, such that a RNA duplex formed between the guide sequence and the target sequence. Accordingly, the degree of complementarity is preferably less than 99%. For instance, where the guide sequence consists of 24 nucleotides, the degree of complementarity is more particularly about 96% or less. In particular embodiments, the guide sequence is designed to have a stretch of two or more adjacent mismatching nucleotides, such that the degree of complementarity over the entire guide sequence is further reduced. For instance, where the guide sequence consists of 24 nucleotides, the degree of complementarity is more particularly about 96% or less, more particularly, about 92% or less, more particularly about 88% or less, more particularly about 84% or less, more particularly about 80% or less, more particularly about 76% or less, more particularly about 72% or less, depending on whether the stretch of two or more mismatching nucleotides encompasses 2, 3, 4, 5, 6 or 7 nucleotides, etc. In some embodiments, aside from the stretch of one or more mismatching nucleotides, the degree of complementarity, when optimally aligned using a suitable alignment algorithm, is about or more than about 50%, 60%, 75%, 80%, 85%, 90%, 95%, 97.5%, 99%, or more. Optimal alignment may be determined with the use of any suitable algorithm for aligning sequences, non-limiting example of which include the Smith-Waterman algorithm, the Needleman-Wunsch algorithm, algorithms based on the Burrows-Wheeler Transform (e.g., the Burrows Wheeler Aligner), ClustalW, Clustal X, BLAT, Novoalign (Novocraft Technologies; available at www.novocraft.com), ELAND (Illumina, San Diego, CA), SOAP (available at soap.genomics.org.cn), and Maq (available at maq.sourceforge.net). The ability of a guide sequence (within a nucleic acid-targeting guide RNA) to direct sequence-specific binding of a nucleic acid-targeting complex to a target nucleic acid sequence may be assessed by any suitable assay. For example, the components of a nucleic acid-targeting CRISPR system sufficient to form a nucleic acid-targeting complex, including the guide sequence to be tested, may be provided to a host cell having the corresponding target nucleic acid sequence, such as by transfection with vectors encoding the components of the nucleic acid-targeting complex, followed by an assessment of preferential targeting (e.g., cleavage) within the target nucleic acid sequence, such as by Surveyor assay as described herein. Similarly, cleavage of a target nucleic acid sequence (or a sequence in the vicinity thereof) may be evaluated in a test tube by providing the target nucleic acid sequence, components of a nucleic acid-targeting complex, including the guide sequence to be tested and a control guide sequence different from the test guide sequence, and comparing binding or rate of cleavage at or in the vicinity of the target sequence between the test and control guide sequence reactions. Other assays are possible, and will occur to those skilled in the art. A guide sequence, and hence a nucleic acid-targeting guide RNA may be selected to target any target nucleic acid sequence.

In certain embodiments, the guide sequence or spacer length of the guide molecules is from 15 to 50 nt. In certain embodiments, the spacer length of the guide RNA is at least 15 nucleotides. In certain embodiments, the spacer length is from 15 to 17 nt, e.g., 15, 16, or 17 nt, from 17 to 20 nt, e.g., 17, 18, 19, or 20 nt, from 20 to 24 nt, e.g., 20, 21, 22, 23, or 24 nt, from 23 to 25 nt, e.g., 23, 24, or 25 nt, from 24 to 27 nt, e.g., 24, 25, 26, or 27 nt, from 27-30 nt, e.g., 27, 28, 29, or 30 nt, from 30-35 nt, e.g., 30, 31, 32, 33, 34, or 35 nt, or 35 nt or longer. In certain example embodiment, the guide sequence is 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 nt.

In some embodiments, the guide sequence is an RNA sequence of between 10 to 50 nt in length, but more particularly of about 20-30 nt advantageously about 20 nt, 23-25 nt or 24 nt. The guide sequence is selected so as to

ensure that it hybridizes to the target sequence. This is described more in detail below. Selection can encompass further steps which increase efficacy and specificity.

In some embodiments, the guide sequence has a canonical length (e.g., about 15-30 nt) is used to hybridize with the target RNA or DNA. In some embodiments, a guide molecule is longer than the canonical length (e.g., >30 nt) is used to hybridize with the target RNA or DNA, such that a region of the guide sequence hybridizes with a region of the RNA or DNA strand outside of the Cas-guide target complex. This can be of interest where additional modifications, such deamination of nucleotides is of interest. In alternative embodiments, it is of interest to maintain the limitation of the canonical guide sequence length.

In some embodiments, the sequence of the guide molecule (direct repeat and/or spacer) is selected to reduce the degree secondary structure within the guide molecule. In some embodiments, about or less than about 75%, 50%, 40%, 30%, 25%, 20%, 15%, 10%, 5%, 1%, or fewer of the nucleotides of the nucleic acid-targeting guide RNA participate in self-complementary base pairing when optimally folded. Optimal folding may be determined by any suitable polynucleotide folding algorithm. Some programs are based on calculating the minimal Gibbs free energy. An example of one such algorithm is mFold, as described by Zuker and Stiegler (Nucleic Acids Res. 9 (1981), 133-148). Another example folding algorithm is the online webserver RNAfold, developed at Institute for Theoretical Chemistry at the University of Vienna, using the centroid structure prediction algorithm (see e.g., A. R. Gruber et al., 2008, Cell 106(1): 23-24; and PA Carr and GM Church, 2009, Nature Biotechnology 27(12): 1151-62).

In some embodiments, it is of interest to reduce the susceptibility of the guide molecule to RNA cleavage, such as to cleavage by Cas13. Accordingly, in particular embodiments, the guide molecule is adjusted to avoid cleavage by Cas13 or other RNA-cleaving enzymes.

In certain embodiments, the guide molecule comprises non-naturally occurring nucleic acids and/or non-naturally occurring nucleotides and/or nucleotide analogs, and/or chemically modifications. Preferably, these non-naturally occurring nucleic acids and non-naturally occurring nucleotides are located outside the guide sequence. Non-naturally occurring nucleic acids can include, for example, mixtures of naturally and non-naturally occurring nucleotides. Non-naturally occurring nucleotides and/or nucleotide analogs may be modified at the ribose, phosphate, and/or base moiety. In an embodiment of the invention, a guide nucleic acid comprises ribonucleotides and non-ribonucleotides. In one such embodiment, a guide comprises one or more ribonucleotides and one or more deoxyribonucleotides. In an embodiment of the invention, the guide comprises one or more non-naturally occurring nucleotide or nucleotide analog such as a nucleotide with phosphorothioate linkage, a locked nucleic acid (LNA) nucleotides comprising a methylene bridge between the 2' and 4' carbons of the ribose ring, or bridged nucleic acids (BNA). Other examples of modified nucleotides include 2'-O-methyl analogs, 2'-deoxy analogs, or 2'-fluoro analogs. Further examples of modified bases include, but are not limited to, 2-aminopurine, 5-bromouridine, pseudouridine, inosine, 7-methylguanosine. Examples of guide RNA chemical modifications include, without limitation, incorporation of 2'-O-methyl (M), 2'-O-methyl 3'phosphorothioate (MS), S-constrained ethyl(cEt), or 2'-O-methyl 3'thioPACE (MSP) at one or more terminal nucleotides. Such chemically modified guides can comprise increased stability and increased activity as compared to unmodified guides, though on-target vs. off-target specificity is not predictable. (See, Hendel, 2015, Nat Biotechnol. 33(9):985-9, doi: 10.1038/nbt.3290, published online 29 Jun. 2015 Ragdarm et al., 0215, *PNAS, E*7110-E7111; Allerson et al., *J. Med. Chem.* 2005, 48:901-904; Bramsen et al., *Front. Genet.,* 2012, 3:154; Deng et al., *PNAS,* 2015, 112:11870-11875; Sharma et al., *MedChemComm.,* 2014, 5:1454-1471; Hendel et al., *Nat. Biotechnol.* (2015) 33(9): 985-989; Li et al., *Nature Biomedical Engineering,* 2017, 1, 0066 DOI:10.1038/s41551-017-0066). In some embodiments, the 5' and/or 3' end of a guide RNA is modified by a variety of functional moieties including fluorescent dyes, polyethylene glycol, cholesterol, proteins, or detection tags. (See Kelly et al., 2016, *J. Biotech.* 233:74-83). In certain embodiments, a guide comprises ribonucleotides in a region that binds to a target RNA and one or more deoxyribonucleotides and/or nucleotide analogs in a region that binds to Cas13. In an embodiment of the invention, deoxyribonucleotides and/or nucleotide analogs are incorporated in engineered guide structures, such as, without limitation, stem-loop regions, and the seed region. For Cas13 guide, in certain embodiments, the modification is not in the 5'-handle of the stem-loop regions. Chemical modification in the 5'-handle of the stem-loop region of a guide may abolish its function (see Li, et al., *Nature Biomedical Engineering,* 2017, 1:0066). In certain embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, or 75 nucleotides of a guide is chemically modified. In some embodiments, 3-5 nucleotides at either the 3' or the 5' end of a guide is chemically modified. In some embodiments, only minor modifications are introduced in the seed region, such as 2'-F modifications. In some embodiments, 2'-F modification is introduced at the 3' end of a guide. In certain embodiments, three to five nucleotides at the 5' and/or the 3' end of the guide are chemically modified with 2'-O-methyl (M), 2'-O-methyl 3' phosphorothioate (MS), S-constrained ethyl(cEt), or 2'-O-methyl 3' thioPACE (MSP). Such modification can enhance genome editing efficiency (see Hendel et al., Nat. Biotechnol. (2015) 33(9): 985-989). In certain embodiments, all of the phosphodiester bonds of a guide are substituted with phosphorothioates (PS) for enhancing levels of gene disruption. In certain embodiments, more than five nucleotides at the 5' and/or the 3' end of the guide are chemically modified with 2'-O-Me, 2'-F or S constrained ethyl(cEt). Such chemically modified guide can mediate enhanced levels of gene disruption (see Ragdarm et al., 0215, *PNAS*, E7110-E7111). In an embodiment of the invention, a guide is modified to comprise a chemical moiety at its 3' and/or 5' end. Such moieties include, but are not limited to amine, azide, alkyne, thio, dibenzocyclooctyne (DBCO), or Rhodamine. In certain embodiment, the chemical moiety is conjugated to the guide by a linker, such as an alkyl chain. In certain embodiments, the chemical moiety of the modified guide can be used to attach the guide to another molecule, such as DNA, RNA, protein, or nanoparticles. Such chemically modified guide can be used to identify or enrich cells generically edited by a CRISPR system (see Lee et al., *eLife,* 2017, 6:e25312, DOI:10.7554).

In some embodiments, the modification to the guide is a chemical modification, an insertion, a deletion or a split. In some embodiments, the chemical modification includes, but is not limited to, incorporation of 2'-O-methyl (M) analogs, 2'-deoxy analogs, 2-thiouridine analogs, N6-methyladenosine analogs, 2'-fluoro analogs, 2-aminopurine, 5-bromouridine, pseudouridine (Ψ), N1-methylpseudouridine (me1Ψ), 5-methoxyuridine(5moU), inosine, 7-methyl-

guanosine, 2'-O-methyl 3'phosphorothioate (MS), S-constrained ethyl(cEt), phosphorothioate (PS), or 2'-O-methyl 3'thioPACE (MSP). In some embodiments, the guide comprises one or more of phosphorothioate modifications. In certain embodiments, at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, or 25 nucleotides of the guide are chemically modified. In certain embodiments, one or more nucleotides in the seed region are chemically modified. In certain embodiments, one or more nucleotides in the 3'-terminus are chemically modified. In certain embodiments, none of the nucleotides in the 5'-handle is chemically modified. In some embodiments, the chemical modification in the seed region is a minor modification, such as incorporation of a 2'-fluoro analog. In a specific embodiment, one nucleotide of the seed region is replaced with a 2'-fluoro analog. In some embodiments, 5 to 10 nucleotides in the 3'-terminus are chemically modified. Such chemical modifications at the 3'-terminus of the Cas13 CrRNA may improve Cas13 activity. In a specific embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 nucleotides in the 3'-terminus are replaced with 2'-fluoro analogues. In a specific embodiment, 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 nucleotides in the 3'-terminus are replaced with 2'-O-methyl (M) analogs.

In some embodiments, the loop of the 5'-handle of the guide is modified. In some embodiments, the loop of the 5'-handle of the guide is modified to have a deletion, an insertion, a split, or chemical modifications. In certain embodiments, the modified loop comprises 3, 4, or 5 nucleotides. In certain embodiments, the loop comprises the sequence of UCUU, UUUU, UAUU, or UGUU.

In some embodiments, the guide molecule forms a stemloop with a separate non-covalently linked sequence, which can be DNA or RNA. In particular embodiments, the sequences forming the guide are first synthesized using the standard phosphoramidite synthetic protocol (Herdewijn, P., ed., Methods in Molecular Biology Col 288, Oligonucleotide Synthesis: Methods and Applications, Humana Press, New Jersey (2012)). In some embodiments, these sequences can be functionalized to contain an appropriate functional group for ligation using the standard protocol known in the art (Hermanson, G. T., Bioconjugate Techniques, Academic Press (2013)). Examples of functional groups include, but are not limited to, hydroxyl, amine, carboxylic acid, carboxylic acid halide, carboxylic acid active ester, aldehyde, carbonyl, chlorocarbonyl, imidazolylcarbonyl, hydrozide, semicarbazide, thio semicarbazide, thiol, maleimide, haloalkyl, sulfonyl, ally, propargyl, diene, alkyne, and azide. Once this sequence is functionalized, a covalent chemical bond or linkage can be formed between this sequence and the direct repeat sequence. Examples of chemical bonds include, but are not limited to, those based on carbamates, ethers, esters, amides, imines, amidines, aminotrizines, hydrozone, disulfides, thioethers, thioesters, phosphorothioates, phosphorodithioates, sulfonamides, sulfonates, fulfones, sulfoxides, ureas, thioureas, hydrazide, oxime, triazole, photolabile linkages, C—C bond forming groups such as Diels-Alder cyclo-addition pairs or ring-closing metathesis pairs, and Michael reaction pairs.

In some embodiments, these stem-loop forming sequences can be chemically synthesized. In some embodiments, the chemical synthesis uses automated, solid-phase oligonucleotide synthesis machines with 2'-acetoxyethyl orthoester (2'-ACE) (Scaringe et al., J. Am. Chem. Soc. (1998) 120: 11820-11821; Scaringe, Methods Enzymol. (2000) 317: 3-18) or 2'-thionocarbamate (2'-TC) chemistry (Dellinger et al., J. Am. Chem. Soc. (2011) 133: 11540-11546; Hendel et al., Nat. Biotechnol. (2015) 33:985-989).

In certain embodiments, the guide molecule comprises (1) a guide sequence capable of hybridizing to a target locus and (2) a tracr mate or direct repeat sequence whereby the direct repeat sequence is located upstream (i.e., 5') from the guide sequence. In a particular embodiment the seed sequence (i.e. the sequence essential critical for recognition and/or hybridization to the sequence at the target locus) of the guide sequence is approximately within the first 10 nucleotides of the guide sequence.

In a particular embodiment the guide molecule comprises a guide sequence linked to a direct repeat sequence, wherein the direct repeat sequence comprises one or more stem loops or optimized secondary structures. In particular embodiments, the direct repeat has a minimum length of 16 nts and a single stem loop. In further embodiments the direct repeat has a length longer than 16 nts, preferably more than 17 nts, and has more than one stem loops or optimized secondary structures. In particular embodiments the guide molecule comprises or consists of the guide sequence linked to all or part of the natural direct repeat sequence. A typical Type V or Type VI CRISPR-cas guide molecule comprises (in 3' to 5' direction or in 5' to 3' direction): a guide sequence a first complimentary stretch (the "repeat"), a loop (which is typically 4 or 5 nucleotides long), a second complimentary stretch (the "anti-repeat" being complimentary to the repeat), and a poly A (often poly U in RNA) tail (terminator). In certain embodiments, the direct repeat sequence retains its natural architecture and forms a single stem loop. In particular embodiments, certain aspects of the guide architecture can be modified, for example by addition, subtraction, or substitution of features, whereas certain other aspects of guide architecture are maintained. Preferred locations for engineered guide molecule modifications, including but not limited to insertions, deletions, and substitutions include guide termini and regions of the guide molecule that are exposed when complexed with the CRISPR-Cas protein and/or target, for example the stemloop of the direct repeat sequence.

In particular embodiments, the stem comprises at least about 4 bp comprising complementary X and Y sequences, although stems of more, e.g., 5, 6, 7, 8, 9, 10, 11 or 12 or fewer, e.g., 3, 2, base pairs are also contemplated. Thus, for example X2-10 and Y2-10 (wherein X and Y represent any complementary set of nucleotides) may be contemplated. In one aspect, the stem made of the X and Y nucleotides, together with the loop will form a complete hairpin in the overall secondary structure; and, this may be advantageous and the amount of base pairs can be any amount that forms a complete hairpin. In one aspect, any complementary X:Y basepairing sequence (e.g., as to length) is tolerated, so long as the secondary structure of the entire guide molecule is preserved. In one aspect, the loop that connects the stem made of X:Y basepairs can be any sequence of the same length (e.g., 4 or 5 nucleotides) or longer that does not interrupt the overall secondary structure of the guide molecule. In one aspect, the stemloop can further comprise, e.g. an MS2 aptamer. In one aspect, the stem comprises about 5-7 bp comprising complementary X and Y sequences, although stems of more or fewer basepairs are also contemplated. In one aspect, non-Watson Crick basepairing is contemplated, where such pairing otherwise generally preserves the architecture of the stemloop at that position.

In particular embodiments the natural hairpin or stemloop structure of the guide molecule is extended or replaced by an extended stemloop. It has been demonstrated that extension of the stem can enhance the assembly of the guide molecule with the CRISPR-Cas protein (Chen et al. Cell. (2013);

155(7): 1479-1491). In particular embodiments the stem of the stemloop is extended by at least 1, 2, 3, 4, 5 or more complementary basepairs (i.e. corresponding to the addition of 2, 4, 6, 8, 10 or more nucleotides in the guide molecule). In particular embodiments these are located at the end of the stem, adjacent to the loop of the stemloop.

In particular embodiments, the susceptibility of the guide molecule to RNAses or to decreased expression can be reduced by slight modifications of the sequence of the guide molecule which do not affect its function. For instance, in particular embodiments, premature termination of transcription, such as premature transcription of U6 Pol-III, can be removed by modifying a putative Pol-III terminator (4 consecutive U's) in the guide molecules sequence. Where such sequence modification is required in the stemloop of the guide molecule, it is preferably ensured by a basepair flip.

In a particular embodiment, the direct repeat may be modified to comprise one or more protein-binding RNA aptamers. In a particular embodiment, one or more aptamers may be included such as part of optimized secondary structure. Such aptamers may be capable of binding a bacteriophage coat protein as detailed further herein.

In some embodiments, the guide molecule forms a duplex with a target RNA comprising at least one target cytosine residue to be edited. Upon hybridization of the guide RNA molecule to the target RNA, the cytidine deaminase binds to the single strand RNA in the duplex made accessible by the mismatch in the guide sequence and catalyzes deamination of one or more target cytosine residues comprised within the stretch of mismatching nucleotides.

A guide sequence, and hence a nucleic acid-targeting guide RNA may be selected to target any target nucleic acid sequence. The target sequence may be mRNA.

In certain embodiments, the target sequence should be associated with a PAM (protospacer adjacent motif) or PFS (protospacer flanking sequence or site); that is, a short sequence recognized by the CRISPR complex. Depending on the nature of the CRISPR-Cas protein, the target sequence should be selected such that its complementary sequence in the DNA duplex (also referred to herein as the non-target sequence) is upstream or downstream of the PAM. In the embodiments of the present invention where the CRISPR-Cas protein is a Cas13 protein, the complementary sequence of the target sequence is downstream or 3' of the PAM or upstream or 5' of the PAM. The precise sequence and length requirements for the PAM differ depending on the Cas13 protein used, but PAMs are typically 2-5 base pair sequences adjacent the protospacer (that is, the target sequence). Examples of the natural PAM sequences for different Cas13 orthologues are provided herein below and the skilled person will be able to identify further PAM sequences for use with a given Cas13 protein.

Further, engineering of the PAM Interacting (PI) domain may allow programing of PAM specificity, improve target site recognition fidelity, and increase the versatility of the CRISPR-Cas protein, for example as described for Cas9 in Kleinstiver B P et al. Engineered CRISPR-Cas9 nucleases with altered PAM specificities. Nature. 2015 Jul. 23; 523 (7561):481-5. doi: 10.1038/nature14592. As further detailed herein, the skilled person will understand that Cas13 proteins may be modified analogously.

In particular embodiment, the guide is an escorted guide. By "escorted" is meant that the CRISPR-Cas system or complex or guide is delivered to a selected time or place within a cell, so that activity of the CRISPR-Cas system or complex or guide is spatially or temporally controlled. For example, the activity and destination of the 3 CRISPR-Cas system or complex or guide may be controlled by an escort RNA aptamer sequence that has binding affinity for an aptamer ligand, such as a cell surface protein or other localized cellular component. Alternatively, the escort aptamer may for example be responsive to an aptamer effector on or in the cell, such as a transient effector, such as an external energy source that is applied to the cell at a particular time.

The escorted CRISPR-Cas systems or complexes have a guide molecule with a functional structure designed to improve guide molecule structure, architecture, stability, genetic expression, or any combination thereof. Such a structure can include an aptamer.

Aptamers are biomolecules that can be designed or selected to bind tightly to other ligands, for example using a technique called systematic evolution of ligands by exponential enrichment (SELEX; Tuerk C, Gold L: "Systematic evolution of ligands by exponential enrichment: RNA ligands to bacteriophage T4 DNA polymerase." Science 1990, 249:505-510). Nucleic acid aptamers can for example be selected from pools of random-sequence oligonucleotides, with high binding affinities and specificities for a wide range of biomedically relevant targets, suggesting a wide range of therapeutic utilities for aptamers (Keefe, Anthony D., Supriya Pai, and Andrew Ellington. "Aptamers as therapeutics." Nature Reviews Drug Discovery 9.7 (2010): 537-550). These characteristics also suggest a wide range of uses for aptamers as drug delivery vehicles (Levy-Nissenbaum, Etgar, et al. "Nanotechnology and aptamers: applications in drug delivery." Trends in biotechnology 26.8 (2008): 442-449; and, Hicke B J, Stephens A W. "Escort aptamers: a delivery service for diagnosis and therapy." J Clin Invest 2000, 106:923-928). Aptamers may also be constructed that function as molecular switches, responding to a que by changing properties, such as RNA aptamers that bind fluorophores to mimic the activity of green fluorescent protein (Paige, Jeremy S., Karen Y. Wu, and Samie R. Jaffrey. "RNA mimics of green fluorescent protein." Science 333.6042 (2011): 642-646). It has also been suggested that aptamers may be used as components of targeted siRNA therapeutic delivery systems, for example targeting cell surface proteins (Zhou, Jiehua, and John J. Rossi. "Aptamer-targeted cell-specific RNA interference." Silence 1.1 (2010): 4).

Accordingly, in particular embodiments, the guide molecule is modified, e.g., by one or more aptamer(s) designed to improve guide molecule delivery, including delivery across the cellular membrane, to intracellular compartments, or into the nucleus. Such a structure can include, either in addition to the one or more aptamer(s) or without such one or more aptamer(s), moiety(ies) so as to render the guide molecule deliverable, inducible or responsive to a selected effector. The invention accordingly comprehends an guide molecule that responds to normal or pathological physiological conditions, including without limitation pH, hypoxia, O_2 concentration, temperature, protein concentration, enzymatic concentration, lipid structure, light exposure, mechanical disruption (e.g. ultrasound waves), magnetic fields, electric fields, or electromagnetic radiation.

Light responsiveness of an inducible system may be achieved via the activation and binding of cryptochrome-2 and CIB1. Blue light stimulation induces an activating conformational change in cryptochrome-2, resulting in recruitment of its binding partner CIB1. This binding is fast and reversible, achieving saturation in <15 sec following pulsed stimulation and returning to baseline <15 min after

the end of stimulation. These rapid binding kinetics result in a system temporally bound only by the speed of transcription/translation and transcript/protein degradation, rather than uptake and clearance of inducing agents. Cytochrome-2 activation is also highly sensitive, allowing for the use of low light intensity stimulation and mitigating the risks of phototoxicity. Further, in a context such as the intact mammalian brain, variable light intensity may be used to control the size of a stimulated region, allowing for greater precision than vector delivery alone may offer.

The invention contemplates energy sources such as electromagnetic radiation, sound energy or thermal energy to induce the guide. Advantageously, the electromagnetic radiation is a component of visible light. In a preferred embodiment, the light is a blue light with a wavelength of about 450 to about 495 nm. In an especially preferred embodiment, the wavelength is about 488 nm. In another preferred embodiment, the light stimulation is via pulses. The light power may range from about 0-9 mW/cm^2. In a preferred embodiment, a stimulation paradigm of as low as 0.25 sec every 15 sec should result in maximal activation.

The chemical or energy sensitive guide may undergo a conformational change upon induction by the binding of a chemical source or by the energy allowing it act as a guide and have the Cas13 CRISPR-Cas system or complex function. The invention can involve applying the chemical source or energy so as to have the guide function and the Cas13 CRISPR-Cas system or complex function; and optionally further determining that the expression of the genomic locus is altered.

There are several different designs of this chemical inducible system: 1. ABI-PYL based system inducible by Abscisic Acid (ABA) (see, e.g., stke.sciencemag.org/cgi/content/abstract/sigtrans;4/164/rs2), 2. FKBP-FRB based system inducible by rapamycin (or related chemicals based on rapamycin) (see, e.g., www.nature.com/nmeth/journal/v2/n6/full/nmeth763.html), 3. GID1-GAI based system inducible by Gibberellin (GA) (see, e.g., www.nature.com/nchembio/journal/v8/n5/full/nchembio.922.html).

A chemical inducible system can be an estrogen receptor (ER) based system inducible by 4-hydroxytamoxifen (4OHT) (see, e.g., www.pnas.org/content/104/3/1027.abstract). A mutated ligand-binding domain of the estrogen receptor called ERT2 translocates into the nucleus of cells upon binding of 4-hydroxytamoxifen. In further embodiments of the invention any naturally occurring or engineered derivative of any nuclear receptor, thyroid hormone receptor, retinoic acid receptor, estrogen receptor, estrogen-related receptor, glucocorticoid receptor, progesterone receptor, androgen receptor may be used in inducible systems analogous to the ER based inducible system.

Another inducible system is based on the design using Transient receptor potential (TRP) ion channel based system inducible by energy, heat or radio-wave (see, e.g., www-.sciencemag.org/content/336/6081/604). These TRP family proteins respond to different stimuli, including light and heat. When this protein is activated by light or heat, the ion channel will open and allow the entering of ions such as calcium into the plasma membrane. This influx of ions will bind to intracellular ion interacting partners linked to a polypeptide including the guide and the other components of the Cas13 CRISPR-Cas complex or system, and the binding will induce the change of sub-cellular localization of the polypeptide, leading to the entire polypeptide entering the nucleus of cells. Once inside the nucleus, the guide protein and the other components of the Cas13 CRISPR-Cas complex will be active and modulating target gene expression in cells.

While light activation may be an advantageous embodiment, sometimes it may be disadvantageous especially for in vivo applications in which the light may not penetrate the skin or other organs. In this instance, other methods of energy activation are contemplated, in particular, electric field energy and/or ultrasound which have a similar effect.

Electric field energy is preferably administered substantially as described in the art, using one or more electric pulses of from about 1 Volt/cm to about 10 kVolts/cm under in vivo conditions. Instead of or in addition to the pulses, the electric field may be delivered in a continuous manner. The electric pulse may be applied for between 1 μs and 500 milliseconds, preferably between 1 μs and 100 milliseconds. The electric field may be applied continuously or in a pulsed manner for 5 about minutes.

As used herein, "electric field energy" is the electrical energy to which a cell is exposed. Preferably the electric field has a strength of from about 1 Volt/cm to about 10 kVolts/cm or more under in vivo conditions (see WO97/49450).

As used herein, the term "electric field" includes one or more pulses at variable capacitance and voltage and including exponential and/or square wave and/or modulated wave and/or modulated square wave forms. References to electric fields and electricity should be taken to include reference the presence of an electric potential difference in the environment of a cell. Such an environment may be set up by way of static electricity, alternating current (AC), direct current (DC), etc, as known in the art. The electric field may be uniform, non-uniform or otherwise, and may vary in strength and/or direction in a time dependent manner.

Single or multiple applications of electric field, as well as single or multiple applications of ultrasound are also possible, in any order and in any combination. The ultrasound and/or the electric field may be delivered as single or multiple continuous applications, or as pulses (pulsatile delivery).

Electroporation has been used in both in vitro and in vivo procedures to introduce foreign material into living cells. With in vitro applications, a sample of live cells is first mixed with the agent of interest and placed between electrodes such as parallel plates. Then, the electrodes apply an electrical field to the cell/implant mixture. Examples of systems that perform in vitro electroporation include the Electro Cell Manipulator ECM600 product, and the Electro Square Porator T820, both made by the BTX Division of Genetronics, Inc (see U.S. Pat. No. 5,869,326).

The known electroporation techniques (both in vitro and in vivo) function by applying a brief high voltage pulse to electrodes positioned around the treatment region. The electric field generated between the electrodes causes the cell membranes to temporarily become porous, whereupon molecules of the agent of interest enter the cells. In known electroporation applications, this electric field comprises a single square wave pulse on the order of 1000 V/cm, of about 100 .mu.s duration. Such a pulse may be generated, for example, in known applications of the Electro Square Porator T820.

Preferably, the electric field has a strength of from about 1 V/cm to about 10 kV/cm under in vitro conditions. Thus, the electric field may have a strength of 1 V/cm, 2 V/cm, 3 V/cm, 4 V/cm, 5 V/cm, 6 V/cm, 7 V/cm, 8 V/cm, 9 V/cm, 10 V/cm, 20 V/cm, 50 V/cm, 100 V/cm, 200 V/cm, 300 V/cm, 400 V/cm, 500 V/cm, 600 V/cm, 700 V/cm, 800

V/cm, 900 V/cm, 1 kV/cm, 2 kV/cm, 5 kV/cm, 10 kV/cm, 20 kV/cm, 50 kV/cm or more. More preferably from about 0.5 kV/cm to about 4.0 kV/cm under in vitro conditions. Preferably the electric field has a strength of from about 1 V/cm to about 10 kV/cm under in vivo conditions. However, the electric field strengths may be lowered where the number of pulses delivered to the target site are increased. Thus, pulsatile delivery of electric fields at lower field strengths is envisaged.

Preferably the application of the electric field is in the form of multiple pulses such as double pulses of the same strength and capacitance or sequential pulses of varying strength and/or capacitance. As used herein, the term "pulse" includes one or more electric pulses at variable capacitance and voltage and including exponential and/or square wave and/or modulated wave/square wave forms.

Preferably the electric pulse is delivered as a waveform selected from an exponential wave form, a square wave form, a modulated wave form and a modulated square wave form.

A preferred embodiment employs direct current at low voltage. Thus, Applicants disclose the use of an electric field which is applied to the cell, tissue or tissue mass at a field strength of between IV/cm and 20V/cm, for a period of 100 milliseconds or more, preferably 15 minutes or more.

Ultrasound is advantageously administered at a power level of from about 0.05 W/cm2 to about 100 W/cm2. Diagnostic or therapeutic ultrasound may be used, or combinations thereof.

As used herein, the term "ultrasound" refers to a form of energy which consists of mechanical vibrations the frequencies of which are so high they are above the range of human hearing. Lower frequency limit of the ultrasonic spectrum may generally be taken as about 20 kHz. Most diagnostic applications of ultrasound employ frequencies in the range 1 and 15 MHz' (From Ultrasonics in Clinical Diagnosis, P. N. T. Wells, ed., 2nd. Edition, Publ. Churchill Livingstone [Edinburgh, London & NY, 1977]).

Ultrasound has been used in both diagnostic and therapeutic applications. When used as a diagnostic tool ("diagnostic ultrasound"), ultrasound is typically used in an energy density range of up to about 100 mW/cm2 (FDA recommendation), although energy densities of up to 750 mW/cm2 have been used. In physiotherapy, ultrasound is typically used as an energy source in a range up to about 3 to 4 W/cm2 (WHO recommendation). In other therapeutic applications, higher intensities of ultrasound may be employed, for example, HIFU at 100 W/cm up to 1 kW/cm2 (or even higher) for short periods of time. The term "ultrasound" as used in this specification is intended to encompass diagnostic, therapeutic and focused ultrasound.

Focused ultrasound (FUS) allows thermal energy to be delivered without an invasive probe (see Morocz et al 1998 Journal of Magnetic Resonance Imaging Vol. 8, No. 1, pp. 136-142. Another form of focused ultrasound is high intensity focused ultrasound (HIFU) which is reviewed by Moussatov et al in Ultrasonics (1998) Vol. 36, No. 8, pp. 893-900 and TranHuuHue et al in Acustica (1997) Vol. 83, No. 6, pp. 1103-1106.

Preferably, a combination of diagnostic ultrasound and a therapeutic ultrasound is employed. This combination is not intended to be limiting, however, and the skilled reader will appreciate that any variety of combinations of ultrasound may be used. Additionally, the energy density, frequency of ultrasound, and period of exposure may be varied.

Preferably the exposure to an ultrasound energy source is at a power density of from about 0.05 to about 100 Wcm−2. Even more preferably, the exposure to an ultrasound energy source is at a power density of from about 1 to about 15 Wcm−2.

Preferably the exposure to an ultrasound energy source is at a frequency of from about 0.015 to about 10.0 MHz. More preferably the exposure to an ultrasound energy source is at a frequency of from about 0.02 to about 5.0 MHz or about 6.0 MHz. Most preferably, the ultrasound is applied at a frequency of 3 MHz.

Preferably the exposure is for periods of from about 10 milliseconds to about 60 minutes. Preferably the exposure is for periods of from about 1 second to about 5 minutes. More preferably, the ultrasound is applied for about 2 minutes. Depending on the particular target cell to be disrupted, however, the exposure may be for a longer duration, for example, for 15 minutes.

Advantageously, the target tissue is exposed to an ultrasound energy source at an acoustic power density of from about 0.05 Wcm−2 to about 10 Wcm−2 with a frequency ranging from about 0.015 to about 10 MHz (see WO 98/52609). However, alternatives are also possible, for example, exposure to an ultrasound energy source at an acoustic power density of above 100 Wcm−2, but for reduced periods of time, for example, 1000 Wcm−2 for periods in the millisecond range or less.

Preferably the application of the ultrasound is in the form of multiple pulses; thus, both continuous wave and pulsed wave (pulsatile delivery of ultrasound) may be employed in any combination. For example, continuous wave ultrasound may be applied, followed by pulsed wave ultrasound, or vice versa. This may be repeated any number of times, in any order and combination. The pulsed wave ultrasound may be applied against a background of continuous wave ultrasound, and any number of pulses may be used in any number of groups.

Preferably, the ultrasound may comprise pulsed wave ultrasound. In a highly preferred embodiment, the ultrasound is applied at a power density of 0.7 Wcm−2 or 1.25 Wcm−2 as a continuous wave. Higher power densities may be employed if pulsed wave ultrasound is used.

Use of ultrasound is advantageous as, like light, it may be focused accurately on a target. Moreover, ultrasound is advantageous as it may be focused more deeply into tissues unlike light. It is therefore better suited to whole-tissue penetration (such as but not limited to a lobe of the liver) or whole organ (such as but not limited to the entire liver or an entire muscle, such as the heart) therapy. Another important advantage is that ultrasound is a non-invasive stimulus which is used in a wide variety of diagnostic and therapeutic applications. By way of example, ultrasound is well known in medical imaging techniques and, additionally, in orthopedic therapy. Furthermore, instruments suitable for the application of ultrasound to a subject vertebrate are widely available and their use is well known in the art.

In particular embodiments, the guide molecule is modified by a secondary structure to increase the specificity of the CRISPR-Cas system and the secondary structure can protect against exonuclease activity and allow for 5' additions to the guide sequence also referred to herein as a protected guide molecule.

In one aspect, the invention provides for hybridizing a "protector RNA" to a sequence of the guide molecule, wherein the "protector RNA" is an RNA strand complementary to the 3' end of the guide molecule to thereby generate a partially double-stranded guide RNA. In an embodiment of the invention, protecting mismatched bases (i.e. the bases of the guide molecule which do not form part of the guide

sequence) with a perfectly complementary protector sequence decreases the likelihood of target RNA binding to the mismatched basepairs at the 3' end. In particular embodiments of the invention, additional sequences comprising an extended length may also be present within the guide molecule such that the guide comprises a protector sequence within the guide molecule. This "protector sequence" ensures that the guide molecule comprises a "protected sequence" in addition to an "exposed sequence" (comprising the part of the guide sequence hybridizing to the target sequence). In particular embodiments, the guide molecule is modified by the presence of the protector guide to comprise a secondary structure such as a hairpin. Advantageously there are three or four to thirty or more, e.g., about 10 or more, contiguous base pairs having complementarity to the protected sequence, the guide sequence or both. It is advantageous that the protected portion does not impede thermodynamics of the CRISPR-Cas system interacting with its target. By providing such an extension including a partially double stranded guide molecule, the guide molecule is considered protected and results in improved specific binding of the CRISPR-Cas complex, while maintaining specific activity.

In particular embodiments, use is made of a truncated guide (tru-guide), i.e. a guide molecule which comprises a guide sequence which is truncated in length with respect to the canonical guide sequence length. As described by Nowak et al. (Nucleic Acids Res (2016) 44 (20): 9555-9564), such guides may allow catalytically active CRISPR-Cas enzyme to bind its target without cleaving the target RNA. In particular embodiments, a truncated guide is used which allows the binding of the target but retains only nickase activity of the CRISPR-Cas enzyme.

CRISPR RNA-Targeting Effector Proteins

In one example embodiment, the CRISPR system effector protein is an RNA-targeting effector protein. In certain embodiments, the CRISPR system effector protein is a Type VI CRISPR system targeting RNA (e.g., Cas13a, Cas13b, Cas13c or Cas13d). Example RNA-targeting effector proteins include Cas13b and C2c2 (now known as Cas13a). It will be understood that the term "C2c2" herein is used interchangeably with "Cas13a". "C2c2" is now referred to as "Cas13a", and the terms are used interchangeably herein unless indicated otherwise. As used herein, the term "Cas13" refers to any Type VI CRISPR system targeting RNA (e.g., Cas13a, Cas13b, Cas13c or Cas13d). When the CRISPR protein is a C2c2 protein, a tracrRNA is not required. C2c2 has been described in Abudayyeh et al. (2016) "C2c2 is a single-component programmable RNA-guided RNA-targeting CRISPR effector"; Science; DOI: 10.1126/science.aaf5573; and Shmakov et al. (2015) "Discovery and Functional Characterization of Diverse Class 2 CRISPR-Cas Systems", Molecular Cell, DOI: dx.doi.org/10.1016/j.molcel.2015.10.008; which are incorporated herein in their entirety by reference. Cas13b has been described in Smargon et al. (2017) "Cas13b Is a Type VI-B CRISPR-Associated RNA-Guided RNases Differentially Regulated by Accessory Proteins Csx27 and Csx28," Molecular Cell. 65, 1-13; dx.doi.org/10.1016/j.molcel.2016.12.023., which is incorporated herein in its entirety by reference.

In some embodiments, one or more elements of a nucleic acid-targeting system is derived from a particular organism comprising an endogenous CRISPR RNA-targeting system. In certain example embodiments, the effector protein CRISPR RNA-targeting system comprises at least one HEPN domain, including but not limited to the HEPN domains described herein, HEPN domains known in the art, and domains recognized to be HEPN domains by comparison to consensus sequence motifs. Several such domains are provided herein. In one non-limiting example, a consensus sequence can be derived from the sequences of C2c2 or Cas13b orthologs provided herein. In certain example embodiments, the effector protein comprises a single HEPN domain. In certain other example embodiments, the effector protein comprises two HEPN domains.

In one example embodiment, the effector protein comprise one or more HEPN domains comprising a RxxxxH motif sequence. The RxxxxH motif sequence can be, without limitation, from a HEPN domain described herein or a HEPN domain known in the art. RxxxxH motif sequences further include motif sequences created by combining portions of two or more HEPN domains. As noted, consensus sequences can be derived from the sequences of the orthologs disclosed in U.S. Provisional Patent Application 62/432,240 entitled "Novel CRISPR Enzymes and Systems," U.S. Provisional Patent Application 62/471,710 entitled "Novel Type VI CRISPR Orthologs and Systems" filed on Mar. 15, 2017, and U.S. Provisional Patent Application 62/484,786 entitled "Novel Type VI CRISPR Orthologs and Systems," filed on Apr. 12, 2017.

In certain other example embodiments, the CRISPR system effector protein is a C2c2 nuclease. The activity of C2c2 may depend on the presence of two HEPN domains. These have been shown to be RNase domains, i.e. nuclease (in particular an endonuclease) cutting RNA. C2c2 HEPN may also target DNA, or potentially DNA and/or RNA. On the basis that the HEPN domains of C2c2 are at least capable of binding to and, in their wild-type form, cutting RNA, then it is preferred that the C2c2 effector protein has RNase function. Regarding C2c2 CRISPR systems, reference is made to U.S. Provisional 62/351,662 filed on Jun. 17, 2016 and U.S. Provisional 62/376,377 filed on Aug. 17, 2016. Reference is also made to U.S. Provisional 62/351,803 filed on Jun. 17, 2016. Reference is also made to U.S. Provisional 62/432,240, entitled "Novel Crispr Enzymes and Systems" filed Dec. 9, 2016 bearing Broad Institute No. 10035.PA4. Reference is further made to East-Seletsky et al. "Two distinct RNase activities of CRISPR-C2c2 enable guide-RNA processing and RNA detection" Nature doi:10/1038/nature19802 and Abudayyeh et al. "C2c2 is a single-component programmable RNA-guided RNA targeting CRISPR effector" bioRxiv doi:10.1101/054742.

In certain embodiments, the C2c2 effector protein is from an organism of a genus selected from the group consisting of: *Leptotrichia, Listeria, Corynebacterium, Sutterella, Legionella, Treponema, Filifactor, Eubacterium, Streptococcus, Lactobacillus, Mycoplasma, Bacteroides, Fluviicola, Flavobacterium, Sphaerochaeta, Azospirillum, Gluconacetobacter, Neisseria, Roseburia, Parvibaculum, Staphylococcus, Nitratifractor, Mycoplasma, Campylobacter*, and *Lachnospira*, or the C2c2 effector protein is an organism selected from the group consisting of: *Leptotrichia shahii, Leptotrichia. wadei, Listeria seeligeri, Clostridium aminophilum, Camobacterium gallinarum, Paludibacter propionicigenes, Listeria* weihenstephanensis, or the C2c2 effector protein is a *L. wadei* F0279 or *L. wadei* F0279 (Lw2) C2C2 effector protein. In another embodiment, the one or more guide RNAs are designed to detect a single nucleotide polymorphism, splice variant of a transcript, or a frameshift mutation in a target RNA or DNA.

In certain example embodiments, the RNA-targeting effector protein is a Type VI-B effector protein, such as Cas13b and Group 29 or Group 30 proteins. In certain example embodiments, the RNA-targeting effector protein

comprises one or more HEPN domains. In certain example embodiments, the RNA-targeting effector protein comprises a C-terminal HEPN domain, a N-terminal HEPN domain, or both. Regarding example Type VI-B effector proteins that may be used in the context of this invention, reference is made to U.S. application Ser. No. 15/331,792 entitled "Novel CRISPR Enzymes and Systems" and filed Oct. 21, 2016, International Patent Application No. PCT/US2016/058302 entitled "Novel CRISPR Enzymes and Systems", and filed Oct. 21, 2016, and Smargon et al. "Cas13b is a Type VI-B CRISPR-associated RNA-Guided RNase differentially regulated by accessory proteins Csx27 and Csx28" Molecular Cell, 65, 1-13 (2017); dx.doi.org/10.1016/j.molcel.2016.12.023, and U.S. Provisional Application No. to be assigned, entitled "Novel Cas13b Orthologues CRISPR Enzymes and System" filed Mar. 15, 2017. In particular embodiments, the Cas13b enzyme is derived from *Bergeyella zoohelcum.*

In certain example embodiments, the RNA-targeting effector protein is a Cas13c effector protein as disclosed in U.S. Provisional Patent Application No. 62/525,165 filed Jun. 26, 2017, and PCT Application No. US 2017/047193 filed Aug. 16, 2017.

In some embodiments, one or more elements of a nucleic acid-targeting system is derived from a particular organism comprising an endogenous CRISPR RNA-targeting system. In certain embodiments, the CRISPR RNA-targeting system is found in *Eubacterium* and Ruminococcus. In certain embodiments, the effector protein comprises targeted and collateral ssRNA cleavage activity. In certain embodiments, the effector protein comprises dual HEPN domains. In certain embodiments, the effector protein lacks a counterpart to the Helical-1 domain of Cas13a. In certain embodiments, the effector protein is smaller than previously characterized class 2 CRISPR effectors, with a median size of 928 aa. This median size is 190 aa (17%) less than that of Cas13c, more than 200 aa (18%) less than that of Cas13b, and more than 300 aa (26%) less than that of Cas13a. In certain embodiments, the effector protein has no requirement for a flanking sequence (e.g., PFS, PAM).

In certain embodiments, the effector protein locus structures include a WYL domain containing accessory protein (so denoted after three amino acids that were conserved in the originally identified group of these domains; see, e.g., WYL domain IPR026881). In certain embodiments, the WYL domain accessory protein comprises at least one helix-turn-helix (HTH) or ribbon-helix-helix (RHH) DNA-binding domain. In certain embodiments, the WYL domain containing accessory protein increases both the targeted and the collateral ssRNA cleavage activity of the RNA-targeting effector protein. In certain embodiments, the WYL domain containing accessory protein comprises an N-terminal RHH domain, as well as a pattern of primarily hydrophobic conserved residues, including an invariant tyrosine-leucine doublet corresponding to the original WYL motif. In certain embodiments, the WYL domain containing accessory protein is WYL1. WYL1 is a single WYL-domain protein associated primarily with Ruminococcus.

In other example embodiments, the Type VI RNA-targeting Cas enzyme is Cas13d. In certain embodiments, Cas13d is *Eubacterium siraeum* DSM 15702 (EsCas13d) or Ruminococcus sp. N15.MGS-57 (RspCas13d) (see, e.g., Yan et al., Cas13d Is a Compact RNA-Targeting Type VI CRISPR Effector Positively Modulated by a WYL-Domain-Containing Accessory Protein, Molecular Cell (2018), doi.org/10.1016/j.molcel.2018.02.028). RspCas13d and EsCas13d have no flanking sequence requirements (e.g., PFS, PAM).

Cas13 RNA Editing

In one aspect, the invention provides a method of modifying or editing a target transcript in a eukaryotic cell. In some embodiments, the method comprises allowing a CRISPR-Cas effector module complex to bind to the target polynucleotide to effect RNA base editing, wherein the CRISPR-Cas effector module complex comprises a Cas effector module complexed with a guide sequence hybridized to a target sequence within said target polynucleotide, wherein said guide sequence is linked to a direct repeat sequence. In some embodiments, the Cas effector module comprises a catalytically inactive CRISPR-Cas protein. In some embodiments, the guide sequence is designed to introduce one or more mismatches to the RNA/RNA duplex formed between the target sequence and the guide sequence. In particular embodiments, the mismatch is an A-C mismatch. In some embodiments, the Cas effector may associate with one or more functional domains (e.g. via fusion protein or suitable linkers). In some embodiments, the effector domain comprises one or more cytidine or adenosine deaminases that mediate endogenous editing of via hydrolytic deamination. In particular embodiments, the effector domain comprises the adenosine deaminase acting on RNA (ADAR) family of enzymes. In particular embodiments, the adenosine deaminase protein or catalytic domain thereof capable of deaminating adenosine or cytidine in RNA or is an RNA specific adenosine deaminase and/or is a bacterial, human, cephalopod, or *Drosophila* adenosine deaminase protein or catalytic domain thereof, preferably TadA, more preferably ADAR, optionally huADAR, optionally (hu)ADAR1 or (hu)ADAR2, preferably huADAR2 or catalytic domain thereof.

The present application relates to modifying a target RNA sequence of interest (see, e.g, Cox et al., Science. 2017 Nov. 24; 358(6366):1019-1027). Using RNA-targeting rather than DNA targeting offers several advantages relevant for therapeutic development. First, there are substantial safety benefits to targeting RNA: there will be fewer off-target events because the available sequence space in the transcriptome is significantly smaller than the genome, and if an off-target event does occur, it will be transient and less likely to induce negative side effects. Second, RNA-targeting therapeutics will be more efficient because they are cell-type independent and not have to enter the nucleus, making them easier to deliver.

A further aspect of the invention relates to the method and composition as envisaged herein for use in prophylactic or therapeutic treatment, preferably wherein said target locus of interest is within a human or animal and to methods of modifying an Adenine or Cytidine in a target RNA sequence of interest, comprising delivering to said target RNA, the composition as described herein. In particular embodiments, the CRISPR system and the adenosine deaminase, or catalytic domain thereof, are delivered as one or more polynucleotide molecules, as a ribonucleoprotein complex, optionally via particles, vesicles, or one or more viral vectors. In particular embodiments, the invention thus comprises compositions for use in therapy. This implies that the methods can be performed in vivo, ex vivo or in vitro. In particular embodiments, when the target is a human or animal target, the method is carried out ex vivo or in vitro.

A further aspect of the invention relates to the method as envisaged herein for use in prophylactic or therapeutic treatment, preferably wherein said target of interest is within a human or animal and to methods of modifying an Adenine or Cytidine in a target RNA sequence of interest, comprising delivering to said target RNA, the composition as described

herein. In particular embodiments, the CRISPR system and the adenosine deaminase, or catalytic domain thereof, are delivered as one or more polynucleotide molecules, as a ribonucleoprotein complex, optionally via particles, vesicles, or one or more viral vectors.

In one aspect, the invention provides a method of generating a eukaryotic cell comprising a modified or edited gene. In some embodiments, the method comprises (a) introducing one or more vectors into a eukaryotic cell, wherein the one or more vectors drive expression of one or more of: Cas effector module, and a guide sequence linked to a direct repeat sequence, wherein the Cas effector module associate one or more effector domains that mediate base editing, and (b) allowing a CRISPR-Cas effector module complex to bind to a target polynucleotide to effect base editing of the target polynucleotide within said disease gene, wherein the CRISPR-Cas effector module complex comprises a Cas effector module complexed with the guide sequence that is hybridized to the target sequence within the target polynucleotide, wherein the guide sequence may be designed to introduce one or more mismatches between the RNA/RNA duplex formed between the guide sequence and the target sequence. In particular embodiments, the mismatch is an A-C mismatch. In some embodiments, the Cas effector may associate with one or more functional domains (e.g. via fusion protein or suitable linkers). In some embodiments, the effector domain comprises one or more cytidine or adenosine deaminases that mediate endogenous editing of via hydrolytic deamination. In particular embodiments, the effector domain comprises the adenosine deaminase acting on RNA (ADAR) family of enzymes. In particular embodiments, the adenosine deaminase protein or catalytic domain thereof capable of deaminating adenosine or cytidine in RNA or is an RNA specific adenosine deaminase and/or is a bacterial, human, cephalopod, or *Drosophila* adenosine deaminase protein or catalytic domain thereof, preferably TadA, more preferably ADAR, optionally huADAR, optionally (hu)ADAR1 or (hu)ADAR2, preferably huADAR2 or catalytic domain thereof.

A further aspect relates to an isolated cell obtained or obtainable from the methods described herein comprising the composition described herein or progeny of said modified cell, preferably wherein said cell comprises a hypoxanthine or a guanine in replace of said Adenine in said target RNA of interest compared to a corresponding cell not subjected to the method. In particular embodiments, the cell is a eukaryotic cell, preferably a human or non-human animal cell, optionally a therapeutic T cell or an antibody-producing B-cell.

In some embodiments, the modified cell is a therapeutic T cell, such as a T cell suitable for adoptive cell transfer therapies (e.g., CAR-T therapies). The modification may result in one or more desirable traits in the therapeutic T cell, as described further herein.

The invention further relates to a method for cell therapy, comprising administering to a patient in need thereof the modified cell described herein, wherein the presence of the modified cell remedies a disease in the patient. In one embodiment, the modified cell for cell therapy is a epithelial cell (e.g., tuft cell).

The present invention may be further illustrated and extended based on aspects of CRISPR-Cas development and use as set forth in the following articles and particularly as relates to delivery of a CRISPR protein complex and uses of an RNA guided endonuclease in cells and organisms:

Multiplex genome engineering using CRISPR-Cas systems. Cong, L., Ran, F. A., Cox, D., Lin, S., Barretto, R., Habib, N., Hsu, P. D., Wu, X., Jiang, W., Marraffini, L. A., & Zhang, F. Science February 15; 339(6121):819-23 (2013);

RNA-guided editing of bacterial genomes using CRISPR-Cas systems. Jiang W., Bikard D., Cox D., Zhang F, Marraffini L A. Nat Biotechnol March; 31(3):233-9 (2013);

One-Step Generation of Mice Carrying Mutations in Multiple Genes by CRISPR-Cas-Mediated Genome Engineering. Wang H., Yang H., Shivalila C S., Dawlaty M M., Cheng A W., Zhang F., Jaenisch R. Cell May 9; 153(4): 910-8 (2013);

Optical control of mammalian endogenous transcription and epigenetic states. Konermann S, Brigham M D, Trevino A E, Hsu P D, Heidenreich M, Cong L, Platt R J, Scott D A, Church G M, Zhang F. Nature. August 22; 500(7463): 472-6. doi: 10.1038/Nature12466. Epub 2013 Aug. 23 (2013);

Double Nicking by RNA-Guided CRISPR Cas9 for Enhanced Genome Editing Specificity. Ran, F A., Hsu, P D., Lin, C Y., Gootenberg, J S., Konermann, S., Trevino, A E., Scott, D A., Inoue, A., Matoba, S., Zhang, Y., & Zhang, F. Cell August 28. pii: S0092-8674(13)01015-5 (2013-A);

DNA targeting specificity of RNA-guided Cas9 nucleases. Hsu, P., Scott, D., Weinstein, J., Ran, F A., Konermann, S., Agarwala, V., Li, Y., Fine, E., Wu, X., Shalem, O., Cradick, T J., Marraffini, L A., Bao, G., & Zhang, F. Nat Biotechnol doi:10.1038/nbt.2647 (2013);

Genome engineering using the CRISPR-Cas9 system. Ran, F A., Hsu, P D., Wright, J., Agarwala, V., Scott, D A., Zhang, F. Nature Protocols November; 8(11):2281-308 (2013-B);

Genome-Scale CRISPR-Cas9 Knockout Screening in Human Cells. Shalem, O., Sanjana, N E., Hartenian, E., Shi, X., Scott, D A., Mikkelson, T., Heckl, D., Ebert, B L., Root, D E., Doench, J G., Zhang, F. Science December 12. (2013);

Crystal structure of cas9 in complex with guide RNA and target DNA. Nishimasu, H., Ran, F A., Hsu, P D., Konermann, S., Shehata, S I., Dohmae, N., Ishitani, R., Zhang, F., Nureki, O. Cell February 27, 156(5):935-49 (2014);

Genome-wide binding of the CRISPR endonuclease Cas9 in mammalian cells. Wu X., Scott D A., Kriz A J., Chiu A C., Hsu P D., Dadon D B., Cheng A W., Trevino A E., Konermann S., Chen S., Jaenisch R., Zhang F., Sharp P A. Nat Biotechnol. April 20. doi: 10.1038/nbt.2889 (2014);

CRISPR-Cas9 Knockin Mice for Genome Editing and Cancer Modeling. Platt R J, Chen S, Zhou Y, Yim M J, Swiech L, Kempton H R, Dahlman J E, Parnas O, Eisenhaure T M, Jovanovic M, Graham D B, Jhunjhunwala S, Heidenreich M, Xavier R J, Langer R, Anderson D G, Hacohen N, Regev A, Feng G, Sharp P A, Zhang F. Cell 159(2): 440-455 DOI: 10.1016/j.cell.2014.09.014 (2014);

Development and Applications of CRISPR-Cas9 for Genome Engineering, Hsu P D, Lander E S, Zhang F., Cell. June 5; 157(6):1262-78 (2014).

Genetic screens in human cells using the CRISPR-Cas9 system, Wang T, Wei J J, Sabatini D M, Lander E S., Science. January 3; 343(6166): 80-84. doi:10.1126/science.1246981 (2014);

Rational design of highly active sgRNAs for CRISPR-Cas9-mediated gene inactivation, Doench J G, Hartenian E, Graham D B, Tothova Z, Hegde M, Smith I, Sullender M, Ebert B L, Xavier R J, Root D E., (published online 3 Sep. 2014) Nat Biotechnol. December; 32(12):1262-7 (2014);

In vivo interrogation of gene function in the mammalian brain using CRISPR-Cas9, Swiech L, Heidenreich M,

Banerjee A, Habib N, Li Y, Trombetta J, Sur M, Zhang F., (published online 19 Oct. 2014) Nat Biotechnol. January; 33(1):102-6 (2015);

Genome-scale transcriptional activation by an engineered CRISPR-Cas9 complex, Konermann S, Brigham M D, Trevino A E, Joung J, Abudayyeh 00, Barcena C, Hsu P D, Habib N, Gootenberg J S, Nishimasu H, Nureki O, Zhang F., Nature. January 29; 517(7536):583-8 (2015).

A split-Cas9 architecture for inducible genome editing and transcription modulation, Zetsche B, Volz S E, Zhang F., (published online 2 Feb. 2015) Nat Biotechnol. February; 33(2):139-42 (2015);

Genome-wide CRISPR Screen in a Mouse Model of Tumor Growth and Metastasis, Chen S, Sanjana N E, Zheng K, Shalem O, Lee K, Shi X, Scott D A, Song J, Pan J Q, Weissleder R, Lee H, Zhang F, Sharp P A. Cell 160, 1246-1260, Mar. 12, 2015 (multiplex screen in mouse), and

In vivo genome editing using *Staphylococcus aureus* Cas9, Ran F A, Cong L, Yan W X, Scott D A, Gootenberg J S, Kriz A J, Zetsche B, Shalem O, Wu X, Makarova K S, Koonin E V, Sharp P A, Zhang F., (published online 1 Apr. 2015), Nature. April 9; 520(7546):186-91(2015).

Shalem et al., "High-throughput functional genomics using CRISPR-Cas9," Nature Reviews Genetics 16, 299-311 (May 2015).

Xu et al., "Sequence determinants of improved CRISPR sgRNA design," Genome Research 25, 1147-1157 (August 2015).

Parnas et al., "A Genome-wide CRISPR Screen in Primary Immune Cells to Dissect Regulatory Networks," Cell 162, 675-686 (Jul. 30, 2015).

Ramanan et al., "CRISPR-Cas9 cleavage of viral DNA efficiently suppresses hepatitis B virus," Scientific Reports 5:10833. doi: 10.1038/srep10833 (Jun. 2, 2015).

Nishimasu et al., "Crystal Structure of *Staphylococcus aureus* Cas9," Cell 162, 1113-1126 (Aug. 27, 2015).

BCL11A enhancer dissection by Cas9-mediated in situ saturating mutagenesis, Canver et al., Nature 527(7577): 192-7 (Nov. 12, 2015) doi: 10.1038/nature15521. Epub 2015 Sep. 16.

*Cpf*1 *Is a Single RNA-Guided Endonuclease of a Class* 2 *CRISPR-Cas System*, Zetsche et al., Cell 163, 759-71 (Sep. 25, 2015).

Discovery and Functional Characterization of Diverse Class 2 *CRISPR-Cas Systems*, Shmakov et al., Molecular Cell, 60(3), 385-397 doi: 10.1016/j.molcel.2015.10.008 Epub Oct. 22, 2015.

*Rationally engineered Cas*9 *nucleases with improved specifcity*, Slaymaker et al., Science 2016 Jan. 1 351 (6268): 84-88 doi: 10.1126/science.aad5227. Epub 2015 Dec. 1.

Gao et al, "Engineered Cpf1 Enzymes with Altered PAM Specificities," bioRxiv 091611; doi: http://dx.doi.org/10.1101/091611 (Dec. 4, 2016).

Cox et al., "RNA editing with CRISPR-Cas13," Science. 2017 Nov. 24; 358(6366):1019-1027. Doi: 10.1126/science.aaq0180. Epub 2017 Oct. 25.

each of which is incorporated herein by reference, may be considered in the practice of the instant invention, and discussed briefly below:

Cong et al. engineered type II CRISPR-Cas systems for use in eukaryotic cells based on both *Streptococcus thermophilus* Cas9 and also *Streptococcus pyogenes* Cas9 and demonstrated that Cas9 nucleases can be directed by short RNAs to induce precise cleavage of DNA in human and mouse cells. Their study further showed that Cas9 as converted into a nicking enzyme can be used to facilitate homology-directed repair in eukaryotic cells with minimal mutagenic activity. Additionally, their study demonstrated that multiple guide sequences can be encoded into a single CRISPR array to enable simultaneous editing of several at endogenous genomic loci sites within the mammalian genome, demonstrating easy programmability and wide applicability of the RNA-guided nuclease technology. This ability to use RNA to program sequence specific DNA cleavage in cells defined a new class of genome engineering tools. These studies further showed that other CRISPR loci are likely to be transplantable into mammalian cells and can also mediate mammalian genome cleavage. Importantly, it can be envisaged that several aspects of the CRISPR-Cas system can be further improved to increase its efficiency and versatility.

Jiang et al. used the clustered, regularly interspaced, short palindromic repeats (CRISPR)-associated Cas9 endonuclease complexed with dual-RNAs to introduce precise mutations in the genomes of *Streptococcus pneumoniae* and *Escherichia coli*. The approach relied on dual-RNA:Cas9-directed cleavage at the targeted genomic site to kill unmutated cells and circumvents the need for selectable markers or counter-selection systems. The study reported reprogramming dual-RNA:Cas9 specificity by changing the sequence of short CRISPR RNA (crRNA) to make single- and multinucleotide changes carried on editing templates. The study showed that simultaneous use of two crRNAs enabled multiplex mutagenesis. Furthermore, when the approach was used in combination with recombineering, in *S. pneumoniae*, nearly 100% of cells that were recovered using the described approach contained the desired mutation, and in *E. coli,* 65% that were recovered contained the mutation.

Wang et al. (2013) used the CRISPR-Cas system for the one-step generation of mice carrying mutations in multiple genes which were traditionally generated in multiple steps by sequential recombination in embryonic stem cells and/or time-consuming intercrossing of mice with a single mutation. The CRISPR-Cas system will greatly accelerate the in vivo study of functionally redundant genes and of epistatic gene interactions.

Konermann et al. (2013) addressed the need in the art for versatile and robust technologies that enable optical and chemical modulation of DNA-binding domains based CRISPR Cas9 enzyme and also Transcriptional Activator Like Effectors.

Ran et al. (2013-A) described an approach that combined a Cas9 nickase mutant with paired guide RNAs to introduce targeted double-strand breaks. This addresses the issue of the Cas9 nuclease from the microbial CRISPR-Cas system being targeted to specific genomic loci by a guide sequence, which can tolerate certain mismatches to the DNA target and thereby promote undesired off-target mutagenesis. Because individual nicks in the genome are repaired with high fidelity, simultaneous nicking via appropriately offset guide RNAs is required for double-stranded breaks and extends the number of specifically recognized bases for target cleavage. The authors demonstrated that using paired nicking can reduce off-target activity by 50- to 1,500-fold in cell lines and to facilitate gene knockout in mouse zygotes without sacrificing on-target cleavage

efficiency. This versatile strategy enables a wide variety of genome editing applications that require high specificity.

Hsu et al. (2013) characterized SpCas9 targeting specificity in human cells to inform the selection of target sites and avoid off-target effects. The study evaluated >700 guide RNA variants and SpCas9-induced indel mutation levels at >100 predicted genomic off-target loci in 293T and 293FT cells. The authors that SpCas9 tolerates mismatches between guide RNA and target DNA at different positions in a sequence-dependent manner, sensitive to the number, position and distribution of mismatches. The authors further showed that SpCas9-mediated cleavage is unaffected by DNA methylation and that the dosage of SpCas9 and guide RNA can be titrated to minimize off-target modification. Additionally, to facilitate mammalian genome engineering applications, the authors reported providing a web-based software tool to guide the selection and validation of target sequences as well as off-target analyses.

Ran et al. (2013-B) described a set of tools for Cas9-mediated genome editing via non-homologous end joining (NHEJ) or homology-directed repair (HDR) in mammalian cells, as well as generation of modified cell lines for downstream functional studies. To minimize off-target cleavage, the authors further described a double-nicking strategy using the Cas9 nickase mutant with paired guide RNAs. The protocol provided by the authors experimentally derived guidelines for the selection of target sites, evaluation of cleavage efficiency and analysis of off-target activity. The studies showed that beginning with target design, gene modifications can be achieved within as little as 1-2 weeks, and modified clonal cell lines can be derived within 2-3 weeks.

Shalem et al. described a new way to interrogate gene function on a genome-wide scale. Their studies showed that delivery of a genome-scale CRISPR-Cas9 knockout (GeCKO) library targeted 18,080 genes with 64,751 unique guide sequences enabled both negative and positive selection screening in human cells. First, the authors showed use of the GeCKO library to identify genes essential for cell viability in cancer and pluripotent stem cells. Next, in a melanoma model, the authors screened for genes whose loss is involved in resistance to vemurafenib, a therapeutic that inhibits mutant protein kinase BRAF. Their studies showed that the highest-ranking candidates included previously validated genes NF1 and MED12 as well as novel hits NF2, CUL3, TADA2B, and TADA1. The authors observed a high level of consistency between independent guide RNAs targeting the same gene and a high rate of hit confirmation, and thus demonstrated the promise of genome-scale screening with Cas9.

Nishimasu et al. reported the crystal structure of *Streptococcus pyogenes* Cas9 in complex with sgRNA and its target DNA at 2.5 A° resolution. The structure revealed a bilobed architecture composed of target recognition and nuclease lobes, accommodating the sgRNA:DNA heteroduplex in a positively charged groove at their interface. Whereas the recognition lobe is essential for binding sgRNA and DNA, the nuclease lobe contains the HNH and RuvC nuclease domains, which are properly positioned for cleavage of the complementary and non-complementary strands of the target DNA, respectively. The nuclease lobe also contains a carboxyl-terminal domain responsible for the interaction with the protospacer adjacent motif (PAM). This high-resolution structure and accompanying functional analyses have revealed the molecular mechanism of RNA-guided DNA targeting by Cas9, thus paving the way for the rational design of new, versatile genome-editing technologies.

Wu et al. mapped genome-wide binding sites of a catalytically inactive Cas9 (dCas9) from *Streptococcus pyogenes* loaded with single guide RNAs (sgRNAs) in mouse embryonic stem cells (mESCs). The authors showed that each of the four sgRNAs tested targets dCas9 to between tens and thousands of genomic sites, frequently characterized by a 5-nucleotide seed region in the sgRNA and an NGG protospacer adjacent motif (PAM). Chromatin inaccessibility decreases dCas9 binding to other sites with matching seed sequences; thus 70% of off-target sites are associated with genes. The authors showed that targeted sequencing of 295 dCas9 binding sites in mESCs transfected with catalytically active Cas9 identified only one site mutated above background levels. The authors proposed a two-state model for Cas9 binding and cleavage, in which a seed match triggers binding but extensive pairing with target DNA is required for cleavage.

Platt et al. established a Cre-dependent Cas9 knockin mouse. The authors demonstrated in vivo as well as ex vivo genome editing using adeno-associated virus (AAV)-, lentivirus-, or particle-mediated delivery of guide RNA in neurons, immune cells, and endothelial cells.

Hsu et al. (2014) is a review article that discusses generally CRISPR-Cas9 history from yogurt to genome editing, including genetic screening of cells.

Wang et al. (2014) relates to a pooled, loss-of-function genetic screening approach suitable for both positive and negative selection that uses a genome-scale lentiviral single guide RNA (sgRNA) library.

Doench et al. created a pool of sgRNAs, tiling across all possible target sites of a panel of six endogenous mouse and three endogenous human genes and quantitatively assessed their ability to produce null alleles of their target gene by antibody staining and flow cytometry. The authors showed that optimization of the PAM improved activity and also provided an on-line tool for designing sgRNAs.

Swiech et al. demonstrate that AAV-mediated SpCas9 genome editing can enable reverse genetic studies of gene function in the brain.

Konermann et al. (2015) discusses the ability to attach multiple effector domains, e.g., transcriptional activator, functional and epigenomic regulators at appropriate positions on the guide such as stem or tetraloop with and without linkers.

Zetsche et al. demonstrates that the Cas9 enzyme can be split into two and hence the assembly of Cas9 for activation can be controlled.

Chen et al. relates to multiplex screening by demonstrating that a genome-wide in vivo CRISPR-Cas9 screen in mice reveals genes regulating lung metastasis.

Ran et al. (2015) relates to SaCas9 and its ability to edit genomes and demonstrates that one cannot extrapolate from biochemical assays.

Shalem et al. (2015) described ways in which catalytically inactive Cas9 (dCas9) fusions are used to synthetically repress (CRISPRi) or activate (CRISPRa) expression, showing. advances using Cas9 for genome-scale

screens, including arrayed and pooled screens, knockout approaches that inactivate genomic loci and strategies that modulate transcriptional activity.

Xu et al. (2015) assessed the DNA sequence features that contribute to single guide RNA (sgRNA) efficiency in CRISPR-based screens. The authors explored efficiency of CRISPR-Cas9 knockout and nucleotide preference at the cleavage site. The authors also found that the sequence preference for CRISPRi/a is substantially different from that for CRISPR-Cas9 knockout.

Parnas et al. (2015) introduced genome-wide pooled CRISPR-Cas9 libraries into dendritic cells (DCs) to identify genes that control the induction of tumor necrosis factor (Tnf) by bacterial lipopolysaccharide (LPS). Known regulators of Tlr4 signaling and previously unknown candidates were identified and classified into three functional modules with distinct effects on the canonical responses to LPS.

Ramanan et al (2015) demonstrated cleavage of viral episomal DNA (cccDNA) in infected cells. The HBV genome exists in the nuclei of infected hepatocytes as a 3.2 kb double-stranded episomal DNA species called covalently closed circular DNA (cccDNA), which is a key component in the HBV life cycle whose replication is not inhibited by current therapies. The authors showed that sgRNAs specifically targeting highly conserved regions of HBV robustly suppresses viral replication and depleted cccDNA.

Nishimasu et al. (2015) reported the crystal structures of SaCas9 in complex with a single guide RNA (sgRNA) and its double-stranded DNA targets, containing the 5'-TTGAAT-3' PAM and the 5'-TTGGGT-3' PAM. A structural comparison of SaCas9 with SpCas9 highlighted both structural conservation and divergence, explaining their distinct PAM specificities and orthologous sgRNA recognition.

Canver et al. (2015) demonstrated a CRISPR-Cas9-based functional investigation of non-coding genomic elements. The authors developed pooled CRISPR-Cas9 guide RNA libraries to perform in situ saturating mutagenesis of the human and mouse BCL11A enhancers which revealed critical features of the enhancers.

Zetsche et al. (2015) reported characterization of Cpf1, a class 2 CRISPR nuclease from *Francisella novicida* U112 having features distinct from Cas9. Cpf1 is a single RNA-guided endonuclease lacking tracrRNA, utilizes a T-rich protospacer-adjacent motif, and cleaves DNA via a staggered DNA double-stranded break.

Shmakov et al. (2015) reported three distinct Class 2 CRISPR-Cas systems. Two system CRISPR enzymes (C2c1 and C2c3) contain RuvC-like endonuclease domains distantly related to Cpf1. Unlike Cpf1, C2c1 depends on both crRNA and tracrRNA for DNA cleavage. The third enzyme (C2c2) contains two predicted HEPN RNase domains and is tracrRNA independent.

Slaymaker et al (2016) reported the use of structure-guided protein engineering to improve the specificity of *Streptococcus pyogenes* Cas9 (SpCas9). The authors developed "enhanced specificity" SpCas9 (eSpCas9) variants which maintained robust on-target cleavage with reduced off-target effects.

Cox et al., (2017) reported the use of catalytically inactive Cas13 (dCas13) to direct adenosine-to-inosine deaminase activity by ADAR2 (adenosine deaminase acting on RNA type 2) to transcripts in mammalian cells. The system, referred to as RNA Editing for Programmable A to I Replacement (REPAIR), has no strict sequence constraints and can be used to edit full-length transcripts. The authors further engineered the system to create a high-specificity variant and minimized the system to facilitate viral delivery.

The methods and tools provided herein are may be designed for use with or Cas13, a type II nuclease that does not make use of tracrRNA. Orthologs of Cas13 have been identified in different bacterial species as described herein. Further type II nucleases with similar properties can be identified using methods described in the art (Shmakov et al. 2015, 60:385-397; Abudayeh et al. 2016, Science, 5; 353 (6299)). In particular embodiments, such methods for identifying novel CRISPR effector proteins may comprise the steps of selecting sequences from the database encoding a seed which identifies the presence of a CRISPR Cas locus, identifying loci located within 10 kb of the seed comprising Open Reading Frames (ORFs) in the selected sequences, selecting therefrom loci comprising ORFs of which only a single ORF encodes a novel CRISPR effector having greater than 700 amino acids and no more than 90% homology to a known CRISPR effector. In particular embodiments, the seed is a protein that is common to the CRISPR-Cas system, such as Cas1. In further embodiments, the CRISPR array is used as a seed to identify new effector proteins.

Also, "Dimeric CRISPR RNA-guided FokI nucleases for highly specific genome editing", Shengdar Q. Tsai, Nicolas Wyvekens, Cyd Khayter, Jennifer A. Foden, Vishal Thapar, Deepak Reyon, Mathew J. Goodwin, Martin J. Aryee, J. Keith Joung Nature Biotechnology 32(6): 569-77 (2014), relates to dimeric RNA-guided FokI Nucleases that recognize extended sequences and can edit endogenous genes with high efficiencies in human cells.

With respect to general information on CRISPR/Cas Systems, components thereof, and delivery of such components, including methods, materials, delivery vehicles, vectors, particles, and making and using thereof, including as to amounts and formulations, as well as CRISPR-Cas-expressing eukaryotic cells, CRISPR-Cas expressing eukaryotes, such as a mouse, reference is made to: U.S. Pat. Nos. 8,999,641, 8,993,233, 8,697,359, 8,771,945, 8,795,965, 8,865,406, 8,871,445, 8,889,356, 8,889,418, 8,895,308, 8,906,616, 8,932,814, and 8,945,839; US Patent Publications US 2014-0310830 (U.S. application Ser. No. 14/105,031), US 2014-0287938 A1 (U.S. application Ser. No. 14/213,991), US 2014-0273234 A1 (U.S. application Ser. No. 14/293,674), US2014-0273232 A1 (U.S. application Ser. No. 14/290,575), US 2014-0273231 (U.S. application Ser. No. 14/259,420), US 2014-0256046 A1 (U.S. application Ser. No. 14/226,274), US 2014-0248702 A1 (U.S. application Ser. No. 14/258,458), US 2014-0242700 A1 (U.S. application Ser. No. 14/222,930), US 2014-0242699 A1 (U.S. application Ser. No. 14/183,512), US 2014-0242664 A1 (U.S. application Ser. No. 14/104,990), US 2014-0234972 A1 (U.S. application Ser. No. 14/183,471), US 2014-0227787 A1 (U.S. application Ser. No. 14/256,912), US 2014-0189896 A1 (U.S. application Ser. No. 14/105,035), US 2014-0186958 (U.S. application Ser. No. 14/105,017), US 2014-0186919 A1 (U.S. application Ser. No. 14/104,977), US 2014-0186843 A1 (U.S. application Ser. No. 14/104,900), US 2014-0179770 A1 (U.S. application Ser. No. 14/104,837) and US 2014-0179006 A1 (U.S. application Ser. No. 14/183,486), US 2014-0170753 (U.S. application Ser. No. 14/183,429); US 2015-0184139 (U.S. application Ser. No. 14/324,960); Ser. No. 14/054,414 European Patent Applications EP 2 771 468 (EP13818570.7), EP 2 764 103 (EP13824232.6), and EP 2 784 162

(EP14170383.5); and PCT Patent Publications WO2014/093661 (PCT/US2013/074743), WO2014/093694 (PCT/US2013/074790), WO2014/093595 (PCT/US2013/074611), WO2014/093718 (PCT/US2013/074825), WO2014/093709 (PCT/US2013/074812), WO2014/093622 (PCT/US2013/074667), WO2014/093635 (PCT/US2013/074691), WO2014/093655 (PCT/US2013/074736), WO2014/093712 (PCT/US2013/074819), WO2014/093701 (PCT/US2013/074800), WO2014/018423 (PCT/US2013/051418), WO2014/204723 (PCT/US2014/041790), WO2014/204724 (PCT/US2014/041800), WO2014/204725 (PCT/US2014/041803), WO2014/204726 (PCT/US2014/041804), WO2014/204727 (PCT/US2014/041806), WO2014/204728 (PCT/US2014/041808), WO2014/204729 (PCT/US2014/041809), WO2015/089351 (PCT/US2014/069897), WO2015/089354 (PCT/US2014/069902), WO2015/089364 (PCT/US2014/069925), WO2015/089427 (PCT/US2014/070068), WO2015/089462 (PCT/US2014/070127), WO2015/089419 (PCT/US2014/070057), WO2015/089465 (PCT/US2014/070135), WO2015/089486 (PCT/US2014/070175), WO2015/058052 (PCT/US2014/061077), WO2015/070083 (PCT/US2014/064663), WO2015/089354 (PCT/US2014/069902), WO2015/089351 (PCT/US2014/069897), WO2015/089364 (PCT/US2014/069925), WO2015/089427 (PCT/US2014/070068), WO2015/089473 (PCT/US2014/070152), WO2015/089486 (PCT/US2014/070175), WO2016/049258 (PCT/US2015/051830), WO2016/094867 (PCT/US2015/065385), WO2016/094872 (PCT/US2015/065393), WO2016/094874 (PCT/US2015/065396), WO2016/106244 (PCT/US2015/067177).

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Each of these patents, patent publications, and applications, and all documents cited therein or during their prosecution ("appln cited documents") and all documents cited or referenced in the appln cited documents, together with any instructions, descriptions, product specifications, and product sheets for any products mentioned therein or in any document therein and incorporated by reference herein, are hereby incorporated herein by reference, and may be employed in the practice of the invention. All documents (e.g., these patents, patent publications and applications and the appln cited documents) are incorporated herein by reference to the same extent as if each individual document was specifically and individually indicated to be incorporated by reference.

In particular embodiments, pre-complexed guide RNA and CRISPR effector protein, (optionally, adenosine deaminase fused to a CRISPR protein or an adaptor) are delivered as a ribonucleoprotein (RNP). RNPs have the advantage that they lead to rapid editing effects even more so than the RNA method because this process avoids the need for transcription. An important advantage is that both RNP delivery is transient, reducing off-target effects and toxicity issues. Efficient genome editing in different cell types has been observed by Kim et al. (2014, Genome Res. 24(6):1012-9), Paix et al. (2015, Genetics 204(1):47-54), Chu et al. (2016, BMC Biotechnol. 16:4), and Wang et al. (2013, Cell. 9; 153(4):910-8).

In particular embodiments, the ribonucleoprotein is delivered by way of a polypeptide-based shuttle agent as described in WO2016161516. WO2016161516 describes efficient transduction of polypeptide cargos using synthetic peptides comprising an endosome leakage domain (ELD) operably linked to a cell penetrating domain (CPD), to a histidine-rich domain and a CPD. Similarly these polypeptides can be used for the delivery of CRISPR-effector based RNPs in eukaryotic cells.

Tale Systems

As disclosed herein editing can be made by way of the transcription activator-like effector nucleases (TALENs) system. Transcription activator-like effectors (TALEs) can be engineered to bind practically any desired DNA sequence. Exemplary methods of genome editing using the TALEN system can be found for example in Cermak T. Doyle E L. Christian M. Wang L. Zhang Y. Schmidt C, et al. Efficient design and assembly of custom TALEN and other TAL effector-based constructs for DNA targeting. Nucleic Acids Res. 2011; 39:e82; Zhang F. Cong L. Lodato S. Kosuri S. Church G M. Arlotta P Efficient construction of sequence-specific TAL effectors for modulating mammalian transcription. Nat Biotechnol. 2011; 29:149-153 and U.S. Pat. Nos. 8,450,471, 8,440,431 and 8,440,432, all of which are specifically incorporated by reference.

In advantageous embodiments of the invention, the methods provided herein use isolated, non-naturally occurring, recombinant or engineered DNA binding proteins that comprise TALE monomers as a part of their organizational structure that enable the targeting of nucleic acid sequences with improved efficiency and expanded specificity.

Naturally occurring TALEs or "wild type TALEs" are nucleic acid binding proteins secreted by numerous species of proteobacteria. TALE polypeptides contain a nucleic acid binding domain composed of tandem repeats of highly conserved monomer polypeptides that are predominantly 33, 34 or 35 amino acids in length and that differ from each other mainly in amino acid positions 12 and 13. In advantageous embodiments the nucleic acid is DNA. As used herein, the term "polypeptide monomers", or "TALE monomers" will be used to refer to the highly conserved repetitive polypeptide sequences within the TALE nucleic acid binding domain and the term "repeat variable di-residues" or "RVD" will be used to refer to the highly variable amino acids at positions 12 and 13 of the polypeptide monomers. As provided throughout the disclosure, the amino acid residues of the RVD are depicted using the IUPAC single letter code for amino acids. A general representation of a TALE monomer which is comprised within the DNA binding domain is X1-11-(X12X13)-X14-33 or 34 or 35, where the subscript indicates the amino acid position and X represents any amino acid. X12X13 indicate the RVDs. In some polypeptide monomers, the variable amino acid at position 13 is missing or absent and in such polypeptide monomers, the RVD consists of a single amino acid. In such cases the RVD may be alternatively represented as X*, where X represents X12 and (*) indicates that X13 is absent. The DNA binding domain comprises several repeats of TALE monomers and this may be represented as (X1-11-(X12X13)-X14-33 or 34 or 35)z, where in an advantageous embodiment, z is at least 5 to 40. In a further advantageous embodiment, z is at least 10 to 26.

The TALE monomers have a nucleotide binding affinity that is determined by the identity of the amino acids in its RVD. For example, polypeptide monomers with an RVD of NI preferentially bind to adenine (A), polypeptide monomers with an RVD of NG preferentially bind to thymine (T), polypeptide monomers with an RVD of HD preferentially bind to cytosine (C) and polypeptide monomers with an RVD ofNN preferentially bind to both adenine (A) and guanine (G). In yet another embodiment of the invention, polypeptide monomers with an RVD of IG preferentially bind to T. Thus, the number and order of the polypeptide monomer repeats in the nucleic acid binding domain of a TALE determines its nucleic acid target specificity. In still further embodiments of the invention, polypeptide monomers with an RVD ofNS recognize all four base pairs and may bind to A, T, G or C. The structure and function of TALEs is further described in, for example, Moscou et al., Science 326:1501 (2009); Boch et al., Science 326:1509-1512 (2009); and Zhang et al., Nature Biotechnology 29:149-153 (2011), each of which is incorporated by reference in its entirety.

The TALE polypeptides used in methods of the invention are isolated, non-naturally occurring, recombinant or engineered nucleic acid-binding proteins that have nucleic acid or DNA binding regions containing polypeptide monomer repeats that are designed to target specific nucleic acid sequences.

As described herein, polypeptide monomers having an RVD of HN or NH preferentially bind to guanine and thereby allow the generation of TALE polypeptides with high binding specificity for guanine containing target nucleic acid sequences. In a preferred embodiment of the invention, polypeptide monomers having RVDs RN, NN, NK, SN, NH, KN, HN, NQ, HH, RG, KH, RH and SS

preferentially bind to guanine. In a much more advantageous embodiment of the invention, polypeptide monomers having RVDs RN, NK, NQ, HH, KH, RH, SS and SN preferentially bind to guanine and thereby allow the generation of TALE polypeptides with high binding specificity for guanine containing target nucleic acid sequences. In an even more advantageous embodiment of the invention, polypeptide monomers having RVDs HH, KH, NH, NK, NQ, RH, RN and SS preferentially bind to guanine and thereby allow the generation of TALE polypeptides with high binding specificity for guanine containing target nucleic acid sequences. In a further advantageous embodiment, the RVDs that have high binding specificity for guanine are RN, NH RH and KH. Furthermore, polypeptide monomers having an RVD of NV preferentially bind to adenine and guanine. In more preferred embodiments of the invention, polypeptide monomers having RVDs of H*, HA, KA, N*, NA, NC, NS, RA, and S* bind to adenine, guanine, cytosine and thymine with comparable affinity.

The predetermined N-terminal to C-terminal order of the one or more polypeptide monomers of the nucleic acid or DNA binding domain determines the corresponding predetermined target nucleic acid sequence to which the TALE polypeptides will bind. As used herein the polypeptide monomers and at least one or more half polypeptide monomers are "specifically ordered to target" the genomic locus or gene of interest. In plant genomes, the natural TALE-binding sites always begin with a thymine (T), which may be specified by a cryptic signal within the non-repetitive N-terminus of the TALE polypeptide; in some cases this region may be referred to as repeat 0. In animal genomes, TALE binding sites do not necessarily have to begin with a thymine (T) and TALE polypeptides may target DNA sequences that begin with T, A, G or C. The tandem repeat of TALE monomers always ends with a half-length repeat or a stretch of sequence that may share identity with only the first 20 amino acids of a repetitive full length TALE monomer and this half repeat may be referred to as a half-monomer (FIG. **8**), which is included in the term "TALE monomer". Therefore, it follows that the length of the nucleic acid or DNA being targeted is equal to the number of full polypeptide monomers plus two.

As described in Zhang et al., Nature Biotechnology 29:149-153 (2011), TALE polypeptide binding efficiency may be increased by including amino acid sequences from the "capping regions" that are directly N-terminal or C-terminal of the DNA binding region of naturally occurring TALEs into the engineered TALEs at positions N-terminal or C-terminal of the engineered TALE DNA binding region. Thus, in certain embodiments, the TALE polypeptides described herein further comprise an N-terminal capping region and/or a C-terminal capping region.

An exemplary amino acid sequence of a N-terminal capping region is:

(SEQ ID NO: 1)

M D P I R S R T P S P A R E L L S G P Q P D G V Q

P T A D R G V S P P A G G P L D G L P A R R T M S

R T R L P S P P A P S P A F S A D S F S D L L R Q

F D P S L F N T S L F D S L P P F G A H H T E A A

T G E W D E V Q S G L R A A D A P P P T M R V A V

T A A R P P R A K P A P R R R A A Q P S D A S P A

-continued

A Q V D L R T L G Y S Q Q Q Q E K I K P K V R S T

V A Q H H E A L V G H G F T H A H I V A L S Q H P

A A L G T V A V K Y Q D M I A A L P E A T H E A I

V G V G K Q W S G A R A L E A L L T V A G E L R G

P P L Q L D T G Q L L K I A K R G G V T A V E A V

H A W R N A L T G A P L N

An exemplary amino acid sequence of a C-terminal capping region is:

(SEQ ID NO: 2)

R P A L E S I V A Q L S R P D P A L A A L T N D H

L V A L A C L G G R P A L D A V K K G L P H A P A

L I K R T N R R I P E R T S H R V A D H A Q V V R

V L G F F Q C H S H P A Q A F D D A M T Q F G M S

R H G L L Q L F R R V G V T E L E A R S G T L P P

A S Q R W D R I L Q A S G M K R A K P S P T S T Q

T P D Q A S L H A F A D S L E R D L D A P S P M H

E G D Q T R A S

As used herein the predetermined "N-terminus" to "C terminus" orientation of the N-terminal capping region, the DNA binding domain comprising the repeat TALE monomers and the C-terminal capping region provide structural basis for the organization of different domains in the d-TALEs or polypeptides of the invention.

The entire N-terminal and/or C-terminal capping regions are not necessary to enhance the binding activity of the DNA binding region. Therefore, in certain embodiments, fragments of the N-terminal and/or C-terminal capping regions are included in the TALE polypeptides described herein.

In certain embodiments, the TALE polypeptides described herein contain a N-terminal capping region fragment that included at least 10, 20, 30, 40, 50, 54, 60, 70, 80, 87, 90, 94, 100, 102, 110, 117, 120, 130, 140, 147, 150, 160, 170, 180, 190, 200, 210, 220, 230, 240, 250, 260 or 270 amino acids of an N-terminal capping region. In certain embodiments, the N-terminal capping region fragment amino acids are of the C-terminus (the DNA-binding region proximal end) of an N-terminal capping region. As described in Zhang et al., Nature Biotechnology 29:149-153 (2011), N-terminal capping region fragments that include the C-terminal 240 amino acids enhance binding activity equal to the full length capping region, while fragments that include the C-terminal 147 amino acids retain greater than 80% of the efficacy of the full length capping region, and fragments that include the C-terminal 117 amino acids retain greater than 50% of the activity of the full-length capping region.

In some embodiments, the TALE polypeptides described herein contain a C-terminal capping region fragment that included at least 6, 10, 20, 30, 37, 40, 50, 60, 68, 70, 80, 90, 100, 110, 120, 127, 130, 140, 150, 155, 160, 170, 180 amino acids of a C-terminal capping region. In certain embodiments, the C-terminal capping region fragment amino acids are of the N-terminus (the DNA-binding region proximal end) of a C-terminal capping region. As described in Zhang et al., Nature Biotechnology 29:149-153 (2011), C-terminal

capping region fragments that include the C-terminal 68 amino acids enhance binding activity equal to the full length capping region, while fragments that include the C-terminal 20 amino acids retain greater than 50% of the efficacy of the full length capping region.

In certain embodiments, the capping regions of the TALE polypeptides described herein do not need to have identical sequences to the capping region sequences provided herein. Thus, in some embodiments, the capping region of the TALE polypeptides described herein have sequences that are at least 50%, 60%, 70%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical or share identity to the capping region amino acid sequences provided herein. Sequence identity is related to sequence homology. Homology comparisons may be conducted by eye, or more usually, with the aid of readily available sequence comparison programs. These commercially available computer programs may calculate percent (%) homology between two or more sequences and may also calculate the sequence identity shared by two or more amino acid or nucleic acid sequences. In some preferred embodiments, the capping region of the TALE polypeptides described herein have sequences that are at least 95% identical or share identity to the capping region amino acid sequences provided herein.

Sequence homologies may be generated by any of a number of computer programs known in the art, which include but are not limited to BLAST or FASTA. Suitable computer program for carrying out alignments like the GCG Wisconsin Bestfit package may also be used. Once the software has produced an optimal alignment, it is possible to calculate % homology, preferably % sequence identity. The software typically does this as part of the sequence comparison and generates a numerical result.

In advantageous embodiments described herein, the TALE polypeptides of the invention include a nucleic acid binding domain linked to the one or more effector domains. The terms "effector domain" or "regulatory and functional domain" refer to a polypeptide sequence that has an activity other than binding to the nucleic acid sequence recognized by the nucleic acid binding domain. By combining a nucleic acid binding domain with one or more effector domains, the polypeptides of the invention may be used to target the one or more functions or activities mediated by the effector domain to a particular target DNA sequence to which the nucleic acid binding domain specifically binds.

In some embodiments of the TALE polypeptides described herein, the activity mediated by the effector domain is a biological activity. For example, in some embodiments the effector domain is a transcriptional inhibitor (i.e., a repressor domain), such as an mSin interaction domain (SID). SID4X domain or a Kriippel-associated box (KRAB) or fragments of the KRAB domain. In some embodiments the effector domain is an enhancer of transcription (i.e. an activation domain), such as the VP16, VP64 or p65 activation domain. In some embodiments, the nucleic acid binding is linked, for example, with an effector domain that includes but is not limited to a transposase, integrase, recombinase, resolvase, invertase, protease, DNA methyltransferase, DNA demethylase, histone acetylase, histone deacetylase, nuclease, transcriptional repressor, transcriptional activator, transcription factor recruiting, protein nuclear-localization signal or cellular uptake signal.

In some embodiments, the effector domain is a protein domain which exhibits activities which include but are not limited to transposase activity, integrase activity, recombinase activity, resolvase activity, invertase activity, protease activity, DNA methyltransferase activity, DNA demethylase activity, histone acetylase activity, histone deacetylase activity, nuclease activity, nuclear-localization signaling activity, transcriptional repressor activity, transcriptional activator activity, transcription factor recruiting activity, or cellular uptake signaling activity. Other preferred embodiments of the invention may include any combination the activities described herein.

ZN-Finger Nucleases

Other preferred tools for genome editing for use in the context of this invention include zinc finger systems and TALE systems. One type of programmable DNA-binding domain is provided by artificial zinc-finger (ZF) technology, which involves arrays of ZF modules to target new DNA-binding sites in the genome. Each finger module in a ZF array targets three DNA bases. A customized array of individual zinc finger domains is assembled into a ZF protein (ZFP).

ZFPs can comprise a functional domain. The first synthetic zinc finger nucleases (ZFNs) were developed by fusing a ZF protein to the catalytic domain of the Type IIS restriction enzyme FokI. (Kim, Y. G. et al., 1994, Chimeric restriction endonuclease, Proc. Natl. Acad. Sci. U.S.A. 91, 883-887; Kim, Y. G. et al., 1996, Hybrid restriction enzymes: zinc finger fusions to FokI cleavage domain. Proc. Natl. Acad. Sci. U.S.A. 93, 1156-1160). Increased cleavage specificity can be attained with decreased off target activity by use of paired ZFN heterodimers, each targeting different nucleotide sequences separated by a short spacer. (Doyon, Y. et al., 2011, Enhancing zinc-finger-nuclease activity with improved obligate heterodimeric architectures. Nat. Methods 8, 74-79). ZFPs can also be designed as transcription activators and repressors and have been used to target many genes in a wide variety of organisms. Exemplary methods of genome editing using ZFNs can be found for example in U.S. Pat. Nos. 6,534,261, 6,607,882, 6,746,838, 6,794,136, 6,824,978, 6,866,997, 6,933,113, 6,979,539, 7,013,219, 7,030,215, 7,220,719, 7,241,573, 7,241,574, 7,585,849, 7,595,376, 6,903,185, and 6,479,626, all of which are specifically incorporated by reference.

Meganucleases

As disclosed herein editing can be made by way of meganucleases, which are endodeoxyribonucleases characterized by a large recognition site (double-stranded DNA sequences of 12 to 40 base pairs). Exemplary method for using meganucleases can be found in U.S. Pat. Nos. 8,163,514; 8,133,697; 8,021,867; 8,119,361; 8,119,381; 8,124,369; and 8,129,134, which are specifically incorporated by reference.

Pharmaceuticals

Another aspect of the invention provides a composition, pharmaceutical composition or vaccine comprising the intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) or populations thereof as taught herein.

A "pharmaceutical composition" refers to a composition that usually contains an excipient, such as a pharmaceutically acceptable carrier that is conventional in the art and that is suitable for administration to cells or to a subject.

The term "pharmaceutically acceptable" as used throughout this specification is consistent with the art and means compatible with the other ingredients of a pharmaceutical composition and not deleterious to the recipient thereof.

As used herein, "carrier" or "excipient" includes any and all solvents, diluents, buffers (such as, e.g., neutral buffered saline or phosphate buffered saline), solubilisers, colloids, dispersion media, vehicles, fillers, chelating agents (such as,

e.g., EDTA or glutathione), amino acids (such as, e.g., glycine), proteins, disintegrants, binders, lubricants, wetting agents, emulsifiers, sweeteners, colorants, flavourings, aromatisers, thickeners, agents for achieving a depot effect, coatings, antifungal agents, preservatives, stabilisers, antioxidants, tonicity controlling agents, absorption delaying agents, and the like. The use of such media and agents for pharmaceutical active components is well known in the art. Such materials should be non-toxic and should not interfere with the activity of the cells or active components.

The precise nature of the carrier or excipient or other material will depend on the route of administration. For example, the composition may be in the form of a parenterally acceptable aqueous solution, which is pyrogen-free and has suitable pH, isotonicity and stability. For general principles in medicinal formulation, the reader is referred to Cell Therapy: Stem Cell Transplantation, Gene Therapy, and Cellular Immunotherapy, by G. Morstyn & W. Sheridan eds., Cambridge University Press, 1996; and Hematopoietic Stem Cell Therapy, E. D. Ball, J. Lister & P. Law, Churchill Livingstone, 2000.

The pharmaceutical composition can be applied parenterally, rectally, orally or topically. Preferably, the pharmaceutical composition may be used for intravenous, intramuscular, subcutaneous, peritoneal, peridural, rectal, nasal, pulmonary, mucosal, or oral application. In a preferred embodiment, the pharmaceutical composition according to the invention is intended to be used as an infuse. The skilled person will understand that compositions which are to be administered orally or topically will usually not comprise cells, although it may be envisioned for oral compositions to also comprise cells, for example when gastro-intestinal tract indications are treated. Each of the cells or active components (e.g., modulants, immunomodulants, antigens) as discussed herein may be administered by the same route or may be administered by a different route. By means of example, and without limitation, cells may be administered parenterally and other active components may be administered orally.

Liquid pharmaceutical compositions may generally include a liquid carrier such as water or a pharmaceutically acceptable aqueous solution. For example, physiological saline solution, tissue or cell culture media, dextrose or other saccharide solution or glycols such as ethylene glycol, propylene glycol or polyethylene glycol may be included.

The composition may include one or more cell protective molecules, cell regenerative molecules, growth factors, anti-apoptotic factors or factors that regulate gene expression in the cells. Such substances may render the cells independent of their environment.

Such pharmaceutical compositions may contain further components ensuring the viability of the cells therein. For example, the compositions may comprise a suitable buffer system (e.g., phosphate or carbonate buffer system) to achieve desirable pH, more usually near neutral pH, and may comprise sufficient salt to ensure isoosmotic conditions for the cells to prevent osmotic stress. For example, suitable solution for these purposes may be phosphate-buffered saline (PBS), sodium chloride solution, Ringer's Injection or Lactated Ringer's Injection, as known in the art. Further, the composition may comprise a carrier protein, e.g., albumin (e.g., bovine or human albumin), which may increase the viability of the cells.

Further suitably pharmaceutically acceptable carriers or additives are well known to those skilled in the art and for instance may be selected from proteins such as collagen or gelatine, carbohydrates such as starch, polysaccharides, sugars (dextrose, glucose and sucrose), cellulose derivatives like sodium or calcium carboxymethylcellulose, hydroxypropyl cellulose or hydroxypropylmethyl cellulose, pregelatinized starches, pectin agar, carrageenan, clays, hydrophilic gums (acacia gum, guar gum, arabic gum and xanthan gum), alginic acid, alginates, hyaluronic acid, polyglycolic and polylactic acid, dextran, pectins, synthetic polymers such as water-soluble acrylic polymer or polyvinylpyrrolidone, proteoglycans, calcium phosphate and the like.

If desired, cell preparation can be administered on a support, scaffold, matrix or material to provide improved tissue regeneration. For example, the material can be a granular ceramic, or a biopolymer such as gelatine, collagen, or fibrinogen. Porous matrices can be synthesized according to standard techniques (e.g., Mikos et al., Biomaterials 14: 323, 1993; Mikos et al., Polymer 35:1068, 1994; Cook et al., J. Biomed. Mater. Res. 35:513, 1997). Such support, scaffold, matrix or material may be biodegradable or non-biodegradable. Hence, the cells may be transferred to and/or cultured on suitable substrate, such as porous or non-porous substrate, to provide for implants.

For example, cells that have proliferated, or that are being differentiated in culture dishes, can be transferred onto three-dimensional solid supports in order to cause them to multiply and/or continue the differentiation process by incubating the solid support in a liquid nutrient medium of the invention, if necessary. Cells can be transferred onto a three-dimensional solid support, e.g. by impregnating the support with a liquid suspension containing the cells. The impregnated supports obtained in this way can be implanted in a human subject. Such impregnated supports can also be re-cultured by immersing them in a liquid culture medium, prior to being finally implanted. The three-dimensional solid support needs to be biocompatible so as to enable it to be implanted in a human. It may be biodegradable or non-biodegradable.

The cells or cell populations can be administered in a manner that permits them to survive, grow, propagate and/or differentiate towards desired cell types (e.g. differentiation) or cell states. The cells or cell populations may be grafted to or may migrate to and engraft within the intended organ.

In certain embodiments, a pharmaceutical cell preparation as taught herein may be administered in a form of liquid composition. In embodiments, the cells or pharmaceutical composition comprising such can be administered systemically, topically, within an organ or at a site of organ dysfunction or lesion.

Preferably, the pharmaceutical compositions may comprise a therapeutically effective amount of the specified intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) and/or other active components. The term "therapeutically effective amount" refers to an amount which can elicit a biological or medicinal response in a tissue, system, animal or human that is being sought by a researcher, veterinarian, medical doctor or other clinician, and in particular can prevent or alleviate one or more of the local or systemic symptoms or features of a disease or condition being treated.

A further aspect of the invention provides a population of the intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) as taught herein. The terms "cell population" or "population" denote a set of cells having characteristics in common. The characteristics may include in particular the one or more marker(s) or gene or gene product signature(s) as taught herein. The intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably

intestinal epithelial cells) cells as taught herein may be comprised in a cell population. By means of example, the specified cells may constitute at least 40% (by number) of all cells of the cell population, for example, at least 450/a, preferably at least 50%, at least 55%, more preferably at least 60%, at least 65%, still more preferably at least 70%, at least 75%, even more preferably at least 80%, at least 85%, and yet more preferably at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or even 100% of all cells of the cell population.

The isolated intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) of populations thereof as disclosed throughout this specification may be suitably cultured or cultivated in vitro. The term "in vitro" generally denotes outside, or external to, a body, e.g., an animal or human body. The term encompasses "ex vivo". The terms "culturing" or "cell culture" are common in the art and broadly refer to maintenance of cells and potentially expansion (proliferation, propagation) of cells in vitro. Typically, animal cells, such as mammalian cells, such as human cells, are cultured by exposing them to (i.e., contacting them with) a suitable cell culture medium in a vessel or container adequate for the purpose (e.g., a 96-, 24-, or 6-well plate, a T-25, T-75, T-150 or T-225 flask, or a cell factory), at art-known conditions conducive to in vitro cell culture, such as temperature of 37° C., 5% v/v CO_2 and >95% humidity.

The term "medium" as used herein broadly encompasses any cell culture medium conducive to maintenance of cells, preferably conducive to proliferation of cells. Typically, the medium will be a liquid culture medium, which facilitates easy manipulation (e.g., decantation, pipetting, centrifugation, filtration, and such) thereof.

Differentiation

A relatively more specialised cell may differ from an unspecialised or relatively less specialised cell in one or more demonstrable phenotypic characteristics, such as, for example, the presence, absence or level of expression of particular cellular components or products, e.g., RNA, proteins or other substances, activity of certain biochemical pathways, morphological appearance, proliferation capacity and/or kinetics, differentiation potential and/or response to differentiation signals, electrophysiological behaviour, etc., wherein such characteristics signify the progression of the relatively more specialised cell further along the developmental pathway. Non-limiting examples of differentiation may include, e.g., the change of a pluripotent stem cell into a given type of multipotent progenitor or stem cell, the change of a multipotent progenitor or stem cell into a given type of unipotent progenitor or stem cell, or the change of a unipotent progenitor or stem cell to more specialised cell types or to terminally specialised cells within a given cell lineage.

The terms "diagnosis" and "monitoring" are commonplace and well-understood in medical practice. By means of further explanation and without limitation the term "diagnosis" generally refers to the process or act of recognising, deciding on or concluding on a disease or condition in a subject on the basis of symptoms and signs and/or from results of various diagnostic procedures (such as, for example, from knowing the presence, absence and/or quantity of one or more biomarkers characteristic of the diagnosed disease or condition).

The term "monitoring" generally refers to the follow-up of a disease or a condition in a subject for any changes which may occur over time.

The terms "prognosing" or "prognosis" generally refer to an anticipation on the progression of a disease or condition and the prospect (e.g., the probability, duration, and/or extent) of recovery. A good prognosis of the diseases or conditions taught herein may generally encompass anticipation of a satisfactory partial or complete recovery from the diseases or conditions, preferably within an acceptable time period. A good prognosis of such may more commonly encompass anticipation of not further worsening or aggravating of such, preferably within a given time period. A poor prognosis of the diseases or conditions as taught herein may generally encompass anticipation of a substandard recovery and/or unsatisfactorily slow recovery, or to substantially no recovery or even further worsening of such.

The terms also encompass prediction of a disease. the terms "predicting" or "prediction" generally refer to an advance declaration, indication or foretelling of a disease or condition in a subject not (yet) having the disease or condition. For example, a prediction of a disease or condition in a subject may indicate a probability, chance or risk that the subject will develop the disease or condition, for example within a certain time period or by a certain age. The probability, chance or risk may be indicated inter alia as an absolute value, range or statistics, or may be indicated relative to a suitable control subject or subject population (such as, e.g., relative to a general, normal or healthy subject or subject population). Hence, the probability, chance or risk that a subject will develop a disease or condition may be advantageously indicated as increased or decreased, or as fold-increased or fold-decreased relative to a suitable control subject or subject population. As used herein, the term "prediction" of the conditions or diseases as taught herein in a subject may also particularly mean that the subject has a 'positive' prediction of such, i.e., that the subject is at risk of having such (e.g., the risk is significantly increased vis-à-vis a control subject or subject population). The term "prediction of no" diseases or conditions as taught herein as described herein in a subject may particularly mean that the subject has a 'negative' prediction of such, i.e., that the subject's risk of having such is not significantly increased vis-à-vis a control subject or subject population.

As used throughout this specification, the terms "treat", "treating" and "treatment" refer to the alleviation or measurable lessening of one or more symptoms or measurable markers of a pathological condition such as a disease or disorder. Measurable lessening includes any statistically significant decline in a measurable marker or symptom. Generally, the terms encompass both curative treatments and treatments directed to reduce symptoms and/or slow progression of the disease. The terms encompass both the therapeutic treatment of an already developed pathological condition, as well as prophylactic or preventative measures, wherein the aim is to prevent or lessen the chances of incidence of a pathological condition. In certain embodiments, the terms may relate to therapeutic treatments. In certain other embodiments, the terms may relate to preventative treatments. Treatment of a chronic pathological condition during the period of remission may also be deemed to constitute a therapeutic treatment. The term may encompass ex vivo or in vivo treatments as appropriate in the context of the present invention.

As used throughout this specification, the terms "prevent", "preventing" and "prevention" refer to the avoidance or delay in manifestation of one or more symptoms or measurable markers of a pathological condition, such as a disease or disorder. A delay in the manifestation of a symptom or marker is a delay relative to the time at which

such symptom or marker manifests in a control or untreated subject with a similar likelihood or susceptibility of developing the pathological condition. The terms "prevent", "preventing" and "prevention" include not only the avoidance or prevention of a symptom or marker of the pathological condition, but also a reduced severity or degree of any one of the symptoms or markers of the pathological condition, relative to those symptoms or markers in a control or non-treated individual with a similar likelihood or susceptibility of developing the pathological condition, or relative to symptoms or markers likely to arise based on historical or statistical measures of populations affected by the disease or disorder. By "reduced severity" is meant at least a 10% reduction in the severity or degree of a symptom or measurable marker relative to a control or reference, e.g., at least 15%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, 99% or even 100% (i.e., no symptoms or measurable markers).

The terms "disease" or "disorder" are used interchangeably throughout this specification, and refer to any alternation in state of the body or of some of the organs, interrupting or disturbing the performance of the functions and/or causing symptoms such as discomfort, dysfunction, distress, or even death to the person afflicted or those in contact with a person. A disease or disorder can also be related to a distemper, ailing, ailment, malady, disorder, sickness, illness, complaint, indisposition, or affliction.

In certain embodiments, the pathological condition may be an infection, inflammation, proliferative disease, autoimmune disease, or allergy.

The term "infection" as used herein refers to presence of an infective agent, such as a pathogen, e.g., a microorganism, in or on a subject, which, if its presence or growth were inhibited, would result in a benefit to the subject. Hence, the term refers to the state produced by the establishment, more particularly invasion and multiplication, of an infective agent, such as a pathogen, e.g., a microorganism, in or on a suitable host. An infection may produce tissue injury and progress to overt disease through a variety of cellular and toxic mechanisms.

The term "inflammation" generally refers to a response in vasculated tissues to cellular or tissue injury usually caused by physical, chemical and/or biological agents, that is marked in the acute form by the classical sequences of pain, heat, redness, swelling, and loss of function, and serves as a mechanism initiating the elimination, dilution or walling-off of noxious agents and/or of damaged tissue. Inflammation histologically involves a complex series of events, including dilation of the arterioles, capillaries, and venules with increased permeability and blood flow, exudation of fluids including plasma proteins, and leukocyte migration into the inflammatory focus.

Further, the term encompasses inflammation caused by extraneous physical or chemical injury or by biological agents, e.g., viruses, bacteria, fungi, protozoan or metazoan parasite infections, as well as inflammation which is seemingly unprovoked, e.g., which occurs in the absence of demonstrable injury or infection, inflammation responses to self-antigens (auto-immune inflammation), inflammation responses to engrafted xenogeneic or allogeneic cells, tissues or organs, inflammation responses to allergens, etc. The term covers both acute inflammation and chronic inflammation. Also, the term includes both local or localised inflammation, as well as systemic inflammation, i.e., where one or more inflammatory processes are not confined to a particular tissue but occur generally in the endothelium and/or other organ systems.

Systemic inflammatory conditions may particularly encompass systemic inflammatory response syndrome (SIRS) or sepsis. "SIRS" is a systemic inflammatory response syndrome with no signs of infection. It can be characterised by the presence of at least two of the four following clinical criteria: fever or hypothermia (temperature of 38.0° C.) or more, or temperature of 36.0° C. or less; tachycardia (at least 90 beats per minute); tachypnea (at least 20 breaths per minute or $PaCO_2$ less than 4.3 kPa (32.0 mm Hg) or the need for mechanical ventilation); and an altered white blood cell (WBC) count of 12×10^6 cells/mL or more, or an altered WBC count of 4×10^6 cells/mL or less, or the presence of more than 10% band forms. "Sepsis" can generally be defined as SIRS with a documented infection, such as for example a bacterial infection. Infection can be diagnosed by standard textbook criteria or, in case of uncertainty, by an infectious disease specialist. Bacteraemia is defined as sepsis where bacteria can be cultured from blood. Sepsis may be characterised or staged as mild sepsis, severe sepsis (sepsis with acute organ dysfunction), septic shock (sepsis with refractory arterial hypotension), organ failure, multiple organ dysfunction syndrome and death.

The term "proliferative disease" generally refers to any disease or disorder characterised by neoplastic cell growth and proliferation, whether benign, pre-malignant, or malignant. The term proliferative disease generally includes all transformed cells and tissues and all cancerous cells and tissues. Proliferative diseases or disorders include, but are not limited to abnormal cell growth, benign tumours, pre-malignant or precancerous lesions, malignant tumors, and cancer.

The terms "tumor" or "tumor tissue" refer to an abnormal mass of tissue resulting from excessive cell division. A tumor or tumor tissue comprises "tumor cells" which are neoplastic cells with abnormal growth properties and no useful bodily function. Tumors, tumor tissue and tumor cells may be benign, pre-malignant or malignant, or may represent a lesion without any cancerous potential. A tumor or tumor tissue may also comprise "tumor-associated non-tumor cells", e.g., vascular cells which form blood vessels to supply the tumor or tumor tissue. Non-tumor cells may be induced to replicate and develop by tumor cells, for example, the induction of angiogenesis in a tumor or tumor tissue.

The term "cancer" refers to a malignant neoplasm characterised by deregulated or unregulated cell growth. The term "cancer" includes primary malignant cells or tumors (e.g., those whose cells have not migrated to sites in the subject's body other than the site of the original malignancy or tumor) and secondary malignant cells or tumors (e.g., those arising from metastasis, the migration of malignant cells or tumor cells to secondary sites that are different from the site of the original tumor. The term "metastatic" or "metastasis" generally refers to the spread of a cancer from one organ or tissue to another non-adjacent organ or tissue. The occurrence of the proliferative disease in the other non-adjacent organ or tissue is referred to as metastasis.

As used throughout the present specification, the terms "autoimmune disease" or "autoimmune disorder" used interchangeably refer to a diseases or disorders caused by an immune response against a self-tissue or tissue component (self-antigen) and include a self-antibody response and/or cell-mediated response. The terms encompass organ-specific autoimmune diseases, in which an autoimmune response is directed against a single tissue, as well as non-organ specific autoimmune diseases, in which an autoimmune response is

directed against a component present in two or more, several or many organs throughout the body.

Non-limiting examples of autoimmune diseases include but are not limited to acute disseminated encephalomyelitis (ADEM); Addison's disease; ankylosing spondylitis; antiphospholipid antibody syndrome (APS); aplastic anemia; autoimmune gastritis; autoimmune hepatitis; autoimmune thrombocytopenia; Behçet's disease; coeliac disease; dermatomyositis; diabetes mellitus type I; Goodpasture's syndrome; Graves' disease; Guillain-Barre syndrome (GBS); Hashimoto's disease; idiopathic thrombocytopenic purpura; inflammatory bowel disease (IBD) including Crohn's disease and ulcerative colitis; mixed connective tissue disease; multiple sclerosis (MS); myasthenia gravis; opsoclonus myoclonus syndrome (OMS); optic neuritis; Ord's thyroiditis; pemphigus; pernicious anaemia; polyarteritis nodosa; polymyositis; primary biliary cirrhosis; primary myxedema; psoriasis; rheumatic fever; rheumatoid arthritis; Reiter's syndrome; scleroderma; Sjögren's syndrome; systemic lupus erythematosus; Takayasu's arteritis; temporal arteritis; vitiligo; warm autoimmune hemolytic anemia; or Wegener's granulomatosis.

"Activation" generally refers to the state of a cell, such as preferably T cell, following sufficient cell surface moiety ligation (e.g., interaction between the T cell receptor on the surface of a T cell (such as naturally-occurring TCR or genetically engineered TCR, e.g., chimeric antigen receptor, CAR) and MHC-bound antigen peptide presented on the surface of the immune cell as taught herein) to induce a noticeable biochemical or morphological change of the cell, such as preferably T cell. In particular, "activation" may refer to the state of a T cell that has been sufficiently stimulated to induce detectable cellular proliferation of the T cell. Activation can also encompass induced cytokine production, and detectable T cell effector functions, e.g., regulatory or cytolytic effector functions. The T cells and immune cells may be may be suitably contacted by admixing the T cells and immune cells in an aqueous composition, e.g., in a culture medium, in sufficient numbers and for a sufficient duration of time to produce the desired T cell activation.

The terms "increased" or "increase" or "upregulated" or "upregulate" as used herein generally mean an increase by a statically significant amount. For avoidance of doubt, "increased" means a statistically significant increase of at least 10% as compared to a reference level, including an increase of at least 20%, at least 30%, at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 100% or more, including, for example at least 2-fold, at least 3-fold, at least 4-fold, at least 5-fold, at least 10-fold increase or greater as compared to a reference level, as that term is defined herein.

The term "reduced" or "reduce" or "decrease" or "decreased" or "downregulate" or "downregulated" as used herein generally means a decrease by a statistically significant amount relative to a reference. For avoidance of doubt, "reduced" means statistically significant decrease of at least 10% as compared to a reference level, for example a decrease by at least 20%, at least 30%, at least 40%, at least t 50%, or least 60%, or least 70%, or least 80%, at least 90% or more, up to and including a 100% decrease (i.e., absent level as compared to a reference sample), or any decrease between 10-100% as compared to a reference level, as that term is defined herein. The term "abolish" or "abolished" may in particular refer to a decrease by 100/6, i.e., absent level as compared to a reference sample.

Any one or more of the several successive molecular mechanisms involved in the expression of a given gene or polypeptide may be targeted by the intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) cell modification as intended herein. Without limitation, these may include targeting the gene sequence (e.g., targeting the polypeptide-encoding, non-coding and/or regulatory portions of the gene sequence), the transcription of the gene into RNA, the polyadenylation and where applicable splicing and/or other post-transcriptional modifications of the RNA into mRNA, the localization of the mRNA into cell cytoplasm, where applicable other post-transcriptional modifications of the mRNA, the translation of the mRNA into a polypeptide chain, where applicable post-translational modifications of the polypeptide, and/or folding of the polypeptide chain into the mature conformation of the polypeptide. For compartmentalized polypeptides, such as secreted polypeptides and transmembrane polypeptides, this may further include targeting trafficking of the polypeptides, i.e., the cellular mechanism by which polypeptides are transported to the appropriate sub-cellular compartment or organelle, membrane, e.g. the plasma membrane, or outside the cell. Functional genomics can be used to modify cells for therapeutic purposes, and identify networks and pathways. For example, Graham et al ("Functional genomics identifies negative regulatory nodes controlling phagocyte oxidative burst," *Nature Communications* 6, Article number: 7838 (2015)) describes functional genetic screens to identify the phagocytic oxidative burst. With the rapid advancement of genomic technology, it is now possible to associate genetic variation with phenotypes of intestinal epithelial cells, intestinal epithelial stem cells, or intestinal immune cells (preferably intestinal epithelial cells) at the population level. In particular, genome-wide association studies (GWAS) have implicated genetic loci associated with risk for IBD and allowed for inference of new biological processes that contribute to disease. These studies highlight innate defense mechanisms such as antibacterial autophagy, superoxide generation during oxidative burst and reactive nitrogen species produced by iNOS. However, GWAS requires functional analysis to unlock new insights. For example, many risk loci are densely populated with coding genes, which complicates identification of causal genes. Even when fine mapping clearly identifies key genes, a majority have poorly defined functions in host immunity. Moreover, any given gene may have multiple functions depending on the cell type in which it is expressed as well as environmental cues. Such context-specific functions of regulatory genes are largely unexplored. Thus, human genetics offers an opportunity to leverage insight from large amounts of genetic variation within healthy and patient populations to interrogate mechanisms of immunity. Irrespective of their putative roles in IBD pathology, genes within risk loci are likely to be highly enriched for genes controlling signaling pathways.

The invention is further described in the following examples, which do not limit the scope of the invention described in the claims.

EXAMPLES

Example 1—Map of the Cellular and Molecular Composition in the Healthy and Inflamed Gut

Applicants have generated a foundational resource in the healthy and inflamed gut for: (1) Cell composition (i.e., changes in proportions of different cell types/states), (2) Cell

intrinsic states (i.e., changes in gene expression within a cell type), (3) Cell-cell interactions (i.e., changes in cell-cell interaction mechanisms), and (4) the relevant cell types for each gene (e.g., GWAS genes).

GWAS gene→cell type→cell state→cell interaction→disease

Applicants used single cell RNA-seq of colonoscopy samples from healthy individuals and UC patients to generate the cell atlas. The samples were obtained from 10 healthy individuals (37,435 non-inflamed cells were initially analyzed), 10 UC patients (17,400 cells (10,688 uninflamed; 6,712 inflamed) were initially analyzed). Three additional samples were analyzed. In total 117,819 cells were analyzed (49,765 epithelial, 11,556 stromal, 56,498 immune). The samples were small biopsies containing about <80,000 cells. The biopsies were fresh and dislocation and processing were performed by applicants. A subset of greater than 50,000 cells are presented on some plots herein.

FIG. **1** shows that initial clustering analysis partitioned cells by patient in the UC samples and by cell type in the healthy samples. This result was similar as in Tirosh, et al. (Dissecting the multicellular ecosystem of metastatic melanoma by single-cell RNA-seq. Science 2016, 352, 189-196) where malignant cells partitioned by patient and non-malignant cells partitioned by cell type. Applicants used computational modeling to address the batch effects and partition the cells by cell type (FIG. **2**).

FIGS. **3** and **4** show that the atlas uncovers almost all cell types and subtypes in the colon. Applicants identified the following cell types and subtypes in the colon: Plasma B cells, Class switching B cells, Follicular B cells, T cells, Macrophages, Dendritic cells, Mast cells, Cycling monocytes, Tolerogenic DCs, Neutrophils, Activated CD4 cells loFos, Activated CD4 cells hiFos, CD8 IELs, CD8 LP cells, Tregs, Memory T cells, NK cells, Cycling CD8 cells, Microvascular cells, Post-capillary venules, Vitamin metabolizing, Endothelial pericytes, Enterocytes, Tuft cells, Goblet 2, Absorptive TA 1, Secretory TA, Absorptive TA 2, Cycling TA, Goblet 1, Stem cells, Enteroendocrine, Glial cells, Inflammatory fibroblasts, Fibroblast pericytes, Myofibroblasts, Villus fibroblasts, Crypt fibroblasts (hiFos) and Crypt fibroblasts (loFos). Applicants identified markers specific for each cell type. Table 1 A-D shows the top 250 genes expressed in each cell type.

TABLE 1A

Plasma_B_cells	Class_switching_B_cells	Follicular_B_cells	Microvascular_cells	Post-capillary_venules
HERPUD1	IGLL5	CD79A	PRSS23	DARC
IGJ	IGJ	MS4A1	RGCC	NPC2
SSR4	TMSB10	CD79B	PLVAP	CLDN5
SEC11C	CFL1	VPREB3	VWA1	CPE
XBP1	TMSB4X	TCL1A	PASK	MADCAM1
MZB1	PFN1	FCRLA	GNG11	CLU
FKBP11	MYL6	CD37	CA4	DUSP23
DERL3	FTH1	CD19	CD36	JAM2
SPCS2	GAPDH	SMIM14	CD320	PLVAP
TNFRSF17	ACTB	CST3	VWF	LY6E
CD79A	IGLL1	CD63	ENG	ECSCR
SSR3	TNFRSF17	LTB	RAMP2	SDCBP
UBE2J1	CD79A	LIMD2	SLC9A3R2	TSPAN7
SPCS1	DERL3	CD22	ESAM	EGFL7
DNAJB9	MT-CO1	BLK	CRIP2	VWF
EAF2	MZB1	LGALS3	GSN	GNG11
FKBP2	SERF2	PTPRCAP	SPARCL1	RAMP2
MANF	AL928768.3	AL928768.3	FKBP1A	APLNR
PRDX4	ACTG1	HLA-DQA1	TMEM204	RAMP3
SDF2L1	RPL28	CD53	ITM2B	ITM2B
SERP1	RPS24	BANK1	RBP5	CTNNAL1
AL928768.3	MT-CO3	RHOH	TM4SF18	IGFBP4
SPCS3	ATP5E	S100A6	RAMP3	NNMT
CYBA	COX4I1	GPR18	EGFL7	HLA-E
WT1-AS	HLA-A	CORO1A	HSPG2	GIMAP7
CRELD2	PPAPDC1B	BCAS4	CCDC85B	GPR126
VIMP	GNG7	CXCR5	ECSCR	ICAM1
SEC61B	UBA52	CD74	TMEM88	HHEX
PDIA6	ICAM3	SERPINA9	SDPR	GIMAP4
HSP90B1	UQCR11	LRMP	VAMP5	TNFSF10
GNG7	RPS12	FCGRT	BCAM	LINC01013
PPAPDC1B	SSR4	EAF2	CAV1	AC011526.1
CD27	S100A6	RGS13	MGP	CLEC14A
FAM46C	PPDPF	CXCR4	EMCN	IGFBP7
PDIA4	RPL31	POU2AF1	ELTD1	NPDC1
ISG20	CHCHD2	SMARCB1	PLAT	NCOA7
PABPC4	BTF3	CD52	KDR	CAV1
TRAM1	SRP14	SPIB	CLEC14A	LMO2
ANKRD37	CD27	MGST3	HLA-E	SNCG
RPL36AL	TOMM7	BLNK	IGFBP7	CTGF
C19orf10	PFDN5	HLA-DRA	FLT1	TM4SF1
CCR10	MYL12B	CD72	PODXL	FAM213A
IGLL5	YBX1	POU2F2	SEPW1	SPARCL1
HSPA5	EAF2	ACTR3	IGFBP4	CRIP2
ACTB	UBE2J1	FCRL2	HTRA1	ITM2A
LMAN2	SRGN	HMGN1	SPARC	FAM167B
MEI1	RPL30	CD40	CAV2	FKBP1A
DUSP5	EIF3K	ARPC2	SLC14A1	ESAM
SELK	NDUFA11	GGA2	AC011526.1	IFITM3
UBC	CYTIP	EZR	SH3BP5	TMEM100

TABLE 1A-continued

FCRL5	RPL23	HERPUD1	FAM167B	CCL14
CST3	TRAM1	NCF1	FAM213A	BCAM
TXNDC11	ATP5G2	IRF8	SNCG	GIMAP1
UAP1	FAM46C	HLA-DPA1	GIMAP7	CD34
PIM2	TCEB2	HLA-DQB1	CDC37	IFI27
CFL1	PTMA	HLA-DPB1	IFITM3	TGFBR2
SPAG4	ERLEC1	LAPTM5	RP11-536018.2	CYBA
YPEL5	SH3BGRL3	UBE2J1	PPAP2A	RBP5
PFN1	EDF1	HLA-DOB	TSC22D1	CYYR1
S100A6	HM13	FCER2	IFITM2	ZNF385D
TPD52	RPS7	C12orf75	ICAM2	NRN1
CHPF	KDELR1	SWAP70	PTRF	HLA-DRA
RP11-90F5.1	ARHGDIB	HMCES	EHD4	ADIRF
HSPA1B	FKBP11	BTG1	NQO1	CD320
POU2AF1	PABPC4	P2RX5	CLDN5	CD59
JUN	SPCS3	LY86	CD59	SRPX
BTG2	RPL38	CYTIP	COL4A1	ENG
TXNDC15	COX6B1	METAP2	PPAP2B	CFI
TSC22D3	ALDOA	CD180	HLA-C	HLA-A
TMEM258	RPS11	AICDA	CXorf36	HSPB1
TMED10	CLIC1	CD9	NPDC1	HLA-DPB1
MCL1	TPI1	LY9	ARHGAP29	PIM3
TMSB10	TXNDC15	HLA-DRB1	ANGPT2	HLA-DRB5
TPST2	RPL10A	ANXA2	HSPB1	SEPW1
ACTG1	CHST12	ISG20	CD34	SDPR
NR4A1	NDUFA13	SEPW1	TM4SF1	ENPP2
S100A10	TRMT112	ARHGDIB	APP	NOSTRIN
TNFRSF18	DPP7	HMGA1	BAALC	DNAJA1
ERLEC1	IFNAR2	TCEA1	C16orf80	PTRF
NUCB2	RPL11	POLD4	EFNA1	KCTD12
TMSB4X	MYL12A	CD83	ACVRL1	IFITM2
RPN2	RPSA	BASP1	LXN	HLA-DRB1
SUB1	RPL26	STAG3	IGFBP3	MYCT1
PNOC	ISG20	S100A11	CYYR1	GIMAP5
SELM	ATP6V1G1	SNX29P2	MYL12A	CCDC85B
SLAMF7	RPL27	TPD52	MGLL	CNN3
IFNAR2	POU2AF1	IFI27	HLA-A	LMCD1
DDOST	ALG5	ARPC3	HLA-DRA	KANK3
MYL12B	PSMA7	HTR3A	STOM	CD74
TNFRSF13B	RPL24	GCSAM	EGLN3	HLA-DPA1
FGF23	SLC25A3	PNOC	ROBO4	HLA-C
LMAN1	SEC62	E2F5	SPTBN1	CDH5
ANKRD28	CNPY2	CD27	ABI3	ADM5
CD38	BST2	RAC2	HLX	NFKBIA
ICAM3	TMEM230	AC023590.1	RASIP1	SPARC
GAPDH	RPL37	STX7	HLA-B	PALMD
DNAJB11	CD63	LYL1	TGFBR2	CHCHD10
ARF4	SLAMF7	TMSB10	S100A13	LPCAT4
AC104699.1	LGALS1	UCP2	MMRN2	ERG
CDK2AP2	GYPC	IL32	IVNS1ABP	SH3BP5
TMEM59	RPS9	HLA-DMA	CTGF	STXBP6
ALG5	NDUFA4	SELT	F2RL3	BST2
C16orf74	COX5B	LAT2	ENPP2	CAV2
SRPRB	DUSP5	IFITM3	WWTR1	SMAD1
CIRBP	RPS13	BFSP2	EXOC3L2	CLIC2
FTH1	HNRNPDL	GDI2	B2M	IFIT1
TMED2	LRPAP1	HLA-DMB	NOTCH4	TPD52L1
RGS2	PARK7	HHEX	GABARAPL2	SOCS3
IGFBP7	MEI1	LGALS4	IFI27	GALNT15
RABAC1	RPL19	EPCAM	S100A16	HLA-DQA1
CD74	RHEB	MZB1	HES1	CYP1B1
SSR2	VIM	SIT1	GMFG	ICAM2
ARHGDIB	RPL32	PLEKHF2	IL3RA	HSPA1A
DNAJB1	COX7C	TNFRSF13B	GAS6	IRF1
CYTIP	COX6A1	RHOC	IDO1	FBLN2
ZBP1	PTPRCAP	OAZ1	COL4A2	HYAL2
HM13	SMARCB1	KRT18	MSN	EIF1
AMPD1	COMMD3	LCP1	FSCN1	SELP
MYL12A	LSP1	HVCN1	HHEX	LIFR
RHOC	PSENEN	C15orf48	MYCT1	S100A16
GSN	RPS25	KRT8	ACE	TCF4
IFI27	ARL6IP4	ITM2B	TSPAN7	MPZL2
REEP5	EMC4	MBD4	EPAS1	YBX3
TMEM208	ARPC3	BIK	FAM110D	EGR1
SDC1	ATP5O	TXN	C9orf3	ARL2
GLA	MT-ND4	CCND3	CALCRL	MTUS1
TUBA1A	GMFG	DEF8	HLA-DRB1	B2M
EEF1D	SRPRB	RASGRP2	SOX18	SNHG7
KDELR2	ATP5B	MARCKSL1	FABP5	FAM110D
B4GALT3	NDUFA1	NEIL1	GALNT18	CALCRL

TABLE 1A-continued

PDE4B	RPL37A	SUGCT	ITM2A	ELTD1
RGCC	RAC1	RP11-64H13.1	A2M	PIR
LGALS1	EIF3F	RFTN1	IFITM1	JUNB
RGS1	DNAJB11	ITM2C	IGFBP6	IL3RA
LGALS3	ATP5J	MT2A	NOSTRIN	RNASE1
PDK1	MT-ATP6	TNFAIP8	JAM2	IL33
TMEM176B	RPS20	ZCCHC7	RNASE1	VGLL4
SH3BGRL3	MGAT1	LINC00926	MYL12B	IFIT3
IFITM3	CRELD2	AIM2	SLCO2A1	EFEMP1
KIAA0125	UBL5	STK17A	CALM1	AC116035.1
MYL6	MT-CYB	CISD3	NES	KLF4
SRGN	SELM	CYB561A3	KANK3	TESC
RP11-92E3.2	VAMP2	SLBP	ARHGAP18	EPCAM
TRIB1	OSTC	TMEM156	RND1	STOM
CITED2	ICAM2	BACH2	FTH1	CD55
ID2	EMP3	LMNA	CLIC2	RND1
EVI2B	NACA	ATP1A1	LDB2	CDC42EP3
KRTCAP2	CALM2	GYPC	MPZL2	TIMP1
BEX5	RPS3	RMI2	PEA15	HES1
CISD2	NDUFS8	PPP1CC	MCAM	TSPAN4
SEPW1	COX7A2	UBE2N	DLL4	PLK2
ANXA1	PLP2	AGR2	MFNG	ATP5G3
RPN1	CCR10	PARP1	C8orf4	TXNIP
EIF1	TPD52	MME	HLA-DPB1	HLA-DMA
FOSB	SELT	HCLS1	BST2	BAG3
HAX1	ZNF706	PABPC1	PTPRB	PDLIM4
IL32	PIM2	IGLL5	TSPAN4	MGP
IFITM2	HINT1	RGS16	ACTN4	ID3
TMED4	UAP1	CD1C	IPO11	PHGR1
SEMA4A	SNRPD2	RGS19	DUSP6	TIE1
RAB30	S100A10	PAX5	TEK	AGR2
SLC17A9	SLC35B1	ETHE1	GUK1	SEMA6A
SLC38A5	REEP5	HLA-DQA2	ID3	HLA-B
CAPZB	TMEM66	DCK	CDH5	TAGLN2
PTPRCAP	ATRAID	ITSN2	IMP3	KRT222
H3F3B	SOD1	SH2B2	TBCD	TMEM176A
COPE	RPS23	SUSD3	CABP1	SORBS2
WNT10A	GUK1	SRSF3	GIMAP1	ST8SIA4
TMED9	TMED4	LYN	JUP	IFI16
CUTA	RPS21	SYPL1	TNFRSF4	LGALS4
E2F5	DNAJC1	ARPC1B	ARHGDIB	GIMAP8
HSPA1A	NDUFB2	CTSD	PRX	KRT8
SELT	MT-ND5	IL16	GRB10	BAALC
HES1	NUCB2	ZFAND6	PCDH12	FAM107A
EZR	PABPC1	PRPSAP2	NRP1	JUN
DUSP1	RPL12	MAP3K7CL	SRGN	S100A13
RNU12	ATF4	S100A10	ERG	ZFP36
PAIP2B	DNAJB9	PXK	NKX2-3	A2M
SPINK2	B4GALT3	RP11-960L18.1	CLIC4	DTL
SLC35B1	HNRNPA1	CCR7	TUBA1B	EID1
SMARCB1	NEDD8	LSM10	SLC25A6	PKP4
SEPP1	CISD2	LYPLA1	LAYN	CCL21
DNAJC1	KRTCAP2	DCAF12	TMEM255B	HLA-DQB1
SEL1L	ERGIC2	CTSH	GIMAP4	LIMCH1
HSP90AA1	UQCRQ	TMEM243	LIMCH1	GADD45B
AC093818.1	CNBP	TFEB	THBD	CD9
HLA-A	LAMTOR4	AC079767.4	CD74	CXorf36
ICAM2	COX6C	UBE2G1	HLA-DPA1	HAPLN3
TPI1	CD44	WIPF1	TSPAN12	VIM
EMB	LMAN1	KIAA0125	CDC42EP1	ADCY4
QPCT	TMBIM4	HNRNPC	COX7A1	WARS
SPATS2	CST3	FXYD3	SCARF1	PLAT
RHOH	C4orf3	ID2	TXNIP	ACVRL1
APOE	EIF4A2	CBX3	SEMA3F	MEOX1
MANEA	FXYD5	SNAP23	RHOA	CYB5A
IRF4	NDUFB8	MOB1A	LDHB	INPP1
ANXA2	AUP1	DBNL	SORBS2	LDB2
IFITM1	DDOST	DOK3	TACC1	IL1R1
JSRP1	GSTK1	PLCG2	ITGA6	TMEM176B
COMMD3	C19orf43	KRT19	KIFC3	ARL4A
SRM	PRDX2	IGJ	LGALS4	CTHRC1
CXCL14	SKP1	SQRDL	TIE1	PRCP
SMDT1	A1BG	FCRL3	HLA-DRB5	IFIT2
MT-CO3	SAP18	RRAS2	PRDX1	TMEM173
RPS5	TMA7	CERS4	PELO	FAM198B
IL2RG	UBE2D3	OSER1	TP53I11	FABP1
SRPR	DHRS7	LMO2	SERPINI1	GPR146
ERGIC2	RPS15	TAGAP	PPA1	MLEC
PTMS	LGALS3	FTL	FAM101B	MMP28
PLP2	PSMB6	BTK	S100A6	SQSTM1

TABLE 1A-continued

OSTC	SDF2L1	ATP5I	PPFIBP1	KRT18
CNPY2	CHID1	ANP32B	RPL12	SERTAD1
S100A4	ATP5G3	PTPRC	TMEM173	IFITM1
SRP14	RBM39	RCSD1	ANKRD65	LPAR6
PPIB	LAMP2	TUBB4B	PLXNA2	RASIP1
SIL1	ATP6V0E1	RPS4Y1	APLN	ALDH1A1
GLRX	ITM2B	MLEC	CD93	MX1
CD69	EVI2B	GSTP1	ITGA1	PTPRB
RPL28	EIF3H	CCNI	C10orf54	NKX2-3
SLC25A4	SEC11C	HLA-A	VAT1	PPP1R15A
TMBIM6	UFM1	RP11-138I18.2	KLHDC8B	NEAT1
S100A11	OS9	NPM1	PHGR1	IGJ
TNFRSF4	C11orf31	SGPP1	TINAGL1	MEIS2
LGALS4	ANXA7	HSH2D	CYBA	GIMAP6
JTB	CALM1	BLVRB	ME3	SRGN
RPL8	PSMB3	ORAI2	TNFSF10	CLDN7
THAP2	TPT1	TNFRSF17	SERPINE1	LAPTM4A
COTL1	TAPBP	ALOX5	RHOC	PLA1A
TIFA	CHPF	PTPN6	EPHX1	EPAS1
TXNIP	ERGIC3	ACTG1	NDUFA12	SLC41A3
FCRLA	DERL2	GPSM3	PTMA	LAYN
ENO1	HIGD2A	MTMR14	CCND1	ASRGL1
CD151	15-Sep	FAM65B	GIMAP5	FOS
BRSK1	ARPC2	TFF3	RPLP1	IFI6
ARPC1B	NDUFB4	KLHL5	GPX1	CSF2RB
A2M	RPLP2	GRB2	RBP7	CSRP2
AC104024.1	ST13	GNG7	KRT8	C10orf128
LMTK3	JTB	CCDC69	SEC14L1	DDX5
SSR1	ATP5D	CR2	CHCHD10	GBP2
RNASET2	NUDT22	TMEM141	PRIG	IFI44L
COX5B	GNL3	DDX39A	PSMB5	TIMP3
SEC61A1	NDUFB11	SRGN	ARHGEF15	EIF4A2
HSH2D	NHP2L1	MEF2C	SCARB1	EVA1C
ATP5E	ARF1	HLA-DRB5	PRKCH	IDH2
DCN	SEC61A1	LAMTOR4	MCF2L	RAB13
CHID1	CHMP2A	REL	GPR116	NEDD9
MT-CO1	RPL14	KIAA0226L	DYNLL1	DNAJB4
RP11-16E12.2	NPM1	PRDX5	HEG1	NR2F2
ERGIC3	ARMCX3	CCDC109B	OSBPL1A	CAPG
TXNDC5	SRPR	PPDPF	ARL2	IPO11

Vitamin_metabolizing	Endothelial_pericytes	Enterocytes	Tuft_cells	Goblet_2
CD320	RGS5	RPL15	AZGP1	MUC2
RAMP2	HIGD1B	RPS2	LRMP	TFF1
CLDN5	CD320	RPL13	SH2D6	RPL13
PLVAP	PLVAP	RPS6	MARCKSL1	ZG16
SLC9A3R2	CLDN5	GUCA2A	AVIL	RPL10
GNG11	CRIP2	RPL10	BIK	RPL15
IGFBP4	RAMP2	AQP8	SH2D7	RPS4X
TXNIP	CAV1	RPL32	HCK	RPS2
ENPP2	ESAM	RPS4X	ANXA4	RPS18
CLEC14A	GNG11	RPS19	PTGS1	RPS19
TMEM88	CD36	SLC26A3	ALOX5	RPL32
ESAM	COX4I2	RPLP1	ANXA13	FCGBP
CRIP2	NDUFA4L2	RPS18	KRT18	RPL19
SPARCL1	IGFBP4	PLAC8	IL17RB	S100P
HLA-E	MGP	CEACAM7	TPM1	CEACAM5
RAMP3	EGFL7	FXYD3	TRPM5	TSPAN1
CD59	TMEM88	KRT20	EIF1B	RPL11
CAV1	SPARCL1	FABP1	BMX	RPS9
VAMP5	RBP7	PRAP1	HPGDS	RPS14
IFI27	IGFBP7	TSPAN1	POU2F3	FXYD3
JAM2	MYL9	CEACAM5	GNG13	RPL10A
ECSCR	SLC9A3R2	SDCBP2	HTR3E	RPL35
SEPW1	TINAGL1	SRI	PSTPIP2	LYPD8
EGFL7	NOTCH3	MS4A12	SPIB	RPL12
BCAM	CLEC14A	PHGR1	PLCG2	RPS5
GIMAP7	TXNIP	C19orf33	ELF3	MUC1
CD36	ENPP2	RPS8	MATK	ENTPD8
NPDC1	JAM2	RPS9	KRT8	RPLP1
RBP7	SDPR	RPL10A	C11orf53	RPS8
GSN	GIMAP7	CTD-2228K2.5	TFF3	RPL35A
CYYR1	RAMP3	RPL35	EPCAM	RPL26
SDPR	TM4SF1	MISP	RASSF6	CLDN4
EFNA1	ECSCR	GUCA2B	RGS13	RPS13
ICAM2	HLA-E	RPS5	FYB	TFF3
TM4SF1	CYYR1	TMEM54	CRYM	REP15
EMCN	IFITM3	RPS7	PRSS3	FAM3D
IFITM3	SPARC	SLC51B	IGJ	RPS27A

TABLE 1A-continued

MGP	A2M	RPL19	TREH	RPS3
TSPAN7	GSN	RPL11	SPINT2	GNB2L1
FKBP1A	CALD1	CDHR5	IL13RA1	RPS7
IL3RA	HSPA1A	RPL5	NMU	RPS16
IFITM1	CAV2	RPL35A	SOX4	CLDN7
PODXL	CCDC85B	RPS13	DPYSL3	RPL6
IFITM2	VWF	CLDN7	ASCL2	RPLP2
TGFBR2	VAMP5	RPL12	LGALS4	RPS15
STOM	ZFP36	RPS23	HEPACAM2	RPS15A
PPA1	HLA-C	CEACAM1	LGALS1	MUC13
ENG	HSPB1	CA2	HOTAIRM1	RPLP0
HES1	HLA-DRA	ANPEP	PLEKHB1	SDCBP2
CD34	EGR1	LYPD8	CLDN4	RPL8
VWF	TM4SF18	KRT8	PPAP2C	ELF3
HLA-C	IFI27	LINC01133	PPDPF	GDPD3
RBP5	CSRP2	RPS3	PTPN18	NACA
CAV2	JUNB	RPS12	OGDHL	RPS12
SLC14A1	NOSTRIN	RPLP0	MDK	RPL23A
PRSS23	FOS	RPL26	FXYD3	RPL5
PLAT	CDH5	GNB2L1	OCIAD2	CLDN3
CDC37	RNASE1	SFN	RP11-39B14.5	PHGR1
A2M	GADD45B	RPS15A	CLDN3	RPS23
CCDC85B	IFITM2	RPL14	ESPL1	C19orf33
TNFSF10	FRZB	RPS14	FABP1	GUCA2B
EPAS1	IER2	PRSS3	ALOX5AP	PLAC8
RNASE1	ENG	LGALS3	ANXA3	RPL4
OAZ2	CTGF	RPL6	CD74	BCAS1
SRP14	JUN	RPL4	FURIN	RPS6
CTGF	ICAM2	RPS16	PPP1R1B	RPL13A
HLA-DRB1	BGN	RPS15	MT-CO3	TBX10
GIMAP4	TPPP3	RPL23A	ANKS4B	TUBB2A
HLA-DRA	FOSB	PTMA	HSPB1	TM4SF5
ELTD1	RBP5	PKIB	NCMAP	SMIM6
ITM2B	HLA-DPB1	RPS27A	DEFB1	VSIG2
FAM107A	HES1	AMN	ZFP36	SERPINA1
AC011526.1	HLA-DRB1	RPL27A	CC2D1A	IFI27
APP	HLA-DRB5	GPA33	COX5A	LGALS9B
MPZL2	MGLL	GCNT3	MT-CO1	KRT20
IGFBP7	SLC14A1	PRDX6	EHF	ZG16B
TMEM204	SEPW1	AGPAT2	CALM2	MT-CO1
GPR146	EPAS1	AOC1	SOX9	PTMA
CD74	FKBP1A	SULT1A2	IFT172	SERINC2
FLT1	ITM2B	MEP1A	7SK	RPL14
C16orf80	SNCG	RPL8	ITM2C	TRIM31
ACVRL1	C8orf4	RPL31	CASP6	RPL24
FAM167B	SOCS3	SMIM22	EMP3	AMN
MMRN2	LDB2	TMIGD1	COX6C	TPSG1
MGLL	ELTD1	KRT19	ATP1A1	FFAR4
HLA-DPB1	PLAT	CA4	PHGR1	KLK1
NOSTRIN	EMCN	CLDN3	CCDC115	TMEM54
GIMAP1	ID3	SERINC2	GFI1B	RPL27A
BST2	GIMAP4	RPL13A	HSPA1A	RPS20
HYAL2	PRSS23	PIGR	S100A11	CDHR5
TIMP3	BST2	NEAT1	KIAA1324	CLTB
TM4SF18	CD59	RPL29	EPS8L3	RPL29
HHEX	FAM167B	FTH1	NREP	CREB3L1
GIMAP5	TSC22D1	TST	HLA-DPB1	RPL3
RPLP1	HSPA1B	CLCA4	HLA-DRA	EPCAM
SLCO2A1	RGS16	RPL7A	HLA-DRB1	FOXA3
SNCG	PDGFRB	PPP1R14D	MYO1B	RPL31
FAM213A	ADIRF	MUC12	B2M	CAPN8
HLA-DPA1	GJA4	MUC13	GADD45B	GPA33
HEY1	TGFBR2	TMEM171	KLK11	CFDP1
SOX17	KLF2	HIST1H1C	CLRN3	TMSB10
PTRF	MFGE8	CLDN4	ATP2A3	RPS25
EMP2	APP	C2orf88	NDUFB4	RPS24
RPL12	PODXL	TRIM31	COX7A2	AQP8
NKX2-3	TIMP3	MYO15B	S100A14	KRT18
SYNPO	HLA-A	ETHE1	EIF5	RPL30
SOCS3	BCAM	RPL18	PRDX2	FAM177B
NRN1	SLC2A3	RPS25	CYB5A	RPL18
RPLP0	DNAJA1	S100A6	C15orf48	LGALS4
IFIT3	MCAM	RETSAT	CLDN7	RPL7A
CDH5	SERPING1	RPS20	CHPT1	SPATS2L
HLA-A	CD74	CES2	CKB	KRT8
IER2	SYNPO	CA1	COX7C	PRR15L
TSC22D1	ISYNA1	RPL24	SLC25A6	PRSS3
RND1	COX7A1	RPL3	MAP7	DHRS9
KANK3	LHFP	RPL28	VSNL1	PIGR
THBD	SRGN	C11orf86	MT-ND4	NEAT1

TABLE 1A-continued

NQO1	THBD	SPINT2	BUB3	PLA2G10
C8orf4	EFNA1	RPL30	KRT19	EEF1D
LDB2	MMRN2	RPLP2	CCDC28B	RPL27
ARHGAP29	HLA-DPA1	CYSTM1	SRI	SCNN1A
C10orf10	FAM107A	SLC26A2	SMIM22	FABP1
EHD4	IRF1	MT-CO1	FBP1	RPL28
HSPB1	CLIC2	RPSA	H1F0	SMIM22
HLA-DRB5	PTRF	COL17A1	ALDH2	FAM101A
GABARAPL2	CYGB	S100A10	PAFAH1B3	FTL
NOTCH4	RPLP0	LINC00035	MAOB	FAU
GPR116	PPA1	MYH14	HLA-DRB5	HIST1H1C
HEG1	MYCT1	EPCAM	HLA-DMA	PARM1
CLIC2	H3F3B	RPS24	ACTG1	CEACAM6
SRGN	B2M	C15orf48	MIEN1	CEACAM7
FABP5	SPINT2	NACA	MT-CYB	GSN
NFIB	GPX3	HSD17B2	HOXB6	ARL14
AIF1L	TSPAN7	SLC17A4	TIMP1	MISP
ADAM15	COL18A1	TMSB10	GPX2	CA2
NOV	FLT1	RPL36	ZFHX3	GUCA2A
C9orf3	SOD3	EEF1D	CD9	MLPH
S100A16	EIF1	SLC44A4	MALAT1	CEACAM1
SH3BP5	COL1A2	CDKN2B-S1	RPL37A	SPINT2
HLA-B	PPAP2B	LGALS4	NCK2	YBX1
B2M	TCF4	IFI27	TAS1R3	RPL36
PIK3R3	SERTAD1	PPDPF	PIK3CG	SCGB2A1
PLLP	STOM	BTNL3	RBM38	C15orf48
C10orf54	C16orf80	NPM1	LDHA	NAAA
SPARC	HLA-DMA	BTNL8	COX5B	MT-ND2
CFI	APOLD1	ELF3	ESPN	RPSA
GAS6	NRN1	HN1	ESYT2	CLDN8
PPAP2A	HES4	POLD4	PSMD9	ASS1
LY6E	SOX17	ST14	ANXA2	S100A6
SERTAD1	LGALS1	SLC6A8	MT-ND1	POLD4
TIE1	ZFP36L1	CLTB	TXN	MXD1
MYCT1	REM1	LAMB3	STMN1	PFDN5
TMEM109	ID1	SLC51A	DEGS2	SLC25A6
CD93	NPDC1	CLDN23	PMM1	MYO15B
RPS2	AC011526.1	CDHR2	HOXA11-AS	MLLT3
GIMAP6	CFI	TMEM45B	IP6K2	TP53INP2
ID1	CYB5R3	TMEM37	TMEM176B	RPL18A
TAGLN2	EFHD1	CHP2	ZNHIT3	UBA52
ZFP36	OAZ2	GPRC5A	ATP5B	MT-CO2
S100A13	CD34	HPGD	IFITM2	ST3GAL4
CYBA	NES	CKB	RPL36	ITM2C
TACC1	SRP14	FCGBP	HMX2	ATP5G2
LAP3	HHEX	AK1	TSC22D3	LMO7
CFLAR	TMEM204	ASS1	ACADSB	RPL34
HSPA1A	C1QTNF1	PRR15	S100A4	AGR2
LMCD1	GABARAPL2	ITM2C	RHEB	AC009133.21
TINAGL1	COL3A1	TMPRSS2	SPINT1	SYTL2
DLL4	MYH9	YBX1	IMP4	RAB27A
TNFRSF4	DNAJB1	S100A11	LSMD1	RPL37
PTP4A3	PHGR1	PRR13	ATPIF1	CKB
KDR	LGALS4	KRT18	ADH5	VILL
SPTBN1	ITGA7	DHRS11	H2AFJ	CA4
HLX	HEY1	HNRNPA1	IGFBP2	LINC01133
ROBO4	FAM222B	GNA11	RAB4A	RP11-94O2.2
PTPRB	HSPG2	NDRG1	SPATS2L	S100A14
IFI6	GPR116	CCL15	AFAP1L2	MEP1A
FAM110D	TACC1	RPL27	WFDC2	CYBA
ATOH8	BBX	SPINT1	DNAJB1	MT-CO3
APLNR	SH3BP5	DEFB1	SKAP2	PKIB
LPAR6	C10orf10	CFDP1	HLA-DQB1	KCNK1
PRMT1	EHD2	DHRS9	ANXA5	MAST2
PALMD	TNS1	PFDN5	RPL31	EIF4A1
COL15A1	FAM213A	PTPRH	PBXIP1	CLDN23
SEMA3G	LCN6	FLNB	COL27A1	HPGD
NDUFA12	PPP1R14A	ACAA2	MT-ND5	SMIM5
RGS3	FAM110D	PRSS8	RAB25	MALAT1
TMEM255B	RPLP1	RPS11	FRAT2	SPINT1
CHCHD10	SDCBP	RPL37	AOC1	MT-ATP6
COX4I1	SOX7	C10orf99	GSTP1	PRSS8
CD151	GEM	RHOC	MT-CO2	CLCA4
ARL2	EMP2	RPL34	RTN4	MT-ND4
SLC25A6	LMO2	EIF4A1	TUBA1A	RPS3A
ID3	NEAT1	CDA	RPS27L	EEF2
SCARF1	TIE1	BLOC1S1	CCDC14	ST14
GALNT18	IGFBP6	HHLA2	FUT3	MUC12
LIFR	COL4A1	AHCYL2	TP53I3	HIST1H2AC
SWAP70	APLNR	LDHB	MCL1	RHOC

TABLE 1A-continued

RPL29	SEPP1	GDPD3	TSPO	RP11-665N17.4
SEC14L1	PLK2	HRCT1	ZFP36L1	RPL37A
RPS19	HYAL2	MT-CO2	CMTM8	MT-ND1
RPL10A	RPS29	FAM3D	PRDX5	TSPAN3
HLA-DMA	RNASET2	ATP5G2	HES6	IGJ
RRAS	TAGLN2	FAM132A	PTMA	RPS11
LCN6	SLCO2A1	SLC9A3R1	NDUFB11	EIF1
WARS	PRIG	PKP3	CHN2	KRT19
EPHX1	KRT8	STAP2	TMEM63A	HSP90AB1
DUSP6	RPS2	SLC22A18	RASSF7	BEST2
JUNB	CXorf36	ESPN	VIL1	RASEF
PRKCDBP	LRRC32	MT-CO3	MT-ATP6	AOC1
RPL18	RHOA	VIM	CERS6	SPDEF
RALB	GIMAP1	TJP3	ID3	LGALS9C
SORBS2	LIFR	PCK1	CDH17	NPM1
EIF1	HDAC7	CTSA	TMSB10	PCK1
ALPL	TSPAN4	BSG	ARPC1B	PABPC1
FOS	C10orf54	ARL14	IFI6	NLN
RPS5	CYBA	TSPAN8	FAM200B	SEPP1
TMEM173	IFIT3	ENTPD8	CDX2	VIPR1
CALM1	HEG1	CDH17	HOXB9	HNRNPA1
KLF2	GIMAP5	MT-ND5	COX6A1	GPRIN2
VWA1	NQO1	CDKN2B	AP1M2	BTNL3
ADCY4	IL3RA	PEX26	RNF186	QSOX1
NES	PTPRB	SLC25A6	RPS21	SMIM14
ETS2	KANK3	SLC25A5	SHC1	BTNL8
MGAT1	IFITM1	GGT6	CD14	ITLN1
SERPING1	NKX2-3	LSR	DPP7	NEDD4L
SNX3	TMEM176B	NLN	LYZ	GPR153
COX7A1	GPRC5B	RPL18A	SEPP1	TDP2
ACTN4	TCF21	APOBEC3B	PERP	CYSTM1
CARHSP1	NDUFA12	PABPC1	RNF24	SH3BGRL3
ERG	ARID5B	EIF1	TBC1D2B	CDHR2
RPS4X	RAC1	IL32	MACROD1	PTPRF
RAC1	TNFSF10	SULT1A1	MYO10	ISG20
CYB5R3	EPHX1	LMO7	RPS11	LSR
LRRC32	PRKCDBP	CGN	IFITM3	FBXO32
IMP3	ITGA1	RPL37A	EPHB3	OASL
RNASET2	PLAU	S100A14	ASMTL	RPL23
BTNL9	FAM162B	LLGL2	YPEL5	CYP3A5
RPL13	DUSP1	IFITM3	H2AFY2	SLC26A3
YBX3	ACTN4	MVP	STK38	PRAP1
HPCAL1	APOL3	CLCN2	JUNB	MT-ND5
RPS18	COL6A2	TPRN	PPAP2A	SLC44A4
ELK3	ROBO4	ACOX1	LACTB2	KCNK5
KLF4	UBC	AKR1B10	TAGLN2	RASSF7
PVRL2	IGJ	CA12	SMARCC1	H2AFJ
RHOC	WNT6	MT-ATP6	GAPDH	CA1
SNHG7	TMEM255B	MPST	AC005355.2	STARD10
CTNNBIP1	COL15A1	TSPAN3	TMPRSS2	CDH1
RPL28	ADAMTS1	FAU	C7orf55	STAP2
RASIP1	RPL10	PARK7	TSPAN13	STX19
HYAL1	PTMA	C1orf106	SNX3	PLAUR

TABLE 1B

Absorptive__TA__1	Secretory__TA	Absorptive__TA__2	Cycling__A	Goblet__1
TXN	MT-ND1	FABP1	EPCAM	TFF3
GPX2	B2M	SELENBP1	LGALS4	KLK1
MGST1	TFF3	CA2	MGST1	ITLN1
EPCAM	MT-ATP6	LGALS4	AGR2	FCGBP
AGR2	PRDX5	C15orf48	C15orf48	AGR2
C15orf48	MUC2	S100A14	GPX2	CLCA1
PPP1R1B	FCGBP	PHGR1	KRT8	LRRC26
LGALS4	KLK1	KRT19	CLDN7	RETNLB
HMGCS2	RPL36	ETHE1	CLDN3	MUC2
TSPAN8	AGR2	FXYD3	PIGR	WFDC2
C10orf99	PIGR	LGALS3	HLA-DPA1	SPINK1
UGT2B17	ITLN1	UQCRQ	PHGR1	SPINK4
ATP5B	GPX2	PIGR	FXYD3	KRT18
CLDN7	ATP5G1	COX5B	TXN	REP15
S100A14	MT-ND4	MT-ND1	ARHGDIB	ZG16
PHGR1	EPCAM	MT-CO2	VIM	SERPINA1
ELF3	LGALS4	COX4I1	ELF3	TPSG1
PIGR	ZG16	C10orf99	HLA-DPB1	LGALS4
CDX1	MT1G	MT-CO3	BST2	ST6GALNAC1

TABLE 1B-continued

MT1G	CLDN3	MT-ND4	TUBB4B	FAM3D
CLDN3	FABP1	MT-ATP6	CD74	KRT8
FABP1	PHGR1	MT1G	KRT18	EPCAM
FXYD3	KRT8	TST	S100A14	STARD10
KRT8	CLCA1	ATP5G3	MT1G	PHGR1
COX5A	COX4I1	KRT8	ARPC1B	SMIM22
ATP5G3	CLDN7	CA1	ATP5G1	FXYD3
KRT18	H3F3B	TMEM54	HMGCS2	GMDS
PRDX5	FXYD3	CHCHD10	KRTCAP3	HEPACAM2
CYC1	MT-ND2	ATP5G1	CD9	RNASE1
RPLP0	RPS14	SLC26A2	HLA-DRB1	KRT19
ATP5G1	MALAT1	TXN	PPP1R1B	MT-ND1
MT1E	IGJ	B2M	CLDN4	CLDN3
SLC25A5	KRT18	CLDN7	TSPAN8	VSIG2
TIMP1	CLDN4	CES2	HLA-DRA	C15orf48
LEFTY1	RPL37A	COX7A2	SUCLG1	PIGR
FAM3D	RPS29	UQCR10	CDX1	CLDN7
UQCRH	MT-CO2	COX6C	NUPR1	ANXA13
KLF5	RPS18	COX6B1	FAM3D	SPDEF
CHCHD10	C15orf48	HMGCS2	CYC1	MT-CO3
CLDN4	MT-CO3	AKR1C3	FABP1	TMEM141
LGALS3	TSPAN8	CKB	PRDX5	ANG
SUCLG2	EIF1	EPCAM	SMIM22	COX6C
CD9	SPINK1	HSD11B2	LGALS1	ELF3
TSPO	RPL35	AGR2	TMEM141	S100A14
KRT19	SMIM22	SMIM22	TMEM54	HMGCS2
SMIM22	SPINK4	MT-ND5	CKB	BEST2
C19orf33	STARD10	AMN	CST3	MB
NXPE4	FAM3D	MGST1	NDUFAB1	FABP1
B2M	MT-CYB	MT-CYB	C10orf99	CREB3L1
SUCLG1	MT-ND3	COX8A	ITM2C	RPL36
ATP5A1	RPS21	C19orf33	TMSB4X	GPX2
ATP5F1	CD74	TMEM141	ARPC2	CLDN4
GAPDH	HLA-DPA1	COX6A1	HLA-DRB5	S100A6
COX4I1	HLA-C	AKR7A3	SPINK1	RP11-234B24.2
COX5B	WFDC2	MT1E	PLP2	URAD
RP11-519G16.5	ATP5I	GOLM1	SPINT2	TCEA3
TMEM54	TMEM141	AKR1B10	HLA-DMA	TSPAN8
ETHE1	ELF3	PRSS3	HLA-DMB	MT1G
UQCRC2	RETNLB	CLDN3	MT1E	TSPAN1
CA2	TIMP1	CISD3	COX5A	TMEM61
TMEM141	HMGCS2	ATP5D	ATP5B	RAP1GAP
HLA-E	RPS3	MT-CO1	ECH1	C10orf99
CDX2	PPP1R1B	MT-ND2	TUBA1A	REG4
COX6C	RPS15	CHP2	IGJ	PRDX5
C1QBP	TMEM54	H3F3B	FXYD5	MT-ND4
RPSA	KRT19	KRT18	SELENBP1	CCL15
KRTCAP3	MT1E	NDUFA1	ETFB	UQCRH
OLFM4	ZFP36	VSIG2	HLA-DQB1	H3F3B
UQCRFS1	RPL12	TIMP1	SRI	NANS
S100A10	KRTCAP3	COX7C	KRT19	NPDC1
ATP5C1	COX5B	FAM3D	KLF5	MT-ATP6
H3F3B	IGLL5	PDE4C	IGLL5	MT-CYB
GSN	RPS9	EIF1	LGALS3	MT-CO2
MRPL12	MGST1	COX5A	HADH	IGJ
CD74	C10orf99	LGALS1	CDX2	MT-ND2
CKMT1B	RPL8	CD74	UQCRC1	IGFBP2
SLC25A6	ITM2B	TSPAN1	SMAGP	SPINT2
ARHGDIB	RPLP2	CLDN4	TIMP1	EIF1
RPS2	CHCHD10	TSPAN8	ACTB	C2orf82
MPC2	UBC	SLC22A18AS	LY6E	COX5A
SELENBP1	HLA-DRB1	CYC1	COA3	IFI27
RPS24	COX6B1	MT-ND3	COTL1	HES6
RPS18	ATP5D	ATPIF1	IGFBP2	COX5B
MAOA	NDUFB11	UQCR11	ACADS	TIMP1
RPL8	C19orf33	ELF3	PLA2G2A	CDC42EP5
CKB	S100A14	SDCBP2	STARD10	FOXA3
MPST	HLA-DRA	ATP5I	CES2	S100A4
IGJ	RPS5	IGJ	TST	PPDPF
TRABD2A	COX5A	CDX1	LEFTY1	ZG16B
ATP5O	RPS12	TSPO	CKMT1B	MT-CO1
RPS6	RPL13	SRI	ATP5G3	IL1R2
HINT1	ARHGDIB	UQCRC1	CISD3	TMEM176B
SPINK1	C2orf82	MGST3	ISG15	HSD11B2
HLA-DPA1	RPS8	S100A6	RARRES2	CD9
ECH1	RPS2	MRPL41	MPC2	BTG1
PHB	TCEA3	TCEA3	HLA-E	UQCR10
CES2	HLA-DPB1	NDUFB9	ECHS1	IFT172
AKR1C3	LEFTY1	COX7B	CKMT1A	COX6B1
CKMT1A	ACTB	ZFP36	UQCRQ	TPM1

TABLE 1B-continued

PLA2G2A	LRRC26	ATP5J	GGH	ZFP36
RPL5	MUC5B	ATP5B	TSPO	SERF2
UQCR10	NUPR1	SLC39A5	MPST	TSTA3
IGFBP2	MT-ND5	KRTCAP3	ATP5F1	MGST1
COX7C	CKB	NXPE4	COX4I1	TSPAN13
COX6B1	UQCR10	GPT	ATPIF1	C19orf33
LCN2	SELENBP1	MS4A12	CYCS	MT-ND3
RPL7A	RPL27A	ANXA5	UQCRH	ATP5G3
ZFP36	MT-CO1	ACADS	ZFP36	FAM195A
RPS8	UQCRQ	SLPI	MACROD1	ITM2B
CMBL	STRA13	PXMP2	COX5B	RAB25
FAM84A	RPL7A	NDUFB2	STAP2	FTL
PEBP1	RPL32	FAM162A	RPLP0	CDX1
S100A4	RPS19	DBI	RP11-519G16.5	STAP2
STARD10	CISD3	ARHGDIB	COX6C	DNAJA1
HLA-C	TPSG1	PPP1R14D	RGS10	TMEM54
IGFBP7	AMN	GPX2	SLC44A4	FABP2
PPP1R14D	URAD	UQCRH	NANS	ATP5I
HLA-DPB1	MT2A	TMEM45B	NDUFV1	CHCHD10
PDE4C	RPLP1	CYSTM1	RPS18	ARPC1B
RPS3A	TSPO	MYO1A	B2M	TSTD1
PCK1	COX6C	CDHR5	NBL1	UBC
GSTA1	RPL18	SLC44A4	ALDH2	PPP1R1B
RPL26	DUSP1	DHRS11	GNAI2	DDX5
STAP2	HERPUD1	ADIRF	C1QBP	ACTB
RPS3	RPS6	PPP1R1B	S100A4	MLPH
RPL10A	TMSB10	CKMT1B	MLEC	ETHE1
SEPP1	RPSA	MT1M	SUCLG2	SH3BGRL3
ATP5I	ARPC1B	HLA-C	MINOS1	KIAA1324
FAM162A	DDX5	ITM2B	S100A10	KRT20
UQCRC1	ATP5G3	PKIB	OAZ1	HSPA1A
TCEA3	UQCRH	USMG5	PSAP	STRA13
CHP2	NDUFA1	FAM195A	ATP5I	IFITM2
RPL31	ANXA5	FCGBP	TIMM13	CKB
ATP5D	TIMM13	IFITM3	SEPP1	AC011523.2
RPL37A	HLA-B	MPC2	HSPD1	HLA-C
SRI	COX8A	S100A10	RPL36	UGT2B17
HLA-DRB1	CDX1	MISP	UQCRFS1	ENTPD8
SELK	HLA-E	STAP2	ATP5A1	COX4I1
TSPAN1	SEPP1	MGAT4B	ANXA5	CST3
RPS23	CDC42EP5	SULT1A1	HLA-C	RGCC
SOCS3	SNX3	PYCARD	S100A6	B2M
RAB25	CYC1	ATP1A1	SFN	RAB15
MT1X	HLA-DRB5	DNAJA1	ATP5O	CD74
COX6A1	MRPL12	ZG16	AP1M2	NDUFA1
NACA	HLA-DMA	ASL	MT2A	MT1E
RPS29	IFITM2	NPM1	RAC2	ERI3
GMDS	RPL28	MPST	RGCC	TST
COA3	RPL38	MUC4	GSN	ERN2
UBC	RPS11	UBC	STRA13	TNNC2
RPL36	DNAJA1	SLC26A3	ATP5J2	NEURL1
SPINT2	HLA-A	SLC51B	CA2	GSN
ITM2C	RPL37	URAD	PEBP1	LGALS3
IFITM3	COX7C	HLA-B	TYMP	CAMK2N1
RPL13A	ETHE1	S100A4	PRDX2	SMAGP
DNPH1	HLA-DQB1	HLA-E	H3F3B	IFITM3
ISG15	MZT2B	CDH17	SQRDL	TSPO
SLC25A3	LITAF	CKMT1A	GJB1	CAPN9
UGT2A3	ISG15	ANPEP	PBK	MALAT1
SLC39A5	TRABD2A	SLC25A5	RPL37A	CDX2
RPL12	MZT2A	ABCC3	UCP2	TMEM176A
RPL29	TSC22D3	UQCRFS1	TPM4	IGLL5
FAM195A	TSTD1	IGLL5	CHCHD10	SLC44A4
URAD	ARPC2	DUSP1	TMEM98	TTC39A
NDUFA10	ECI1	TRMT112	ADIRF	COX7B
SQRDL	ETFB	IFITM2	DDT	OAZ1
HSPD1	MPC2	SHD	AKR1B10	COX8A
DDT	IGFBP2	JUNB	S100A16	JUNB
IFITM2	PLA2G2A	TSC22D3	PLEKHJ1	UQCRQ
NUPR1	TST	ATP5E	LGALS3BP	MARCKSL1
TPI1	GSTP1	TMSB10	ARPC3	SCNN1A
NOX1	HIST1H4C	TXNDC17	NOX1	LYPD8
ACADS	SDCBP	HLA-DRA	EEF1B2	COX7A2
ATPIF1	DNPH1	SQRDL	FAM162A	CTD-2547H18.1
TSC22D3	RPL31	CIRBP	RPS14	RASD1
TMSB10	SOCS3	SERINC2	GGCT	CIRBP
RPS27A	S100A4	DDT	RPS8	KRTCAP3
ANXA5	PRDX2	LDHB	TCEA3	H1F0
PRSS3	RP11-357H14.17	NDUFB7	GMDS	NXPE4
TFF3	COX7B	CMBL	RPS6	RPS24

TABLE 1B-continued

GOLM1	HSPA1A	IFI27	ETHE1	RPL37A
RPS15A	RARRES2	AOC1	LAMTOR4	PCBD1
HLA-B	CLUH	RAB25	MT-ND1	YPEL5
MACROD1	RPLP0	KLF5	RPL8	HLA-E
PXMP2	MPST	PCK1	SH3BGRL3	MUC1
TST	SPINT2	SPINT2	HLA-B	ITM2C
COX7A2	TXN	TCEB2	IMPDH2	ATP5G1
AP1M2	GSN	NDUFA2	TUFM	KCNMA1
TUBB	UQCRC1	C2orf82	PXMP2	PRR15L
IGLL5	CES2	HERPUD1	NDUFA10	RPL26
GJB1	RPL29	S100A16	LYZ	HLA-DRB1
EIF1	ATPIF1	GSN	PHB	CYC1
ARPC1B	ST6GALNAC1	HNRNPA1	VIL1	AGR3
CISD3	MGAT4B	BCL2L15	NDUFA1	FFAR4
PKIB	MLEC	LAPTM4A	ACTR3	AMN
GPR160	REP15	UGT2B17	HINT1	RPS29
MRPS33	IFI27	STARD10	RAB25	SCGB2A1
DCTPP1	FBL	EID1	IRF8	KLF5
AKR1B1	DNAJB1	NDUFB3	CHP2	DUSP1
CDH17	UQCR11	MRPL12	AKR1B1	DNAJC12
AKR7A3	RNASE1	ESRRA	FCGRT	MUC4
HSPA1A	NDUFS5	MT2A	RPS3	ATP5J2
RPS14	IMPA2	PNRC1	RPL26	RAB27A
PLP2	DDT	NDUFV1	RPL10A	COX7C
RGS10	MYL12A	GJB1	HOXB7	IL32
MT-CYB	RHOA	MYO1D	MAOA	PSAP
TKT	RPL11	NAP1L1	AMN	RP11-357H14.17
MDH2	RPL10A	VIL1	TSPAN1	HLA-DRA
ITM2B	NDUFB7	DDX5	MT1M	HSPA8
HLA-DRA	RAB25	TMC4	MRPL12	MUC5B
EEF1B2	SUCLG1	NDUFS7	ITM2B	PLA2G10
DUSP1	FAM195A	SOCS3	NPC2	MPC2
PSMB9	MUC4	MAOA	NXPE4	DUSP2
AMN	SFN	KRT20	UQCRC2	TRABD2A
AKR1B10	MT1X	PLCD3	SDC1	DYRK4
FBL	GCHFR	SFN	ACAT1	KLK15
NDUFAB1	MUC1	ROMO1	IFITM2	LXN
DBI	FKBP1A	SSR2	RPS21	NDUFB4
MTCH2	RAB7A	EEF1D	HERPUDI	C12orf57
RPL14	GMDS	ITM2C	RPL13	SLC12A2
RPL3	TMEM176B	PADI2	TPM1	DCTPP1
RPL11	FOS	NDUFB1	SH3YL1	TMSB10
RPS9	TRPM4	DPP7	HSD17B11	GADD45B

Stem_cells	Enteroendocrine	Glial_cells	Inflammatory_fibroblasts	Fibroblast_pericytes
B2M	PCSK1N	CRYAB	VCAM1	RGS5
LEFTY1	CRYBA2	ALDH1A1	NNMT	BGN
TMSB4X	SCGN	GPM6B	LUM	CSRP2
ASCL2	CHGA	PLP1	SOD2	NDUFA4L2
MT-ND4	PYY	SPP1	CCL2	MYL9
LGALS4	SCG5	S100B	TDO2	MFGE8
SMOC2	GCG	FXYD1	COL3A1	TINAGL1
PRDX5	FEV	PRNP	C1S	TSC22D1
RGMB	MS4A8	PMP22	MFAP4	COX4I2
MT-CYB	TTR	CLU	C1R	FRZB
FXYD3	CACNA1A	TUBA1A	MMP2	ADIRF
GPX2	PRDX5	CD9	CTSK	TPPP3
CDCA7	HLA-C	MPZ	PDPN	HIGD1B
MT-CO3	HOXB9	SPARC	FBLN1	COL18A1
TSPAN8	FXYD3	NRXN1	DCN	GPX3
PHGR1	STARD10	DKK3	CTSC	SOD3
MT-ND2	RAB26	CYR61	RARRES2	IGFBP7
MT-ND1	B2M	LGI4	GPX3	NET1
EPCAM	LGALS4	MATN2	APOE	CALD1
ELF3	PHGR1	TUBB2B	SELM	4-Sep
PIGR	RAB3B	ANXA2	CALD1	TPM2
HLA-C	KRT18	PMEPA1	IFITM3	SERPINI1
MT-ATP6	MARCKSL1	PCSK2	TMEM176A	NOTCH3
MT-ND3	MDK	PEBP1	CYGB	PGF
KRT8	SLC29A4	GFRA3	DYNLT1	HES4
MT-CO1	KRT8	CAPS	COL1A2	ACTA2
PPP1R1B	EPCAM	CALM2	ADAMDEC1	MGP
EPHB3	ELF3	MYOT	WARS	ISYNA1
SMIM22	SST	L1CAM	TMEM176B	PDGFRB
KRT18	HLA-B	S100A1	COL6A2	SPARC
HSPB1	TMSB4X	COMT	CFD	FAM162B
CLDN7	ARX	CD59	GGT5	HSPB1
CLDN4	VIM	PLEKHB1	NDN	H2AFJ

TABLE 1B-continued

RPS18	CLDN3	TIMP3	FOXF1	BCAM
C15orf48	HLA-DPA1	CDH19	NINJ1	PLXDC1
HMGCS2	C15orf48	SMIM5	PLAU	CD36
HLA-B	FABP1	TSPAN11	LAP3	CAV1
RPS24	RPL37A	NTM	EMILIN1	DSTN
RPS21	MLXIPL	C8orf4	IGFBP7	PRSS23
CLDN3	COX6C	CNN3	STMN2	REM1
RPL36	C19orf77	MAL	CXCL14	LHFP
SPINK1	HLA-DRA	FIBIN	EPSTI1	COL4A2
RPL37	NEUROD1	FBLN2	HAPLN3	RGS16
MT-CO2	CPE	CCL2	CD63	LURAP1L
RPS6	SMIM22	CBR1	GBP1	TPM1
SLC12A2	TSPAN1	FGFBP2	SPARC	TAGLN
RPL37A	HLA-DRB1	ARHGAP15	COL1A1	EGR1
S100A14	TFF3	LGALS1	PKIG	IFITM3
RPL31	IGJ	JUN	LGALS1	HLA-C
RPL12	HLA-DPB1	PRKCDBP	SERPING1	EHD2
MT1G	CLDN4	SNCA	CFH	MEST
BST2	ITM2B	RPS6	DMKN	PKIG
ACTB	SEPP1	IGFBP7	SERPINF1	LGALS1
MARCKSL1	IFITM3	NDRG2	PAQR5	STOM
PDZK1IP1	RTN1	COL9A3	THY1	A2M
MGST1	SPINK1	ST6GALNAC2	SOD3	STEAP4
RNF186	LDHA	TTR	COL6A1	PTGIR
GNB2L1	VWA5B2	TMEM176B	CNOT4	RPLP2
RPS3	CD74	RPS2	LINC01082	PTK2
RPLP0	RPL36	FOS	TNFRSF1A	RBPMS
ETS2	SOX4	AP1S2	PMP22	EPS8
HLA-A	SCT	WISP2	GSTT1	PPP1R14A
CD63	BEX2	HES1	SGCE	SRGN
CST3	ISL1	VIM	TPM2	COL3A1
ARHGDIB	ANXA5	RGS16	A2M	GEM
FAM3D	GSN	FEZ1	TFPI	CRIP2
MT-ND5	RPS29	SORBS2	CLEC11A	ZFP36L1
CKB	S100A14	FCGR2B	FTH1	ARID5A
RPS4X	HOXB8	IFITM3	MFGE8	ARVCF
GSN	CHGB	RP4-792G4.2	SPON2	EPHX1
C10orf99	GUCY2C	RHOB	GBP4	HLA-A
FABP1	FXYD5	TMEM176A	C2	ADAMTS1
ALDH1B1	CLDN7	ART3	SFTA1P	PRKCDBP
MT1E	HLA-DMA	EGR1	LAPTM4A	MAP3K7CL
TRABD2A	HLA-DRB5	RPL8	TIMP1	NDUFAF4
KLK1	KRT19	TUBB2A	CDH11	C1R
SELENBP1	PRDX2	PDLIM4	LY6E	CALM2
STARD10	SPINT2	IL11RA	PLAT	C8orf4
AGR2	EIF1	RPS19	CEBPB	SDC2
RPL26	ETV1	ANXA5	APOL1	TCF21
SPINT2	HLA-E	SOCS3	PROCR	ESAM
ARPC1B	QPCT	RPS18	TMEM205	HEYL
KRT19	KIF12	PHLDA3	GADD45G	KNOP1
RPS5	DDC	NRN1	EVA1A	EFHD1
RPS2	LITAF	TSPAN15	ICAM1	SERPING1
RPL13	TMEM141	MIA	FHL2	RCAN2
TFF3	TMEM61	COL18A1	KLF6	C1QTNF1
S100A11	MT-ND3	RPLP1	LGALS3BP	RBPMS2
MYL6	COX5A	SPARCL1	RCN1	SERPINH1
AQP1	IGLL5	TPT1	BST2	NDRG2
FERMT1	LY6E	C1orf198	CCL8	FXYD6
MT-ND4L	MPC2	SCCPDH	GALNT11	COL6A1
RABAC1	IFITM2	S100A10	IGFBP3	GPRC5C
HLA-DPA1	UCP2	S100A4	ECM1	MAP1LC3A
RPL29	NDUFB11	RPL11	CYR61	RERG
LY6E	COX6B1	RASSF4	F3	GUCY1B3
HLA-E	HEPACAM2	TNFAIP6	HSD11B1	ASPN
SLC25A6	HLA-A	SGCE	CEBPD	EPAS1
TIMP1	COX4I1	COL1A2	IGFBP6	CTSF
RPL8	CXXC4	NNMT	EFEMP2	UBA2
CD74	KIAA1324	CADM4	SEPP1	GUCY1A3
RPL35A	TPH1	TAX1BP3	PRR24	RPS14
RPL10A	VAMP5	RPL19	COL18A1	LRRC32
KRTCAP3	ATP5G1	RPS3	NAB2	MSC
UBB	RPS9	TFAP2A	SCARA5	NR2F2
RPS12	MT-ND4	RCAN1	TNFAIP6	LGALS3BP
KLF5	SLC25A6	IER2	TNIP2	ANGPT2
NOS2	MT-ND1	MYL9	TCF21	CD151
RPL5	ERI3	RPS14	PRR16	SORBS3
OLFM4	ZFP36	GPNMB	IFI35	MCAM
SOX4	S100A11	TUBA1B	PTGIR	COL1A2
RPL32	RPS14	GPX3	BRCC3	GNG11
RPS23	NPC2	FAM210B	EID1	PTMS

TABLE 1B-continued

SEPP1	PCBD1	ID3	POSTN	MYH11
GUK1	RPS21	CADM2	PSMA2	RNASET2
COX5A	CKB	GATM	APOC1	RPLP1
RPS8	ATP5G2	HSPB2	CXCL1	THY1
MLXIP	GPBAR1	RHOC	S100A13	TGFBI
CEACAM5	SELENBP1	RPLP2	CD302	COL6A2
RPS19	NDUFA3	RPL18	RBP1	ASAH1
QTRT1	SMIM6	NGFR	EMP3	PLOD2
IFITM3	RPS11	HSPA2	BSG	RARRES2
STXBP6	KLK1	ASPA	SPG20	EFEMP1
RPL14	BAIAP3	FST	TNFRSF11B	SOCS3
CDX1	RPS2	MARCKS	UBE2L6	RPS18
RPL30	RPS18	KCNMB4	IL7	RPS19
RPS9	RPL12	SBSPON	PSME2	LBH
RHOC	MYL12A	PSAP	SCT	SELM
RPL7A	TM4SF5	OLFML2A	IL11	NEXN
CDX2	CADPS	RPL10	SRGN	CDS2
HLA-DRB1	C21orf58	SEPP1	IGJ	GADD45B
IFI27	DNAJC12	C1S	ARID5B	COX7A1
RPS14	CTSC	RPL13A	EDEM2	FKBP7
IFITM2	PPT1	CXXC5	PSMA4	HLA-B
TXN	RARRES1	S100A6	TAP2	CD248
RPL34	RPS3	EMP2	IFI6	PTRF
ISG15	DNAJA1	RPL13	FBLIM1	F2R
HLA-DPB1	SNX3	MXRA8	COL5A2	MRVI1
IGJ	NGFRAP1	SERPING1	FOSB	NFASC
PFN1	ISG15	RPS4X	ATP5E	PPIL4
AP003774.1	CDX1	RPL31	PCOLCE	STK16
GPR160	RPL38	RPL28	COL14A1	SMDT1
H3F3B	C12orf75	SRGN	ETHE1	NF2
CD9	TAX1BP3	FGL2	CDK2AP2	ATF3
CDHR1	RPS8	TBCB	IFITM2	APOE
HLA-DRB5	PPP1R1B	ENTPD2	ANXA5	FLNA
HLA-DMA	LYZ	SELM	TRIM47	TUBA1A
S100A4	HMGCS2	PHLDA1	TSPAN4	RRAD
NUPR1	PAM	EID1	PDGFRA	TRIB2
RPL18	PLA2G12A	NGFRAP1	ISG15	OAZ2
RPL27A	ACTB	ANGPTL7	CD276	RPL19
RPS15	SPINK4	RPS8	ADM	HRC
HLA-DRA	IFITM1	RPL26	APH1A	HCFC1R1
RPS15A	COX8A	JUNB	IL34	HEY2
ANXA5	IGFBP2	SLITRK6	FILIP1L	C11orf96
RPL38	TSTD1	RPS12	MAD2L2	LAPTM4A
TMEM54	LYPD8	RPL15	ADD3	RPL27A
FXYD5	RPSA	RPL12	TAGLN2	RPL11
RPL24	C4orf48	SLC22A17	PHGR1	ARHGEF17
RPS29	HLA-DQB1	RERG	SQSTM1	CACNA1H
PSMB9	GPX2	PCBP4	PLAC9	TGFB1I1
ARSE	MLXIP	CADM1	MESDC2	COTL1
RPSA	LAP3	RPS23	NR2F1	PLEKHA4
RPL11	ATP5E	ATF3	SERPINH1	RPS13
CTSC	HSPA1A	RPS27A	NUBP2	GULP1
EEF1B2	AGR2	ITPR1	LAMA4	PARM1
ARPC2	TNNC1	LGALS3BP	CYB5R1	OLFM2
CAPZB	TPPP3	FSTL3	TSPAN9	RPS5
ZKSCAN1	SOCS3	RPS5	SEC63	RASL12
TYMP	MT-ATP6	FAU	DKK3	S100A10
KIAA1324	QTRT1	RPL32	F10	RPS6
LRIG1	HERPUD1	ZFP36L1	AGT	ITGA7
IMPDH2	ETFB	SOD1	COX5B	DOCK7
GLTSCR2	MRPL41	SERTAD1	BBIP1	ANGPT1
RNF43	CD55	RPS16	TNIP1	CD74
RPS27A	PEMT	PCMT1	COTL1	CLMN
ATP1A1	PRSS3	RARRES2	IFIT1	ENTPD3
PSME2	C10orf54	ITGB1BP1	IFITM1	RPL36
RPL23	CKMT1A	RPLP0	PTGDS	MAB21L2
RPS7	TCEA3	CTNNAL1	CD40	ILK
DYNLL1	TYMP	RPS20	ALDH1A3	COASY
RPLP2	S100A4	HSPA1A	ACP5	RPL28
LGR5	PSMB9	YWHAE	NUPR1	MSRB3
OAZ1	RPL18	CST3	GSN	CYGB
SOCS3	RPS15	RPS9	OS9	PDE1A
EIF3D	MT1G	SLC15A3	MRFAP1	FHL2
SUCLG1	RPL32	CLIC4	CLEC2B	CCL2
HSPA1A	PIGR	DYNLL1	ARHGDIB	ZNF580
URAD	MT-CO3	RPS15A	GNG11	CASC3
PTGDR	CUTA	RPSA	NUMA1	SH3BGRL3
CHDH	KIAA1456	MT2A	PPAP2B	HLA-F
KCNN4	CTSD	S100A16	LGALS4	TMEM98
PSMA7	RAC1	WDR86	SYPL1	RRAGA

TABLE 1B-continued

TAGLN2	QDPR	DLX2	FBN1	LINC00152
C19orf33	C19orf45	GSN	FABP1	LGI4
EPHB2	RPL13	LAMP1	TMEM119	MXRA8
ETHE1	WFDC2	ID4	MMP3	GPI
PABPC1	HSPB1	POLR2F	ATPIF1	10-Sep
SELM	RPL31	RXRG	S100A3	MYLK
ITM2B	CD59	SECISBP2L	C1RL	CCDC146
IGLL5	OCIAD2	RPS7	AKR1B1	PTP4A3
MPST	KIAA1377	TMOD2	HTRA3	NNT-AS1
UQCRH	CENPV	RPL6	NBL1	ARHGAP29
UBC	EMC10	SH3BGRL3	SLC9A3R2	FILIP1
TDGF1	PLAUR	DEPDC7	TYMP	SCN4B
PPAP2C	DNAJB9	ERBB3	PUS3	FOS
NQO1	RPL37	PON2	EZR	RPS15
RARRES2	EPHB3	STARD13	PRKCDBP	MOCS1
S100A6	GADD45B	RPL23A	ANG	PPP1R15A
HLA-DQB1	HIST1H4C	SCD	OLFML3	EPC1
TSC22D3	SERINC2	GRAMD3	CXCL6	FXYD5
CDKN1A	CTSS	AHNAK	GPX8	VIM
TGIF1	URAD	CDC42EP1	CPQ	SERTAD3
AP000344.3	RGS2	IFIT3	CCL13	RPL8
C10orf54	NDUFA11	RPL27A	TNFRSF12A	ID3
SH3BGRL3	ATP6AP2	RPL5	PGRMC1	HN1
WNK2	NUDT16L1	C1R	PSMB9	EFEMP2
RPS2O	SAT1	CMTM5	TPST1	EBF1
RHOA	ANXA2	TNFRSF12A	PAPPA	TIMP1
MYL12A	TIMM13	RPL29	FAM105A	LPL
COPE	UQCR10	RPS29	COPA	GNAI1
VAMP8	PRR15L	ARHGAP12	EHD2	RSBN1L

TABLE 1C

Myofibroblasts	Villus_fibroblasts	Crypt_fibroblasts_(hiFos)	Crypt_fibroblasts_(loFos)	T_cells
ACTA2	NSG1	ADAMDEC1	CFD	DCN
TAGLN	F3	CFD	DCN	LUM
MYL9	FRZB	DCN	ADAMDEC1	CFD
TPM2	CXCL14	C1S	FBLN1	ADAMDEC1
PDLIM3	DMKN	LUM	LUM	C1R
ACTG2	VSTM2A	FBLN1	MFAP4	C1S
HHIP	POSTN	HAPLN1	C1R	FBLN1
SOSTDC1	BMP4	CCL8	APOE	TCF21
MYLK	ENHO	C1R	C1S	APOE
FHL1	PLAT	MFAP4	SOD3	COL3A1
HSD17B6	MMP2	APOE	TCF21	CXCL12
MYL6	EDNRB	CTSC	COL1A2	MFAP4
TPM1	HSD17B2	CCL2	ABCA8	GPX3
MYH11	COL6A1	COL1A2	COL3A1	HAPLN1
DSTN	COL6A2	TCF21	CTSC	CFH
CNN1	SDC2	COL3A1	CYGB	SERPINF1
NDUFA4	AGT	CYGB	CXCL12	COL1A2
TGFB1I1	TMEM176B	ABCA8	CXCL14	CCL2
NPNT	IGFBP3	SOD3	CTSK	PPAP2B
DCN	NBL1	STMN2	TMEM176B	PLAC9
PDLIM7	CYGB	CXCL14	GPX3	PTN
PRKCDBP	FENDRR	PROCR	RBP1	PTGDS
WFDC1	RARRES2	GPX3	PROCR	IGFBP7
CXCL14	FOXF1	CXCL12	COL6A2	PROCR
COL3A1	MFGE8	A2M	PLAC9	COL6A2
COL1A2	CAV1	RBP1	CCL8	CTSC
SMTN	ECM1	COL1A1	PTN	CXCL14
FLNA	TPM2	SERPINF1	IGFBP7	SOD3
HHIP-AS1	MFAP4	PTN	LINC01082	CYGB
C1S	PDGFRA	CCL13	CALD1	CCL13
SELM	COL3A1	TMEM176B	A2M	CCL8
PPIC	COL1A2	CTSK	TMEM176A	IFITM3
LUM	GPX3	LINC01082	COL1A1	PMP22
PPP1R14A	C1S	PPAP2B	SERPINF1	CCL11
ADAMDEC1	LGALS1	GSN	IFITM3	RARRES2
COL1A1	CALD1	CFH	CFH	GSN
TM4SF1	TMEM119	IGFBP7	ADH1B	CD2
COL6A2	FAM150B	CCL11	SERPING1	COL14A1
NBL1	WFDC1	CLEC11A	CCL2	ADH1B
NEXN	APLP2	ADH1B	CLEC11A	SCARA5
LGALS1	COL1A1	GGT5	HAPLN1	A2M
C1R	BMP5	PLAC9	GGT5	COL1A1
ILK	PDLIM1	SCARA5	RARRES2	FXYD1

TABLE 1C-continued

KCNMB1	TMSB4X	VCAM1	SCARA5	DKK3
SPARC	SCPEP1	DKK3	CCL13	CALD1
CSRP1	PDGFD	COL6A2	LGALS3BP	CD3D
MFAP4	MMP11	PMP22	GSN	PPAP2A
CALD1	MMP1	TMEM176A	MMP2	ADAM28
IGFBP7	SPARC	SEPP1	DKK3	TMEM176B
LINC01082	TMEM176A	MATN2	CCL11	CLEC11A
HSPB1	IGFBP7	PPAP2A	PMP22	CTSK
APOE	PROCR	CYR61	PPAP2B	EFEMP1
POSTN	LGALS3BP	CALD1	HAAO	PCOLCE
APOC1	PPP1R14A	ADAM28	ADAM28	CD69
FBLN1	PKIG	RARRES2	CD63	EMILIN1
TMEM176B	IGFBP6	MMP2	PCOLCE	STMN2
SPARCL1	TRPA1	BMP4	BMP4	MMP2
CAV1	TIMP1	SERPING1	COL6A1	GGT5
LMOD1	MYL9	VIM	SEPP1	HAAO
AOC3	MRPS6	SGCE	SPON2	NDN
CFD	PCOLCE	EFEMP1	SPARC	SPON2
RBPMS	SLITRK6	PCOLCE	PPP1R14A	RBP1
TCEAL4	C1R	IFITM3	PPAP2A	CD52
IFITM3	IFITM3	ECM1	FHL2	THY1
TUBB6	TCF21	LTBP4	LGALS1	BMP4
MMP2	SERPINF1	PTGDS	PTGDS	VCAN
MXRA8	TGFBI	LAPTM4A	MFGE8	GNG11
CD151	REEP2	SPARC	EMILIN1	SCT
TCF21	SOX6	CD63	VIM	PPP1R14A
ACTN1	TSLP	COL6A1	PRKCDBP	ABCA8
PDIA5	CLEC11A	PPP1R14A	THY1	LAPTM4A
PMP22	INSC	SPON2	SELM	TMEM176A
EFEMP2	CTC-276P9.1	HAAO	GNG11	LGALS1
LGALS3BP	SRGN	FOS	LAPTM4A	LTB
CD9	RBP4	SNAI2	LTBP4	LINC01082
EMILIN1	LTBP4	NNMT	TIMP1	PAMR1
TUBA1A	PITX1	FHL2	STMN2	PLTP
GSN	LAPTM4A	GNG11	EFEMP2	IGFBP6
MRGPRF	EMILIN1	MEG3	SNAI2	NDUFA4L2
MFGE8	MAGED2	TM4SF1	ECM1	VIM
COL6A1	GLP2R	FABP4	SGCE	SELM
UBE2E3	LAMA4	EMILIN1	VCAM1	CIRBP
C9orf3	A2M	LGALS3BP	IL34	FABP4
PTMS	PROM1	EFEMP2	IGFBP6	S100A4
SERPINF1	RGS10	CXCL1	SPARCL1	QSOX1
JUNB	LHFP	LGALS1	NOVA1	RGCC
RCN1	BAMBI	PLAT	FBLN5	FBLN5
FXYD1	RBPMS	IGFBP6	NGFRAP1	PLAT
CES1	ANXA5	SOCS3	PLTP	MEG3
NUPR1	AKR1B1	TPM2	MATN2	SRGN
RARRES2	BSG	SMPDL3A	FXYD1	TIMP1
SRGN	PRR16	NDN	EDIL3	GSTT1
FN1	MAP1B	SELM	TPM2	EMIDI
SDC2	GADD45G	FXYD1	SFTA1P	SERPING1
FOXF1	TSPAN4	C2	TSPAN4	CD3E
PCOLCE	S100A13	PLTP	MEG3	ANXA1
SERPING1	GLT8D2	VCAN	EPHX1	LTBP4
SCPEP1	HSPB1	NGFRAP1	QSOX1	CCL5
AC131025.8	C11orf96	QSOX1	MYL9	SPARCL1
SGCE	EFEMP2	SDC2	SRGN	MXRA8
MIR145	FGF9	EPHX1	TM4SF1	IFI27L2
CRYAB	EID1	GSTM3	EFEMP1	FN1
LTBP1	PTMS	SPARCL1	PLAT	GSTM3
CRIP2	COL5A1	TIMP1	OLFML3	MYL9
DUSP1	MXRA8	FHL1	GSTM3	PHGR1
CERCAM	FKBP10	SRGN	CCDC80	CD63
TPPP3	PTGDR2	COLEC11	DPT	SEPP1
SH3BGRL	CPE	EDIL3	RAB13	TPM2
VIM	SGCE	IL34	ITIH5	GATA3
CKB	TNC	PRKCDBP	NNMT	TFPI
NGFRAP1	TAGLN	C11orf96	SDC2	LEPROT
PTCH1	DCN	ARHGDIB	FSTL1	C16orf89
SOD3	TXNL1	FBLN5	LOXL1	SGCE
COL4A2	EMID1	SFTA1P	FABP4	LGALS3BP
LRRC17	CRISPLD2	EID1	S100A13	LCK
GNG11	SRPX2	FXYD6	COL14A1	DPT
CYBA	C1orf21	MYL9	NDN	SNAI2
RBP1	NDN	THY1	MXRA8	ZFP36L1
IER2	ISCU	LINC01116	UBE2E3	IL32
CPQ	CD9	TFPI	FHL1	TSC22D3
MAP1LC3A	ACP1	LOXL1	TAC3	LAMB1
BMP5	PALLD	MXRA8	IFITM2	MATN2
OSR1	F2R	IRF1	EID1	C6orf48

TABLE 1C-continued

AKR7A2	BST2	PITX1	PITX1	SPARC
NDN	CPM	MFGE8	C2	CNBP
PKIG	SELM	UBE2E3	LRP1	NANS
S100A13	PTN	FGF7	NUPR1	FSTL1
HMG20B	WNT5B	SERPINH1	VKORC1	EEF1D
RP11-332H18.4	SERPING1	OLFML3	APOC1	AEBP1
CFH	RBP1	ARID5B	FKBP10	SERPINH1
GAS6	FBLN1	PPIC	FXYD6	NNMT
FOSB	NDUFA4L2	RAB13	LAMA4	WNT2B
LPP	PCDH18	CFL1	PPIC	C11orf96
PALLD	APOD	JUNB	DMKN	PDPN
TTLL7	KREMEN1	KCNS3	EMID1	GZMK
IGFBP5	TUBAlA	S100A13	NDUFA4L2	ELANE
LAPTM4A	ID1	CEBPD	PLAU	TRIM22
WLS	ADM	TSPAN4	FOXF1	CLEC14A
EDNRB	PRKCDBP	APOC1	FN1	PITX1
FAM127A	IFITM1	LAMA4	GLT8D2	SLC25A5
ARHGDIB	CXCL12	C6orf48	COL5A1	CXCL1
CSRP2	TSHZ2	ZFP36L1	CTC-276P9.1	COL6A3
TIMP2	LRRN4CL	GLT8D2	COLEC11	IDH2
MAMDC2	PTCHI	NDUFA4L2	CFL1	COLEC11
P2RY14	LAMB1	EMID1	EHD2	COX5A
S100A4	HHIP	CCL7	RBPMS	MXRA5
TRIP6	VIM	SRPX	COL18A1	EDIL3
SH3BGRL3	NNMT	TIMP3	SCPEP1	EFEMP2
CBR1	CIRBP	ANGPTL4	SMPDL3A	PPIC
MMP14	CAPZB	SCPEP1	WFDC1	TDO2
SEPW1	CD63	DPT	DUSP1	C4orf3
MFAP5	TGFB1I1	ADM	COX5A	VPS25
FENDRR	IL32	GADD45B	FOSB	FNDC1
CALU	PLK2	NUPR1	C6orf48	CYP7B1
TMEM176A	TBX2	LRP1	SERPINE2	SPRY1
CTSK	ANGPTL4	CYBA	FAM127A	PCDH7
C1QTNF2	PCSK6	RAB34	TMEM119	ZFP36L2
SNAI2	TSPAN2	PRNP	GSTM5	DMKN
COL4A1	WLS	EGR1	CPQ	ALDOA
CD63	AEBP1	ZFP36	RAB34	COL6A1
COX7A1	SCUBE2	PROS1	AKR1B1	HTRA3
LOXL2	LANCL2	ITIH5	CD81	PRKCDBP
CYB5R3	LOXL2	CD81	SLC9A3R2	CXCR4
FOS	FIP1L1	CIRBP	TNFAIP6	KRT8
IL32	RTN4	FOXF1	FILIP1L	KLRB1
RPL28	ADH5	CCDC80	VCAN	PHLDA1
CFL2	TM4SF1	NEGR1	TGFB1I1	FGF7
LTBP4	C7orf50	COX5A	COL15A1	LAMA4
EHD2	IL1R1	NOVA1	ATRAID	TAC3
ITM2C	EMP3	FN1	TFPI	COL18A1
STMN2	CYBA	CPQ	WNT2B	SPINT2
BSG	CAV2	ID3	SERPINH1	THNSL2
VCAN	TMEM100	FKBP10	PRNP	NEXN
LAMB1	MAP1LC3A	BST2	CTSF	RNASE1
MAP1B	IFI27	WFDC1	MDK	FXYD6
VCL	SEMA4D	TDO2	ACTA2	LOXL1
P2RX1	PXDN	DMKN	CST3	CD81
WNT2B	HAAO	COL5A2	KLF6	TMEM66
PARVA	NPY	COL14A1	TGFBI	CRIP2
S100A6	RGCC	PGRMC1	TIMP3	TIMP3
ECM1	SGCB	PHGR1	ABCA6	H3F3B
TCEAL1	FHL1	SH3BGRL3	FGF7	IRF1
LAMA4	TPBG	ANXA5	CYBRD1	ECM1
VKORC1	NUPR1	EHD2	MMP23B	IFI27
NME4	TBX3	TAC3	EVA1A	DDR2
TMEM98	RGS1	VASN	PTMS	SLC9A3R2
RPLP2	LEPROT	SLC25A5	TNFRSF1A	SGCA
TIMP1	GNAI1	AEBP1	C7	CD74
CD74	MSC	RBPMS	RP11-14N7.2	COL15A1
PPP1CC	PTX3	CCNI	RGCC	SFTA1P
A2M	ACTA2	CNBP	CDH11	CDK2AP2
CTSS	CD74	SPRY1	FGFR4	PTGER2
PTS	LRP1	SEC11C	BST2	FABP1
PPAP2A	TMEM98	PLAU	IGFBP5	TNFAIP3
TTC3	PLBD1	IFITM2	CXCL1	FGFR2
ADH5	CPQ	4-Sep	CP	FHL1
MCL1	VASN	GSTM5	C16orf89	KRT18
FAM105A	AMPD3	ABCA6	LINC01116	RND3
MAGED2	IGFBP5	FILIP1L	CIRBP	SCPEP1
NKX2-3	MXRA5	MT-ND2	SAMD11	MAPK10
RAB34	PHGR1	LEPROT	SAT1	LY6E
SGCA	STMN2	FSTL1	SH3BGRL3	CLEC2B
CCDC107	GULP1	MT-CO2	MIR497HG	FTH1

TABLE 1C-continued

SERPINH1	CCDC68	TUBA1A	PHGR1	NUPR1
FILIP1L	SPON2	HES1	HTRA3	CD5
MINOS1	CH25H	CSF1	AEBP1	IL34
AEBP1	PLAU	CDK2AP2	TMEM9	EMP3
NEO1	MRVI1	CDH11	S100A4	NUDT16L1
EID1	CD151	PFN1	SCT	CCDC80
PDGFC	CNTFR	HTRA3	MXRA5	IL1R1
DCTN2	COL6A3	RND3	CNBP	EVL
CBR3	PDLIM4	HSPA1A	IFITM1	RP11-14N7.2
RCAN2	CYTL1	JUN	PDLIM3	CSF1
RERG	COL4A5	MT-ND4	KCNS3	GNAO1
CLEC11A	HMGB1	CST3	ISLR	LRP1
FSTL1	ST5	HINT1	HSPA8	ITIH5
C2	GADD45B	TNFAIP6	PFN1	MFGE8
FHL3	ID3	CHL1	BDH2	DUSP2
TGM2	CYR61	ADAMTS1	ELANE	FHL2
MORF4L2	CTSF	ACTA2	HINT1	TRAT1
TMEM47	CTSK	SERPINE2	WARS	FARP1
ISG20	ENPP6	C16orf89	COX7A1	MRPL23
ACTB	LUM	MYL12A	PAMR1	TM4SF1
CD99	HOXA10	RCN1	LY6E	LAMA2
EFEMP1	SERPINH1	IGJ	CRYAB	GZMA
ZYX	FILIP1L	TMEM98	MYL12A	PAM
SAMD11	SEC62	ELANE	SPRY1	RNASET2
SSPN	GPC1	MAMDC2	IL6ST	GPC6
RBBP7	ARPC1B	CTC-276P9.1	ANGPTL1	IL7R
CPED1	PDPN	CD302	GAS6	IFITM2
RGS10	TUSC3	PCDH18	NENF	FBN1
CREB3	RP11-332H18.4	FAM92A1	RUNX1T1	ACTA2
DDAH2	C12orf57	GRK5	CYBA	RARRES3
SEPP1	NOVA1	WNT2B	ANXA1	ADM
MIR143HG	WFS1	MDK	NEGR1	FKBP10
NENF	NGFRAP1	POSTN	CYCS	COL5A1
PITX1	CDH11	ISLR	COL6A3	CCDC127
COL6A3	OLFML3	EPHA7	SLC25A5	GAPDH
KANK2	ZFP36L1	ANGPTL1	PAM	MGST1
NUDT4	PDE1A	PHLDA1	IL32	VKORC1
ARHGEF25	ECHDC2	HSD11B1	CRIP2	HSD11B1
MMP23B	BRK1	FTH1	TDO2	DUSP23
THYN1	HLA-A	RGCC	COL4A2	CHCHD10
RGS1	TCF4	IL6ST	RGS1	SSBP3
ARPC1B	SEC11C	SMIM10	PCDH18	NGFRAP1
RCN3	COL4A6	TMEM150C	P4HA2	ARHGAP24
SQRDL	RCAN2	CTSF	CYB5R3	EID1
APCDD1	SCARB2	ATP6AP2	TSTD1	ID4
RP11-532F6.3	MMP14	AKR1B1	EEF1D	C11orf58
NDUFB9	SH3BGRL3	SVEP1	MT-CO2	CREG1

	Macrophages	Dendritic__cells	Mast__cells	Cycling__monocytes	Tolerogenic__DCs
	FTL	CST3	TPSAB1	FTL	SNX3
	C1QB	CLEC10A	VWA5A	PSAP	CPVL
	C1QC	HLA-DPB1	LTC4S	MS4A6A	IDO1
	PSAP	HLA-DPA1	C1orf186	GPX1	CST3
	C1QA	HLA-DQB1	CPA3	AIF1	CLEC9A
	CTSB	FCER1A	SLC18A2	C1QA	LGALS2
	CD68	HLA-DQA1	HPGDS	C1QC	C1orf54
	CTSD	HLA-DRA	MAOB	C1QB	HLA-DPB1
	TYROBP	HLA-DRB1	HDC	CST3	DNASE1L3
	SAT1	CD74	CLU	TYROBP	IRF8
	LGMN	AIF1	NFKBIZ	IGSF6	HLA-DPA1
	FCER1G	LST1	RP11-354E11.2	CD68	CD74
	MS4A7	IL1B	SAMSN1	CTSB	HLA-DQB1
	MS4A6A	LYZ	GATA2	DNASE1L3	LSP1
	AIF1	CPVL	ANXA1	FCER1G	COTL1
	ACP5	AMICA1	GLUL	MS4A7	HLA-DQA1
	MS4A4A	HLA-DMA	FCER1A	MS4A4A	HLA-DRA
	DNASE1L3	TYROBP	KRT1	NPC2	AIF1
	GPX1	FCER1G	CAPG	LYZ	HLA-DQB2
	IGSF6	SPI1	CTSG	IL1B	HLA-DRB1
	FUCA1	MS4A6A	PPP1R15A	VSIG4	SPI1
	FCGRT	HLA-DQB2	SLC45A3	LST1	LYZ
	SEPP1	HLA-DMB	HPGD	SDS	HLA-DOB
	HLA-DMB	CFP	HS3ST1	CTSD	HLA-DRB5
	NPC2	HLA-DRB5	GMPR	GRN	HLA-DQA2
	HLA-DPA1	IGSF6	KIT	CPVL	ACTB
	STAB1	LGALS2	RGS13	FGL2	LST1
	HLA-DQA1	PLAUR	CD9	SPI1	RGS10
	HLA-DPB1	CD83	FCER1G	HLA-DPB1	BATF3
	RNASET2	IFI30	NFKBIA	SAT1	CADM1

TABLE 1C-continued

LST1	PLD4	BTK	CD74	MPEG1
LYZ	CD1C	HSP90AB1	HLA-DRB1	ASB2
HLA-DRA	MNDA	CD44	HLA-DQA1	C1orf162
CD14	COTL1	MITF	HLA-DPA1	PPT1
HLA-DMA	GPX1	SERPINB1	RNASE6	FGL2
GPNMB	HLA-DQA2	LMNA	FAM26F	S100A6
HLA-DRB1	ITGB2	ADRB2	PLAUR	HLA-DMB
PLA2G7	SGK1	VIM	CTSZ	BASP1
APOC1	GPR183	TYROBP	HLA-DRA	CD83
CD74	FGL2	SRGN	HLA-DRB5	KIAA0226L
SDS	C1orf162	IL1RL1	RNASET2	HLA-DMA
CTSS	SRGN	SDPR	PLA2G7	SGK1
LAPTM5	FAM26F	FAM46A	SEPP1	TMSB4X
CD163L1	LY86	BTG2	CD14	RGCC
RNASE6	RNASE6	ALOX5	HLA-DQB1	PLEK
VSIG4	RGS2	NSMCE1	STAB1	S100B
HLA-DQB1	DNASE1L3	CTNNBL1	HLA-DMA	SERPINF2
GRN	CTSH	MIR24-2	LAPTM5	ARPC2
ADORA3	CD1E	LEO1	CLEC10A	SMCO4
CTSZ	FCGR2B	SDCBP	ACP5	ITGB2
S100A11	MS4A7	PTGS1	HLA-DMB	HCK
SPI1	LAPTM5	LAT2	AP2S1	CST7
PLD3	SAT1	ALOX5AP	NCF4	UCP2
TREM2	CD1D	FTH1	S100A11	WDFY4
FOLR2	C1QA	DDX5	IGF1	CPNE3
CYBA	CXCL16	AC020571.3	A2M	TNNI2
CST3	ACTB	DNAJA1	CCL3	GLIPR1
RNASE1	RNASET2	BACE2	ITGB2	DUSP2
ATP6V1F	HCK	CD69	SLC7A7	PTPRE
CCL3	CACNA2D3	DUSP6	CD300A	RNASET2
SLC40A1	CORO1A	MLPH	LGMN	ARPC1B
LIPA	MPEG1	JUN	SLC40A1	LY86
GLUL	ARPC1B	IL1RAPL1	TYMP	SLAMF8
CSTB	VSIG4	SIGLEC8	C1orf162	SLAMF7
CPVL	BID	RAB27B	GLUL	C20orf27
ASAH1	STX11	LAT	RGS10	LIMD2
VAMP8	CTSS	UBB	VAMP8	FLT3
ATP6V0D2	FTL	ACOT7	SRGN	FAM49B
RENBP	SAMHD1	STMN1	P2RY6	PARVG
CREG1	GLIPR1	FXYD5	C1orf54	CORO1A
CLEC10A	CSF2RA	EGR2	MNDA	BID
FCGR2A	CD68	ALDH1A1	AMICA1	GCSAM
FAM26F	LSP1	NCOA4	IFI30	RAB32
RGS10	INSIG1	GCSAML	CTSH	FAM26F
TMSB4X	IL8	CD33	FCGRT	CD9
CTSL	NR4A3	STX3	CSF1R	LCP1
NCF4	ARPC3	SVOPL	FCGR2A	ARHGDIB
AP2S1	DUSP2	ATP6V0A2	TGFBI	CKS2
LY86	FAM110A	LAPTM4A	LGALS1	SUSD3
IGF1	CD33	HSP90AA1	MPEG1	PABPC1
HLA-DRB5	TMSB4X	CD63	GPR183	FKBP1B
FGL2	C1QC	ANKRD28	SERPINF1	GSTP1
AKR1B1	CD86	LAPTM5	TBXAS1	PPDPF
MALAT1	RGS10	EGR1	IL8	P2RY6
AMICA1	PHACTR1	ARL5B	CTSS	FCER1G
APOE	PPDPF	CATSPER1	APOC1	NAP1L1
IFI30	AOAH	HSPH1	RNF130	CD48
CD163	PYCARD	KLRG1	HCK	TYMP
ITGB2	PTPRE	CLIC1	ALOX5AP	LAPTM5
HLA-DQB2	ARHGDIB	TSC22D1	CD36	MT-ND2
S100A9	RNF130	S100A4	ADORA3	ID2
CD300A	PLEK	ATP6V1F	SIRPA	AMICA1
UCP2	TYMP	CTD-3203P2.2	CYBA	AIM2
CSF1R	GRN	SGK1	PLD3	CLNK
OAZ1	NCF4	RENBP	PDLIM1	LGALS3
GM2A	TBXAS1	PLIN2	RGS1	IFI27
PLAUR	C1QB	PTPN6	GPNMB	CSF2RA
NPL	ARRB2	ANXA2	CD4	VMO1
HCK	IFI27	FAM212A	RGS2	DUSP4
LILRB4	UCP2	FOSB	TIMP1	ID3
C1orf54	ARL5B	ASAH1	APOE	SAT1
C5AR1	DUSP1	HSPA8	OAZ1	TLR10
LGALS1	CD48	ASRGL1	VIM	TYROBP
RNF130	RHOG	LYL1	ATP6V0B	MIR142
CD209	RGS1	EIF4G2	CORO1A	GPR183
TTYH3	NR4A2	STXBP6	HLA-DQA2	TSPO
PRDX1	NCF2	TNFSF10	CREG1	MNDA
RAB42	HCLS1	GRAP2	HLA-DQB2	PFN1
IL1B	ARPC2	NFKBID	S100A9	LGALS1
FABP3	PILRA	CSF2RB	PPT1	GPX1

TABLE 1C-continued

MPEG1	CD53	RAC2	LY86	HSPA1A
CD36	P2RY13	NR4A1	TXN	ACTG1
SLC7A7	CLEC4A	HSPA1B	EPCAM	CCND1
NINJ1	PPT1	H3F3B	LILRB4	CNN2
C3AR1	CHMP1B	SMYD3	FUCA1	LTB
CHMP1B	GPSM3	MPP1	FXYD5	SAMHD1
CAPG	ZNF385A	FAR2	GNAI2	NAAA
ADAP2	ATF3	LMO4	ADAP2	ITM2C
OTOA	LITAF	SRSF5	CSF2RA	HCLS1
CFD	ZNF331	ARHGDIB	LGALS4	TACSTD2
HSD17B14	PARVG	EIF3D	NINJ1	PSMB9
CD83	MIR142	EGR3	ATP5G1	XCR1
LILRB5	NAMPT	CD82	FCGR1A	PLCD1
P2RY6	P2RY6	MYADM	EMP3	SERPINB9
CMKLR1	FAM49B	TESPA1	KRT18	TMEM176B
SERPINF1	FTH1	RASSF5	CAMK1	GMFG
CTSC	GAPT	CALB2	PHGR1	COX7A2
BLVRA	NPC2	BIRC3	CD163L1	CD99
TYMP	ITGB2-AS1	HINT1	KRT8	PPM1J
TBXAS1	HLA-DOA	CD22	C3AR1	H2AFY
RGS1	CYBA	IL18	IFI27	PYCARD
CXCL16	OAZ1	HSPD1	S100A4	RGS1
CD86	P1D1	STXBP2	RAB31	TMEM59
CD4	CCL3	MBOAT7	DAB2	SRGN
A2M	RILPL2	RGCC	ANXA1	ZYX
IL8	CXCR4	IER2	ATP6V1F	CLEC7A
C1orf162	CSF1R	MSRA	TUBB4B	NABP1
NAGK	ARL4C	JUNB	CD209	ZFP36L2
ATP6VOB	PDLIM1	BHLHE40	TFF3	ABI3
HLA-DQA2	IGJ	ARHGEF6	LSP1	MT-ND1
FTH1	NCF1	CST3	ARHGDIB	CD37
CAMK1	G0S2	DUSP10	UCP2	FNBP1
GPR34	HSPA1A	SCYL1	CXCL16	EVI2A
SLAMF8	VAMP8	RGS10	HBEGF	HAVCR2
S100A6	TNFSF13B	PRDX6	ZNF331	ARPC3
IL18BP	H2AFY	ACTG1	FCGR2B	CD63
CTSH	OLR1	CHST2	CTSC	HES1
ARHGDIB	HCST	CD37	RBI	KIAA1598
PLTP	MT-CYB	DDX3X	SRI	VAC14
COTL1	TMEM59	ESYT1	YWHAH	IGFBP7
ARL4C	CXorf21	CRBN	RENBP	TAP1
FPR3	CNPY3	SYTL2	SGK1	LDLRAD4
SRGN	EIF4A1	CTSD	CD163	ELOVL5
HMOX1	THEMIS2	HNRNPM	C5AR1	IL16
TNFSF13B	C20orf27	P2RY14	LILRB2	RGS19
CYBB	CD300A	CD83	COTL1	DUSP10
LAIR1	S100A11	SLC2A6	CLEC4A	PDLIM7
GLIPR1	YBX1	CKS2	TMSB4X	TWF2
ITM2B	LGALS1	ARHGAP18	LAIR1	CTSZ
YWHAH	IGFBP7	TIMP3	ASAH1	IFITM3
TGFBI	ANXA1	TMEM154	EEF2	CXCR4
HLA-DOA	PTPRC	CMA1	PLD4	COX5B
CCL4	AGPAT9	MALAT1	MAFB	VIM
DAB2	FCGR2A	RGS1	RPL24	SELPLG
EBI3	CTSZ	DNAJB1	FCER1A	CFL1
GATM	PPIF	FCGRT	PLTP	ATG3
ATOX1	DOK2	PFN1	TUBA1B	C12orf5
FCGR3A	MT-ND2	EXD3	RPS27A	PNMA1
ARPC3	GNA15	LIF	GMFG	APOL3
TNFAIP8L2	KRT18	GBE1	AXL	RAB31
ABI3	HERPUD1	CHORDC1	CLEC7A	MT-CYB
RHOG	HBEGF	GAPT	PRDX5	MYCL
RGS2	SCIMP	HSPE1	CD83	IFNGR1
CCL18	LCP1	ITM2B	HCST	GYPC
HN1	PTGS2	UBXN10	GNPDA1	GPSM3
RAC1	LIMD2	CNIH1	IGJ	PLEKHO1
TMEM176B	PMAIP1	SLC16A3	TUBB	LSM6
KRT8	PABPC1	GNPTAB	RPL31	MSL3
PYCARD	KDM6B	TSPO	DUSP1	UQCR10
PILRA	IL32	RPL28	RPL35A	LGALS4
LGALS4	FPR3	MAML1	P2RY13	CXCR3
SLCO2B1	PFN1	TUBA1B	CD9	CIITA
SMS	BSG	UBE3A	BLVRA	BCL2A1
CORO1A	GMFG	NFE2L2	GLIPR1	ROGDI
ZNF331	SLC31A2	SH3BGRL3	TNFSF13B	TGFBI
ARRB2	SNX10	ELF1	GATM	MIR4435-1HG
IFI27	SEPW1	PRKAR1A	OSM	CKLF
SIGLEC7	ZFP36	ENPP3	CLDN7	IGJ
GPR183	FOSB	GALNT6	NCF1	BST2
DOK2	KYNU	CCL2	CTSL	DGAT2

TABLE 1C-continued

CLEC4A	RGS19	ACTR3	GM2A	NDUFB9
CECR1	PHGR1	TMEM66	LRRC25	COX6C
TMEM37	SDS	NCF4	C15orf48	MT-ND5
RHOC	AKIRIN2	BEX4	AKR1B1	KLF6
ANXA1	DSTN	BLVRA	RAB42	KRT18
PHGR1	VIM	SERP2	GSN	1-Mar
AP1B1	S100A4	TM6SF1	TREM2	EVI2B
NCF1	RB1	ITM2A	RPL34	CPPED1
GRB2	ARPC5	DHRS7	SLCO2B1	FERMT3
GAL3ST4	H3F3B	IFI27	ADAMDEC1	ST8SIA4
ID1	PAK1	2-Sep	TSPO	PTPRC
NINJ2	RAB32	CD84	TRPM2	GNAI2
SDSL	CSF3R	HSPA9	RPL18	ATP5J
CD63	GSN	FECH	RPL5	GPR137B
ABHD12	RAB31	PRDX5	H2AFZ	HSPA1B
GNPDA1	ID3	IFITM10	SDSL	RNASE6
CD81	TNFAIP8L2	HSPA1A	MT1E	AKIRIN2
LRRC25	SOD2	DLC1	FABP1	LITAF
YBX1	SLAMF8	HIF1A	ENG	TOMM34
GPSM3	CCL3L1	LYN	TNFAIP8L2	PTPRCAP
TFPT	LILRB2	DDX3Y	LIPA	AP1S2
MKNK1	PRDX5	ZEB2	NCF2	BSG
SLC15A3	ANXA5	RHOG	ARL4C	MT-ND4
BRI3	RABAC1	RBMX	MGST1	MCL1
ADAMDEC1	S100A6	CDK5	GPSM3	ACTR3
IL2RA	FCGRT	DDX39A	RAC1	CD40
IGJ	COX6C	TMSB10	CECR1	MT-ATP6
RBI	CD52	EIF1	ARPC1B	PPA1
MPP1	NGFRAP1	NEK6	PARVB	KCNMB1
SLC7A8	PLEKHO1	CSF2	CYBB	MAP4K1
TNFAIP2	RAB20	CSF1	VMO1	EPCAM
SCIMP	ITM2C	CXCL14	SLC16A3	MYADM
TFF3	CEBPD	PIK3R6	DOK2	CAP1
NCKAP1L	CD9	GPR65	TNFAIP2	SIGLEC10
FXYD3	CD151	RPS4Y1	ARRB2	CECR1
ARPC1B	NUDT1	VAV1	ATPIF1	ACTN1
SIGLEC1	CCDC88A	IL4R	COX5B	RAB7L1
TUBA1B	MAT2A	SELM	ITGB7	FAM110A
BSG	PRMT10	EVL	NAGK	LINC00152
EEF2	GCA	HNRNPA2B1	ATF3	INPP5D
BST2	LINC00936	BCL2A1	IL1RN	PHGR1
HCST	COX5B	RALB	SUCLG1	GRN
LGALS3	MCL1	CORO1A	HSD17B14	AC093673.5
MNDA	CARD9	RAB32	CD86	C12orf57
RAB20	REL	WDR45B	KRT19	PHACTR1
FCGR1A	BCL2A1	LINC00863	TTYH3	CD86
PTAFR	TUBA1B	ABCB8	ANXA5	S100A4
CD53	FGR	EIF2AK1	SOD2	DAPP1
HCLS1	ABI3	SAR1B	BST2	RHOG
LSP1	SOCS3	RHBDD2	CAPG	CYB5R3
AGR2	IFNGR1	DHRS9	FOLR2	C10orf128
C12orf57	JUNB	SEMA7A	PRDX2	RHOF
AOAH	GHRL	CCDC28A	STX11	KRT8
STMN1	MT-ND5	TRAPPC2P1	SNCA	ANXA6
GMFG	NAGK	IGFBP7	PTGS2	ITM2B
IRF8	CIITA	GPR35	CMKLR1	SCNM1
AXL	CPPED1	PAK1	ATP5B	PRDX5
MMP14	LGALS3BP	PARVB	RPL37A	CAT
C15orf48	KLF4	RARRES1	RASSF4	PTRHD1
TRPM2	WAS	IL5RA	S100A6	CD72

TABLE 1D

Neutrophils	Activated_CD4_cells_loFos	Activated_CD4_cells_hiFos	CD8_IELs	CD8_LP_cells
S100A9	RPLP1	IL32	CCL5	CCL5
SOD2	RPS3	ANXA1	CD7	IL32
IL1B	IL32	KLF6	GZMA	NKG7
PLAUR	RPL10A	S100A4	NKG7	CCL4
LST1	RPS25	CD69	HOPX	GZMA
AIF1	RPSA	DNAJA1	IL32	DUSP2
SPI1	RPL32	HSPA8	CKLF	CD8A
G0S2	ANXA1	CD3D	KLRC2	SH3BGRL3
LYZ	RPLP2	RPLP1	CD160	CST7
SAT1	RPL19	LTB	GZMB	CD8B
FPR1	RPS19	CCL5	PTPRCAP	CD52
TYROBP	TPT1	CD52	TMIGD2	GZMK

TABLE 1D-continued

FCER1G	RPS15A	ID2	HCST	ZFP36L2
SERPINA1	RPLP0	SH3BGRL3	EVL	HCST
FTH1	RPL13	BTG1	CD52	HOPX
FCGR1A	RPL11	TNFAIP3	CD3D	PFN1
S100A8	RPL28	TNFRSF25	GNLY	TMSB4X
IGSF6	RPS12	CALM1	CD3E	BTG1
CFP	RPL13A	TSC22D3	SH3BGRL3	GZMB
IL1RN	RPL30	EIF1	RAC2	CD3D
HLA-DRA	RPS27A	TMEM66	CTSW	CD3E
CTSS	RPL4	CD2	PHGR1	GZMH
TYMP	RPS14	ZFP36L2	IGJ	CKLF
FAM26F	RPS6	RPS3	TMSB4X	MYL12A
HLA-DQB1	RPL23A	RPSA	GAPDH	CXCR4
FGL2	RPS2	CD3E	CORO1A	CFL1
CPVL	CD52	TMSB4X	ABI3	NR4A2
STX11	RPS18	RPS19	PRF1	B2M
HLA-DRB1	RPL6	SRSF7	ACTB	ARHGDIB
CD14	LTB	HSP90AA1	CD3G	LYAR
FTL	RPL27A	DUSP1	ARHGDIB	ANXA1
HLA-DPB1	S100A4	MYL12A	SIRPG	RPL28
HLA-DQA1	RPL10A	ARHGDIB	LCK	CTSW
COTL1	RPL3	ACTB	ACTG1	TMEM66
NCF2	RPS16	RPL28	RARRES3	C9orf142
HLA-DRB5	RPS5	CORO1A	PFN1	PSMB9
LILRB2	IL7R	RPLP2	CD247	RPLP2
APOBEC3A	RPL31	PFN1	STK17A	RPS3
EREG	RPL14	ABRACL	CAPG	PTPRCAP
C1orf162	UBA52	IL7R	TBC1D10C	LAG3
S100A11	RPS15	LEPROTL1	XCL2	CORO1A
CDC42EP2	RPL18	RAC2	FABP1	HLA-B
PLEK	SH3BGRL3	B2M	ARPC2	GZMM
MS4A7	RPS20	CD47	CD96	IFNG
LY86	RPS13	IFITM3	C9orf142	TUBA4A
HLA-DPA1	RPL27	APRT	LGALS4	ID2
IFI30	RPS8	HLA-DRA	FTH1	S100A4
HLA-DMB	EEF1B2	RPLP0	XCL1	RPS19
LGALS2	RPS23	IL2RG	CD8A	CD69
ITGB2	RPS4X	TPT1	1-Sep	CD7
C5AR1	RPL12	RPL10	CST3	ACTB
SRGN	ARHGDIB	CD53	AC092580.4	HLA-A
CYBA	RPS3A	DNAJB1	CFL1	CD2
TIMP1	RPL35A	PTGER4	CST7	PSME1
CD74	RPL5	ID3	CLIC1	ALOX5AP
CST3	RPL15	PPP2R5C	PPP1CA	RPL27A
CD36	RPL37	CD40LG	IL2RB	HSPA8
TNFSF13B	RPL8	HLA-DPB1	ALOX5AP	LEPROTL1
MS4A6A	TMEM66	CKLF	TIGIT	SRGN
BID	RPL34	RPS12	RPS19	HSPB1
GBP1	CD3D	RPS27A	IGLL5	SRRT
GLRX	RPL29	PHLDA1	PLEKHF1	RPS27A
NFKBIA	IGFBP7	RPL19	ACAP1	RPL30
MNDA	PTGER4	FTL	PTPN6	CXCR3
CXCL10	RPL35	DRAP1	P2RY11	CALM1
ACTB	CD3E	CD63	ID2	KLF6
FCN1	RPS7	DEDD2	MYL12A	RPL13A
IL8	TOMM7	GPSM3	FASLG	CREM
ARPC1B	CXCR4	DDX5	CYTIP	BIN1
HLA-DQA2	MYL12A	1-Sep	KLRD1	RPL23A
PILRA	RPL18A	UBE2D3	DRAP1	APRT
LILRB1	BTG1	CFL1	CD8B	RPS20
FGR	RPL9	GRN	CLIC3	HLA-C
NINJ1	RPL7A	PSMB9	IFITM3	CYBA
CD86	TMSB4X	TPM3	CXCR3	ABRACL
LINC00877	CD63	CD48	PPP1R18	TC2N
OAZ1	CORO1A	RPL14	RPS4Y1	1-Sep
TREM1	FAU	PDCL3	ACTR3	CD99
ASGR1	CD2	SAMSN1	GRN	EVL
HLA-DMA	TNFAIP3	PSME2	RGL4	ICAM3
TNFAIP2	RPL36	RPS6	TPI1	IFITM3
ARPC3	CCL5	SRGN	COTL1	LCK
CAMK1	EEF1D	RPL32	TRAPPC1	C12orf75
S100A4	GPSM3	ALOX5AP	KLRC1	ARPC2
CPPED1	LDHB	RPS20	HSPA1A	FYN
RAB20	RPS9	ARHGDIA	CIB1	XCL1
RIPK2	LEPROTL1	SOCS1	PSMB10	PRF1
CXCL9	PFN1	DDIT4	ITGA1	PSAP
LAP3	KLF6	MIR24-2	LAT2	ATP5E
ATP6V0B	CALM1	HLA-B	CD244	YPEL5
HCK	CD69	HLA-DRB1	ITGAE	DRAP1
GCA	APRT	PGK1	ENO1	MCL1

TABLE 1D-continued

RP11-290F20.3	GLTSCR2	LAPTM4A	BCAS4	CRTAM
LILRB4	GPR183	FDX1	CDK2AP2	PPP1CA
CD37	RPL26	RPL27A	NFKBIA	RPLP1
PRELID1	RPL36AL	RPS4X	PTMA	RPS15A
RNASET2	GIMAP7	CITED2	GIMAP7	GSTK1
GCH1	HSPB1	PSME1	RPLP2	TIMP1
CYBB	ABRACL	RAN	NPC2	CLIC1
NCF4	PSAP	MALAT1	ARPC1B	ID3
IL23A	HLA-DPB1	H3F3B	VASP	TMA7
RP11-701P16.5	RPL24	RPS15A	LSP1	PTPRC
SERPINB9	HLA-DRB1	FOSB	HERPUD1	PPP2R5C
MPEG1	PTPRCAP	CXCR4	RGCC	RGCC
CCL3	KLRB1	BCAS2	PTPN22	RNF167
CFD	IFITM3	ALG13	CISH	MYL12B
UBE2D1	HLA-DPA1	LCK	MATK	PSME2
THEMIS2	FTL	RPL11	HSPA1B	HMOX2
STXBP2	EVL	CDC42SE2	SOCS3	RPL13
ARRB2	APOE	RPL13	RPS3	CD59
GPX1	FXYD5	CACYBP	RPL13A	SAMSN1
TIFAB	CD74	IDS	PSME1	RARRES3
CORO1A	HLA-DRA	GALM	PTPN7	TRAPPC1
DUSP2	DDX5	CD6	CD2	TAPBP
TESC	RPS4Y1	CCL20	ASB2	SH3KBP1
CD68	RGCC	RPS2	OSTF1	APOBEC3G
SPHK1	TC2N	RPL31	DOK2	GLIPR2
KYNU	HSPA1A	UBE2D2	ITGB7	PSMB10
BCL2A1	CMPK1	IL4I1	MT-CO1	DHRS7
GLUL	CD6	SLAMF1	CD59	RPL19
BLVRA	IL2RG	FOS	TNFRSF18	TSC22D3
KDM6B	SRGN	MGAT4A	RPLP1	MALAT1
NAMPT	NPM1	TRMT112	FCER1G	STK17A
SLC31A2	TSC22D3	FAM96B	LAG3	DENND2D
NUP214	PDCL3	IL12RB1	HSPB1	RPL31
ABI3	ZFP36L2	SVIP	ARL6IP5	ITM2A
SELK	CD59	CCR6	WAS	CDK2AP2
PSAP	CFL1	RPL36AL	BUB3	MZT2A
SAMSN1	SOCS1	PLP2	RGS1	RGS1
PPIF	NACA	CYCS	CD69	SOCS1
ATF5	RPL38	TTC39C	SLC16A3	GUK1
AMICA1	CKLF	HLA-DPA1	HLA-DRA	GRAP2
IGJ	CD37	NOP58	RPS3A	C19orf60
ITM2C	SH2D2A	ENO1	PTTG1	TNFAIP3
YBX1	GNB2L1	MYADM	LDLRAD4	IL2RG
ACSL1	IGJ	RPS25	CD53	DDX5
RNASE6	BTF3	HNRNPA0	PSAP	EEF1D
ZFAND5	NPC2	JUN	PTGER2	RPS12
GRN	CXCL14	YPEL5	SH3BP1	ARPC1B
WAS	CCDC109B	PPP1R15A	CHMP4A	PTGER4
TNFAIP8	LGALS1	SERP1	IDH2	ZNF331
JUN	HSPA8	RPS14	RPS27A	BUB3
ASGR2	CRIP1	EVL	LSM2	RBM8A
CXCL2	HSPA1B	PSAP	EEF1A1	CAP1
FCGR1B	CCR6	FAU	HCLS1	RPS18
LIMD2	RPS29	RPL13A	MYL12B	7-Sep
DOK2	PFDN5	PTPRCAP	CRIP1	C19orf24
PFN1	TTC39C	TAGAP	PABPC1	HLA-DRB1
LILRA2	RPS21	DHRS7	LYAR	FAM177A1
PYCARD	C9orf142	H2AFZ	FYN	CRIP1
ISG15	RPL37A	AMD1	BIN1	ABT1
KMO	RPL17	CD74	RGS19	CXCL14
IL10	PABPC1	ODF2L	DEF6	RPS25
CTSH	EIF1	SND1	RPL18A	SNRPB
CD48	GSTK1	OSTF1	IFI27	RPS2
RTN1	ARL4A	ERP29	LCP1	EIF1
IKZF1	YPEL5	PNP	HENMT1	CTSB
SH3BGRL3	CD7	ARL4A	CXCR6	BAX
C19orf38	HCST	RPL30	RPL9	MFSD10
RIN3	LAPTM5	MRPL11	FCGRT	RPL36AL
PSME2	ITM2C	AATF	RPS10	RORA
HCLS1	ID2	RPL4	CCL4	SRSF7
CD83	FYB	MCL1	RPS27	HNRNPUL1
AP1S2	TUBA4A	JUNB	APOBEC3G	COPE
LCP1	1-Sep	BAZ1A	CD99	FTL
ITGAX	RPL22	EIF4A3	TPM3	C9orf78
PKM	RORA	CREM	RPL17	PDCL3
CFL1	LAPTM4A	SRSF2	GYPC	TAGAP
VAMP8	PLD3	RPS5	GSTK1	UBE2D3
IFNGR2	SNRPD2	MRPL34	IL2RG	C14orf1
NPC2	METTL9	SNHG8	ATP5E	PLP2
RILPL2	B2M	C9orf142	GYG1	GPSM3

TABLE 1D-continued

GPBAR1	CACYBP	MTFP1	FOSB	UBE2L3
CSF1R	SAMSN1	RPS8	SASH3	GPR65
OSM	HIGD2A	PRR5	C19orf53	ATP6V0E1
CCRL2	ARPC1B	ACTG1	7-Sep	RAC2
CLEC10A	9-Sep	CHCHD7	FXYD3	KLRD1
IL4I1	GPR171	RPS13	TSEN54	HLA-DRA
CD52	AES	PTGER2	COMMD8	EBP
SYK	LAT	HSPE1	CYBA	RPSA
CHMP1B	ACTB	TC2N	PSME2	TMUB1
NLRP3	NKG7	SAP18	EGR1	RNF149
HBEGF	DYNLT3	RORA	CD74	HLA-DQA1
CCL3L1	TRAT1	CCDC109B	GZMM	GAPDH
IFI27	EIF3E	CDK2AP2	CAPN12	STUB1
IL27	RARRES3	UBE2S	SPINT2	SNRPD2
ATP6V1F	OXNAD1	LAT	C9orf78	CSNK1D
ARHGDIB	SERPINB6	CD97	POLR3GL	HSPA1A
TMSB10	SPINT2	GSTK1	PDLIM1	RPL14
VSIG4	COMMD6	PSENEN	C9orf16	RALY
ANXA2	HNRNPA1	LDHA	GUK1	RPL22L1
VASP	ACP5	EIF4A1	CCND2	FAM96B
PPDPF	RAP1A	FUS	GPR68	TOMM7
ARL5B	RPSAP58	HNRNPUL1	TNFSF14	SNRPB2
MT-CYB	EEF1A1	C14orf166	RHOC	METTL5
GBP5	CREM	SPINT2	IL16	RPL32
PSTPIP2	RCAN3	SURF4	SLC9A3R1	PNN
GPR183	CD48	MZT2A	MIF	MBP
HCAR2	SPOCK2	CXXC1	MT-CYB	CLDND1
SAMHD1	TNFSF13B	PCBP1	TTC1	GTF3A
HAPLN3	EIF3H	RPS18	SAT1	ATF6B
CAPG	SAT2	ANXA5	TSC22D4	CDC42SE2
EPSTI1	LYAR	HMGN1	LAPTM4A	ALG13
RNF130	PLP2	HCST	SCML4	RPS16
ID3	MZT2A	PSMA7	PTPN4	RBCK1
CREM	MGAT4A	LAPTM5	COMMD6	CD9
LITAF	SMDT1	TIMP1	HLA-DRB5	CD74
CXCL3	ANXA5	EML4	RP11-47L3.1	PHGR1
PLA2G7	ENO1	AMICA1	SSNA1	EPSTI1
UBE2E2	TMEM14B	ICAM3	CASP4	CD53
H2AFY	PSME1	IL17A	CTSB	OAZ1
UBXN11	CYCS	EIF1AX	ARPC3	PPP1R18
RGS2	ATP5L	DYNLT3	APRT	RPS14
RHOG	RBM3	IFITM2	RPL7	CSRNP1
CASP1	ICAM3	PRKCQ-AS1	VAMP8	BLVRB
CD274	ALOX5AP	RBL2	RPL4	RPL27
HCAR3	C19orf24	HSP90B1	HLA-DQB1	RPL3
LINC00936	GMFG	SNRPB	FAM173A	OXNAD1
TUBA1B	NEAT1	FERMT3	SLA2	NEDD8
IL18BP	EGR1	GHITM	GPR171	C11orf31
C12orf57	PTPRC	SELT	SAMSN1	HSPA9
EMG1	CD97	NFKBIA	PSMB9	TPM3
PTGS2	UBE2D2	RPS16	CD37	CHMP4A
MYO1F	TXNIP	RPL22L1	ANAPC16	PSENEN
NADK	GTF3A	ISG20	RPL21	MLX
RABAC1	RPS11	SNRPD2	RPSA	RPL34
A2M	PPP2R5C	IFI35	HMOX2	CIB1
GDI2	SNRPG	CASP1	LSM10	OCIAD2
GLIPR1	TMA7	NPC2	PSMD13	SLC38A1
HSPB1	RPL22L1	SLC1A5	PGK1	TADA3
DSTN	IFITM2	TRAPPC1	TYROBP	IDH2
NMI	DUSP2	TUBA4A	HLA-DRB1	GHITM
CD9	RPL23	MAX	C11orf48	NHP2L1
DUSP1	SCML4	UXT	RPL28	ATP5D
MCL1	C19orf53	HSPB1	GGA1	ACADVL
BSG	GGA1	RBM3	EEF1D	ATP8A1
MT-ND3	MZB1	RAB8A	LAPTM5	GATA3
RNF19B	ARHGEF1	TAPBP	GPR34	NAA50
GLIPR2	HERPUD1	RPL23A	TSTA3	AKR1A1
PSMB9	JUN	EMP3	BANF1	CD97
GAPT	PHLDA1	UBA52	CDIP1	MZB1
NAGK	PRKCQ-AS1	CRIP1	C11orf31	MEA1
C10orf54	ZFAS1	NR4A2	STXBP2	PSMB8
CTSB	EEF2	TAP1	RPL22	MYEOV2
CD53	COTL1	SS18L2	CALM1	UBE2I
CSF3R	TRAPPC6A	FLT3LG	RPL36A	ZFP36
SCIMP	CTSD	GPR183	NUDT14	FIBP

TABLE 1D-continued

MT-ND4	NDUFS5	IRF1	IRF2	C14orf166
PSMA4	CLIC1	CXCR3	MRPL46	SIGIRR
HCST	RPS24	PPP6C	YPEL5	RPL10

Tregs	Memory_T_cells	NK_cells	Cycling_CD8_cells	Inflammatory_CD2_DCs
IL32	LDHB	NKG7	CD3D	LST1
CORO1B	RPL11	TYROBP	CD3E	IL4I1
BATF	CCR7	FCER1G	NKG7	KRT86
TIGIT	RPS12	XCL2	CD2	LTB
PFN1	RPL32	CTSW	CCL5	FXYD5
BTG1	RPS3	XCL1	CD7	ALDOC
CD3D	RPL19	CLIC3	IL32	KRT81
ARHGDIB	RPLP2	IL2RB	GZMA	ID2
CREM	RPL13	GZMB	CST3	LTA4H
ICA1	RPS15A	CCL4	ITM2A	NFKBIA
C9orf16	RPS14	GSTP1	TUBB4B	ZFP36L1
DNPH1	RPL23A	KLRC1	CTSW	CASP3
TNFRSF4	RPL31	MATK	PTPRCAP	TNFRSF25
CARD16	RPSA	APOBEC3G	GZMB	HSPA8
RAP1A	RPS4X	CST7	VIM	MIR24-2
LTB	RPL18	GZMA	CD8A	LIF
ARPC1B	RPS6	GNLY	CD8B	TYROBP
CTLA4	RPS13	GZMK	B2M	DUSP1
NDUFV2	RPL28	CD7	CD96	NXT1
FOXP3	RPL27A	KLRD1	AC092580.4	HNRNPA0
PMVK	RPS2	HCST	SH3BGRL3	MPG
PBXIP1	RPS25	EIF3G	CD3G	HMGN3
LCK	LTB	PFN1	RGL4	CXCR4
CD63	RPS18	PRF1	LGALS1	NR4A1
BIRC3	RPL30	FGR	FCGRT	CSF2
PTPRCAP	RPL4	KRT81	HCST	PRMT10
ITM2C	RPS9	HOPX	PLA2G16	CD83
UCP2	RPL35A	CAPG	TMIGD2	DNAJA1
IL2RG	RPS27A	CCL3	IFNG	H2AFY
AC017002.1	RPS8	KLRF1	RAC2	SRSF2
SRGN	RPL10A	MAP3K8	GYPC	TMIGD2
LGALS1	GNB2L1	SRGN	SPINT2	OTUD5
CD44	CD63	IFITM2	LGALS4	CD300LF
CALM3	RPS23	CD3D	HLA-DRA	SPINK2
DUSP4	RPS20	STK17A	CD69	TPT1
RGS1	RPL14	FAM177A1	LY6E	TLE1
TNFRSF1B	RPL36	PTP4A1	LDHA	DLL1
MIR4435-1HG	RPL37	ITGB2	ARHGDIB	PTGDR
LAIR2	RPL13A	CCL5	GIMAP7	NCOA7
ICOS	IL32	BTG1	SRGN	CD52
TNFRSF18	RPL27	NR4A2	TBC1D10C	AMICA1
HLA-A	PABPC1	APMAP	CD52	MAFF
ACTB	RPL26	DUSP2	RPL8	BIRC3
SPOCK2	RPL8	PTGDR	EPCAM	JUNB
ANKRD12	SELL	GZMH	RARRES3	TOX2
EIF3H	RPS21	CORO1A	CD9	DRAP1
GSTP1	RPL5	KRT86	H2AFZ	CD69
B2M	RPS15	CD160	ATPIF1	IL23R
CORO1A	RPL10	LAT2	MSN	ARL4A
CD27	LGALS1	ID2	APOBEC3G	TCIRG1
CCL5	RPS16	MIB2	GZMM	UBB
LAT	BTG1	ALOX5AP	SLC9A3R1	IER2
PKM	RPL34	BCO2	CDKN2A	CAT
PPP1R18	RPL29	NCR3	COX5B	EIF1
ANXA1	RPL12	ARPC5L	C15orf48	AREG
EEF1D	TMEM66	MYL12A	ICAM3	FOSB
HINT1	FXYD5	FTL	TXN	ZFP36
IL10	ARHGDIB	CD97	CD37	TCP1
RAC2	RPS5	PPP1R2	SKAP1	CD164
ASB2	RPLP1	CD247	PIM1	DDX3X
LAG3	RPS7	GLIPR2	SLA2	METTL9
FOS	EEF1B2	CLIC1	TRAT1	ZNF75A
ATP5L	RPS19	SLC35E1	CXCR3	C16orf91
TBC1D4	CD52	7-Sep	TCEA2	NR4A2
COTL1	FAU	CHST12	PRKCH	TNFRSF18
RPL28	RPL7A	CDC42SE1	ATP5B	MAP3K8
RHOH	GLTSCR2	C20orf24	EMP3	TEX30
NINJ2	NOSIP	LSP1	MARCKSL1	BZW1
RHOG	NPM1	SAMD3	HLA-DRB1	H3F3B
GMFG	LEF1	PTPRCAP	HLA-B	DDX18
CST3	RPL6	HSPB1	PEBP1	MRPL18
CD52	ZFP36L2	ABHD17A	TRAF3IP3	PRPF6
PPP1R2	RPL15	RGCC	ATP5G1	PRAM1
UBE2D2	EIF3E	CD44	RPL37A	SLC43A2

TABLE 1D-continued

FYB	TCF7	MAPK1	HLA-DPB1	RAN
TNFRSF9	HINT1	LDLRAD4	PRF1	FCER1G
PTTG1	RPS29	ACTB	HOPX	MGAT4A
CD2	RPLP0	EVL	GSTP1	SLC25A39
TRAF3IP3	UBA52	TMIGD2	PDLIM7	NFKBIZ
NTMT1	LEPROTL1	MRPL3	CST7	BLVRA
RPS15A	RPL22	GZMM	GRN	FOS
ADTRP	RPL38	ZFP36L2	HLA-DPA1	RNASET2
CACYBP	ITM2C	NUDT14	IFITM2	IL2RG
S100A4	HSPA1A	TESC	LCK	EIF4A1
GPR183	RPL3	SH2D1B	EVL	LINC00299
JUN	TRAT1	CHD2	GZMK	EMP3
ENO1	EEF1D	FAM49B	SIRPG	DNAJB1
UBC	EEF2	VDAC1	LGALS3	IL7R
TNIP2	BTF3	BIN2	NANS	BST2
1-Sep	LGALS3	ARHGDIA	CD74	CREM
EVL	SMDT1	CDHR1	CYC1	SLC16A3
CXCR6	PFDN5	SIGIRR	AGR2	KIAA1324
HSPA8	TOMM7	VPS37B	HLA-C	UNC93B1
TAPSAR1	HNRNPA1	TNFRSF18	SH2D1A	ENO1
GNB2L1	EIF3F	GRK6	LAPTM5	SKIL
XRCC6	CCDC109B	DUSP1	SLC25A5	RNF139
CYTIP	PTPRCAP	ZFP36	CORO1A	HSP90AA1
CD37	CD3D	SELM	HLA-A	BEX2
RPL13A	CD37	IDS	HSPD1	TMEM243
NSA2	RPL23	PRDX1	RPL36	DDIT4
CD3E	RPS3A	RHOF	IL2RB	RBM39
HMGN1	PSAP	LGALS3	LSP1	SIK1
TRAPPC4	GIMAP7	CFL1	TSPAN5	PSMD13
TRAPPC1	RPL24	CMC1	GCHFR	RASD1
SH2D1A	LIMD2	RNF113A	ATP5G3	AQP3
TIMP1	RPL37A	IL2RG	HIST1H4C	MED30
ARID5B	RPL9	TIMM8B	GPX2	HHEX
SKAP1	RPS11	FASLG	RPL38	ZNF331
DOK2	TRAF3IP3	TMSB4X	SAMSN1	BTG2
SNRPB	RPS24	SRSF5	COX5A	RPL22L1
ISG20	PASK	LAMTOR5	HN1	NCR3
TNFRSF14	TPT1	AKNA	HLA-DQA1	MYADM
FXYD5	NACA	USF2	ATP5O	LPXN
CDKN2A	CORO1A	RAC2	UQCR10	RBPJ
RPL36AL	COX7C	NDUFB8	UBE2C	UBE2S
PCBP1	IFITM3	SDHC	GMFG	DPAGT1
LAPTM5	EIF3H	RANGRF	GNG2	NHP2
PTPN2	CXCR4	KLRB1	FYN	CYCS
UXS1	ANAPC5	PSMB2	HES1	PRR5
PMAIP1	RPL18A	SLC16A3	GNLY	CCT4
UGP2	CD7	RIN3	ID2	HMGN1
9-Sep	DENND2D	RBM38	UQCRQ	BCAS2
ARF6	MZT2A	IDI1	XCL1	BTG1
CMC2	RPL35	UBXN2B	HLA-DMA	MAP2K1
LIMD2	FAIM3	LINC00667	RPS29	CXXC5
PSME1	OCIAD2	CST3	ANXA1	ATG4B
LEPROTL1	GPSM3	PPP5C	RGCC	SFPQ
TMSB4X	C6orf48	ID3	CCNB1	SRGN
IGBP1	UBB	DRAP1	BST2	NPC2
PYHIN1	RNF138	NFKBIA	ATP5A1	TUBA4A
BCAS2	CYTH1	CCNL1	CLEC2D	CALM1
PHLDA1	SERPINB6	NXT1	ECHS1	TXK
PRR13	CCL5	ARID5A	CCNB2	SPTLC2
ZNHIT1	FAM177A1	AGTRAP	ATP5J2	ANP32A
SOD1	DCXR	ARHGDIB	TNFRSF18	CCR6
MAPK1IP1L	NUCB1	CBX3	CKS2	PROSC
OSER1	DAP3	TCEB2	NCAPH	TXNL1
CASP4	P4HB	RPS3	RPL5	TRAF4
RGCC	FYB	ZNF814	RAC1	HSP90AB1
NAMPT	HLA-DPA1	LINC00996	ARPC1B	SRSF5
6-Sep	FOSB	PSMA7	ABI3	SLA
IDI1	6-Sep	CD69	GPX1	RNF19B
GBP2	CHI3L2	YPEL3	MT1G	COL9A2
SSU72	ID3	APRT	CYTIP	NFKB1
COPE	CST3	HMGN1	SURF4	PPP2CA
YWHAZ	ARPC1B	CPNE1	CTSH	NAP1L1
COMMD3	JUNB	IGFBP7	FXYD5	SRP9
GLRX	RARRES3	PPP1CA	PFKP	BEX4
RBBP4	BEX2	YWHAZ	CRIP1	TMEM123
PTPRC	ICOS	EBP	ZAP70	TUBB4B
HIGD2A	HLA-DRB1	MIR24-2	ICOS	LGALS3BP
SMS	IFITM1	ZNF331	MT1E	TNF
CCL20	PFN1	GCHFR	RPL12	HSPD1
ANP32A	CD3E	TRAPPC1	RORA	SAMD10

TABLE 1D-continued

NPM1	TBC1D10C	DDIT4	IL2RG	CSTB
NAPA	RNASET2	GRB2	IFI16	CRIP1
APOE	EIF2S3	OCIAD2	ETFB	CD47
RPL15	CASP8	MPG	UPP1	EMC10
HSPB11	FXN	RALA	ATP5J	SACM1L
ACTR3	CYLD	C19orf25	S100A4	ANXA5
CDC42SE2	SC5D	SNRPA1	PSMB9	IFI44L
TMEM66	LMNA	BUB3	STK17A	CAPG
SNX5	MAL	PLAC8	RPS14	FAM213B
CHCHD10	AIM1	PDCD4	KRT19	EIF3D
ICAM3	TMSB4X	SLC25A39	TIMM13	EIF4G2
JUNB	MRPL16	RPL7L1	CD247	ERBB2IP
LIMSI	COTL1	NSMCE1	RPS4Y1	ARF1
EPSTI1	CRLF3	BUD31	RPL7A	PARL
C19orf43	H2AFV	PAPOLA	TMSB4X	HSPA5
PIM2	AAK1	CALM1	RPS18	ZFAS1
LINC00152	SLC2A3	MRPS11	GZMH	GSN
GTF3C6	CTSD	C1orf162	SRI	WDR45B
SOCS1	AC013264.2	PSME2	PIGR	TPM3
RPL11	TMSB10	LDHB	KRT18	SERTAD2
UFC1	1-Sep	CD59	COX4I1	CA13
TSC22D1	IGBP1	RBCK1	CCL4	AKAP17A
ARPC4	RPS4Y1	GRN	CENPW	CUTA
NUDT1	ZFP36	BCAP31	STOM	CDC42SE1
ANAPC16	COMMD6	AIM1	CREM	PRKAR1A
TPRKB	DNMT1	TGFB1	PTTG1	EPS8L2
PHGR1	GIMAP4	TIPARP	RPL35A	H2AFX
WDR1	CXCL14	MYO1F	FKBP11	CXCL2
RPS2	YPEL5	SF3B2	PHB	ALG13
CD58	WHSC1L1	NDUFS8	PTGER2	SNRPB
DDX5	ZNF331	RTN3	SUCLG1	B3GALT5
RPS27A	CD27	NDUFA3	ACAP1	NRBP1
SMCO4	GSTK1	PPP1R14B	AIP	AUP1
EEF2	SSU72	PTMA	PLEKHF1	GPATCH3
LDHB	HLA-DPB1	SH2D1A	UQCR11	TRIAPI
CUTA	SPOCK2	PIGX	HSPE1	SF1
TNIP1	TIMP1	PTPN4	TPM1	GPR65
SKP1	SLC25A6	JAK1	HINT1	VEZT
ITM2A	C1orf228	IRF8	DBI	PCBP1
HCLS1	LCK	TADA3	CCND3	NR1H2
HLA-G	NAA38	HSPE1	ITK	FKBP3
GYPC	DCK	GGA1	RPS6	TNFRSF4
RPS3	GPR18	RTCA	CLDN7	CD3E
SH3BGRL3	CTSC	TLN1	CD53	GPR68
RPS27L	HERPUD1	TRMT2A	EEF2	TNFSF4
GPX1	TPI1	PSTPIP1	SH2D2A	H2AFZ
SNRPB2	RGCC	GGNBP2	COX6B1	PSME1
AKIRIN2	LINC00861	NHP2	HMGA1	JMY
PSMD8	CD59	PSD4	RNF187	NUP54
COX17	EVL	RTFDC1	NDUFA11	XCL1
UBE2I	CORO1B	PSMD6	HMGN1	GNA15
SELT	CYCS	DCXR	STMN1	LTC4S
IL2RA	ZNHIT3	TSPAN32	UQCRC2	TXNDC17
FAIM3	TOMM20	CUTC	LAT	GATA3
GK	TUBA4A	ATP6V1G1	HLA-DQB1	N4BP2L2
NAA38	9-Sep	IFITM1	AK2	CTSH
PSMA2	DGUOK	C19orf66	WDR54	SLC39A4
SNRPD2	LYRM4	PPP1R18	RPS24	PER1
RPL24	FTL	TMEM14C	TSC22D3	AC022182.3
PIK3IP1	JUN	ALKBH2	MTPN	HCST
ID3	LAT	POLR2L	MYO1G	PCDH9
SLAMF1	PIK3IP1	METRNL	KLRG1	TPI1
RPL18	OAZ2	SERBP1	NRM	RP11-425D10.10
UBXN1	FOS	C9orf16	FOSL2	SERTAD1
FTL	HSPB1	BHLHE40	1-Sep	KIT
H2AFV	AES	TSC22D4	PRDX5	ERGIC3
CMTM7	COX4I1	S100A6	SSBP4	ZNF814
LINC00649	LRRFIP1	RBM39	RPS13	FOSL2
RPL34	RAB1A	RNF125	GIMAP1	LYPLA2
HSD17B10	MALAT1	MAFF	MPC2	SIVA1
BAX	RILPL2	SLC9A3R1	COX7C	JTB
CLPP	HLA-DRA	STXBP2	GMNN	ANP32E
HSPA1B	GTF3A	CLDND1	GNB2L1	RNFT1
CD7	ABHD14B	AP2M1	PABPC1	EIF5
RPS25	ACP5	PSMD8	HLA-DRB5	BAD
HLA-DRA	CHCHD7	VAPA	FAM162A	PNP
ZNF706	RAN	SOCS1	OASL	HNRNPK
RPL12	CD74	HNRNPA2B1	OSTF1	MGMT
DCXR	VAMP2	DHRS7	DOK2	TCTN3
CUL9	APRT	AKIRIN2	C1QBP	C6orf57

TABLE 1D-continued

RNF213	C19orf43	COA5	LIMD2	PCNP
ZC2HC1A	TSC22D4	COMMD6	CD160	TP53I13
ALDOA	BRMS1	ATG12	TUBB	C3orf17
G3BP2	RASAL3	ARPC2	RPL24	MRPS15
HCST	NDUFS6	KLHDC4	DDT	GPX7
CIB1	NPC2	LRRFIP1	GTPBP1	CASP6
PDCL3	LSM14A	APOBR	ATP2B4	HLA-B
SSBP1	CCDC104	ETF1	NDUFC1	CRTC2
CCT7	WDR82	CASP4	RAB27A	MBOAT7
HPRT1	MEA1	CASP3	PRDX3	TNFAIP3
PTGES3	GADD45B	CD53	CXCR6	DCAF11
MRPS35	ANXA2	U2AF1	RPL23	SRSF7
SRP19	CD28	TSEN15	CDC20	PPP1R11
HSP90B1	FCGRT	AOAH	NASP	ZNF207
BUB3	LINC00649	HLA-DPA1	RHOF	FURIN
BTG3	PHGR1	OBFC1	CDKN3	WDR83OS

FIGS. **5** and **6** show that the cell composition changes between UC and healthy controls. Applicants can use the expression profiles to deconvolute bulk expression data. Thus, Applicants can determine the cell composition of a colonoscopy sample obtained from a subject and analyzed by RNA-seq.

Applicants also determined genes that were associated with disease. FIG. **7** shows genes differentially expressed across the entire colon and FIG. **8** shows genes differentially expressed in specific cell types. FIG. **9** shows differential gene expression in UC cell types for uninflamed and inflamed tissue. IL-32 and MHC-II are two of the strongest signals and are also genes identified by GWAS. Genes differentially expressed in each cell type during disease is shown in Table 2 A-E.

TABLE 2A

NA 1-50	NA 51-100	NA 101-150	NA 151-200	NA 201-250	Plasma_B_cells	Class_switching_B_cells
MTRNR2L1	EMP1	TAGLN	RPS29	MMP10	G0S2	TIMP1
HLA-B	AKR1C1	TFF1	TMEM258	VSIG2	FABP1	RPL3
CHI3L1	CD63	HGF	CLDN7	RAMP1	TNFRSF18	HSP90AA1
EIF5A	FKBP1A	PDIA3	PHLDA2	MT1M	PHGR1	LMNA
RPL3	PTMA	CDH13	TMSB10	APOA4	AGR2	ILVBL
S100P	COL6A3	ACADS	F2R	TFPI2	GAS6	CD69
TIMP1	REG3A	KDELR2	PXMP2	FXYD3	RPL3	CTHRC1
REG1A	BACE2	NOP10	SRM	MORF4L1	LMNA	TNFRSF4
C8orf4	C10orf99	SELM	CFB	PEBP1	TIMP1	G0S2
HMGCS2	CNN3	HAPLN3	NDUFA4L2	STAP2	SMOC1	PABPC4
DMBT1	CEBPB	FABP4	CBX3	NFKBIA	HIST1H1C	ITM2C
AC005540.3	RPL13A	PTGES	NXPE4	MT-CO3	HSP90AA1	AGR2
OLFM4	LCN2	DSTN	ACAA2	DHRS11	TNFRSF4	RPS3A
IL13RA2	HSPA1B	CCL5	NDRG2	SPINT2	HSPA1A	RNASE6
MMP3	CKB	VAMP8	KANSL1-AS1	PRRX2	HSPA1B	LGALS4
REG4	PHGR1	MT-ND1	KLF2	RCN3	CYP20A1	HLA-DMA
IGJ	CD59	SERPINH1	LAPTM4A	EIF4A1	KRT19	FXYD3
DEFA5	C11orf96	HYI	ITGA5	TUBB	CXCR4	PTMA
TNFRSF12A	ANXA5	POLR2L	DHRS4	TSHZ2	DNAJB1	TNFRSF18
BGN	RPL18A	PPIB	CDX2	KRT8	XBP1	RP11-16E12.2
SELENBP1	COL4A1	HLA-DMA	PRKCDBP	ACTN1	GOLGA2	H3F3B
TPM4	CTHRC1	TST	RPL6	VAMP5	CADM1	KLF6
IFITM2	PCOLCE	AQP1	SOCS3	RPL10	NA	QPRT
TNFRSF11B	COL1A1	SPARC	GPR160	IL11	NA	TPM4
PKM	FTL	CA2	PPDPF	AGT	NA	SMOC1
PHLDA1	EMP3	CCL13	SEPP1	SERPINA1	NA	NA
MT1G	GEM	MT-CYB	TMEM141	SLC26A2	NA	NA
LGALS4	COL4A2	HLA-DPB1	ELP5	CLU	NA	NA
IGFBP5	PRSS23	SPINK1	NRG1	APOBEC3B	NA	NA
URAD	S100A6	AQP8	SPON2	DNAJB1	NA	NA
ANXA2	S100A3	ATOX1	CXCL1	THBS2	NA	NA
HLA-DRA	CA1	RPL37A	ID3	UBD	NA	NA
PLA2G2A	REG1B	IER3	PTRF	PIM3	NA	NA
PDPN	TNC	ENO1	CALR	PRKAR1A	NA	NA
S100A11	CCR7	MT1H	TMEM165	IL32	NA	NA
SELL	MEOX1	HSPA5	HSP90B1	IGFBP7	NA	NA
SOD2	FGF7	HSPA1A	CLEC9A	UGT2A3	NA	NA
LDHA	MMP1	ITM2C	INHBA	HLA-DRB5	NA	NA
SMDT1	RPS3A	SDC2	SPHK1	PPA1	NA	NA
CCL8	THY1	ID1	FABP1	CHCHD10	NA	NA
FCGRT	RPS26	AMN	LGALS2	COL6A2	NA	NA
RPL9	PKIB	FABP6	PDLIM4	CD55	NA	NA
CYR61	CHP2	PIGZ	TMEM158	RNASET2	NA	NA
NNMT	SERPINE1	COL8A1	CKMT1A	CTGF	NA	NA
LMNA	TXNIP	DUOXA2	TRMT112	MT-CO1	NA	NA
HIF1A	COL6A1	TPM2	CCDC3	CTSK	NA	NA

TABLE 2A-continued

CD82	RPS4Y1	CRIP2	HOXB13	C19orf10	NA	NA
LINC00152	PSME2	HYAL2	MRGPRF	SERPINE2	NA	NA
TAGLN2	CAV1	CPXM1	CALU	HSD17B12	NA	NA
IFITM3	ANGPTL2	NCOA7	ACSF2	SAA1	NA	NA

	Follicular_B_cells 1-50	Follicular_B_cells 51-87	Microvascular_cells
	C12orf75	LTB	PLAT
	METAP2	CLIC4	AQP1
	CCND3	LSM10	CD9
	HLA-DQB1	GDI2	HLA-A
	HLA-DRB5	RGS16	HLA-DRA
	RPS4Y1	CAPG	EGLN3
	TUBB2A	SRSF2	LDHB
	LCK	ZFAND2A	HLA-C
	RMI2	RPL36	RBP5
	SMARCB1	CBX3	CD99
	HLA-DPB1	AGR2	PASK
	TCEA1	MRPL47	S100A10
	MME	TRA2A	SERPINE1
	RPL9	FBL	CXCL12
	SLBP	SELT	JUN
	CD63	SUMO2	ANXA2
	UBE2D3	HADHB	TESC
	A4GALT	DEF8	IGJ
	PLD4	FGD2	FOSB
	SIT1	LIMD2	LIMS1
	PPP1CC	PSIP1	HSPA1A
	PAIP2	RBBP7	CALU
	CCDC109B	BZW1	RCN3
	DCAF12	TSTD1	S100A6
	SRSF3	MTF2	CST3
	HLA-DQA1	IKZF1	PRSS23
	HLA-C	RUVBL1	SEPP1
	ISG20	BACH2	HSPA1B
	HMGN1	PIM1	WWTR1
	HMCES	CHRAC1	RAMP1
	HNRNPC	EZR	GPX4
	HLA-DPA1	MCM5	PSMB9
	TUBB2B	IGJ	PSME2
	HNRNPA3	COX6B1	CTGF
	CD27	PRPSAP2	CD82
	EIF1AY	TK1	LGALS4
	ITGAE	CCR7	SNED1
	TPD52		TNFRSF4
	ECHS1		IER3
	RAP1B		VAMP8
	HLA-DQA2		ALDOA
	GGA2		HLA-B
	CHCHD10		TAP1
	ACTR3		CD36
	HLA-DRA		F2RL3
	SGPP1		KDR
	PGAM1		COL15A1
	DCK		PLAU
	TSG101		NA
	HNRNPM		NA

TABLE 2B

Post-capillary_venules	Vitamin_metabolizing	Endothelial_pericytes	Enterocytes	Tuft_cells
PTGS1	PLAT	FAM222B	SPINK1	PTGS1
RAMP1	CXCL12	RP11-490M8.1	PLA2G2A	ESYT2
PDLIM1	ENPP2	TWF2	IL18	SHC1
HLA-A	TXNIP	ZNF205	ATP1B3	HPGDS
OLFML3	IGFBP4	HYI	MTRNR2L1	HOOK1
PLAT	CD36	NA	GSTP1	BCKDK
STXBP6	ANXA2	NA	GPX2	RALGAPA1
UBD	OAZ2	NA	CYBA	NA
LY6E	CD320	NA	TAX1BP3	NA
TNFSF10	AQP1	NA	S100A14	NA
CD9	CTGF	NA	NQO1	NA
MGP	RGS5	NA	TSPAN3	NA
CPE	TGFBR2	NA	NAALADL1	NA
PSMB8	RAMP1	NA	CTSA	NA
PHLDA1	CD9	NA	RARRES3	NA

TABLE 2B-continued

EIF4A2	C16orf80	NA	OAS1	NA
GIMAP7	CXCR4	NA	LGALS1	NA
TMEM100	CLDN5	NA	HMGCS2	NA
CST3	STC1	NA	PCK1	NA
HLA-C	GJA1	NA	PRDX5	NA
RPL9	FAM213A	NA	MUC1	NA
RPL10	PLAU	NA	TMEM37	NA
LPCAT4	HLA-E	NA	KRTCAP3	NA
AQP1	PRKCDBP	NA	MT2A	NA
GIMAP1	RBP5	NA	MX1	NA
SRPX	RPL9	NA	S100A11	NA
MALAT1	SAT1	NA	NA	NA
RPL3	TNFSF10	NA	NA	NA
AGR2	S100A4	NA	NA	NA
PRSS23	TSPAN7	NA	NA	NA
COL4A3BP	AKR1C3	NA	NA	NA
EFEMP1	C8orf4	NA	NA	NA
SNHG7	HLA-DPB1	NA	NA	NA
TUBA1B	SRP14	NA	NA	NA
PTGES	TNFRSF4	NA	NA	NA
NFKBIZ	TIMP1	NA	NA	NA
B2M	ANXA1	NA	NA	NA
FTH1	C1orf54	NA	NA	NA
C19orf66	RND1	NA	NA	NA
CDKN3	ANGPT2	NA	NA	NA
RNF181	EGR1	NA	NA	NA
EEF1B2	STAT3	NA	NA	NA
MDK	SH3BP5	NA	NA	NA
CLIC1	RPL29	NA	NA	NA
TPTEP1	CTNNBIP1	NA	NA	NA
TFF3	LSMD1	NA	NA	NA
S100A10	HLA-C	NA	NA	NA
JUN	RBM17	NA	NA	NA
CRIP1	GYPC	NA	NA	NA
MED24	NDUFA7	NA	NA	NA
NA	IER2	NA	NA	NA
NA	COTL1	NA	NA	NA
NA	RPLP0	NA	NA	NA
NA	SDPR	NA	NA	NA
NA	IDI1	NA	NA	NA
NA	SLC6A6	NA	NA	NA
NA	RPL10A	NA	NA	NA
NA	MYL6	NA	NA	NA
NA	AQP3	NA	NA	NA
NA	NKX2-3	NA	NA	NA
NA	COASY	NA	NA	NA
NA	SOD2	NA	NA	NA

Goblet__2	Absorptive__TA__1	Secretory__TA	Absorptive__TA__2	Cycling__TA
SPINK4	REG1A	HLA-DRA	AGR2	RARRES2
NUPR1	CD74	HLA-DRB1	HLA-DRA	ARHGDIB
S100A14	RPL3	RARRES2	CD74	IGJ
BAIAP2L1	HLA-DRB1	ID3	S100A11	BST2
BDKRBI	MT2A	HLA-DMA	HSPB1	PKIG
MT-ND2	RPS3A	UGT2B17	SPINK1	PITX1
FAM3B	ARHGDIB	CD74	HLA-DRB1	ETS2
MUC13	TIMP1	HLA-DRB5	TIMP1	HLA-DRA
TFF1	LIN7C	REG1A	RARRES3	TIMP1
ANO9	MTRNR2L1	HLA-DPB1	SELENBP1	MTRNR2L1
TUBB2A	KCNK6	HLA-DPA1	GPX2	HRCT1
NA	RPL18A	GLB1L2	MUC12	ZNF90
NA	TNFRSF12A	NA	ID3	MUC12
NA	SEC11C	NA	ARHGDIB	AKR1B1
NA	NA	NA	REG1A	HLA-DPA1
NA	NA	NA	PLA2G2A	VAMP7
NA	NA	NA	CEACAM5	S100P
NA	NA	NA	IDH2	NQO1
NA	NA	NA	IGJ	DEK
NA	NA	NA	RNASET2	ABRACL
NA	NA	NA	BSG	REG1A
NA	NA	NA	PSMB9	ACAT1
NA	NA	NA	ADIRF	DNAJB1
NA	NA	NA	LEFTY1	HLA-DRB1
NA	NA	NA	RARRES1	IGFBP4
NA	NA	NA	LYZ	NA
NA	NA	NA	MTRNR2L1	NA
NA	NA	NA	TFF1	NA
NA	NA	NA	RPS4Y1	NA
NA	NA	NA	SRSF6	NA

TABLE 2B-continued

NA	NA	NA	CNPY2	NA
NA	NA	NA	GSTP1	NA
NA	NA	NA	ATP1B3	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA
NA	NA	NA	NA	NA

TABLE 2C

Goblet__1	Stem__cells	Enteroendocrine	Glial-cells	Inflammatory-fibroblasts	Fibroblast__pericytes
SPINK4	AQP1	RARRES2	ALDH1A1	COL1A2	NET1
ITLN1	RPL3	HLA-DRA	CLU	GBP1	NA
IGJ	RPS4Y1	SEC11C	ANXA1	IFI27	NA
AGR2	LYZ	MT2A	SPP1	DYNLT1	NA
SDF2L1	LCN2	NIPSNAP1	IL32	PKM	NA
TIMP1	ID3	OLFM4	CAPS	PHLDA1	NA
PDLIM1	HLA-DRA	DDC	FIBIN	DUSP1	NA
MUC2	HLA-DRB1	MDK	RPL3	CNOT4	NA
LYZ	HLA-DMA	CD82	RPL9	CCL8	NA
SELK	HLA-DPA1	NA	HLA-G	LAP3	NA
HMGCS2	C2	NA	MRPS6	ACP5	NA
SEC11C	NQO1	NA	LINC00152	GSTT1	NA
SSR4	B2M	NA	HOXC6	GALNT11	NA
DNAJA1	ARHGDIB	NA	CDKN2A	PSMB9	NA
FKBP11	DNAJB1	NA	TUBA1A	TNIP2	NA
REG4	RARRES2	NA	HLA-DQA2	PSMB8	NA
EZR	MTRNR2L1	NA	SOCS3	HAPLN3	NA
SELM	HLA-C	NA	SEPP1	PERP	NA
CISD1	CD74	NA	IGJ	NA	NA
SYTL1	C19orf70	NA	HLA-DRB5	NA	NA
PHLDA2	GSTT1	NA	KLC1	NA	NA
CHPF	TESC	NA	HLA-DRB1	NA	NA
NA	IFI27	NA	NDUFB4	NA	NA
NA	PSME1	NA	ENTPD2	NA	NA
NA	HMGCS2	NA	SRGN	NA	NA
NA	HLA-DRB5	NA	PMEPA1	NA	NA
NA	RPL6	NA	HSPA1B	NA	NA
NA	UGT2B17	NA	FKBP1A	NA	NA
NA	HLA-DPB1	NA	GLIPR2	NA	NA
NA	PSMB9	NA	UBR4	NA	NA
NA	SCARB2	NA	UBB	NA	NA
NA	NA	NA	COX7A1	NA	NA
NA	NA	NA	LSM3	NA	NA

TABLE 2C-continued

NA	NA	NA	PRDX2	NA	NA
NA	NA	NA	NUPR1	NA	NA
NA	NA	NA	NA	NA	NA

	Myofibroblasts	Villus__fibroblasts	Crypt__fibroblasts__(hiFos)	Crypt__fibroblasts__(loFos)
	PDLIM7	MMP2	TM4SF1	GPX3
	NBL1	SRPX2	VASN	NR4A1
	C12orf75	TNC	GSN	C1S
	PHLDA2	MMP1	FGF7	TM4SF1
	IGFBP5	S100A4	PLAT	DUSP1
	PRSS23	NSG1	CLEC14A	ID1
	TM4SF1	EDNRB	IQGAP2	LGALS3BP
	SQRDL	AGT	ID3	COL15A1
	MRGPRF	TRPA1	FN1	SERPING1
	RERG	CPE	SEPP1	TNFAIP6
	MXRA8	VSTM2A	TNXB	CFD
	RPS4Y1	RBP4	CCL13	ADAMDEC1
	EGR1	TSHZ2	TPBG	MZT2B
	HOXD9	IL32	HSD17B2	MIF
	TDO2	VASN	STMN2	EGR1
	DUSP1	CRIP1	GPX3	DKK3
	LMNA	NR4A2	VIM	NBEAL1
	CYB5R3	PCTP	TNFSF10	GSN
	DDAH2	PRSS23	NA	GGT5
	TFPI2	MCL1	NA	FOXF1
	NA	NDUFA4L2	NA	RPL9
	NA	ANXA1	NA	CD74
	NA	TMSB4X	NA	NA
	NA	PDLIM1	NA	NA
	NA	IGFBP3	NA	NA
	NA	CEBPD	NA	NA
	NA	FOXF1	NA	NA
	NA	ACP1	NA	NA
	NA	C1S	NA	NA
	NA	FRZB	NA	NA
	NA	ECM1	NA	NA
	NA	DMKN	NA	NA
	NA	ID4	NA	NA
	NA	PDGFRA	NA	NA
	NA	GADD45B	NA	NA
	NA	SPARCL1	NA	NA

TABLE 2D

T__cells	Macrophages	Dendritic__cells	Mast__cells	Cyding__monocytes	Tolerogenic__DCs
NUB1	LGMN	CST3	NFKBIZ	TFF3	TXN
CAV1	RNASE1	MARCKSL1	EGR3	ATP2A3	NA
EIF2S1	AKR1B1	CD52	IL1RL1	GSDMD	NA
COL6A1	LGALS2	PPA1	HLA-B	EMP3	NA
POSTN	A2M	IGJ	CAPG	IL12RB1	NA
ALAS1	C15orf48	SERPINB1	EGR2	PSMD11	NA
RGCC	VMO1	TYMP	HLA-C	ENPP2	NA
NA	SERPINF1	STMN1	RPS4Y1	ALOX5AP	NA
NA	SPINT1	FCER1A	CTSW	AK1	NA
NA	ACP5	DNAJB1	EIF4G2	NA	NA
NA	TFF3	PRELID1	ZEB2	NA	NA
NA	RNASET2	NA	NA	NA	NA
NA	ENPP2	NA	NA	NA	NA
NA	LGALS1	NA	NA	NA	NA
NA	MMP9	NA	NA	NA	NA
NA	CORO1A	NA	NA	NA	NA
NA	CSTB	NA	NA	NA	NA
NA	SELK	NA	NA	NA	NA
NA	MT2A	NA	NA	NA	NA
NA	FBP1	NA	NA	NA	NA
NA	PLSCR1	NA	NA	NA	NA
NA	FXYD5	NA	NA	NA	NA
NA	NR1H3	NA	NA	NA	NA
NA	UCHL3	NA	NA	NA	NA

TABLE 2D-continued

NA	SEPP1	NA	NA	NA	NA
NA	AGR2	NA	NA	NA	NA

	Neutrophils	Activated_CD4_cells_loFos	Activated_CD4_cells_hiFos	CD8_IELs
	GBP1	S100A4	IGJ	CCL3
	FCGR2B	RPS29	ADSS	CCL4
	GSTO1	TIMP1	NA	RPL10
	RPL30	RPL9	NA	RPL6
	TMEM176B	CFL1	NA	CD3E
	EMG1	VIM	NA	MTRNR2L1
	GDI2	ANXA1	NA	ARHGDIB
	NA	PHLDA1	NA	CD3G
	NA	S100A11	NA	RPL3
	NA	HLA-A	NA	ITGB2
	NA	NA	NA	KLRB1
	NA	NA	NA	IFNG
	NA	NA	NA	RPL22
	NA	NA	NA	RPL18A
	NA	NA	NA	PTMA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA
	NA	NA	NA	NA

TABLE 2E

CD8_LP_cells	Tregs	Memory_T_cells	NK_cells	Cycling_CD8_cells
RPL9	CD7	RPL9	ILF3	ENTPD1
EMP3	CD2	PFN1	CALCOCO2	CD2
ARFRP1	TIA1	IL32	CD47	EIF5A
NA	GRSF1	ANXA1	NA	LCK
NA	NA	S100A4	NA	HAVCR2
NA	NA	ARPC1B	NA	ATP5L
NA	NA	KLRB1	NA	KLRB1
NA	NA	RPL30	NA	CALR
NA	NA	ANAPC5	NA	MTPN
NA	NA	GAPDH	NA	CENPA
NA	NA	B2M	NA	MIF
NA	NA	RPS28	NA	NA
NA	NA	PSME2	NA	NA
NA	NA	AK5	NA	NA
NA	NA	SERF2	NA	NA
NA	NA	RILPL2	NA	NA
NA	NA	RPS29	NA	NA
NA	NA	TAGLN2	NA	NA
NA	NA	FXYD5	NA	NA
NA	NA	S100A11	NA	NA
NA	NA	ANXA5	NA	NA
NA	NA	S100A6	NA	NA
NA	NA	PNRC1	NA	NA
NA	NA	ARPC2	NA	NA
NA	NA	ZFP36	NA	NA

Applicants were able to determine the cell of origin for genes associated with disease by genome wide association (GWAS) (e.g., IBD). Previous studies have shown 94 IBD loci fine mapped in 67,852 individuals (Hung et al., Nature 2017). FIGS. **10** and **11** show violin plots for key IBD genes in healthy and disease samples. Applicants also show heatmaps for GWAS genes expressed in each cell type (FIGS. **12** and **13**). Applicants show a heatmap for G-protein coupled receptors (GPCR), genes involved in cell-cell interactions, and in epithelial cells in the gut cell types. (FIGS. **14**, **15** and **16**). Key genes are highlighted in FIG. **16**. FIG. **17** shows that genes associated with other disease indications can be localized to specific cell types in the atlas.

Applicants also show that the atlas may be used to determine cell-cell interaction mechanisms within the gut (FIG. **18**). FIG. **19** shows cell-cell interactions in healthy tissue and FIG. **20** shows cell-cell interactions in diseased tissue. Applicants identified for the first time cell types that interact in healthy and disease gut tissue and have determined high specificity ligand receptor pairs that allow the cells to interact. Not being bound by a theory, modulating these interactions can allow modulation of the gut to prevent

and treat disease (e.g., IBD). Not being bound by a theory the interactions may be disrupted using small molecules, antibodies and/or soluble proteins.

Finally, Applicants show that fibroblasts that support the stem cell niche can be identified using the atlas (FIGS. **21**-**24**). FIG. **22** shows genes expressed in the villus (e.g., BMP) and genes expressed in the crypt (e.g., Wnt). Genes associated with either locus can be identified by examining gene expression the tSNE plot. For example, FIGS. **23** and **24** show RSPO3 expression in the tSNE plot and an RSPO3 module may be identified by co-expression in the plot (e.g., MGP, C7, GUCY1A3, TNFSF13B, CXCL12, C3, and C1QTNF3).

The genes and cell types identified in this study can also be used to perform in situ validation, functional tests (e.g., organoids), GWAS covariation studies (e.g., to relate changes in cell types through molecular connections).

Example 2—scRNA-Seq Atlas of Colon Biopsies from Healthy Individuals and Ulcerative Colitis (UC) Patients

To understand the cellular and molecular changes associated with UC, Applicants obtained 115,517 high-quality single cell transcriptomes from 34 colon biopsies (each<2.4 mm^2) that were collected from 7 patients with left-sided colitis and 10 healthy individuals who underwent colonoscopic examination (FIG. **25**, STAR Methods). To investigate the transitions between healthy mucosa and chronic inflammation, while mitigating patient-specific variability, paired samples were collected from each subject during a single procedure. For UC patients, these were assessed as adjacent inflamed and non-inflamed tissue (FIG. **25**, STAR Methods); non-inflamed biopsies may be either "non-colitis" (i.e. no history of inflammation) or "post-colitis" (i.e. resolved inflammation). From healthy subjects, these were two location-matched adjacent samples to estimate transcriptional and compositional variability. Immediately after collection, Applicants separated tissue samples into "epithelial" (EPI) and "lamina propria" (LP) fractions (allowing recovery of sufficient LP cells), dissociated them into single cell suspensions, and profiled the cells using scRNA-seq (FIG. **25** and FIG. **31**, STAR Methods). As expected, EPI samples mostly consisted of epithelial cells (89%±15% epithelial cells on average) with some tissue-resident immune cells, such as intraepithelial lymphocytes and mast cells (FIG. **26**D), whereas LP samples primarily contained immune and stromal cells (84%±18% immune and stromal cells on average).

Example 3—a Comprehensive Census of 51 Cell Subsets and their Molecular Signatures

To construct a cell atlas of the human colon in health and disease, Applicants used the expression levels of known markers to divide the cells into three groups: i) epithelial cells, ii) immune cells, including myeloid and lymphoid lineages, and iii) stromal cells, including fibroblasts, glia, and endothelial cells.

The single cell profiles partitioned into 51 subsets by unsupervised clustering (FIG. **26**B,H, after correction for technical and biological variation, STAR Methods), which Applicants annotated post-hoc known markers (FIG. **26**C) to reveal 15 epithelial, 23 immune (lymphoid and myeloid) and 13 stromal (fibroblasts, glia, and endothelial cells) subsets. The "cell subsets" almost invariably had representation from all specimens, and were proportionally distributed across samples of the same type (FIGS. **26**D and **31**), indicating that the clustering is driven by shared programs across samples, rather than by inter-sample differences.

Even though the cells were isolated from miniscule biopsies (~2.4 mm^2), the 51 subsets recapitulate nearly all of the known cellular diversity within the colonic mucosa (FIG. **26**B) and highlight new subsets (below). This includes 15 subsets of epithelial cells, pseudo=temporally ordered along the differentiation trajectory (FIG. **26**H), from $LGR5^+$ intestinal stem cell to mature absorptive and secretory cell fates and including M cells (below); 8 subsets of fibroblasts partitioned defined by WNT and BMP signaling, including novel inflammation-associated fibroblasts, discussed below (also, including three subsets of WNT2B+ fibroblasts, two subsets of BMP4+ fibroblasts, as well as RSPO3+ fibroblasts, myofibroblasts, and inflammation-associated fibroblasts); four subsets of endothelial cells partitioned; one glia subset; seven myeloid cells (including inflammatory monocytes; below), four B cell subsets, ten T cell subsets across $CD4^+$ Tconv, $CD4^+$ Tregs and $CD8^+$ cells, including $CD8^+$ IL-17^+ T cells, and $CD4^+$PD-1^+ T cells, innate lymphoid cells (a mix of ILC2s and 3s), and NK cells (NKs) (FIG. **26**B,H). To Applicants knowledge, known subsets missing from the census include submucosal enteric neurons, which require a distinct isolation approach (e.g., single nucleus RNA-Seq Habib et al., 2017), plasmacytoid dendritic cells (pDCs; possibly due to either low frequencies or uneven spatial distribution), and neutrophils, which express degradative enzymes that may damage their RNA or membranes. As expected, Applicants do not capture submucosal cells, such as myocytes and adipocytes, which require colon resection material.

Each cell subset is supported by a distinct expression profile, including known and new markers of known subsets and signatures of new subsets (FIG. **26**H), with cell type-specific transcription factors (TFs), G protein-coupled receptors (GPCRs), transporters, cytokines, and pattern recognition receptors (FIGS. **32**-**36**). For example, the $CD4^+$ $FOXP3^+IL10^+$ T_{regs} expressed BATF, a critical TF for the differentiation of tissue-resident T_{regs} (FIG. **32**); inflammatory monocytes, thought to underlie chronic immune activation in many diseases, but not previously profiled in UC patients, express Oncostatin M (OSM), a cytokine associated with resistance to anti-tumor necrosis factor (TNF) therapy in IBD patients (FIG. **35**). Surprisingly, compared to other cell types, plasma cells and cycling B cells expressed relatively high levels of the NOD-like receptor, NLRP7, a gene associated with IBD through GWAS, which recognizes microbial lipopeptides and is not known to be expressed by B cells (FIG. **33**).

Example 4—New $BEST4^+$ Epithelial Cells and Fibroblast Subsets in the Healthy Colon

The census reveled a new subset of chemosensory $BEST4^+$ enterocytes that express genes related to acid and electrolyte sensing (e.g., pH (acid sensing) and electrolyte balance) (FIG. **26**E), including BEST4, OTOP2, CA7, and Renin (REN), to likely complete a local renin-angiotensin system (RAS) in the colon (FIG. **26**E,G). In particular, the otopetrin family encodes proton-selective ion channels, including OTOP1, which is enriched in taste receptor cells and contributes to sour taste perception through the detection of acids. Within the intestine, tuft cells are thought to transduce bitter, sweet, and umami tastes through the calcium channel TRPM5, but distinct pathways are required for sour and salty tastes. $BEST4^+$ enterocytes may therefore be

responsible for pH sensing and sour taste perception within the colon. These cells also express SPIB, a TF also expressed by tuft and microfold cells, suggesting they may be developmentally related. Based on the data (FIG. **26**G), angiotensinogen is produced by WNT5B$^+$ fibroblasts, renin by BEST4$^+$ enterocytes (e.g., in response to local electrolyte levels), Angiotensin Converting Enzyme (ACE) by epithelial and endothelial cells, and the angiotensin receptor AGTR1 by WNT2B$^+$ fibroblasts and pericytes, suggesting this pathway may be involved in local colon vasoconstriction.

Multiple fibroblast subsets differed by the expression of WNT and BMP signaling genes, reflecting distinct positions along the intestinal crypt-villus axis. One subset is transcriptionally similar to subepithelial telocytes, a rare population of mesenchymal cells that supports the epithelium that were recently profiled in mice. Some express higher levels of WNT2B, WNT4, and DKK3, and thus may reside near the intestinal crypt, whereas others highly express BMP4, BMP5, and WNT5, and thus may reside away from the crypt (FIG. **26**F). All subsets express low levels of FOXL1, the defining marker of subepithelial telocytes in mice, a rare population of mesenchymal cells that supports the epithelium, and share additional marker genes with subepithelial telocytes, but the data show that these genes have distinct expression patterns in humans (FIG. **26**F). WNT5B$^+$ subsets (but not Tuft cells) are major sources of expression of thymic stromal lymphopoietin (TSLP), a cytokine that is crucial for the activation of ILC2s and Th2-inducing DCs in the colon, and of the receptor for glucagon-like peptide 2 (GLP2R), a peptide hormone produced by enteroendocrine cells to regulate gut metabolism and physiology (FIG. **26**F).

One subset of WNT2B fibroblasts expresses R-spondin-3 (RSPO3) (FIG. **26**E,F), the ligand for LGR5, a hallmark receptor of ISCs This subset expresses several other genes related to WNT/BMP signaling, including Gremlin 2 (a BMP inhibitor), glypican, and secreted frizzled-related protein, along with the immune recruiting chemokines CCL11, CCL19, CCL21, and CXCL12 (also expressed by secondary lymphoid organs), supporting a role of an inflammatory microenvironment to maintain the ISC niche.

Example 5—the Colon Cellular Composition in Dramatically Remodeled in UC

Changes in the composition of cell types that monitor luminal contents and titrate the immune response may affect the functional integrity of the mucosa in UC. To identify such changes, Applicants searched for cell subsets whose proportion changes in the colon between healthy, non-inflamed, and inflamed specimens. Prior work has examined changes in specific cell types, such as infiltration of neutrophils, mast cells, and IL-17$^+$ T cells into the LP, but typically focused on specific cell types. Conversely, the census captures an extensive range of cells simultaneously, but, by definition, as the frequency of one cell subset increases, the frequencies of others decline. Thus, Applicants tested for changes in each subset proportions with a conservative statistical model that accounts for these dependencies (STAR Methods). (To identify changes that may be statistically dependent but physiologically important, Applicants also performed univariate analysis; FIG. **29**E).

The analysis highlighted a dramatic remodeling of the colon's cell type composition, spanning 9 epithelial subsets, 10 immune subsets and 9 stromal subsets. often with gradual changes from healthy to uninflamed to inflamed tissue. Applicants correctly captured many changes in cell proportions in UC patients that were previously reported, such as the increase in non-inflamed and inflamed samples in proportions of gut resident mast cells, CD8$^+$ IL-17$^+$ T cells, T_{regs}, and endothelial cell subsets in non-inflamed and inflamed samples (FIG. **27**A). The magnitudes of these changes increased progressively from healthy to non-inflamed to inflamed samples, suggesting that even nominally "healthy" tissue from UC patients is altered and may represent a transitional state along the course of disease (pre-inflammation or post-resolution).

Although the total number of immune cells increased with the disease, within the immune compartment, colitis was associated with substantial reductions in plasma B cells and proportional increases in FO B cells (FIG. **27**A). Within plasma cells, the frequency of IgA$^+$ cells decreased and that of IgG$^+$ cells concomitantly increased in both non-inflamed and inflamed tissue (Spearman's ρ=–0.80; P=1.4×10^{-7}; FIG. **38**), suggesting that immunoglobulin class-switching is occurring in the cells and may promote tissue inflammation and the generation of auto-antibodies.

Consistent with studies of inflammation in mice, microfold cells (M cells), specialized follicle associated epithelium (FAE) cells that deliver luminal antigens to immune cells situated in their basolateral pockets, were rarely found in healthy patients, but expanded significantly with UC (FIG. **27**A). M cells play major roles in recognizing the gut microbiota and initiating mucosal immune responses. They highly express chemokines such as CCL20 and CCL23 suggesting that increased antigen sampling from the lumen is coupled to immune cell recruitment at the site of inflammation. Their expansion outside of lymphoid follicles with UC is unexpected, although congruent with studies of inflammation in mice, and suggests that M cells may have previously unappreciated roles in the disease.

Example 6—a New Inflammation-Associated Fibroblast Subset Unique to the UC Colon

Although most fibroblast subsets are present in both healthy subjects and UC patients, Applicants discovered a new subset of fibroblasts found almost exclusively within biopsies from UC patients, particularly in inflamed samples (FIGS. **26**D and **27**A), which Applicants termed colitis-associated inflammatory fibroblasts (CAIFs). CAIFs are enriched for the expression of fibrinolytic enzymes (e.g., MMP3, MMP10, PLAU) and immune signaling molecules (e.g., IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, TNFRSF11B) (FIG. **26**E). In particular, IL13RA2 is a decoy receptor with high affinity for IL-13, suggesting that these cells may reinforce inflammation by neutralizing IL-13. Consistent with this hypothesis, deletion of IL13RA2 led to attenuated colitis in mice treated with dextran sodium sulfate (DSS). CAIFs also express high levels of chitinase 3-like-1 (CHI3L1), a biomarker of chronic inflammation and IBD-associated colonic dysplasia that is also associated with increased cancer-related mortality. CHI3L1 and IL13RA2 are known binding partners that can activate downstream MAPK and Akt signaling, and CAIFs have the greatest mean expression of the PI3K-Akt signaling pathway across all cell subsets ($p<10^{-6}$ in all comparisons, Mann-Whitney test). CAIFs are also enriched for WNT2, one of the most upregulated genes in the intestinal stroma of colorectal cancer patients relative to healthy controls.

Example 7—Shift in Goblet Cell Differentiation May Explain Mucosal Changes in UC

Defects in the mucus layer in UC patients is a diagnostic feature and is widely attributed to goblet cell mucin deple-

tion. However, Applicants generally did not observe cell-intrinsic reductions in mucin gene expression, suggesting that these defects may arise from degradation of the mucus layer or changes in the proportions of mucus-producing cells. While Applicants observed no significant changes in the frequencies of mature goblet cells, inflamed biopsies from UC patients showed a loss of goblet cell progenitors (FIG. **27**A), coincident with a reduction in epithelial "sternness." In particular, along the continuum of epithelial cell differentiation (FIGS. **26**H and **27**B), there were significantly reduced proportions of secretory progenitor cells ($p<10^{-4}$; likelihood ratio test on fixed effect in mixed linear model; STAR Methods), in inflamed samples of UC patients. Defects in the mucus layer may therefore be explained by reduction in goblet cell progenitors. Interestingly, these cells are major sources of antimicrobial peptides, including REG4, ITLN1, and RETNLB, and may therefore correspond to the "deep crypt secretory cells" that help maintain the colon ISC niche.

Example 8—Most Cell-Intrinsic Expression Changes in UC are Shared Between Inflamed and Uninflamed Regions

Intestinal pathology during colitis is likely driven both by alterations in tissue composition and by changes in cell-intrinsic cellular programs. To explore the contribution of cell-intrinsic changes, Applicants modeled the expression of each gene as the sum of distinct components, reflecting cell subset, disease state (healthy, non-inflamed, or inflamed) and technical confounders, as well as correction for ambient RNA contamination in droplets (Macosko et al.) (STAR Methods). Fitting this model at different levels of the cell lineage, Applicants distinguished between general expression changes that are shared across an entire compartment (epithelial, stromal, immune, FIG. **27**C-E) and unique changes within each subset (e.g. M cells, CAIFs, $CD8^+$IL-17^+ T cells) (FIG. **27**F-H, Tables 3-9, 11 and 12, STAR Methods).

Despite being collected from grossly normal tissue, non-inflamed specimens shared much of the differential expression (DE) signature of inflamed tissue (FIG. **39**A-F, Table 13-15), suggesting that the transcriptional signature of the disease may precede inflammation or persist after it resolved. Applicants therefore first focused on this shared signature, and then examined the minority of genes that were unique to inflamed tissue during active disease. (Applicants note that for the cell types which are nearly undetectable in healthy tissue, such as CAIFs and M cells, Applicants cannot robustly assess differential expression vs. healthy tissue).

Within epithelial cells, expression changes largely reflect the attempt of the disrupted epithelial barrier to regain tissue homeostasis by activating mucosal immune responses, antimicrobial defenses, tissue repair and antioxidant defense pathways, biosynthesis of O-glycans and alternative mucins (FIG. **27**C), consistent with the remodeling of the mucosal environment, as well as the MHC class II machinery, which Applicants confirmed by RNA-FISH.

Epithelial subsets downregulated genes involved in fatty acid metabolism (FIG. **27**C), possibly due to reduced production of short chain fatty acids by the gut microbiota. Within specific subsets, chemosensory tuft cells upregulated the diamine oxidase, AOC1, which may degrade mast cell-produced histamine (FIG. **27**F); goblet cells increased importers of sialic acids (FIG. **27**F), which may promote the growth of *Escherichia coli*; cycling TA cells upregulated IL-23, a key cytokine implicated in IBD through GWAS; and goblet cells and enterocytes upregulated genes for retinoic acid (RA) biosynthesis (FIG. **27**F), while M cells induced the RA binding protein, CRABP2 (FIG. **27**F). RA is known to suppress intestinal mucus production and to exacerbate colitis, suggesting that M cells may play an important role in this process.

Within the stromal compartment, expression changes reflected induction of inflammatory cues, tissue repair and fibrosis, and of vascular expansion in the supporting tissue, suggesting a major role of the stroma in disease progression. Multiple subsets activate pro-fibrosis programs, including upregulation of genes involved in collagen deposition and fibrosis (FIG. **27**D), expression of beta-catenin (CTNNB1; FIG. **27**D), a mediator of pro-fibrotic WNT signaling by crypt-associated fibroblasts, and expression of fibrosis-associated ECM components that are normally restricted to the crypt (e.g. DCN, LUM; FIG. **27**D,G) by villus-associated fibroblasts (FIG. **27**D). In contrast to the dramatic increase in CAIFs, other fibroblast subsets downregulated the chemokines CCL8, CXCL12, and CCL13 (FIG. **27**D,G) and produced neprilysin (MME), a metalloprotease that cleaves peptide hormones, including substance P, which could limit inflammation (FIG. **27**D). Post-capillary venules induced CSF3 (FIG. **27**G), which signals for the growth and differentiation of monocytes and granulocytes, and endothelial cell subsets induced angiopoietin 2 (ANGPT2; FIG. **27**G) and the adhesion glycoprotein, THY1 (FIG. **27**D), which may promote angiogenesis and leukocyte recruitment into the diseased tissue.

Although innate immune responses seem to be a prerequisite for the excessive activation of adaptive immunity, the latter is the more proximate driver of tissue damage in UC. In particular, multiple subsets of $CD4^+$ and $CD8^+$ T cells adopted a Th17-like phenotype, with upregulation of both IL-17 (IL17A, IL17F; FIG. **27**E) and of checkpoint genes (e.g. CTLA4, PDCD1, TIGIT; FIG. **27**E). IL-17 expressing cells promote a pro-inflammatory and cytotoxic immune response, which may be reinforced by the expression of cytotoxic granule genes (e.g. GZMK, GNLY; FIG. **27**E) in all subsets of $CD8^+$ T cells, and which may contribute to epithelial tissue damage. More generally, all CD8+ T cells induced cytotoxic programs in inflamed tissue that was accompanied by the expression of a co-inhibitory, checkpoint molecule (FIG. **28**A). Notably, checkpoint activation was already apparent in healthy tissue, which may explain immunotherapy-induced colitis in some cancer patients. Within B cells, the increased expression of the TFs PAX5, IRF8, and BCL6 in multiple subsets and the expression of AICDA in GC B cells, which promotes affinity maturation and class switch recombination, help explain the reduction in plasma cells (FIG. **27**A) and IgG class switching (FIG. **38**). Finally, few changes were shared across the myeloid lineage, whereas subset specific changes reflected modulation of the innate immune response in monocytes (induced calprotectin, an inflammatory biomarker of UC and reduced FCER1A and MHC II), DCs (increased expression HTR3A and IL22R, suggesting increased interaction with mast cells and Th17 cells, respectively); and $CD69^+$ mast cells (upregulated secretory granule genes).

Example 9—Shift in Carbon Metabolism, Fatty Acid Oxidation and Amino Acid Metabolism in Epithelial Cells in UC

Comparison of non-inflamed and inflamed tissue within UC patients revealed several metabolic changes within epithelial cells that may underlie tissue inflammation (FIG.

28E). The expression of purine metabolism genes (e.g. XDH, URAD; FIG. **27**C,F) was altered in epithelial subsets, likely leading to the production of uric acid. Uric acid is induced by *S. cerevisiae* colonization, leading to epithelial damage in mice, and inhibition of uric acid synthesis can ameliorate colitis (e.g., damage is reversed upon inhibition of uric acid synthesis). Epithelial cells in inflamed tissue also reduce HMGCS2, the limiting rate enzyme that catalyzes the first reaction in ketosis, and increased the expression of enzymes in the kynurenine pathway, a pathway that is associated with disease severity [REF] and is thought to promote mucosal inflammation through the rewiring of tryptophan metabolism and the abrogation of IL-22 synthesis (e.g. IDO1, KYNU), which may replenish NAD+ levels for oxidative phosphorylation. Diminished CLCA1 expression by secretory TA cells in inflamed tissue may help explain defects in the mucus layer thickness during inflammation. Such rewiring of epithelial cell metabolism in inflammation in UC is consistent with studies suggesting that stress and inflammation are coupled to the upstream sensing of nutrients, such as carbohydrates, lipids, and amino acids.

Previous studies suggest that stress and inflammation pathways induced in IBD and consisting of many IBD GWAS genes may be coupled to upstream environmental sensing of nutrients, such as oxygen, fatty acids, and amino acids, which in turn may be impacted by the microbiota. To identify such metabolic changes systematically, Applicants scored changes in the expression of 239 pathways related to nutrient sensing, stress, and inflammation across all cell types (FIG. **28**E), relative to a background set of genes selected to have similar expression profiles across all samples.

This analysis revealed metabolic shifts between oxidative phosphorylation and glycolysis, and changes in fatty acid and amino acid metabolism. First, in UC, epithelial cells shifted their metabolism from oxidative phosphorylation to glycolysis and the pentose phosphate pathway (FIG. **28**E), while immune cells shifted towards oxidative phosphorylation, which may reflect efforts to quell immune activity, often coupled to glycolysis, which reflect efforts to quell immune activity, often coupled to glycolysis. Second, across multiple subsets Applicants infer a switch from microbial to dietary sources of fatty acids. There is reduced expression of pathways for beta-oxidation and the metabolism of butyrate and propionate (FIG. **28**E), likely driven by impaired production of short chain fatty acids (SCFAs) by the gut microbiota, along with increased expression of dietary fatty acids metabolism genes (FIG. **28**E) by epithelial cells in non-inflamed and inflamed tissue. Finally, epithelial cells from non-inflamed and inflamed tissue increased expression of pathways for the biosynthesis of arginine and the metabolism of alanine, aspartate, and glutamate, and reduced the metabolism of valine, leucine, isoleucine, lysine, and histidine (FIG. **28**E). Changes in amino acid sensing may explain elevated levels of mTORC1 signaling across multiple subsets (FIG. **28**E). Although metabolism of tryptophan through the kynurenine pathway increased, the combined gene signature for tryptophan metabolism decreased in epithelial cells and fibroblasts (FIG. **28**E).

Example 10—Induction of a Strong IL17 Response and Checkpoints in CD8+ Cells in UC

Although the innate immune response seems to be a prerequisite for the excessive activation of adaptive immunity, the latter is the more proximate driver of tissue damage in UC [REF]. In particular, multiple subsets of $CD4^+$ and $CD8^+$ T cells adopted a Th17-like phenotype, with upregulation of IL-17 (IL17A, IL17F; FIG. **27**E) and checkpoint genes (e.g. CTLA4, PDCD1, TIGIT; FIG. **27**E). The $CD8^+$ $IL\text{-}17^+$ cells promote a pro-inflammatory and cytotoxic immune response, as well as induce the expression of IL23R in non-inflamed and inflamed tissue. This may be further reinforced by the expression of cytotoxic granule genes (e.g. GZMK, GNLY; FIG. **27**E) in all subsets of $CD8^+$ T cells, and which may contribute to epithelial tissue damage. More generally, all CD8+ T cells induced cytotoxic programs in inflamed tissue that were accompanied by the expression of a co-inhibitory, checkpoint molecule (FIG. **28**A). Notably, checkpoint activation was already apparent in healthy tissue, which may explain immunotherapy-induced colitis in some cancer patients.

Example 11—A Shift of TNF Responding Cells to CAIFs May Underlie the Resistance to Anti-TNF Therapy

The differentially expressed genes highlight inflammatory processes occurring in the different stages of colitis from non-inflamed to inflamed tissue across diverse cells. TNF signaling is one of the key pathways contributing to the onset and progression of UC, and monoclonal anti-TNF antibodies have been a major breakthrough in the treatment of IBD. Despite this success, non-response rates are high and treated patients eventually develop resistance to treatment, suggesting that there are both intrinsic and acquired causes of resistance. Additional inflammatory pathways could participate in gut inflammation as etiological causes, effects, or exacerbating factors. To assess those, Applicants compared each cell subset for the change between healthy, non-inflamed and inflamed tissue in seven inflammation signatures, as well as in expression of the TNF response (FIG. **28**B,C).

The transition from healthy to non-inflamed tissue was mostly marked by induction of pathways within fibroblasts. For example, TNFα signaling increased in $WNT2B{+}Fos^{lo}$ fibroblasts and myofibroblasts, Jak-STAT signaling increased in $WNT2B^+$ and $WNT5B^+$ subsets, and TGFP signaling increased in myofibroblasts (FIG. **28**B). Additional pathways were induced in inflamed tissues across multiple lineages, including increases in IFNα/β and IFNγ signaling in epithelial subsets, B cells and $CD69^+$ mast cells, and increases in TNF signaling among some epithelial cells, $CD8^+IL\text{-}17^+$ T cells, GC B cells, and CAIFs. This suggests that TNFα, TGFβ, and Jak-STAT responses in fibroblasts are more related to disease etiology, whereas additional pathways in epithelial cells, mast cells, and B cells are secondary aspects that exacerbate tissue inflammation. This may explain why anti-TNF drugs effectively treat UC symptoms, whereas anti-IFNγ therapy does not.

Remarkably, the largest change in TNF signaling between non-inflamed and inflamed tissue was found in CAIFs (FIG. **28**C), suggesting that these cells may underlie resistance to anti-TNF therapy. To test this hypothesis, Applicants scored each subset for gene signatures related to drug resistance and sensitivity, based on a meta-analysis of bulk expression profiles from 55 drug responders and 55 non-responders to anti-TNF blockade (STAR Methods). Supporting the hypothesis, the drug resistance signature was strongly enriched in CAIFs (FIG. **28**D,F; e.g. IL13RA2, IL11, and TNFRSF11B) and inflammatory monocytes (FIG. **28**D,F; e.g., G0S2, OSM, TREM1), while the drug sensitivity signature was enriched in epithelial cells (FIG. **28**D,E; e.g.,

LGR5, PYY, RETNLB). In fact, the three genes whose expression is most significantly associated with drug resistance, IL13RA2, IL11, and TNFRSF11B, are highly specific markers of CAIFs, and are not expressed by any other cell subsets. Confirming these results, deletion of IL13RA2 ameliorates colitis in mice [REF], while pre-treatment expression of OSM is predictive of anti-TNF resistance in a human clinical trial, although the specific cell subsets or pathways mediating this resistance are unknown.

Moreover, after removing overlapping genes between the gene signatures (STAR Methods), the TNFα signature score was strongly correlated to the drug resistance score (FIG. **28**D, left) and mutually exclusive with the drug sensitivity score (FIG. **28**D, right), suggesting a direct relationship between TNF signaling and clinical resistance. Thus, TNF signaling by these cell subsets, particularly CAIFs, may reflect disease severity or even underlie drug non-responsiveness.

Example 12—Inter-Compartmental Re-Wiring of Cell-Cell Interactions in UC Through CAIFs, Inflammatory Monocytes, and M Cells

Both cell subset proportions and intrinsic expression levels are changed in UC relative to healthy controls. Applicants hypothesized that alterations in cell subset proportions could be explained, at least in part, by cell intrinsic changes in cell-cell interaction genes, such as cytokines, chemokines, growth factors, and their cognate receptors. For example, immune signaling in inflamed tissue was impacted by changes in both stroma and immune cells compared to non-inflamed tissue. For example with multiple fibroblast subsets decreased expression of CCL13 and increased expression of the CGRP receptor (RAMP1) (FIG. **33**) or T cell subsets increasing expression of the B cell chemoattractant, CXCL13 (FIG. **39**C) and the checkpoint gene, PDCD1. For example, several expression changes targeted immune signaling within inflamed tissue, including the downregulation of CCL13 in fibroblast subsets (FIG. **33**) and the upregulation of CXCL13 in T cell subsets (FIG. **39**C), which can propagate into the infiltration, expansion, or inhibition of other cell types. Such intrinsic changes in expression in one cell type, can propagate into the infiltration, migration or expansion of another cell type, reflected in turn by a change it its proportion and/or its state. To test this hypothesis, Applicants first mapped thousands of literature-supported receptor-ligand pairs onto the cell subsets to construct a putative cell-cell network (STAR Methods) for healthy (FIG. **29**A), non-inflamed (FIG. **29**B), and inflamed (FIG. **29**C) tissue, and identified those cell subset pairs with a statistically significant excess of receptor-ligand connections compared to a null model.

Whereas the healthy cellular network was mostly compartmentalized, with cell-cell interactions enriched among subsets from the same lineage (FIG. **29**A,D), differential expression in disease preferentially targeted cross talk across compartments, and reduced compartmentalization (FIG. **29**B-D), with colitis-associated subsets, such as CAIFs, inflammatory monocytes, and M cells, as key cross-compartment connectors. Intra-compartment interactions in health delineated the epithelial compartment ($P<10^{-4}$; all p-values for interactions from network permutation tests, STAR Methods) and spanned many connections reflecting homeostatic tissue organization, such as between DCIs and T cells (e.g. $P<10^{-3}$ for T_{regs}, CD8+ LP, and CD4+ Activated Fos-hi T cells), glia, endothelial cells, and pericytes (possibly comprising the gut-vascular barrier; $P<0.05$ for all pairs), and M cells and T cells ($P<0.05$ for cycling and CD8+ IEL subsets) (FIG. **29**A). Conversely, in both non-inflamed and inflamed UC tissue, CAIFs, M cells, and inflammatory monocytes are the nexus of multiple intracompartmental connections. Differential expression in non-inflamed UC tissue (FIG. **29**B,D) significantly targeted cross-talk between epithelial cells and T cells ($P<10^{-4}$) and fibroblasts ($P<10^{-4}$). Interactions between enterocytes and other cell subsets were especially targeted in non-inflamed UC tissue, including with several subsets of T cells ($P<0.05$ for T_{regs} and CD8+ IELs, $P<10^{-3}$ for MT^{hi} T cells) and fibroblasts (e.g. $P<10^{-4}$ for $WNT2B^{+}$ Fos^{lo} subsets, $P<10^{-3}$ for $WNT5B^{+}$ subsets). Inflamed mucosal tissue (FIG. **29**C,D) showed significant re-wiring of communication between B cells and T cells ($P<10^{-4}$; e.g. $P<0.05$ for $PD1^{+}$ T cells and all B cell subsets), macrophages and $CD8^{+}IL\text{-}17^{+}$ T cells ($P<0.05$), and enterocytes and post-capillary venules ($P<10^{-4}$).

Example 13—Cell-Intrinsic Changes that Underlie Immune Cells Infiltration, Stromal Cell and CAIF Proliferation and Epithelial Cell Differentiation Changes in UC

Next, Applicants systematically queried all pairs of cell subsets, by testing, for each ligand-receptor pair that was differentially expressed during disease, whether the ligand's expression level in one cell type was correlated with the frequency of the cells expressing its cognate receptor across samples (including cells of the same type, to capture both autocrine and paracrine interactions).

The results strongly support the hypothesis that re-wiring of the cell-cell signaling network may drive changes in the cell subset proportions in UC. One set of interactions explains changes in immune cell proportions by effects on their migration and infiltration. For example, the increase in FO B cell proportions within the immune compartment, one of the most significant changes Applicants observed in UC (FIG. **27**A), is correlated with strong upregulation of CXCL12 in $WNT2B^{+}$ Fos^{lo} fibroblasts in UC (FIG. **29**D), known to recruit B cells and induce follicle formation, and whose receptor, CXCR4, is expressed on plasma cells, (FIG. **29**D, Spearman's $\rho=0.44$). In another example, the expression of IL-18, an epithelial-derived cytokine induced in enterocytes within inflamed tissue, is correlated with the frequencies of T_{regs} across samples, which express its receptor IL18R1 (FIG. **29**D, Spearman's $\rho=0.68$). IL18R1, inhibits colonic Th17 differentiation, is critical for T_{reg}-mediated control of intestinal inflammation, and has been associated with IBD through GWAS.

Second, within the stroma, multiple interactions reflect expansion of a stromal cell subset through growth factors expressed by other cells. For example, there is a high correlation across samples between the induction of platelet-derived growth factor (PDGFD) in $WNT2B^{+}Fos^{hi}$ fibroblasts and the frequency of pericytes, which express its receptor, PDGFRB (FIG. **29**D, Spearman's $\rho=0.59$). PDGF plays an important role in blood vessel formation.

Third, some interactions reflect an impact of immune cells or fibroblasts on cell differentiation or state transition among epithelial cells, which can impact epithelial repair. For example, the frequency of enterocytes across samples was correlated with the expression by $CD4^{+}$ Activated Fos^{hi} T cells of IL-22, a cytokine that promotes mucosal healing and epithelial renewal known to be reduced in (FIG. **29**D, Spearman's $\rho=0.55$). Conversely, there is a negative correlation between CAIFs expression of CYR61 and the pro-

portion of enterocytes, which express its receptor, ITGAV (FIG. **29**D, Spearman's ρ=. −0.76). Interestingly, RBP4 expression in enterocytes is positively regulated with the proportions of CAIF, which express its receptor (FIG. **29**D), suggesting a negative feedback loop between these two cell types.

Finally, autocrine signals may regulate cell frequencies both positively and negatively. For example, BEST4+ enterocytes expression of the hepatocyte growth factor-like gene, MST1, is strongly correlated to their frequencies across samples (FIG. **29**D, Spearman's ρ=0.66), and they express its receptor, MST1R (implicated in IBD through GWAS). Similarly, post-capillary venule expression of TRAIL, for which they express the receptors, TNFSF10B, C and D, is negatively correlated to their frequencies across samples (FIG. **29**D, Spearman's rho=0.38).

Applicants integrated this analysis across multiple interactions with LASSO regression, to predict the frequency of each cell subset using the expression levels of all cognate ligands of its receptors in other cells (FIG. **29**E, STAR Methods). These provided highly significant explanation to the variance in the proportion of some of the key interacting cells, including inflammatory fibroblasts, CD8+IL17+ T cells, and M cells (FIG. **29**E and FIG. **37**). For example, the frequencies of $CD8^{+}IL\text{-}17^{+}$ T cells were explained by the combination of positive signals from (1) autocrine sources through CCL5, and FASLG; (2) CDH1 by absorptive TA cells, which may mediate adhesion between these cells and epithelial cells; (3) CCL4 by $CD8^{+}$ IELs and (4) IL-18 by immature enterocytes, both are known T cell chemoattractants; and (5) negatively regulation by CCL13 from $WNT2B^{+}Fos^{lo}$ fibroblasts and (6) plasma phospholipid transfer protein (PLTP) from glia.

Example 14—Mapping Disease Associated Variants to Cells of Action and Putative Function

Tissue profiling of patients with active disease captures the pathological state of the tissue, but cannot directly distinguish between cause and effect. Conversely, Genome Wide Association Studies (GWAS) can identify genetic variants that are causally associated with disease risk, but cannot readily determine the molecular, cellular and physiological function of each variant. Tissue profiling by scRNA-Seq can help map variants to function at scale, by determining the cell of action for each associated gene and the genes' differential expression pattern in disease.

Mapping 117 IBD-associated GWAS genes onto the colon cell atlas showed that 53 of the genes were strongly enriched within specific cell lineages (FIG. **30**A), with 40 genes significantly differentially expressed in the cells between health and UC (FIG. **30**A, Table 2, Table 13). In addition to many known associations (e.g. RNF186 in epithelial cells, CARD9 in monocytes), Applicants recovered many previously unappreciated associations. For example, Omentin (ITLN1), a receptor for bacterial arabinoglycans and lactoferrin, is expressed specifically by immature goblet cells that decreased in frequency with disease (FIG. **27**A), rather than by all goblet cells; and plasma B cells expressed high levels of the NOD-like receptor, NLRP7, which is thought to recognize microbial acylated lipoproteins and activate the NLRP7 inflammasome in macrophages.

Some cell types are particularly enriched for UC-induced GWAS genes, most notably M cells, $CD8^{+}IL\text{-}17^{+}$ T cells, GC B cells, enterocytes, DC2s, and ILCs (FIG. **30**B). In particular, multiple IBD-associated GWAS genes were significantly higher in M cells than in all other cell subsets, including MST1R, the receptor for macrophage-stimulating protein, CCL20, NR5A2, NFKB1, and JAK2 (FIG. **30**A,B), and those genes were induced in M cells in UC vs. healthy tissue (FIG. **30**B). Other cells with high mean expression levels of GWAS genes include many UC-related cell subsets, such as $CD8^{+}IL\text{-}17^{+}$ T cells, GC B cells, enterocytes, DC2s, and ILCs (FIG. **30**B,C). Taken together with the changes in M cell proportions, their central cross-compartment interactions and overall differential expression patterns, this suggests that M cell dysfunction may play an underappreciated but pivotal role in UC.

Next, Applicants hypothesized that the variation in expression across individual cells of the same subset can power us to predict the function of GWAS genes. Past approaches to infer function from expression data often use "guilt by association" across bulk tissue samples, but those cannot distinguish between expression and cell proportions changes. In contrast, Applicants can measure the co-variation of genes across single cells within one cell subset, allowing us to isolate co-regulated biological processes (STAR Methods).

Using this approach, Applicants annotated many GWAS genes with new putative biological functions. For example, the function of C1orf106, expressed specifically by epithelial cells, was unknown until Applicants recently showed it was involved in cell-cell junctions. The gene module for this gene within epithelial cells contains many other genes involved in cell adhesion, including E-cadherin (CDH1), tight junction protein 3 (TJP3), and LAMB3, and is significantly enriched for the GO term "cell adhesion" (q-value$<10^{-3}$, Fisher exact test), second only to the response to interferon-gamma, which may reflect a relevant physiological pathway. NLRP7 is a NOD-like receptor that has been shown in macrophages to trigger the assembly of the inflammasome, activation of caspase 1, maturation of IL-1B and IL-18, and rapid pyroptosis. However, the analysis suggests that within plasma B cells, NLRP7 may activate caspase 3, the highest scoring gene in the module. Other top genes include pro- and anti-apoptotic factors, including death-associated protein (DAP), Fas apoptotic inhibitory molecule (FAIM), and BIM (BCL2L11), a key regulator of BCR-mediated apoptosis. Inflammasome assembly can lead to the activation of caspase 3 in cells that do not express caspase 1, which may explain the differential responses observed in macrophages and B cells.

RNF186 is an E3 ubiquitin ligase that is thought to participate in ER stress-mediated apoptosis and is expressed uniquely in epithelial cells (FIG. **30**A).

Example 15—GWAS Genes are Explained by a Small Number of Modules Spanning Key Pathways and Cells

Remarkably, in many cases, multiple IBD-associated GWAS genes map into each others' modules, allowing us to arrange 10 meta-modules that together span nearly 50% of all IBD genetic associations, and may reflect some of the key pathways in the disease (FIG. **30**C). In particular, the PTPN22 module in UC T_{regs} contains 8 IBD-linked genes, including PTPN22, IL23R, RORC, CCL20, ATG16L1, SKAP2, PRDM1, and RASGRP1 (ranks 1, 2, 5, 17, 39, 40, 50, and 98 out of 16,801 analyzed genes, respectively). PTPN22, IL23R, RORC, and ATG16L1 are among the strongest risk factors of IBD, yet their precise roles in the disease are unknown. However, this module also contains caspase-8, BIM, and several other genes enriched in the KEGG terms for apoptosis and TNF signaling

(q-value<10^{-4} for both terms, Fisher's exact test), suggesting that it may reflect pathways that regulate T_{reg} apoptosis vs. survival in response to TNF. In another example, the TNFAIP3 module in healthy DC2s contains 7 IBD-linked genes, including TNFAIP3, TNFSF15, PLAU, STAT4, AHR, NDFIP1, and NCF4 (ranks 1, 11, 12, 21, 25, 88, and 96 out of 15,685 analyzed genes, respectively). This module was significantly enriched for KEGG terms related to TNF and NFκB signaling (q-value<10^{-4} for both terms, Fisher's exact test), along with the expression of several pro-inflammatory and anti-inflammatory cytokines and their receptors (e.g. IL-8, CXCR3, IL-10, IFNGR2, IL10RB), suggesting that this module may regulate DC responses in healthy tissue. In many cases, the genes in these modules are most highly expressed in other cell types, suggesting that the co-regulation of genes within single cells, rather than their absolute levels of expression, may reveal the cell-of-action for at least some GWAS-implicated genes. Some gene modules, such as the TNFAIP3 module in DC2s, were only found in healthy cells and may thus contribute to IBD onset, but the majority of gene modules, such as the PTPN22 module in T_{regs}, were only found in UC cells and may thus contribute to IBD progression (FIG. **30**D). Notably, while, GWAS-enriched gene modules were found in subsets of epithelial cells, microvascular cells, myeloid cells, T cells, and B cells, but not fibroblasts, other endothelial cells, or glia (FIG. **30**D), suggesting that stromal cells may contribute less to the overall genetic disease risk.

Example 16—Co-Regulation of Genes within Single Cells, Rather than their Absolute Expression Levels, Helps Recovers Causal Genes from Candidate Regions of Genetic Association

Finally, Applicants hypothesized that cell type specific expression and co-expression modules can help pinpoint the specific genes that underlie the signal of association for each IBD-related SNP haplotype. To this end, Applicants retrieved all genes associated with each original associated region variant, and for each such candidate gene set, then examined whether the gene's expression level, degree of differential expression, or co-regulation with other candidate genes could be used to successfully recover the "causal" IBD-associated gene, as defined separately by fine mapping (STAR Methods), relative to a null model in which genes were randomly selected. In the null model, the "causal" IBD gene was selected 18 out of 53 total times from gene sets ranging in size from 2-10 genes (mean=4 genes). However, using scRNA-Seq data, Applicants successfully recovered 24 "causal" genes by selecting genes with the highest gene expression from each set of candidate genes (i.e. 33% increase in accuracy), and recovered 28 "causal" genes by selecting genes that were found in the largest co-regulated gene modules consisting of other candidate genes (i.e. 56% increase in accuracy). Importantly, the latter method constructs modules using only candidate genes as seeds, and thus does not rely on any a priori knowledge of disease associations, aside from the genetic regions and the scRNA-seq data. Furthermore, scRNA-seq data can also help prune candidate gene sets to reduce the number of potential hits, by removing genes with no detectable expression in the colon cells, genes that were not differentially expressed, or genes that were not found in any gene modules of candidate genes. Filtering by expression, Applicants successfully eliminated 18 out of 139 total genes, while incorrectly eliminating 5 true hits. Using modules, Applicants successfully eliminated 45 of 139 total genes, while incorrectly eliminating 9 true hits. Taken together, these results suggest that the co-regulation of genes within single cells, rather than their absolute levels of expression, can help recover the causal genes from candidate gene sets. Combining both ranking by co-expression and filtering, Applicants inferred the IBD-associated genes for all regions where the underlying variant is not known (FIG. **30**E). This analysis suggests roles for NCF4, PDGFB, IL10, and CCRL2 in IBD.

Example 17—Discussion

The single cell census of the healthy and IBD colon generated a comprehensive cellular and molecular map of health and disease. This revealed nearly all known cell types, with the notable exception of neutrophils, revealed new cell types and states in the colon, including a subset of chemosensory epithelial cells that may detect pH and contribute to sour taste perception in the colon. Comparison of the cellular composition between healthy, uninflamed and inflamed UC tissue highlighted key disease-specific cell subsets whose contributions to IBD were largely unknown. Analysis of cell intrinsic programs showed that transcriptional programs are larger similarly changed in non-inflamed and inflamed tissue compared to healthy tissue, suggested that non-UC tissue, albeit histologically seemingly normal, is substantially modified, either as a "pre-inflamed" state or as "post-resolution". Analysis of cell interactions showed substantial rewiring from healthy to uninflamed to inflamed, with increased cross-talk between compartments, and allowed to explain some of the most dramatic changes in cellular proportions through cell-cell interactions that impact cell infiltration, proliferation and differentiation. The magnitudes of these reported changes—in cell proportions, intrinsic programs, and cell-cell interactions, emphasize the layer of complexity of colitis in which the three major components of the colon; the epithelial, stromal and immune cell are able to contribute to the initiation and progression of the disease, both inherently and through their effects on each other.

Several cell types, including M cells, CAIFs, inflammatory monocytes, B cells, and $CD8^{+}IL\text{-}17^{+}$ T cells—stand out as particularly prominent in disease and are often the locus of expression of GWAS genes—and manifest both changes in proportions, expression programs, and cell-cell interactions, that can play a role in disease initiation, progression and drug resistance, thus substantially revising the cellular and molecular narrative of disease.

BEST4+ Enterocytes are a New Subset of Chemosensory Epithelial Cells

Within the colon, pH sensing and sour taste perception may help detect members of the gut microbiota, for example, the lactic acid bacteria, many of which have established long-term symbioses with the human host and are thought to inhabit colonic crypts. Recent studies have highlighted the role of tuft cells in chemosensation at the microbiota-epithelium interface. The atlas uncovered also BEST4+ enterocytes, a new subset of chemosensory epithelial cells, which Applicants validated in the colons of healthy subjects and IBD patients (FIG. **26**B). These cells may help detect and modulate salts and acids, and may work alongside tuft cells to transduce taste signals in the intestine. Supporting this hypothesis, they share the TF, SPIB, with tuft cells and M cells, suggesting either a developmental link or a common regulon for their shared functions. That this cell type has not been observed in the earlier census of the mouse small intestine may relate to either species-specific differences or to pH differences between the small and large

intestines. Alternatively, as regulators of salt balance, these cells could be involved in water absorption, a key function of the colon, but not the small intestine. This interpretation is supported by low expression of renin in these cells. The proportion of BEST4$^+$ enterocytes, along with those of several other epithelial subsets, are modestly decreases in inflamed tissue (FIG. **27**A) and few differentially expressed genes with disease. Applicants found significant autocrine and paracrine signals controlling their abundances; most notably, their expression levels of MST1, for which they express the receptor, MST1R, were strongly correlated to their proportions across samples (FIG. **29**D).

Microfold Cells are Expanded in Disease, Mediate Epithelial-T Cell Interactions, Especially with T_{regs}, and are Enriched for GWAS Genes

Microfold cells are critical for the recognition of the gut microbiota by the adaptive immune system and were previously reported to reside in GALT (e.g. isolated lymphoid follicles) in healthy subjects. Microfold cells were rarely detected in healthy subjects, but expanded substantially in multiple inflamed tissue samples (FIG. **27**A), which was unexpected because most biopsy specimens do not capture GALT (e.g. isolated lymphoid follicles). Their expansion during disease may either reflect the development of tertiary lymphoid structures or expansion of small sentinel populations of M cells within normal epithelium, and suggests that they may play an important and previously unrecognized role in the disease. In the cell-cell network, M cells are the sole epithelial cell type in the T cell compartment in healthy tissue, and are a central hub leading to the increased cross-compartment connectivity in non-inflamed and inflamed tissue, especially through connections to myeloid cells (FIG. **29**A-C). Notably, within inflamed tissue, as epithelial cells overall increase production of RA, M cells upregulate the RA binding protein, CRABP2. RA production by DCs leads to the development of gut-homing T_{regs} and it is possible that RA sequestration by CRABP2 from M cells plays a similar role, which also present antigen and form intimate associations with T cells. Moreover, M cells were major producers of CCL20, a cytokine whose expression in enterocytes and M cells was correlated in the analysis to the frequency of T_{regs} across samples (FIG. **29**D). Finally, the analysis implicates M cells causally in IBD through their expression of "GWAS genes": Indeed, they have the highest mean expression of all IBD-associated GWAS genes (FIG. **30**A), including the highest expression levels of CCL20, JAK2, NFKB1, and NR5A2 (FIG. **30**A), and an M-cell expressed gene module consist of 5 IBD-associated, co-regulated GWAS genes, including CCL20, ERAP1, PTGER4, JAK2, and TMEM135.

Inflammatory Fibroblasts and Inflammatory Monocytes are Key Hubs and May be Associated with Response and Resistance to Anti-TNF Therapy

CAIFs are a new subset of fibroblasts that were barely detectable in healthy tissue, increased in non-inflamed tissue from UC patients, and dramatically expanded in inflamed tissue from UC patients (FIG. **27**A). Together with inflammatory monocytes, the two cell types were strongly associated with signatures of clinical resistance to TNF blockade (FIG. **28**D). This association may arise either because these cells are biomarkers of disease severity or are actively involved in drug resistance. Supporting the latter possibility, CAIFs uniquely express several genes that may promote resistance, including IL13RA2 and IL11, while inflammatory monocytes highly express OSM and IL1RN. Both subsets also express high levels of IL-8 and kynureninase (KYNU), which is a known biomarker of disease severity. Applicants additionally found: CAIFs interact with enterocytes; CAIFs and monocytes are "hubs" in disease interaction networks; and Few GWAS genes map to CAIFs.

T Cells

Applicants uncover strong evidence for the role of CD8$^+$ IL-17$^+$ T cells and Tregs in in IBD, which both progressively increase in frequency from healthy to non-inflamed to inflamed tissue (FIG. **27**A). CD8$^+$IL-17$^+$ T cells were previously found in UC patients, but their role in the disease was unclear and they were not known to comprise a large fraction of colon-resident T cells. Surprisingly, these and other T cells simultaneously induce cytotoxic and co-inhibitory pathways. Applicants additionally found: Tregs upregulate TNF with disease; CD8 cells interactions (autocrine+ paracrine interactions); and Re-wiring of T cell interactions with disease; GWAS modules show that Tregs and CD8 T cells are important (apoptosis).

This analysis provides a framework for using scRNA-Seq to understand complex diseases, from a census of cell types and states within healthy and diseased tissue, to identifying changes in cell proportions with disease, and partitioning changes in gene expression into those that are shared by cell lineages or unique to cell subsets or to drug responses; then, integrating these analyses to understand how changes in gene expression propagate into changes in cell-cell interactions, identifying the "cell-of-action" for GWAS genes, and understanding the complex genetic risk factors for the disease.

TABLE 3

Epithelial Healthy specific markers for indicated cell types
E.Enterocyte__Immature__1
SLC16A12, TAC1, EFCAB5 E.Enterocyte__Immature__2
RP11-525K10.3, RP11-576122.2, DRD5, LINC00974, GDPD2 E.Enterocyte__Progenitor,
RP11-800A18.4 E.Enterocytes
KIAA1239, RP11-396O20.1, DUSP21, SLC7A9, ARTN, SAA1, RP11-266L9.5, RP11-77K12.7, RBP2, SLC14A2, ADAMTSL4-AS1, RNU6-1016P, HAS3, LINC00955, G6PC, SAA2, CTB-58E17.9, KCTD4, SLC22A1, CELA3A, SLC6A20, CELA3B, CTC-490G23.2, CTB-171A8.1, GPR110, MAB21L3, RP11-30P6.6, SLC45A2, RAB6B, RP11-202A13.1, RP11-116O18.1, EMP1

TABLE 3-continued

Epithelial Healthy specific markers for indicated cell types
E.Enteroendocrine
DNAH2, MNX1, TNNC1, DACT2, FBXL16, RAB26, RP11-17M24.1, CNNM3, RP11-279F6.1, SYT13, AC114730.3, ADPRHL1, KIAA1456, DDC, C19orf77, SNORD3D, SEZ6L2, STX1A, NAGS, KIF12, C14orf93, ZNF311, PTPRD, MEX3A, PPL, COLCA1, CYP4F3, HOXB9
E.Epithelial
PRSS8, VIL1, PRR15L, PPP1R1B, AQP8, CCL15, SLC26A3, PCK1, CKMT1B, PRAP1, CKMTIA, LYPD8, PKP3, AKR1B10, AP1M2, PLA2G10, NXPE4, MYO1A, TMEM171, PRR15, USH1C, MS4A12, PDZK1IP1, KLK1, GGT6, FUT3, TMPRSS2, CBLC, MUC2, GUCA2B, LAD1, CDH1, MUC1, GJB1, C1orG10, LINC00035, DSG2, LINC00483, C1orf106, GPRC5A, MUC4, LAMB3, ITLN1, CLRN3, CLCA4, LINC00675, MEP1A, CYP3A5, AGR3, TRIM31, MARVELD3, ERN2, CES3, PLA2G2A, MUC5B, RP11-519G16.5, SATB2, CLCA1, MAL2, CGN, NEU4, CFTR, RAPGEFL1, FERMT1, BAIAP2L2, DDC, HNF4A, PLEKHG6, BTNL3, ARL14, CDHR2, FABP2, LCN2, SLC17A4, TM4SF5, ENTPD8, SPINK4, POF1B, MYO5B, C9orf152, VIPR1, PDZD3, COL17A1, LAMA1, PLS1, IHH, B3GNT3, TMIGD1, OVOL1, REP15, RP11-395B7.2, RETNLB, CDKN2B-AS1, GSTA1, MOGAT2, A1CF, SEMA4G, UGT2A3, BTNL8, SGK2, CEACAM6, SLC51A, YBX2, HHLA2, TFF1, TRIM15, NOX1, C11orf86, OLFM4, LRRC19, PITX2, C1orf172, RNF43, PPP1R14C, U47924.27, LIPH, CWH43, EDN3, ANXA13, CAMSAP3, PI3, TMEM184A, F2RL1, CAPN8, SMIM6, HEPACAM2, SH3RF2, TMEM82, ISX, ANKS4B, RBBP8NL, GRB7, SPDEF, ESRP1, EPB41L4B, SLC3A1, AC106876.2, LINC00668, HNF1B, RP11-747D18.1, NGEF, RP11-465B22.8, EPHA10, MB, ZBTB7C, STX19, CA7, SATB2-AS1, ASPG, RP11-680F8.1, PRAC1, NXPE2, REG1A, C12orf36, RP11-465N4.4, CTD-2626G11.2, RP11-708H21.4, SLC9A2, S100P, RP1-278O22.1, L1TD1, KIF12, INPP5J, OVOL2, AC005355.2, WNK4, NR1I2, NAT2, SMIM2-AS1, LINC00992, EDN2, BARX2, C1orf116, HNF1A-AS1, RAP1GAP, SCGB2A1, BEST2, TINAG, GPRIN2, B4GALNT2, RP11-234B24.2, TMEM236, FOXD2, RP11-349K16.1, RHOV, IL22RA1, DMBT1, RP11-304L19.1, RP11-627G23.1, SLC5A1, BEST4, XDH, AC066593.1, RASEF, GLOD5, TMED6, CELA3B, OTOP2, CAPN13, GOLT1A, TMEM61, RP11-59E19.1, GDPD2, ADH6, CYP2B6, IYD, HNF4G, CAPN9, FOXA1, WWC1, SLC30A10, SERPINA6, RP5-881L22.5, IGSF3, PLA2G4F, SLC6A7, FOXA2, MIR194-2, RP3-523K23.2, TMEM92, NOS2, RP11-30P6.6, C3orf83, SLC13A2, SYT13, AGXT, CELA3A, CTD-2547H18.1, CTSE, EPPK1, MYRF, RBP2, TMEM72, FAM83E, GPR39, LINC00704, ACE2, FIBCD1, HOXA13, RP11-297L17.2, RP11-284F21.10, SH2D6, AC009133.21, CTD-2196E14.5, GALNT5, MEP1B, MT3, UGT2B7, CYP2C18, TUBAL3, APOBEC1, CLDN8, RP11-408H20.1, USP43, CTC-210G5.1, HAS3, CTD-2566J3.1, AC011298.2, GLRA4, HSD3B2, CTD-2047H16.2, FAM83B, HOXB13, KRT14, LINC00261, PRAC2, SLC6A19, CASC9, MUC3A, RP11-328M4.2, TM4SF20, PRLR, C6orf141, RP11-150O12.3, RP11-187E13.1, MSLN, ALPI, SI, SOWAHA, GJB3, TBX10, CHAD, RP11-191G24.1, C1QTNF1-AS1, KLK15, PYY, MRAP2, ALDOB, CYP4F2, RP11-91K11.2, RP11-567C2.1, AP000344.3, CASC8, CYP3A4, FAM151A, GRHL2, SLC1A7, TTPA, LCN12, AC007182.6, KLK3, PF4, PVRL4, RP11-542M13.2, TREH, CYP4F11, AC011523.2, GPR115, RP11-1260E13.2, RP11-519G16.3, RP11-6N17.6, MESP2, DMRTA1, AC005152.2, BRINP3, CTA-363E6.2, GPD1, MUC17, NOVA1-AS1, OTOP3, RP11-470P21.2, RP11-595B24.2, RP11-800A3.4, TRPM5, WFIKKN1, BCMO1, GPR128, RP1-170O19.14, RP11-801F7.1, AC005550.3, ACSM1, DPP10, GPR143, HMGA2, KCNE2, LRRC66, PCSK9, PSCA, RP11-202A13.1, RP13-616I3.1, AP001610.9, DACT2, FAM160A1, HTR3E, OGDHL, RP11-28H5.2, RP11-627G18.4, RP11-64K12.10, RP11-800A18.4, SLC5A11, TRIM10, XXyac-YM21GA2.4, B3GALT1, LGR5, RP11-223110.1, RP11-290F24.6, RP11-379B18.6, RP11-93B14.5, RXFP4, UGT1A10, CHGA, DNAH3, C19orf45, CTD-3010D24.3, GNG13, KRT12, LINC00520, NR0B2, RP11-116O18.1, RP11-135A1.2, RP11-276H7.3, RP11-509E16.1, SHH, TFF2, TNNT2, UCA1, RP11-125B21.2, ABHD12B, CTA-221G9.11, CTC-55802.1, DAO, GPR98, LGR6, RP11-432J24.2, RP11-644F5.10, RP4-680D5.8, RP5-1057J7.7, SLC15A1, SLC9A3, TAC1, TRPC7-AS1, LHX4, CASC16, CCDC108, CHRM3, CTD-2611O12.7, KCNK10, KNG1, LINC01071, OXGR1, PHYHIP, POU2F3, RP11-1069G10.1, RP11-1220K2.2, RP11-188P20.3, RP11-339B21.15, RP11-695J4.2, RP11-771K4.1, RP11-809C18.4, SLC45A2, XX-CR54.3, AC024592.9, AC083900.1, AC090673.1, CTD-2026G6.3, CTD-2589M5.4, DUOXA2, GALNT8, HSD17B3, INSL5, KCNV1, KLHL34, LA16c-395F10.2, LINC00941, MAB21L3, RP11-227H15.4, RP11-416N2.4, SLC5A10, SYTL5, FRRS1, AC064834.1, AQP12A, C12orf56, C1orf177, C4BPA, CHST5, CTB-25B13.6, DEFA5, DLG3-AS1, FAM83H-AS1, FEV, GLTPD2, HIST1H4B, LINC00114, LINC00570, MT-TS2, POU5F1B, PRDM7, RP11-209E8.1, RP11-320N21.2, RP11-392E22.12, RP11-426L16.3, RP11-74C1.4, RP11-757F18.5, RP11-806O11.1, RP11-844P9.2, SLC38A4
E.Goblet
CTD-2231E14.4, PLA2G2F, TFF1, TBX10, AC093642.3, RP11-95M15.1, FER1L6, S100P, LINC01022, RN7SKP127, SYTL5, FFAR4, MUC2, SBF2-AS1, RASEF, MUC1, TFF2, NRAP, GALNT5, RP11-379B8.1, HIST1H4A, LINC00842, RP11-363E7.4, AC011718.2, GPR153, RP11-845C23.2, CHAD, CHRNA7, CLDN8, GPRIN2, AC009133.21, FAM101A, SYTL2, RP11-757F18.5, BCAS1, AN RD36C, ZG16, CAPN8, SMIM6, HIST1H2BG, AN RD18A, TM4SF5, RNF39, GLTPD2, LRRC31, EIF2AK3, RECQL5, RP11-276H7.3, RP11-196G18.22, AC147651.3, USP54, LGALS9B, DHX32, CTD-2589M5.4, TSNARE1, CYorf17, NEDD4L, HIST2H2BE, ENTPD8, SCNNIA, GALE, LINC00543, RP11-92K15.3, FAM177B, KAZALD1, HIST1H2BC, LGALS9C, FCGBP, HIST1H3D
E.Immature__Enterocytes
CA1, RP11-439E19.9, XXyac-YM21GA2.7, SLC26A2
E.Immature__Goblet
TMEM210, ITLN1, CLCA1, LA16c-321D4.2, SPINK4, KLK15, LRRC26, KLK1, RP11-234B24.2, RETNLB, WFDC2, GNE, CCDC60, AC011523.2, LA16c-395F10.2, UGT2B7, RAP1GAP, ST6GALNAC1, AGR2, CTD-2547H18.1, KLK3, LINC00261, CACNA2D2, GALNT8, KLK4, GMDS, TMEM61, SPINK1, PFKFB4
E.Secretory
ABCC8, CTD-2231E14.4, HTR3C, NKX2-2, PAX6, PLA2G2F, PRAME, RP11-69G7.1, VWA5B2, HTR3E, GNG13, SCGN, SST, GCG, SH2D6, CHGA, TPH1, FEV, PYY, CRYBA2, SH2D7, TRPM5, TNNI1, OGDHL, POU2F3, NCMAP, TAS1R3, KLHDC7A, TFF1, TBX10, HMX2, AZGP1, TREH, AC093642.3, IL17RB, AC053503.4, FER1L6, KLK11, KCNQ4, PRSS22, SCG5, S100P, AVIL, PROC, RP11-93B14.5, LINC01022,

TABLE 3-continued

Epithelial Healthy specific markers for indicated cell types
C11orf53, SYTL5, ARHGEF38, TGM3, FFAR4, SHB, LCN15, ARX, MUC2, SBF2-AS1, BMX, RASEF, MUC1, TFF2, NRAP, ATP2A3, RP11-384L8.1, GPR153, PSTPIP2, RP11-700H6.1, TMEM198, HIST1H4A, GALNT5, PART1, RP11-379B8.1, 7SK, RP11-845C23.2, RP5-821D11.7, CTA-221G9.11, IGSF21, TM4SF5, LINC00842, RP11-363E7.4, SYT7, CHGB, AC011718.2, CHAD, GPRIN2, RP11-122G18.5, HCG9, MYCBPAP, CNTD1, CHRNA7, FAM101A, CLDN8, GFI1B, RECQL5, ANKRD36C, SYTL2, RP11-757F18.5, CTD-3051D23.4, AC009133.21, GRASP, BCAS1, ANKRD18A, SMIM6, RP11-498E2.9, RAB3B, FAM106A, CAPN8, MYRF, ARHGEF11, FUT6, ZG16, HIST1H2BG, MYO5C, ESPL1, PRUNE2, HCK
E.Secretory_All
HTR3C, GCG, HTR3E, GNG13, SH2D6, FEV, CHGA, SCGN, CRYBA2, ZG16, TBX10, SH2D7, TRPM5, MUC2, PYY, OGDHL, BEST2, LA16c-321D4.2, AC009133.21, CAPN9, REP15, KCNQ4, POU2F3, AC011523.2, NCMAP, MB, FCGBP, SCGB2A1, SYTL5, FFAR4, KLK12, ITLN1, CLCA1, TFF3, TAS1R3, REG4, HMX2, TMEM61, TFF1, SPINK4, FER1L6, TPSG1, RP11-234B24.2, RETNLB, KLK15, RP11-384L8.1, ANXA13, ANO7, CCDC60, HOXA-AS3, KLK1, KLK3, AC093642.3, AZGP1, LRRC26, SPDEF, IL17RB, TREH, CTD-2589M5.4, CCDC108, RAP1GAP, WFDC2, LINC00238, LA16c-395F10.2, FOXA3, LINC00261, RXFP4, CTA-221G9.11, CA9, PFKFB4, CREB3L1, S100P, GPR153, C11orf53, ST6GALNAC1, PROC, FOXP4, ARHGEF38, RP11-93B14.5, WNK4
E.Secretory_TA
RP11-350J20.12
E.Stem
LEFTY1, ASCL2, RGMB, CDCA7, ALDH1B1, EPHB3, OLFM4, SMOC2, PTPRO, SLC39A2, LGR5, CELF5, OXGR1, RP11-84C10.4, FAM201A, TERT, RP11-43505.2, RP11-219E7.4, FMN2, DEC1, TMPRSS13, CLDN1, SNTN, RP11-396C23.2, TRIM74, RP11-22L13.1

TABLE 4

Epithelial UC specific markers for indicated cell types
E.Enterocyte_Progenitor
SLC38A4, AC013268.5, AGMO
E.Enterocytes
BEAN1, CYP24A1, KLK8, MYZAP, PLA2G4E, PNCK, RP11-103J17.2, RP11-317L10.1, RP11-626P14.2, SERPINB4, SLC47A2, ANXA10, INSL4, SERPINB7, RP11-79H23.3, MMP7, FOXE3, SAA4, RP11-381O7.3, KIAA1239, MGAM, C8G, AC104135.3, FAM83A, GLRA4, TPRXL, RP11-30P6.6, PHYHIP, RP11-73G16.1, RP11-345J4.3, RP11-28H5.2, SLC6A14, LINC00955, RP5-1086K13.1, RAB6B, TCHP, PDZK1IP1, RP11-35P15.1, AQP11, LINC00479, CRABP1, LY6D, BMP3, KCNG1, RP11-542M13.2, ABTB2, SLC6A20, TM4SF20, PLIN1
E.Enteroendocrine
MIR7-3HG, NTS, PAX4, PAX6, VWA5B2, PYY, INSL5, SCGN, GCG, FEV, CHGA, CRYBA2, PRPH, SST, TPH1, SCG3, LCN15, KCNH6, KCNJ6, EYS, INSM1, SCG2, CPB1, RFX6, CHGB, NKX2-2, NEUROD1, CNIH2, SLC18A1, LINC00470, SCG5, NEUROG3, PCSK1N, TGM3, MEGT1, MAFA, TNNC1, PCSK1, RTBDN, CACNA1A, RP13-131K19.6, AC034243.1, SYT13, MS4A8, PDX1, ARX, SLC29A4, MAPK8IP2, STX1A, LRRC24, SCT, CTD-3193013.9, MLXIPL, BAIAP3, RIMS2, RIMBP2, DDC, C6orf141, MANEAL, AMBP, CAMK2B, CYP2W1, RXFP4, PELI3, ASCL1, RUNDC3A, PNPO, ATP6V1C2, ACVR2B, NPW, LY6H, PSCA, PPL, CADPS, PAPPA2, DUSP26, NT5DC3, RP11-279F6.1, CXXC4, DNAJC12, NOP9, Z83851.1, CELF4, PEMT, RAB26, GIPR, PGAM2
E.Epithelial
ABCA12, ABO, AC005152.2, AC005550.3, AC007182.6, AC007255.8, AC007292.6, AC009133.21, AC010745.1, AC011298.2, AC011523.2, AC011718.2, AC011747.7, AC024592.9, AC026471.6, AC053503.4, AC066593.1, AC069277.2, AC090673.1, AC104667.3, AC106876.2, AC110619.2, ACE2, AGXT, AL133373.1, ALDH1A2, ALOX12B, AMBP, ANKRD18A, ANKS4B, ANO5, AP001610.9, AQP5, ARTN, B3GALT1, B4GALNT2, BCMO1, BEST2, C12orf56, C1QTNF1-AS1, C1orf168, C21orf88, C2orf54, C2orf70, C3orf83, C4BPA, C5orf52, CALN1, CASC16, CASC9, CASP16, CCDC108, CCDC60, CELA3A, CELF5, CHAD, CHRNA7, CHST5, CNTN3, COL2A1, CRABP1, CRYBA2, CRYBB3, CTA-363E6.2, CTB-175P5.4, CTC-210G5.1, CTC-436P18.3, CTC-490G23.2, CTC-558O2.1, CTD-2377D24.6, CTD-2547H18.1, CTD-2566J3.1, CTD-2589M5.4, CTD-3010D24.3, CTD-3118D7.1, CWH43, CYP2B6, CYP2C18, CYP3A4, CYP4F11, CYP4F2, CYorf17, DACT2, DAO, DEFB4A, DMRTA1, DNAJC6, DPP10, EDN2, EGF, ENKUR, FAM151A, FAM160A1, FAM83A, FAM83B, FAM83H-AS1, FEV, FOXH1, FOXN1, FRMD5, GABRB2, GABRB3, GABRP, GAL3ST1, GALNT8, GJB4, GJB5, GLRA2, GLRA4, GNG13, GPD1, GPR110, GPR115, GPR128, GPR37L1, HMGA2, HS3ST6, HSD3B2, HSPB3, HTR3E, HTR4, IGFALS, IL37, IRX2, ISX, KCNE2, KCNK10, KIAA0319, KLHDC7A, KLK12, KLK15, KLK3, KLK4, KNG1, KRT12, KRT13, KRT14, KRT6B, KRTAP13-2, LA16c-395F10.2, LECT1, LGR5, LHX4, LINC00114, LINC00238, LINC00639, LINC00842, LINC00896, LINC00940, LL22NC03-32F9.1, LRRC66, LRRIQ4, LYPD6, MAB21L3, MAMDC2-AS1, MEP1B, MESP2, MIR194-2, MNX1, MNX1-AS2, MT-TY, MT3, NAT2, NAT8, NKX2-2, NOVA1-AS1, NPSR1, NR0B2, NR1I2, NRAP, OGDHL, PCAT7, PLA2G12B, PLA2G4F, PLCH1, PLSCR2, RBP2, RNF183, RNU1-134P, RP1-170O19.21, RP1-240K6.3, RP1-60O19.1, RP11-1069G10.1, RP11-1157N2_B.2, RP11-11N5.3, RP11-120K24.3, RP11-1220K2.2, RP11-150O12.3, RP11-150O12.6, RP11-164P12.4, RP11-187E13.1, RP11-188P20.3, RP11-202A13.1, RP11-206L10.3, RP11-209E8.1, RP11-211G23.2, RP11-21L23.2, RP11-223I10.1, RP11-231E6.1, RP11-244F12.3, RP11-275F13.1, RP11-307C12.11, RP11-30P6.6, RP11-349K16.1, RP11-352G9.1, RP11-35P15.1,

TABLE 4-continued

Epithelial UC specific markers for indicated cell types
RP11-380P13.1, RP11-382B18.4, RP11-41O4.1, RP11-432J24.2, RP11-439E19.7, RP11-440I14.3, RP11-44F14.8, RP11-465N4.5, RP11-469H8.6, RP11-470P21.2, RP11-511I2.2, RP11-519G16.3, RP11-542M13.2, RP11-595B24.2, RP11-627G18.4, RP11-627G23.1, RP11-63P12.7, RP11-64K12.10, RP11-680F8.1, RP11-6N17.6, RP11-708H21.4, RP11-747D18.1, RP11-757F18.5, RP11-77K12.7, RP11-789C1.1, RP11-796E10.1, RP11-798K3.2, RP11-800A18.4, RP11-801F7.1, RP11-844P9.2, RP11-84C10.4, RP11-93B14.5, RP11-963H4.3, RP13-497K6.1, RP13-616I3.1, RP4-680D5.8, RP5-1013A22.5, RP5-1057J7.7, S100A7, SAA4, SCEL, SCGB2A1, SCGN, SEMA3B-AS1, SERPINA6, SHH, SLC10A5, SLC13A2, SLC15A1, SLC18A1, SLC1A7, SLC28A3, SLC30A10, SLC38A4, SLC39A2, SLC5A11, SLC6A19, SLC6A7, ST6GAL2, SYT8, SYTL5, TMEM72, TNNT2, TRIM10, TRIM40, TRPC7-AS1, TRPM5, TSPO2, TTC6, TTPA, TUBAL3, U47924.27, UCA1, UGT1A1, UGT2B15, UGT2B7, VSTM5, WFIKKN1, WNT11, XX-CR54.3, YBX2, SH2D6, A1CF, TMEM61, TREH, C12orf36, UGT2A3, RP11-465B22.8, NXPE2, TMIGD1, ESRP1, TBX10, FAM83E, TFF2, CDHR2, SI, GRHL2, ZG16, TMEM82, PDZD3, TM4SF5, STX19, TFF1, RETNLB, POU2F3, CELA3B, GUCA2B, RP11-234B24.2, PRAP1, C4orf19, LRRC19, APOBEC1, TRIM31, FCGBP, GUCA2A, TFF3, MUC2, GOLT1A, PCK1, LINC00992, SHD, IL22RA1, CKMT1B, MYH14, PHGR1, CDH1, HSD17B3, CEACAM5, ERN2, KBTBD12, FABP2, LAMA1, ASPG, EPB41L4B, LYPD8, SLC26A3, FERMT1, SLC17A4, CA7, HHLA2, MISP, C9orf152, ELF3, MUC13, TTLL6, TSPAN1, OVOL2, LRRC26, PPP1R14D, REP15, MSLN, C11orf86, PITX2, S100A14, AGR3, CBLC, CDHR5, CAPN8, SMIM22, KRT8, GPT, MEP1A, LCN2, LINC00675, GPRIN2, MS4A12, EPPK1, HOXB13, GCNT3, GDPD2, NXPE4, IRF6, LGALS4, OTOP2, DQX1, FUT3, XDH, NXPE1, SLC9A2, PROM2, MAL2, IGSF9, LIPH, HNF4A, RAB25, CLCA4, SERPINB5, PIGR, HEPACAM2, CCDC64B, GGT6, MS4A8, SLC5A1, MYO1A, PRR15L, MYO5B, FUT2, C10orf99, FAM3D, AGR2, B3GALT5, PRR15, RP5-881L22.5, SPINK4, SLC39A5, CLDN8, PLS1, NOX1, HNF1A-AS1, RP3-406A7.7, ANXA13, RP11-96D1.11, FABP1, EPCAM, PRKCG, CAPN9, PRAC1, RP11-665N17.4, LEFTY1, CLDN7, CYP2C9, CDX1, CHP2, TMPRSS4, AOC1, RP11-22C11.2, FOXA3, URAD, HNF4G, LDHD, C1orf106, POF1B, CCL15, JPH1, TSPAN8, AMN, CAMSAP3, MUC5AC, EFNA2, PLA2G10, GRB7, PI3, SLC44A4, CTD-2196E14.5, LCN12, TMC5, CEACAM7, KRT19, DSG2, EPHA10, AC083900.1, GDA, SEMA4G, SLC6A14, SCNN1A, HMGCS2, AC079602.1, AQP8, TINAG, COL17A1, KLK1, S100P, TMEM54, CNGA1, CLDN3, RP11-304L19.1, SLPI, AKR1B10, KRT20, CA1, SPINK1, RP11-797A18.4, MB, TFCP2L1, RP11-305L7.6, FRMD1, SPDEF, PTPRH, RP11-395B7.2, GPX2, RBBP8NL, GPA33, PDE11A, LINC00483, FZD5, DSP, CA12, ITLN1, NOS2, FFAR4, TMEM184A, SFN, CLRN3, MTIG
E.Goblet
C11orf52, RP11-120K24.5, RP11-43N5.1, RP11-542B15.1, CTD-2231E14.4, LGSN, RN7SKP127, NUTM2E, TBX10, SYTL5, RP11-363E7.4, RP11-143K11.1, TFF1, SCEL, RN7SL676P, FER1L6, SLC25A30-AS1, PCDH20, ANKRD36C, RP11-805124.1, FAM177B, MUC5AC, LINC00342, RP11-845C23.2, RP11-730K11.1, STXBP5-AS1, FRY-AS1, SYTL2, TFF2, SBF2-AS1, RASD2, RP11-757F18.5, AC011718.2, ZG16, MUC1, SYTL4, MUC2, LGALS9B, FAM101A, MLLT3, FFAR4, RP11-452L6.1, TCTEX1D4, RP11-574K11.28, LGALS9C, GPR153, CAPN8, SHH, ADM2, AC007382.1, RP11-167J8.3, LINC01022, SMIM6, MFSD4, GALNT5, TEP1, BCAS1, GPRIN2, SDR16C5, ASPHD2, ZG16B, AC009133.21, C4orD6, GAN, FCGBP, GAREM, LNX1-AS1, MUC4
E.Immature_Enterocytes
F11, RP11-525K10.3, RP11-576122.2, CA1, WFDC12, RP11-164P12.3
E.Immature_Goblet
RP11-7115.4, IGFALS, AC015849.13, CLCA2, GALNTL6, IL37, AC073133.1, PRKCG, ITLN1, RETNLB, SPINK4, TMEM210, DLGAP1, CLCA1, LA16c-425C2.1, LINC00238, CREB3L4, LRRC26, CHRNA3, GALNT8, RP11-234B24.2, CTD-2547H18.1, AGR2, WFDC2, KLK15, KLK1, LINC00261, GIF, ST6GALNAC1, LINC00570, REG4
E.Secretory
C11orf52, HTR3C, KLK13, MIR7-3HG, PAX4, PAX6, RP11-43N5.1, TAS1R1, TNNI1, VWA5B2, HTR3E, B4GALNT4, PYY, SH2D6, INSL5, SCGN, SH2D7, GCG, TRPM5, FEV, CHGA, CRYBA2, GNG13, PRPH, SST, CCDC129, PCP4, TPH1, SCG3, LCN15, KLHDC7A, OGDHL, KCNH6, POU2F3, AZGP1, TAS1R3, EYS, CTD-2231E14.4, KCNJ6, RP11-131L12.2, INSM1, ALOX12B, RAB3B, NCMAP, CCSER1, SCG2, CYP3A7, CPB1, IL17RB, RFX6, RN7SKP127, RIMBP2, CTD-2410N18.3, NKX2-2, NEUROD1, TBX10, SYTL5, SLC25A30-AS1, CNIH2, SLC18A1, C11orf53, RP11-143K11.1, RP11-363E7.4, RP11-93B14.5, MAFA, NRTN, AVIL, TFF1, LINC00470, KCNQ4, ABCA13, SCEL, TREH, GPR153, FER1L6, BMX, SCG5, RN7SK, NEUROG3, PSTPIP2, TGM3, PCDH20, ANKRD36C, KLB, ATP2A3, MEGT1, RASSF6, RP11-805I24.1, KLK11, FAM177B, PAQR7, PROC, ATP8A2, RP11-809C18.4, AC023490.1, RP11-730K11.1, TM4SF5, CACNA1A, HMX2, IGSF21, ADH6, SYTL2, TNNC1, RTBDN, PRSS22, FRY-AS1, GFI1B, FOXP4, RASD2, FAM101A, HOTAIRM1, AGAP1-IT1, HIP1R, SYT7
E.Secretory_All
EYS, KCNH6, LINC01022, NEUROG3, TNNI1, VWA5B2, CRYBA2, HTR3E, SCGN, B4GALNT4, SH2D6, FEV, GCG, CHGA, PRPH, SH2D7, TRPM5, GNG13, RIMBP2, AC009133.21, ZG16, SLC18A1, LCN15, TPH1, SCG3, TBX10, RFX6, INSM1, SCEL, RP11-575A19.2, PKP1, MUC2, MUC5AC, BEST2, PCP4, KLHDC7A, REP15, TGM3, AC011523.2, TAS1R3, AC110619.2, SCG2, CTD-2231E14.4, RAB3B, RAD51AP2, POU2F3, CCDC60, AZGP1, KLK15, FCGBP, CCDC129, KLHL32, ALOX12B, ANO7, CLCA1, OGDHL, B3GNT6, KLK3, MB, ITLN1, TFF3, RN7SKP127, RETNLB, SNORA77, RAB26, CLCA2, NCMAP, KLK11, NKX2-2, KLK1, GALNT8, IL37, ANXA13, SPINK4, RP11-234B24.2, KLK12, TPSG1, CHRNA3, STXBP5-AS1, RAP1GAP, TMEM61, GPR153, IGFALS, TMEM210, SPDEF, CAPN9, SYTL5, SLC25A30-AS1, FOXA3,

TABLE 4-continued

Epithelial UC specific markers for indicated cell types
ABCA13, FFAR4, LRRC26, GALNTL6, LA16c-321D4.2, AGAP1-IT1, SYT7, TFF1, LINC00261, RP11-363E7.4, SCG5, FAM177B, SCGB2A1, KLB, CCDC108, NRTN, GIF, PCDH20, LINC01001, ST6GALNAC1, WFDC2, TFF2, MLLT3, DNAJC12, ATP2A3, PRKCG, CREB3L4, CTD-2547H18.1
E.Secretory_TA
ARHGAP36, DLX4, SIK3-IT1, RP11-430G17.3, RP11-363J20.1, SBSPON, RP11-231G3.1, RP11-396C23.4
E.Stem
RGMB, SMOC2, PTPRO, LPCAT3, LGR5, LGR6, SNX32, RP11-760H22.2, C1orf95, RP11-21817.2, IZUMO2, NANOG, SLC22A11, SHISA6, RP11-219E7.4, HYDIN, RP11-2E11.9, SCN8A, TDRD6, MURC, GABRA4, PARD3-AS1, AC006159.3, RP11-645C24.5, AC068499.10, SERHL, RP1-20N2.6, RP11-130C19.3, FNDC5, RP11-132A1.4, RP11-268P4.4, LINC00924, RN7SL215P, AC078883.4
E.Tuft
KRT18, SH2D6, AZGP1, LRMP, HCK, IFI6, PTPN18, PTGS1, AVIL, ATP2A3, GNG13, TRPM5, PLCG2, BMX, EIFIB, LUC7L3, MATK, BIK, HOTAIRM1, IL17RB, PSTPIP2, ANXA13, SH2D7, AKAP9, HTR3E, DEFB1, RASSF6, PPAP2C, IL13RA1, POU2F3, SPTLC2, SOX9, DPYSL3, IFT172, KLK11, COL27A1, CC2D1A, TREH, TMEM63A, TAS1R3, ZFHX3, CASP6, NCMAP, GRASP, MAP7, VAV1, C11orf53, CHDH, CCSER1, AFAP1L2, CD300LF, OGDHL, 7SK, HIP1R, DEGS2, LIMD1, CRYM, RP11-93B14.5, IGSF21, KCNQ1, GFI1B, SRGAP1, FAM171A1, PRSS22, LRP5, CCDC129, B4GALNT4, PIK3CG, PLCB2, PCP4, RALGAPA2, CTD-3094K11.1, MTSS1, PART1, KCNQ4, KLHDC7A, KDM4A, IRAK1, RN7SK, PAK3, SHB, hsa-mir-1199, FOXP4, ALOX12B, ADH6, CAMP, FUT6, NRTN, PHF12, U47924.27, PROX1, FHDC1, GANC, ZSWIM8, HOXA3, CCM2L, TNNI1, IGSF3, LRRC16A, ARHGEF5, COLCA2, HTR3C, KREMEN2, ARHGEF38, ATP8A2, HMX2, SHF, FAM229A, ABCB9, GKAP1, MADD, KLK13, AC023490.1, TRHDE, ARHGEF11, CEACAM19, RP11-285F7.2, TMEM191C, PAQR7, TAS1R1, TBC1D32, FMN1, USP35, GDPD1, RP11-440L14.1, RP11-1220K2.2, C2orf15, RP1-140A9.1, LINC01001, CDH26, AMER1, SHROOM2, LINC01071, RP11-72M17.1, HIST1H4A, HOXA1, ZNF490, RP1-199J3.7, PLA2G4D, TMEM211, RP11-298I3.4, RP11-219G17.4, CABP4, RP11-712L6.5

TABLE 5

Immune Healthy specific markers for indicated cell types
B.Bcells
CDH15, CR2, CTB-43E15.4, GH1, GLDC, GPRC5D, HBD, HTR3A, IGHE, IGLJ2, IGLV3-12, IGLV5-48, NLRP7, OSTN-AS1, PAX5, RP1-148H17.1, RP11-1084E5.1, RP11-164H13.1, RP11-297B17.3, RP11-301L8.2, RP11-390F4.6, RP4-536B24.4, RP5-921G16.2, SERPINA9, SLC22A31, TRIM55, TSHR, UBE2QL1, ZC2HC1B, FCRLA, IGLL1, TCL1A, IGHD, IGLC2, RP5-887A10.1, FAM92B, CD19, MS4A1, VPREB3, IGKC, AL928768.3, IGHM, IGHA2, IGHG1, CD79A, IGHA1, IGHG2, IGLL5, IGLC7, AC104699.1, MZB1, IGJ, BANK1, CTA-250D10.23, DERL3, RP11-693J15.5, hsa-mir-5195, AC096579.7, TNFRSF17, IGHG3, WT1-AS, MIXL1, IGLV3-1, IGLV6-57, IGLV1-40, IGLV2-8, IGLV2-14, FGF23, IGLV2-11, IGLV3-16, FCRL5, LMTK3, AMPD1, IGLV1-47, TNFRSF13C, AF127936.3, FAM129C, AC104024.1, IGHV1-24, IGLV5-45, IGLV3-21, PKHD1L1, FCER2, AC096579.13, IGLV8-61, E2F5, IGKV1OR2-108, IGLV3-25, RP11-1070N10.3, IGLV3-10, KIAA0125, MEF2BNB-MEF2B, AC079767.4, CCR10, RP11-492E3.2, RP11-325K4.2, MYL2, RP11-138I18.2, IGLV2-23, IGLV4-60, EAF2, RP11-290F5.1, AP001058.3, CNR2, FCRL2, RP11-77H9.8, IGLV1-51, SSR4, CD79B, BLK, IGKV2D-28, IGLV3-9, P2RX5, AICDA, MEF2B, IGLV3-19, CRYBA4, AC096559.1, UBE2J1, RP11-16E12.2, AC007386.2, TEX9, ESR2, RAB30, IGKV4-1, SNX29P2, TXNDC5, RP3-402G11.25, IGKV1-12, IGLV10-54, IGKV1-5
B.Cycling
MIOX, HBD, IGLV3-9, HIST1H1B
B.FO
COL19A1, RP5-887A10.1, FCRL4, IGHE, OSTN-AS1, GYLTL1B, SIDT1, BANK1, TNFRSF13B, IGHD, SELL, TEX9, CCDC50
B.GC
RP11-485G7.5, RP11-624C23.1, RP11-138I18.2, SERPINA9, ANK1, C7orf10, HTR3A, RP11-511B23.1, BACH2, RP1-148H17.1, AC023590.1, IGKV6D-21, DBNDD1, AICDA, ANKLE1, BCL7A, TCL6, TRIM55, RP11-164H13.1, RP11-160H22.5, EYA3, BFSP2, SNX29P2, RP11-558F24.4, RP11-1070N10.3, CCDC144A, TCL1A, ACY3, RP11-960L18.1, NEIL1, WDR66, P2RX5, STAG3, GPR114, RPRD1B, HCAR1, SYVN1, IL21R, SMIM14, KLHL6, SEL1L3, TPD52, TERF2, TRIM59, TIGD1, RP4-739H11.4, BCAS4, LIMD2, LSM10, STAP1, MTMR14, CD180, RP11-16E12.2, GGA2, TNKS2-AS1, STX7, HMCES, DCAF12, MBD4, FBXO16, CD79B, FCRLA, STRBP, IQCB1, NGLY1, PARN, ST6GAL1, FCRL3, DEF8, TCEA1, TMEM156, CD53, RRAS2, NCF1, ZNF296, TOR3A, CD72, RFC1, EPS15, CYB561A3, LYPLAL1
B.Plasma
IGLC3, IGLC7, FGF23, IGLV6-57, IGLV1-40, IGLV2-11, IGLV2-23, IGLV1-51, RP11-492E3.2, PSAT1, IGLV4-69, IGLV3-25, IGLV7-43, LINC00582, IGLV3-10, IGLV8-61, DNAAF1, IGLV10-54, IGLV5-45, IGLV4-60, IGLV3-16, CDH15, SLC22A31, IGLV1-50, RP11-1084E5.1, IGKV1OR2-108, ZC2HC1B, GH1, IGLV3-12, AF127936.3, LINC00525, UGT3A2, IGHV3OR16-9, NLRP11, RNF148, RP11-428K3.1

TABLE 5-continued

Immune Healthy specific markers for indicated cell types
I.Immune
AC004791.2, AC013264.2, AC104820.2, APOC2, ASGR2, ATP6V0D2, BTLA, CA10, CASS4, CATSPER1, CCL18, CCL3L1, CCL4L1, CCL4L2, CD180, CD1E, CD207, CD226, CD28, CD300C, CD300LB, CLEC4E, CLEC4F, CLEC9A, CLECL1, CRHBP, CTLA4, CXCR5, ELAVL4, FAM92B, FCER2, FCGR1A, FCGR1B, FCGR3A, FCN1, FCRL1, FCRL6, FCRLA, FLT3, FPR1, GAPT, GCSAM, GPR34, GPR84, GPRC5D, ICOS, IGHD, IL17A, IL18RAP, IL21R, IL22, ITGAX, JAKMIP1, KIR2DL3, KIR3DL2, KLHDC7B, KRT81, KRT86, LAMP3, LILRA2, LILRA3, LILRA5, LILRB2, LILRB5, LRRC25, LTA, MSR1, NLRC4, NLRP7, OSTN-AS1, P2RY13, PGLYRP2, PIK3R6, PKD2L1, RP11-18H21.1, RP11-291B21.2, RP11-327F22.2, RP11-354E11.2, RP11-365O16.3, RP11-367G6.3, RP11-542M13.3, RP11-556E13.1, RP5-1091N2.9, RP5-899E9.1, S100Z, SIGLEC1, SIGLEC12, SIRPB1, SNAI3, TBX21, TFEC, TIFAB, TNFRSF9, TNFSF8, TRAV4, UBASH3A, ZNF683, RUNX3, CD1C, FASLG, CD160, GZMK, TRDC, CD3D, XCL1, CTSG, CD3E, AC092580.4, TRGC1, TRBC2, KLRB1, TIGIT, CD300A, TPSAB1, IFNG, CD8A, GZMA, SNX20, SH2D1A, CST7, CD52, CCL4, CD247, XCL2, CD2, CCL5, DOK2, GZMB, TMIGD2, GZMM, TRAF3IP3, GNLY, NKG7, SIRPG, THEMIS, CD3G, CD7, ADORA3, MPEG1, KRT1, HCST, PLD4, LTB, TRGC2, IL2RB, SIT1, MAP4K1, RGL4, P2RY10, PTPRC, NCKAP1L, GRAP2, CSF2, CD37, CXCR6, S100A9, GPR18, SLA2, TNFSF14, CTSW, AMICA1, PRF1, ARHGAP9, GPR171, CD86, TBC1D10C, MARCH 1, SAMSN1, GPR183, LCP1, BCL2A1, SDS, RASGRP1, CD5, CMA1, TNFAIP8L2, HDC, LINC00402, FCER1A, IL1B, RP11-455F5.5, STAT4, CD244, IL7R, CD19, ARHGAP30, PCED1B-AS1, KLRD1, TRAT1, PTPN22, KLRC1, GZMH, AC109826.1, CCR5, LINC00996, PARVG, MS4A6A, TNIP3, CD48, NCR3, ITGAM, VPREB3, RNASE6, LCK, FPR3, GNA15, LY86, SASH3, CRTAM, MS4A4A, C1QB, LAPTM5, NCF1, WAS, HOPX, IGHV1OR15-1, CD6, FAM159A, APOBEC3H, CACNA2D3, IGSF6, IKZF1, LY9, CYTIP, MIR142, CSF1R, EVI2A, DUSP2, BFSP2, HLA-DOB, PTPRCAP, PTPN7, SPI1, RHOH, TLR10, CSF3R, TNF, FCER1G, BTK, MYO1F, AC020571.3, CHRM3-AS2, GPR65, CD53, CXCR3, C1orf162, SPN, ITGAL, TXK, CCL3, ADAM8, TCL1A, AIF1, CD96, KLRC2, PDCD1, CPA3, MYO1G, IL10RA, HAVCR2, LILRB4, MMP12, CD40LG, SCIMP, CSF2RA, EVI2B, TREM2, LINC00892, TREM1, DOCK2, EMB, PILRA, CYBB, RGS1, MS4A7, CHI3L2, RP3-522D1.1, C1QC, IL8, KCNA3, SLFN12L, CARD11, CD69, PYHIN1, ITK, LAT2, CORO1A, DNASE1L3, ITGB2, GPR132, KLRG1, RP11-190C22.9, LAIR1, FGD3, SCML4, BLK, SLC18A2, LRRN3, CD8B, FAM26F, PLA2G7, CLEC10A, CD209, C5AR1, SLAMF8, SP140, TESPA1, CD200R1, PRAM1, CXorf21, VSIG4, SKAP1, LPXN, C1orf186, SYTL3, CD163, IFI30, WDFY4, SH2D2A, RP6-91H8.3, RP11-94L15.2, LST1, CD79A, CD27, HLA-DQB2, LYZ, DENND1C, CD70, RP11-222K16.2, CYTH4, RASSF5, CLEC2D, SH2D1B, CLEC4A, C1QA, MS4A1, CCR2, OSCAR, C3AR1, CD101, BATF, ACAP1, CD33, IGLC2, RP3-477O4.14, CD38, CSTA, PIM2, IL4I1, OSM, MMP9, SLAMF7, NCF2, RP11-489E7.4, IFNG-AS1, ITGB7, IL1RN, ZAP70, ITGB2-AS1, STK17A, DUSP4, RP11-693J15.5, FAIM3, FAM179A, CD83, TMEM156, IGLL5, DAPP1, IGFLR1, SLAMF1, CXorf65, RAC2, BIN2, F13A1, C1orf61, OLR1, SAMD3, IGKC, KYNU, AL928768.3, ZNF331, TNNI2, TLR7, OXNAD1, IGLC7, IL16, TAGAP, SLAMF6, WNT10A, P2RY6, NLRP3, KCNAB2, KMO, APBB1IP, CCR1, CD72, RASAL3, EVL, LAT, LIMD2, CREM, POU2F2, ADPGK-AS1, UPK3A, SLC7A5, TNFAIP3, TLR2, HLA-DQA1, SELL, HCLS1, IL23A, AC017104.6, TRAC, GHRL, IRF4, RELT, SEPT1, HLA-DQB1, FAM46C, AC006129.4, TMC8, AP001058.3, SNX10, PLEK, IGHG1, PNOC, LINC00528, CD84, STAP1, IGJ, FGD2, FAM49B, CTA-384D8.34, HENMT1, RGS18, PARP15, MNDA, PHACTR1, P2RY11, EBI3, MZB1, YPEL5, FMNL1, STK4, AOAH, COTL1, MMP25, RP11-324I22.3, SPNS3, IL2RA, PKHD1L1, GATA3, DUSP10, TNFAIP8, SLA, MYBL1, RAB33A, EAF2, FGF23, P2RX5, CRLF3, HLA-DPB1, SEPT6, ARL4C, GPR114, UTS2, RP11-70C1.1, IGLL1, DENND2D, LCP2, RGS19, ARRB2, CLIC3, TYROBP, AIM2, RORA, TC2N, RP11-539L10.2, PDE4B, RP11-347P5.1, IL2RG, PRMT10, PIK3CD, TNFRSF18, SIGLEC10, IL1RAPL1, NCF4, GLIPR1, SMAP2, RP11-863P13.3, CKLF, IGHG2, GALR2, TRAF1, HLA-DRA, ICAM3, PRR7, PRKCB, MAP3K8, PIK3AP1
I.Lymphoid
AC013264.2, AC104820.2, CA10, CR2, CXCR5, DTHD1, GPRC5D, IGHD, IGLV5-48, IL22, JAKMIP1, KIR3DL2, KRT81, KRT86, LINC00861, NCR2, NLRP7, OSTN-AS1, RP11-18H21.1, RP11-291B21.2, RP11-403A21.2, RP11-664D1.1, TBX21, TRAV4, ZNF683, CD160, XCL1, XCL2, GZMK, AC092580.4, TIGIT, GZMA, TRGC1, GNLY, CD3D, IFNG, CD3E, CD2, CD7, CCL5, IL2RB, TRGC2, CD3G, RASGRP1, TRDC, CD247, CD8A, IL18RAP, CXCR6, KLRB1, GZMM, TRBC2, FCRLA, PRF1, KLRC1, VPREB3, ICOS, TRAT1, KLRD1, SIRPG, GZMH, LCK, LINC00402, SLA2, IL17A, HOPX, IGHV1OR15-1, KLRC2, SIT1, FASLG, RGL4, BLK, CHRM3-AS2, CD96, TMIGD2, CD40LG, LRRN3, CD6, PYHIN1, NKG7, SH2D1A, CHI3L2, RP11-542M13.3, TXK, IL7R, SCML4, TCL1A, UBASH3A, IGLL5, THEMIS, FCRL6, SH2D1B, RP11-222K16.2, CD8B, MS4A1, GZMB, STAT4, CD79A, CD27, SLFN12L, SH2D2A, CD70, TNFSF14, IGHG3, IGLC2, CLEC2D, AC017104.6, CD19, IGLL1, FAM179A, RP11-94L15.2, FAM92B, FAM159A, SLAMF1, ZAP70, CD244, RP11-553L6.2, RP11-489E7.4, C1orf61, CD5, PGLYRP2, SLAMF6, PTPRCAP, RP11-284N8.3, IFNG-AS1, AL928768.3, CD28, IGJ, IGKC, SMKR1, GPR171, IGHG1, SAMD3, TRAC, EVL, GAT A3, IL23R, LTA, IGHA2, MZB1, AP001058.3, BCL11B, P2RX5, IGHA1, ITK, PARP15, APOBEC3H, CARD11, TBC1D10C, PCED1B-AS1, AC069363.1, CCR7, LINC00426, RP11-539L10.2, STK17A, TC2N, TPRG1, RP11-279F6.3, CLIC3, CXorf65, IGLC7, AC104699.1, SEPT1, TNFRSF18, AC078883.3, TNFRSF13B, IL2RG, IGHG2, POU2AF1, PLCH2, RORA, MYBL1, CD52, ACAP1, CTLA4, FAM46C, GPR18, DERL3, CACNA1C-AS2, PTPN4, RP11-693J15.5, CCDC65, DEN D2D, ESR2, LTB, TNFRSF17, IGLV2-14, S1PR4, FGF23, NCR3, MIXL1, SPOCK2, OXNAD1, CCR5, AC096579.7, NUGGC, WT1-AS, PKHD1L1, PCED1B, RCAN3, CTSW, KLHDC7B, PARP8, ANKRD44-IT1, FKBP11, SYTL1, TAGAP, PPP1R18, IGLV5-45, ZBP1, EMB, TNFRSF13C, LINC00649, PRKCQ-AS1, FAIM3, RP11-277L2.4, AAK1, P2RY11, GRK6, SPINK2, CYTIP, SASH3, ORMDL3, FYN, LEPROTL1, PTPN22
M.CD69neg__Mast
NTRK1, IL9R, ADAM22, CATSPER1, FAM21B, ABCB8, NSMCE1, AJ271736.10, ARHGEF6, FECH, ACLY, NCOA4, UBA7, BRAP, KRT1, FAM212A, MAML1, SLC43A3, SAMSN1, LPCAT2, GMPR, SPACA3, LTC4S, HPGDS, HSD17B12

TABLE 5-continued

Immune Healthy specific markers for indicated cell types
M.CD69pos_Mast
ADCYAP1, CALB2, RP11-501J20.5, TPSD1, IL13, RP11-557H15.4, IL1RL1, RP4-794H19.2, ARL5B-AS1, RP11-705O1.8, AF213884.2, IL1RAPL1, DKFZP434E1119, IL5RA, ENPP3, PPP1R15A, NFKBIZ, FER, AC020571.3, HDC, FAM46A, EGR3, ANXA1
M.Cycling
SYCE2, ZMYND10, FAM72C, CDC25B, HTR7, SIGLEC15, CDK1, TUBA1B, KPNA2, HJURP, COQ2, FAM64A, H2AFZ, TPK1, RAD51AP1, RP11-556E13.1, TROAP
M.DCs
BAI1, CD1B, CTD-2514K5.2, RFPL4A, RP11-117D22.2, RP11-667K14.3, RUFY4, XCR1, SFTPD, TMEM170B, FLT3, UPK3A, SLAMF9, FAM230A, CLEC4F, NAMPTL, CLEC9A, CD207, RYR1, TBX19, CD1E, CTD-2619J13.17, CX3CR1, SERPINF2, INHBA-AS1, CD1C, CPVL, CTD-2319I12.1, FAM46B, RP11-248J18.2, HLA-DQB2, MYCL, LEKR1, NME8, CD1D
M.Macrophages
AC005082.12, LILRA6, RN7SL138P, GRIN2D, AZU1, KCNC3, SIGLEC11, SLC7A8, FABP3, PLA2G2D, SLC40A1, RP3-414A15.10, FOLR2, CRHBP, TREM2, OTOA, HSD17B14, RP11-848P1.2, RNASE1
M.Mast
ADCYAP1, AMHR2, CALB2, GATA1, GCSAML, MS4A2, NTRK1, RP11-501J20.5, TPSD1, XXbac-BPG13B8.10, IL1RAPL1, ST8SIA6, C1orf186, TPSAB1, RP11-354E11.2, IL13, RP11-557H15.4, SLC45A3, HDC, SLC18A2, CMA1, AC004791.2, SIGLEC8, SVOPL, IL1RL1, CPA3, CTSG, MAOB, KRT1, VWA5A, GATA2, RP4-794H19.2, CTD-3203P2.2, RAB27B, LTC4S, ATP6V0A2, ARL5B-AS1, SPACA3, RP11-705O1.8, HS3ST1, AF213884.2, ADRB2, DKFZP434E1119, LEO1, MITF, IL5RA, CTNNBL1, SMYD3, ENPP3, TIAM2, PPP1R15A, VWC2, NFKBIZ, FER, AC020571.3, GMPR, CAPG, TESPA1, BTK, FAM46A, UBXN10, PLIN2, RP11-169D4.2, CRBN, ANXA1, ALS2, BACE2, LMO4, GLUL, RP11-443B7.1
M.Monocytes
FTL, HLA-DRA, HLA-DRB1, HLA-DPB1, CST3, SAT1, HLA-DPA1, GPX1, AIF1, HLA-DQA1, LYZ, HLA-DQB1, HLA-DRB5, RNASET2, C1QA, HLA-DMB, TYMP, MS4A6A, C1QC, CTSS, DNASE1L3, C1QB, CTSB, SPI1, CTSZ, CPVL, IGSF6, PLAUR, MS4A7, FAM26F, HLA-DQA2, RNASE6, HLA-DQB2, LGMN, IL1B, CLEC10A, FUCA1, IFI30, BID, LGALS2, MPEG1, SLC40A1, VSIG4, STAB1, SDS, MS4A4A, CD68, FCGR2A, MNDA, IL8, PLA2G7, CSF1R, RB1, GM2A, CECR1, CD86, ADORA3, HBEGF, P2RY6, ADAP2, FOLR2, CSF2RA, MMP12, C5AR1, SLAMF8, HLA-DOA, AP1B1, CFP, SLC31A2, G0S2, VMO1, PILRA, S100A9, CD209, TTYH3, NAIP, LILRB4, CLEC7A, CD163, FPR3, TREM2, IL18BP, NCF2, CLEC4A, CLEC9A, ATP6V0D2, NUP214, OTOA, RAB42, LILRB5, CXCL3, LRRC25, CMKLR1, EBI3, P2RY13, FCGR1A, SLC7A8, CACNA2D3, LILRB2, CD1E, EMILIN2, SIGLEC1, RN7SL368P, CSF3R, BATF3, MYCL, DAPK1, TRPM2, CSTA, IL1RN, CRHBP, CD300C, RGS18, OLR1, RP11-426C22.5, TREM1, LY96, RP11-365O16.3, RP3-522D1.1, TIFAB, RP11-1143G9.4, PKD2L1, CCL18, TLR2, HCAR2, ITGAX, MSR1, ASGR2, F13A1, CLEC4G, FLT3, FCN1, RP11-290F20.3, OSCAR, LILRA2, GHRL, CD207, HCAR3, RP3-399L15.3, APOC2, RP5-899E9.1, RP11-863P13.3, CCL3L3, CLEC4E, LILRA3, RP11-556E13.1, FCGR1B, CCDC170, GPR84, RP11-760N9.1, CD300LB, ELAVL4, S100A8, GALR2, CLEC4F, FPR1, NLRC4, RP11-472N13.3, LILRA5, C19orf59, GSDMA, INHBA, GRIP1, RP11-426L16.8, SFTPD, RP11-190C22.9, ALOX15B, MRC1L1, TLR8, XCR1, UPK3A, SYCE2, RP11-680A11.5, CD1B, LILRA6, MS4A14, SLAMF9, CX3CR1, IL27, KCNK13, RNASE2, RP11-701P16.5, GRIN2D, RP11-848P1.2, AC005082.12, RYR1
M.Myeloid
AC004791.2, AC011899.9, AMHR2, ASGR2, ATP6V0D2, CALB2, CD300LB, CLEC4E, CLEC4F, ELAVL4, FCGRIA, FCGRIB, FCN1, FPR1, GATA1, GCSAML, GPR84, INHBA, LILRA3, LILRA5, LILRB2, LILRB5, MS4A2, NLRC4, RP11-365016.3, RP11-472N13.3, RP11-556E13.1, RP11-760N9.1, RP5-899E9.1, S100A8, SIGLEC12, SIGLEC8, TIFAB, XXbac-BPG13B8.10, CTSG, CLEC9A, CMA1, SLC18A2, P2RY13, RP11-557H15.4, CDIE, SDS, MSR1, FPR3, MS4A4A, MS4A6A, KRT1, CSF1R, ADORA3, IGSF6, S100A9, MMP12, IL1B, TREM2, C1QB, FCER1A, C1QC, CD209, CACNA2D3, PLA2G7, CD163, RP3-522D1.1, TPSAB1, AIF1, CSF3R, CD207, DNASE1L3, PKD2L1, C1QA, C5AR1, SIGLEC1, IL1RAPL1, HDC, F13A1, LILRB4, VSIG4, IL8, CLEC10A, MS4A7, LYZ, CSTA, C1orf186, CCL18, SVOPL, TREM1, SFTPD, OSCAR, RP11-190C22.9, TLR2, CSF2RA, IL1RN, CRHBP, RP11-354E11.2, IL13, CPA3, OLR1, P2RY6, SLC45A3, APOC2, LILRA2, PILRA, RAB42, CFP, RASGRP4, FLT3, MNDA, CPVL, MPEG1, IFI30, GSDMA, STAB1, RP11-426L16.8, LRRC25, CCL3L3, CD68, RP11-76E17.3, GALR2, MAOB, LINC00884, CD300C, SLAMF8, IL10RB-AS1, NCF2, RP11-1143G9.4, FAM26F, HCAR3, VWA5A, FTL, HS3ST1, FUCA1, GM2A, SLC40A1, RNASE6, HLA-DPB1, FOLR2, CLEC4A, GLUL, GRIP1, CD86, IL18BP, RP11-426C22.5, ALOX15B, HLA-DRB1, PIK3R6, RP11-42110.1, RGS18, LY96, FCGR2A, GATA2, RP11-70C1.1, GHRL, CST3, CASS4, TBXAS1, HLA-DPA1, CTD-3203P2.2, CXCL16, C19orf59, TNFAIP8L2, TNNI2, HLA-DQA1, HLA-DRB5, PLAUR, RNU1-60P, RAB27B, TTYH3, VMO1, ATP6V0A2, CD33, NUP214, TRPM2, RP11-863P13.3, DAPK1, CTSS, CTSB, SGK1, ARL5B-AS1, HCAR2, CMKLR1, OTOA, RENBP, ATP6V1F, NCF4
M.Neutrophils
S100A8, RP11-701P16.5, S100A9, FCN1, EREG, NLRP3, CSTA, APOBEC3A, G0S2, TLR2, C5AR1, LILRB2, OLR1, FCGR1A, EMILIN2
M.Tissue_DCs
CDIB, CTD-2514K5.2, RFPL4A, RP11-117D22.2, RP11-667K14.3, SFTPD, TMEM170B, SLAMF9, FAM230A, CLEC4F, NAMPTL, CD207, RYR1, TBX19, CD1E, CTD-2619J13.17, CX3CR1, INHBA-AS1, CD1C, GHRL, RP11-248J18.2, LEKR1, NME8, TMEM52B, CD1D, MS4A14, PLD4, FCER1A, CACNA2D3

TABLE 5-continued

Immune Healthy specific markers for indicated cell types
M.Tolerogenic_DCs
XCR1, CLEC9A, CTD-2319I12.1, CLCN4, FBXO27, DGAT2, IDO1, BATF3, WDFY4, FLT3, SERPINF2, FKBP1B, DSCAML1, CPNE3, SNX3, PPM1J, RP11-661A12.7, CPVL, KIAA1598, KIAA0226L, C1orf54, FNIP2, C8orf47, TNNI2, TACSTD2, TOMM34, UCP3, VAC14 T.Activated_CD4_loFos
AC006369.2 T.CD4
CTLA4, LAIR2, RP11-664D1.1, ATG9B, CD40LG, IL17A T.CD8
CD8B, RP11-291B21.2, DRAXIN, CD8A T.CD8_IELs
TRBV20-1, RP11-535A5.1, PAGE5, KLRC2, NCR2, TRGC1, TRGC2, DRAXIN T.CD8_LP
RP11-291B21.2, CD8B T.CXCR6_Th17
RP11-85K15.2, IL12RB1, CCL20, SLAMF1, KLRB1, ZFYVE28 T.Cycling_T
ABCD2, CCT6B, C11orf82, C16orf59, A1BG, C5orf17, ZNF682 T.ILCs
LINC00299, TNFSF11, IL23R, SPINK2, SLC4A10, SAMD10, OTUD5, TRGV9, RP11-425D10.10, IL4I1, LINC00176, ALDOC, FXYD7, CASP3, AREG, KRT86, HINT3, CSF2, PRMT10, LTA4H, FAM167A, ZNF385C, PDZK1, MED30, ZMYM2 T.MT
FSCN3, BZRAP1, AP000350.4, AC132872.2 T.Memory_CD4
RP11-664D1.1 T.NK
PADI4, SPTSSB, KLRF1, RP11-401F2.3, BCO2, SH2D1B, EOMES, XCL1, XCL2, KLRC1, IL2RB, CLIC3, FGR, RP11-222K16.2, AC069363.1, NKG7, GZMB, KLRD1, AC017104.6, PRF1, GEMIN5, EIF3G, FCGR3A, CMC1, GNLY, B3GNT7, CHST12, APOBEC3G T.PD1_CD4
RP5-1028K7.2, NMB, CD200, KIF2A, PDCD1, MPP7, RP11-455F5.5, PVALB, CDK5R1, PRKRIR T.Tcells
CA10, CPA5, FOXP3, RP11-664D1.1, TRAV4, RP11-291B21.2, IL2, IL17A, LINC00402, BCL11B, CD8B, CD3G, CD3D, CTLA4, AC104820.2, CD5, RP11-279F6.3, CD6, CACNA1C-AS2, CD28, CCDC65, TRAT1, TRGC2, SIRPG, GPR171, LINC00649, CD8A, CD3E, FAM115C, TRAC, ACSL6, TNIP3 T.Tregs
RP11-316P17.2, LAIR2, MCF2L2, ANKS1B, FANK1, FOXP3, RP11-580116.2, DUSP16, TRAV8-2, TNFRSF9, IL10, BATF, CTLA4, RP11-382J12.1

TABLE 6

Immune UC specific markers for indicated cell types
B.Bcells
AC007381.3, AC007880.1, AC073072.5, AC104699.1, AL109761.5, AP005530.2, BEND4, C7orf72, CCL25, CHIA, CHIT1, COL19A1, COL24A1, CTB-43E15.4, FAM92B, GPRC5D, HCFC1-AS1, IGHE, IGKV1D-43, IGLV5-48, LINC00494, LINC00582, LINC00643, LRRC4, MYF6, OVOL3, RP1-148H17.1, RP11-138I18.2, RP11-203B7.2, RP11-297B17.3, RP11-301G19.1, RP11-301L8.2, RP11-390F4.6, RP11-428G5.5, RP11-493L12.3, RP11-511B23.1, RP11-624C23.1, RP11-625L16.3, RP11-689B22.2, TREML2, UBE2QL1, UGT3A2, UTS2B, hsa-mir-5195, hsa-mir-5571, HTR3A, IGLL5, IGLC3, CR2, IGLC2, SERPINA9, MED12L, MS4A1, CLEC17A, AC104024.1, AC096579.13, IGHG2, RN7SL17P, IGHA2, PAX5, IGLC7, CD19, IGKC, AL928768.3, AC096579.7, IGHA1, TCL1A, FCRLA, DERL3, IGHD, IGLL1, VPREB3, DKK1, MIXL1, IGHG1, MZB1, WT1-AS, IGHG4, IGLV3-16, FCRL5, IGLV6-57, LINC00525, RP5-887A10.1, BLK, FCER2, RP11-159H10.3, PKHD1L1, TNFRSF17, IGJ, FGF23, NLRP7, RP11-290F5.1, AC009473.1, TNFRSF13C, OSTN-AS1, CD79A, MRVI1-AS1, AF127936.3, FAM129C, IGLV1-40, IGLV2-11, MYL2, RP11-693J15.5, CD79B, IGLV10-54, WDR66, CTD-2306M10.1, FCRL1, IGLV3-1, IGKV2D-30, RP11-485G7.5, AC096559.1, IGHV1-24, KIAA0125, RP11-1070N10.3, AICDA, CD72, C7orf10, BANK1, RP11-492E3.2, DNAAF1, SNX29P2, RP11-480C16.1, EAF2, CLECL1, PNMA6C, IGLV3-25, HVCN1, CRYBA4, BLNK, FCRL4, CD180, AC023590.1,

TABLE 6-continued

Immune UC specific markers for indicated cell types
MEF2BNB-MEF2B , IGKV1-6, SPAG4, CCDC144A, AC007386.2, ZCCHC7, IGKV2-30, UBE2J1, AMPD1, NEIL1, POU2AF1, FCRL2, HBD, SSR4, RP11-960L18.1, IGKV5-2, RP11-16E12.2, XBP1, IGKV1-12, TNFRSF13B, POU2F2, C12orf77, CTC-378H22.1, CD22, AP001058.3, ESR2 B.Cycling
C7orf72, GLT1D1, RP11-301G19.1, STK4-AS1, ZNF730, BTN1A1, CTD-2561J22.5, AKAP2, RP13-494C23.1, RP11-553K8.2, CTC-332L22.1, KCNQ5-IT1, KLLN, RP11-286H14.6, SNORA70, CENPI, STOX1, C6orf99, RP13-20L14.6, RP11-449H11.1, IGHE, WDR76, C11orf65 B.FO
AC002480.5, CCDC78, RP11-444D3.1, COL19A1, RP11-624C23.1, RP5-887A10.1, AC073072.5, RP11-445F6.2, OSTN-AS1, WASIR2, UTS2B, AC007880.1, FCRL4, TNFRSF13B, CLECL1, RP3-455J7.4 B.GC
RP11-567J20.3, RN7SL17P, LRRC4, SERPINA9, RP11-138I18.2, RP11-203B7.2, HRK, NEIL1, C9orf66, PUS10, NPAS1, AC096559.1, RP11-72I8.1, CD22, HTR3A, MIXL1, CD180, C7orf10, CCDC144A, SEMA4A, TRAF4, CD79B, USP6NL, KLHL14, RP11-960L18.1, RP11-542M13.3, IGF2BP3, IFNG-AS1, P2RX5, IL4R, ADORA2A-AS1, RP11-511B23.2, BFSP2, GPR18, RP11-307E17.8, AC023590.1, SMIM14, CYB561A3, SNX29P2, ESR2, GPR114, BCL11A, RP11-164H13.1, BCL7A, AP003419.16, CR2, CNR2, RP11-413H22.2, SYVN1, SYPL1, PLEKHF2, KMO, AMFR, RANBP2, ZNF581, RFTN1, SLC38A9, NCOA3, WDR66, BLNK, HLA-DOB, CD53, FCRLA, FAM105B, VNN2, CD40, AC145110.1, KIAA0922, RP11-158I9.5, ICOSLG, PXK, XKR6, RN7SL172P, VCPKMT, ITSN2, PKHD1L1, MS4A1, TMEM206, CPNE5, LIMD2, RP11-248J18.3, CD72, RAB30, RASGRP3, SYNGR2, MTMR14, GGA2, RNGTT, MGAT3, TMED8, SNX8, MOAP1 B.Plasma
DCC, GH1, IGHJ2, IGKV1D-43, MYBPC2, MYF6, PRRG3, RP11-301L8.2, RP11-625L16.3, RP11-689B22.2, SCARNA16, TNN, TPTE2, TRIM55, UBE2QL1, UGT3A2, hsa-mir-5571, IGLV4-60, IGLV3-16, IGHG2, DKK1, IGLV1-40, AF127936.3, IGKV5-2, IGLV2-8, IGLV3-1, AC096579.7, IGLV6-57, IGHV1-24, FAM92B, IGHA2, DNAAF1, IGLL1, CTB-43E15.4, IGLV10-54, IGKV3-11, IGKV2D-30, AMPD1, IGHG3, PNMA6C, IGLC2, IGHG1, IGKV3-20, IGLV7-43, IGLV7-46, IGKV2-30, IGKV6-21, SPAG4, AL109761.5, IGLV9-49, IGLV3-25, IGLV2-11, IGKV1D-13, IGHG4, IGKV4-1, RP11-390F4.6, RP11-290F5.1, IGLC7, DERL3, SLC22A31, IGHA1, IGLV5-48, GPRC5D, IGKC, RP11-492E3.2, SSR4, IGKV1-6, JSRP1, IGLC3, IGJ, IGKV2-24, IGLL5, XBP1, GUSBP11, LINC00582, RP11-554E23.4, FKBP11, IGHM, TNFRSF17, CHAC1, WNT10A, LINC00525, HERPUD1, LMTK3, IGKV3D-15, IGLV1-36, SEC11C, IGLV2-18, AC093818.1, IGKV1D-39, PDK1 I.Immune
ABCD2, AC004791.2, AC011899.9, AC104699.1, AC104820.2, AC109826.1, AMPD1, AQP9, C11orf21, C19orf59, C20orf201, CA10, CASS4, CCL3L1, CCL3L3, CCL4L1, CCL4L2, CCR2, CCR5, CD1A, CD1B, CD226, CD300C, CD300E, CD300LB, CD80, CEACAM4, CLEC4E, CLEC4F, CLEC5A, CLEC9A, CMA1, CR1, CR2, CRYBB1, CSF3R, CTB-138E5.1, CTC-378H22.1, CTD-2337J16.1, DPEP3, EMR3, F5, FAM92B, FCGR1A, FCGR1B, FCN1, FCRL1, FLT3, FOXP3, FPR2, GPR141, HBD, HK3, IGHV1OR15-1, IKZF3, IL18RAP, IL22RA2, IL26, IL2RA, JAKMIP1, KCNK13, KRT1, LILRA1, LILRA2, LILRA3, LILRA4, LILRA5, LILRA6, LILRB2, LINC00402, LINC00582, LRRN3, MARCO, MEFV, MS4A14, MSR1, NLRC4, OSTN-AS1, P2RY13, PGLYRP2, PIK3R6, PKD2L1, PTCRA, PVALB, RASGRP4, RETN, RN7SL138P, RNASE2, RP11-1381I8.2, RP11-169D4.2, RP11-265P11.2, RP11-291B21.2, RP11-297B17.3, RP11-316P17.2, RP11-354E11.2, RP11-365O16.3, RP11-367G6.3, RP11-403A21.2, RP11-472N13.3, RP11-542M13.3, RP11-556E13.1, RP11-701P16.5, RP11-737O24.5, RP11-76E17.3, RP11-798K3.3, RP11-8L8.2, RP11-960L18.1, RP5-1091N2.9, RP5-899E9.1, RYR1, SIGLEC1, SIGLEC12, SIGLEC14, SIRPB1, SUCNR1, TCHH, TFEC, TIFAB, TLR8, TNFRSF13C, TNFSF8, TRAV4, TREM2, ZFP57, ZNF831, PLD4, FPR1, CD1E, FASLG, OSM, RUNX3, CD1C, KLRB1, GCSAM, GZMH, ITGAX, CD86, LINC00892, C3AR1, CD207, CHRM3-AS2, IL17A, DOCK2, CTLA4, BTLA, CLECL1, HCST, NKG7, NLRP3, FCER1G, CXCR6, CD3D, RP5-1028K7.2, CD247, CD2, SIRPG, GPR34, CCL5, CD52, HDC, AIF1, CD28, GZMA, XCL1, HTR3A, TRDC, FOLR2, SDS, LRRC25, SIT1, SPI1, SH2D1A, UBASH3A, MS4A6A, CD3E, DOK2, CXCR5, THEMIS, C1QA, GPR18, LY9, FCER2, RGL4, AC013264.2, CCL3, MPEG1, STAP1, GZMM, CSF1R, PRF1, TIGIT, CST7, CD209, C1QC, TRGC1, SASH3, CCL4, IFNG, TRGC2, CD3G, CLEC10A, RP11-664D1.1, CTSG, NUGGC, AC092580.4, C1QB, P2RX5, S100A8, LCK, SAMSN1, CTA-250D10.23, TRAF3IP3, LST1, TIMD4, ZBTB32, RP11-164H13.1, GTSF1, ITGB2, PTPRC, IL1B, APOBEC3H, CD69, TXK, RP11-190C22.9, PLA2G7, GNLY, AMICA1, HAVCR2, ATP6V0D2, IKZF1, PTPRCAP, MMP12, MS4A7, XCL2, CD53, RP11-553L6.2, GZMK, C1orf162, TNFAIP8L2, TBC1D10C, IGSF6, LTB, IL22, FXYD7, CD40LG, IGHD, LILRB5, WAS, LCP1, NCR3, TPSAB1, LILRB4, MS4A4A, IGHG2, CYTIP, TRAT1, CD6, CD5, EVI2A, BTK, LAPTM5, TMIGD2, CACNA2D3, TRBC2, IGLL5, CD79A, RGS1, IGLC2, MS4A1, KMO, CYBB, IGHG3, FCER1A, GZMB, CD163, LY86, FAM26F, CD7, FPR3, AC079767.4, PCED1B-AS1, SNX20, CD180, ZAP70, CD300A, SP140, EVI2B, ITGB7, EBI3, NCF2, IFI30, MAP4K1, IGLC3, ITGB2-AS1, CSTA, FCGR3A, GPR183, OLR1, DENND1C, CSF2RA, CCL22, TNF, CD244, STAT4, LAIR1, GPR171, PDCD1, DNASE1L3, NCKAP1L, AC006129.4, NOD2, SERPINA9, RP11-455F5.5, RNASE6, CP A3, BCL2A1, TCL1A, PYHIN1, DUSP2, CD19, C12orf42, IL2RB, MIXL1, LTA, PARVG, CRTAM, CCL18, LAX1, CXorf21, FAIM3, NCF1, VSIG4, GAPT, GRAP2, SLC18A2, FGD2, BFSP2, CD160, TLR10, CD37, MIR142, PRKCB, RP11-693J15.5, RHOH, BLK, TNNI2, TYROBP, IGHG4, PAX5, LINC00861, CX3CR1, CLEC4A, CD38, FAM129C, AC020571.3, C16orf54, CORO1A, IGHG1, ITK, IFNG-AS1, GPR65, SPN, DNAJC5B, LAT2, P2RY10, F13A1, MYO1F, AGAP2, CCR7, TNFSF14, ADORA3, TMEM156, KLRD1, RIC3, BATF, CD8A, IL10RA, SLA2, CD48, ARHGAP30, IL10, SELPLG, ADAM8, RP11-637A17.2, CD84, SNAI3, AL928768.3, CD101, CATSPER1, SKAP1, IL16, HLA-DQA1, TBX21, HLA-DOB, CD96, RASGRP1, SLAMF6, CXCR3, CD22, SH2D2A, CTA-384D8.34, CD70, CD72, ARHGAP9, AIM2, PLEK, TESPA1, FCRL3, RP11-134P9.1, CYTH4, PTPN7, PTPN22, P0U2AF1, AC104024.1, IGKC, SLA, GPR132, MYO1G, STAC3, C1orf186, MZB1, RP11-493L12.4, RP11-284N8.3, PNOC, SLAMF7, FERMT3, PHACTR1, KLHDC7B, AP000783.1, SELL, UTS2, IL12RB1, CD8B, RASSF5, LINC00996, ITGAL, NCF4, AC096579.7, RASGRF1, CLEC2D, S100A9, IGHA2, GHRL, SERPINB9, IGLC7, SCML4, IGHM, CLEC12A, IGJ, AC096579.13, LYZ, HCLS1, TNFRSF18, SIGLEC10, RAC2, TAGAP, BIN2, LPXN, RASAL3,

TABLE 6-continued

Immune UC specific markers for indicated cell types
HCAR3, MYBL1, CD27, SLAMF8, ICOS, RP3-477O4.14, RP11-1143G9.4, SIGLEC7, GATA3, CARD11, CD200R1, PCED1B, CFP, BZRAP1-AS1, CTD-2514K5.2, KLRC2, FGD3, WNT10A, FCRL5, BCL11B, MARCH1, HLA-DPB1, SEPT1, IGLV6-57, MRC1L1, KBTBD8, RP11-158G18.1, EPHA1-AS1, KLRG1, GNA15, ACAP1, TNFRSF13B, FAM110A, HLA-DQB1, TRAC, AC104653.1, HAMP, HLA-DMB, TNFRSF17, BANK1, ATP8B4 I.Lymphoid
AC002331.1, AC006369.2, AC104699.1, AL109761.5, AMPD1, C15orf53, C4orf26, CA10, CCL25, CCR6, DTHD1, F5, FAM179A, FAM92B, FCRL1, FOXP3, GPRC5D, IGHE, IGLV5-48, IL17F, IL2, IL26, JAKMIP1, KISS1R, KRT81, LINC00402, LINC00582, LRRN3, OSTN-AS1, RP11-104L21.3, RP11-222K16.2, RP11-265P11.2, RP11-275I4.2, RP11-291B21.2, RP11-297B17.3, RP11-403A21.2, RP11-686F15.2, RP11-936I5.1, TRAV4, TRBV28, FASLG, XCL1, GZMH, RP5-1028K7.2, CHRM3-AS2, RP11-664D1.1, SIRPG, CD247, CCL5, IL17A, CXCR5, THEMIS, AC013264.2, SH2D1A, IGHV1OR15-1, CD3D, IFNG, GZMM, TIGIT, AC092580.4, LCK, GZMA, XCL2, HTR3A, CD3G, NUGGC, TRGC2, KLRB1, RP11-553L6.2, CD3E, FXYD7, TXK, LINC00861, CD40LG, CD6, GZMK, FCRL4, IGLL5, CD2, TRBC2, FCRL3, EOMES, ZAP70, TRAT1, AC104820.2, LTA, IGLC2, IGHG2, KRT86, CD7, IGLC3, TBX21, GNLY, TRDC, CD160, PYHIN1, IGLV4-60, SERPINA9, CD28, RP4-539M6.22, PGLYRP2, CR2, IL22, SLAMF6, CD8A, P2RX5, IGHG1, MS4A1, RP11-305L7.3, IGHG4, SIT1, KLRD1, CD70, IGLC7, RASGRP1, CD96, TNFRSF13B, TMIGD2, AC096579.13, CLEC2D, CTLA4, IFNG-AS1, RP11-455F5.5, ATG9B, POU2AF1, ABCD2, RGL4, UBASH3A, CARD11, IGKC, AC104024.1, CD8B, IGHD, CD19, PAX5, SCML4, CTC-378H22.1, GATA3, RP11-279F6.3, TCL1A, TRGC1, IGHA2, KLRC2, PTPRCAP, AGAP2, FCRL6, ICOS, CD27, BLK, CXCR6, SLA2, WNT10A, CDK5R1, FCRLA, BCL11B, AL928768.3, MZB1, NELL2, GPR171, IL2RB, KLRC1, PCED1B, TRAC, DERL3, FCRL5, TSHR, RP11-284N8.3, TBC1D10C, VPREB3, GPR18, PRF1, PCED1B-AS1, RP11-290F5.1, MIXL1, AC006129.2, AC096579.7, SAMD3, PDCD1, IL18RAP, AC017104.6, CPA5, SH2D2A, ACAP1, ZNF831, RP11-861A13.4, IGKV6D-21, WT1-AS, SEPT1, FAIM3, IGLL1, BFSP2, IKZF3, IGLV6-57, BCAS4, KCNA3, TNFRSF13C, GZMB, IL23R, CNR2, LAIR2, IGLV2-11, SLFN12L, TPRG1, STAT4, BACH2, PKHD1L1, SPOCK2, RP3-455J7.4, ZBED2, DENND2D, RP11-693J15.5, RP11-316P17.2, RP11-493L12.4, LINC00426, TNFRSF17, TNFSF8, CRTAM, LINC00525, IL7R, FCER2, RORA, STK17A, NKG7, ANKRD44-IT1, CPNE7, RP11-18H21.1, RIC3, LY9, RP11-492E3.2, SLAMF1, CCR4, TNFRSF18, IGJ, RP11-489E7.4, NLRP7, CD79A, RP11-382J12.1, LAG3, HOPX, TNFSF14, RP11-542M13.3, P2RX5-TAX1BP3, FGF23, SUSD4, CD79B, RP11-94L15.2, PIM2, SELL, FAM129C, RP11-539L10.2, SEPT6, EVL, SP140, LINC00649, AP001046.5, P2RY11, TMC8, AC069363.1, MYL2, BZRAP1-AS1, TTC39C, PPP2R2B, SPINK2, SYNGR3, RP3-370M22.8, NCR3, RP11-117D22.2, CD5, TAGAP, ICAM3, RP11-413H22.2, FAM46C, LTB, IKZF2, TMEM156, RAPGEF6, PPP2R5C, OXNAD1, MYBL1, ITGAL, FAM65B, PHTF2, PRKCQ-AS1, BIN2, XKR6 M.CD69neg_Mast
ASIC3, AD000671.6, SIGLEC8, ITGA2B, AMHR2, TSTD3, CYP51A1, EXD3, CDK15, ABCB8, SLC4A2, NSMCE1, FAM212A, KRT1, RSAD2, IL9R, WBP1, NCOA4, MAML1, MS4A2, GPR35, GALNT6, UBA7, ARHGEF6, CAPG, GRAP2, AJ271736.10, IGFLR1, PAQR5 M.CD69pos_Mast
CTC-537E7.3, LINC00323, IL1RAPL1, C19orf81, ATP1A4, PTGER3, ENPP3, IL5RA, RP11-16E12.1, CMA1, AC020571.3, PPM1H, AC004510.3, PPP1R15A, RAB27B, MIR3188, GPR65, RP4-794H19.2, ALAS1, RP11-422J8.1, ST8SIA6 M.Cycling
RP11-6F2.5, HSF2BP, RP11-798K3.3, ZNF565, RP11-190C22.8, RP11-212I21.4, RNASE2, COQ2, RP11-792D21.2, IQGAP3, ZNF724P, RP13-270P17.1, TIMM21, E2F7, C20orf201 M.DCs
RP11-404O13.5, RP11-863P13.4, SLAMF9, CTD-2006K23.1, CLEC4F, CYSLTR2, CD207, RUFY4, CTD-2319I12.1, CD1E, RP11-379F4.9, RN7SL472P, CD1C, RP11-863P13.3, CLEC10A, FLT3, RP11-24F11.2, RP3-399L15.3, CLEC9A, RYR1, AP003774.6, AC144521.1, SIRPB1, CD1B, PPM1J, RN7SL698P, HCAR3, CD80, HCAR2, RP11-192H23.8 M.Macrophages
AC005082.12, ACSM5, NT5DC4, RP11-426L16.8, RP11-452C13.1, RP11-489O18.1, RP11-760N9.1, PLA2G2D, CCL24, CCL18, MERTK, FABP3, MSR1, SIGLEC1, TMEM86A, CTB-138E5.1, CTD-2337J16.1, NPL, ATOX1, FOLR2, ACP5, NR1H3, DNAJC5B, TCHH M.Mast
AMHR2, CDK15, CTC-537E7.3, GCSAML, RP11-501J20.5, TACR1, XXbac-BPG13B8.10, LINC00323, AC004791.2, MS4A2, TPSD1, GATA1, IL1RAPL1, CALB2, RP11-354E11.2, TPSAB1, SLC45A3, C1orf186, CMA1, HDC, SVOPL, CTSG, CTD-3203P2.2, MAOB, KRT1, CPA3, IL13, LTC4S, GATA2, SLC18A2, ATP1A4, DKFZP434E1119, ADCYAP1, VWA5A, SIGLEC8, LEO1, ITGA2B, NTRK1, UTS2, EFHC2, AJ271736.10, RAB27B, RP11-557H15.4, SMYD3, STXBP6, ADRB2, IL9R, HS3ST1, ATP6V0A2, AC020571.3, SAMSN1, P2RX1, GMPR, IL5RA, TIAM2, PLIN2, CTNNBL1, TDRD3, MITF, PIK3R6, MAML1, PPM1H, ACOT7, NSMCE1, ST8SIA6, CATSPER1, CRBN, RP11-620J15.3, SMIM1, GLUL, PPP1R15A, NDST2, CAPG, BMP2K, FAIM, GPR65, ALAS1, RP11-422J8.1 M.Monocytes
ACSM5, AP003774.6, AQP9, C19orf59, CD1B, CD300E, CD300LB, CEACAM4, CLEC4D, CLEC4F, CLEC5A, CLEC9A, CRHBP, CTB-138E5.1, CTD-2337J16.1, EMR3, FCGR1A, FCGR1B, FPR2, HK3, IL22RA2, IL27, KCNK13, LILRA1, LILRA3, LILRA5, LILRA6, MARCO, MEFV, MRC1, MS4A14, NT5DC4, PKD2L1, RETN, RN7SL138P, RNASE2, RP11-365O16.3, RP11-404O13.5, RP11-472N13.3, RP11-489O18.1, RP11-556E13.1, RP11-737O24.5, RP11-760N9.1, RP11-798K3.3, RP5-899E9.1, S100A12, SIGLEC1, SLAMF9, SUCNR1, TCHH, TIFAB, TREM2, VSTM1, ZDHHC19, FCN1, CD1E, LILRB2, CD207, CLEC4E, SDS, C1QA, C1QC, CSF1R, CD209, MS4A6A, C1QB, MSR1, CLEC10A, S100A8, PLA2G7, IGSF6, ATP6V0D2, RP11-190C22.9,

TABLE 6-continued

Immune UC specific markers for indicated cell types
CCL18, CSTA, FPR3, CD163, DNASE1L3, FPR1, MMP12, AIF1, CACNA2D3, CSF2RA, OLR1, VSIG4, F13A1, LILRB5, IL1B, P2RY13, NCF2, LILRB4, GSDMA, RP11-290F20.3, CSF3R, PLA2G2D, MS4A4A, DLEU7, RP11-1143G9.4, LYZ, S100A9, PILRA, MRC1L1, SLAMF8, OSCAR, FCGR2A, HCAR3, CFP, LILRB3, CPVL, CLEC4A, RP11-6F2.5, FLT3, MS4A7, C5AR1, KB-1507C5.4, VMO1, MPEG1, MNDA, FOLR2, GPR84, RP11-426C22.5, RAB42, IL1RN, FUCA1, IFI30, SIGLEC12, G0S2, RP3-460G2.2, MMP9, FTL, RNU5B-1, NLRP3, AURKC, TREM1, SIGLEC15, CLEC7A, TLR2, CD14, SLC7A7, CD68, MERTK, ACP5, NLRC4, RNASE6, TLR4, RP11-792D21.2, CD163L1, TFEC, RRAGD, FAM26F, CTSS, TLR8, ATP6V1B2, STAB1, GPX1, NFAM1, LIP A, TTYH3, SAT1, APOC1, CMKLR1, THEMIS2, ATF5, CTD-2319I12.1, LGMN, SPI1, FABP3, CTSB, CTD-2319I12.2, TNFAIP8L2, CLEC4G, CTD-2006K23.1, NAIP, CTC-205M6.5, TNNI2, OTOA, CST3, MYCL, SLCO2B1, CCL3L1, RB1, HLA-DPB1, RGS18, GRN, HLA-DPA1, EREG, P2RY6, PLAUR, CD1A, SLC31A2, CXCL3, LILRA2, CARD9, NAGA, TYMP, FZD2, GM2A, TRPM2, NUP214 M.Myeloid
AC004791.2, AC011899.9, ADCYAP1, AMHR2, AQP9, C19orf59, CD1B, CD300E, CD300LB, CDK15, CEACAM4, CLEC4D, CLEC4F, CLEC5A, CLEC9A, CMA1, CRHBP, CTB-138E5.1, CTD-2337J16.1, EMR3, FCGR1A, FCGR1B, FPR2, GATA1, GCSAML, GPR141, HK3, IL22RA2, IL27, KCNK13, LILRA1, LILRA3, LILRA5, LILRA6, MARCO, MEFV, MS4A14, MS4A2, PKD2L1, RETN, RN7SL138P, RNASE2, RP11-354E11.2, RP11-365O16.3, RP11-472N13.3, RP11-489O18.1, RP11-501J20.5, RP11-556E13.1, RP11-760N9.1, RP11-798K3.3, RP5-899E9.1, S100A12, SIGLEC1, SIGLEC8, SUCNR1, TCHH, TIFAB, TREM2, XXbac-BPG13B8.10, FCN1, CD1E, LILRB2, HDC, CTSG, CPA3, CD207, SLC18A2, CLEC4E, SDS, C1QA, C1QC, CSF1R, MS4A6A, CD209, FCER1A, C1QB, MSR1, MMP12, CLEC10A, S100A8, LINC00323, IL1B, PLA2G7, IGSF6, ATP6V0D2, RP11-190C22.9, MS4A4A, CCL18, FPR3, AIF1, CD163, DNASE1L3, FPR1, SIGLEC12, SVOPL, CSTA, CACNA2D3, TPSD1, CSF2RA, OLR1, ATP1A4, VSIG4, ADORA3, F13A1, LILRA2, TPSAB1, LILRB5, IL1RAPL1, NCF2, P2RY13, KRT1, RP11-290F20.3, CSF3R, LILRB4, DLEU7, CALB2, S100A9, SLC45A3, GSDMA, LYZ, PLA2G2D, NLRP3, PILRA, RP11-1143G9.4, C1orf186, MRC1L1, UTS2, HCAR3, FCGR2A, SLAMF8, CFP, LILRB3, OSCAR, CTD-3203P2.2, CPVL, CLEC4A, FTL, MAOB, C5AR1, IL13, MS4A7, GPR84, VMO1, CD68, MNDA, RENBP, IL1RN, MPEG1, RP11-426C22.5, RAB42, FLT3, FOLR2, IL10RB-AS1, LTC4S, G0S2, DKFZP434E1119, FUCA1, IFI30, RP3-460G2.2, GATA2, CST6, MMP9, TREM1, ATP6V1B2, GLUL, PLIN2, VWA5A, ACP5, CLEC7A, MERTK, TLR2, AURKC, RRAGD, CD14, RP11-792D21.2, SLC7A7, SLC11A1, CXCL16, RP11-76E17.3, RNASE6, EMILIN2, TLR4, SAT1, LEO1, GM2A, CD163L1, TLR8, GPX1, FAM26F, CTSS, TBXAS1, TNNI2, HS3ST1, ATP6V1F, NLRC4, TFEC, RNF130, CTD-2514K5.2, STAB1, TTYH3, LIPA, NFAM1, ITGA2B, MPP1, RASGRP4 M.Neutrophils
AQP9, C19orf59, S100A8, MARCO, S100A12, FPR2, CD300E, VSTM1, S100A9, APOBEC3A, RP11-290F20.3, RETN, IL1RN, SLC11A1, LILRA3, FCN1, RP11-701P16.5, G0S2, RP4-613B23.1, EREG, NLRP3, RP11-598F7.3, CXCL10, NUP214, FPR1, C5AR1, LUCAT1, TREM1, PLAUR, RP11-47I22.2, CLEC4D, LILRA5, SOD2, KYNU, TLR2, ACSL1, CLEC4E, LILRB2, KB-1507C5.4, STXBP2, CSF3R, CDC42EP2, P2RY2, STX11, OLR1, IL10RB-AS1, CEACAM4, OSM, TYMP, SLC43A2 M.Tissue_DCs
RP11-404O13.5, RP11-863P13.4, SLAMF9, CTD-2006K23.1, CLEC4F, CYSLTR2, CD207, RUFY4, CD1E, RP11-379F4.9, CD1C, RP11-863P13.3, CLEC10A, RP11-24F11.2, RP1-90J20.12, RP3-399L15.3, RYR1, AP003774.6, CTB-113P19.5, SIRPB1, AC144521.1, CD1B, HCAR3, HCAR2, RP11-192H23.8, RP11-737O24.5, UTF1 M.Tolerogenic_DCs
GPR157, PTGES3L, RP3-508I15.22, CTD-2319I12.1, FBXO27, BATF3, CLEC9A, DGAT2, PPM1J, IDO1, AC120194.1, TNNI2, TOMM34, SERPINF2, CPVL, SLAMF7, DICER1-AS1, C1orf54, WDFY4, CPNE3, MREG, CD3EAP, KIAA0226L, VAC14, LGALS2, PPT1, CAMK2D, SNX3 T.Activated_CD4_hiFos
CYP2E1 T.CD4
CCDC81, LINC00880, CCR4, GNG8, FOXP3, F5, RN7SL443P, RP11-265P11.2, ITPKB-AS1, AC013264.2, CDKL2 T.CD8
KIR2DL4, RP11-713M15.1, TMEM155, AC131056.3, ADRB1, RP11-535A5.1, TRGC2, TPRG1, CD8B, CACNA1C-AS2, CCL4L1 T.CD8_IELs
KIR2DL4, RP11-713M15.1, ADRB1, MUCL1, DPH1, KLRC2, DRAXIN, RP11-535A5.1, TRGC1, TRGC2, FBXO2, RP11-446N19.1 T.CD8_LP
TMEM155, AC131056.3, CCL4L1, TRAV38-2DV8, GZMK T.CXCR6_Th17
TRAV17, BTBD16, TMPRSS3, IL17A, INSL3, MATN1-AS1, CA10, CTD-2007H13.3, KLRB1, SMG8, NMRK1, IL17F, AC092580.4, ADAM12

TABLE 6-continued

Immune UC specific markers for indicated cell types
T.Cycling_T
PKHD1, RP11-631N16.2, PRIM1, ASPM, CDCA4, AC010761.8, AC109333.10, CENPF
T.ILCs
LINC00299, SPINK2, RP4-673M15.1, LEKR1, CSF2, ALDOC, RUNX2, IL4I1, RP11-977G19.12, PRAM1, FXYD7, KRT86, COL9A2, LTB4R, ETV3, RP1-102K2.8, BEX2, ARL5B, CASP3, PRMT10, KRT81, CAT, TLR1, LDLRAD4
T.MT
SMC5-AS1, PAQR3, PDE7A, EPHA1-AS1, RP11-277L2.4, ZNF740, BCL11B, LINC00680, ANKRD44, ZNF736, CTB-31N19.3, LSM11
T.NK
KLRF1, GPR97, KIR3DX1, TEX22, CLIC3, KLRC1, S1PR5, SH2D1B, BCO2, C21orf67, SCXA, XCL2, PRF1, GZMB, ZNF114, IL2RB, CTSW, ZNF852, FCGR3A
T.PD1_CD4
IL4, RP11-148O21.6, PHEX, RP11-279F6.3, CXCL13, RP11-431M7.3, TSHR, RP5-1028K7.2, ECEL1, BTLA, AC011893.3, CXXC11, SARDH, RP11-219B17.1, CD200, AC006129.4, SCGB3A1, BZRAP1-AS1, RP11-455F5.5, FKBP5, PDCD1, TMEM232, ANKRD55, TOX, PVALB, XXYLT1-AS2, AP006621.5, MYO7A, NMB, PVRIG, THADA, GAREML, GNG4, NFATC1, KSR2, IL21, PVT1, RNF19A, SYNJ1
T.Tcells
AC002331.1, AC006369.2, CA10, CXXC11, ECEL1, F5, FOXP3, IL17F, IL2, IL26, PAGE5, RP11-104L21.3, RP11-265P11.2, TMEM155, TRAV13-2, TRAV36DV7, TRAV4, TRBV28, CHRM3-AS2, IL17A, RP11-664D1.1, THEMIS, LINC00402, AC131056.3, C15orf53, RP11-291B21.2, RP4-539M6.22, CTLA4, CD8B, NELL2, CD3G, AC013264.2, CD6, CD3D, PDCD1, CPA5, LINC00243, BCL11B, BHLHE40-AS1, SUSD4, RP11-18H21.1, GNG8, LAG3, C12orf79, ABCD2, LINC00649, TRAT1, CD8A, CTC-505O3.3, CD5, HAR1B, CXCR6, CD3E, SLFN12L, PBX4, TRAC, RN7SL443P, SIRPG, GPR171, TRBC2, RP11-85K15.2, C4orf26, RP13-977J11.2, MORN3, BATF, CD28, C14orf64, AC104820.2
T.Tregs
AHSP, PNMA3, SLC8A1-AS1, CARD17, FOXP3, TTBK1, RP4-533D7.5, F5, TNFRSF8, FANK1, RTKN2, IL2RA, CTLA4, CUL9, PPP1R3F, LAIR2, NINJ2, CTD-2325P2.4, BATF, TNFRSF9, AC017002.1, TNFRSF4

TABLE 7

Stromal Healthy specific markers for indicated cell types
F.Crypt
CFD, ADAMDEC1, MFAP4, CCL13, CCL11, HAPLN1, PTGDS, SFTA1P, CXCL1, ABCA6, ELANE, CP, CCL7, NR2F1-AS1, CXCL6, SLIT3, FZD1, CCL19, CFHR3, ADAMTS2, EPHA7, RBFOX1, RP11-93L9.1, GPC3, PTGFR, ABCA10, HAS2, SLCO1C1, FZD10-AS1, RNF112, COL6A5, RP11-222A11.1, AL132709.5, SORCS2, LCE2A, FGF10, RP11-135D11.2, CHODL, RP11-1008C21.2, GALNT9, TWIST2, AC092652.1, TNN, RP11-572C15.6
F.Crypt_RSPO3
CFH, CXCL12, CCL11, EFEMP1, ADH1B, CCDC80, C7, DPT, RSPO3, ASPN, SERPINE2, ANGPTL1, CXCL6, CP, GPC6, CHODL, CCL19, SLIT3, APOD, OGN, GREM2, MAPKAP1, PTGER1, PDE5A, GPC3, RP11-135D11.2, RGMA, C1QTNF3, OSR2, FAIM2, PTGFR, MFAP5, BDKRB1, CAPN6, ECM2, DACT1, SHISA3, CDO1, SFRP2, SFRP4, PI16, RBBP9, FLRT2, CTD-2014B16.3, IL17RD, AL035610.1, APCDD1L-AS1, FOLH1, SORCS2, ENTPD1-AS1, GPC2, AP001626.2, CTD-2085J24.4, CTD-2083E4.4, RP4-545C24.1
F.Crypt_hiFos
CNTN1, ZIC1, TMEM232, AC005592.2, ZDHHC11, SHBG, CECR5-AS1, WASF1, RNU6-450P
F.Crypt_loFos_1
RN7SL374P, BVES, KCNS2, MRAP, RP11-98I9.4
F.Crypt_loFos_2
ZNF836, FAM102B
F.Endothelial
AC004540.4, AC116035.1, APLN, AVPR2, CCDC178, CNTNAP3B, COX4I2, FAM155A, FCN3, FOXC1, GABRD, GIPC3, GJA4, GPIHBP1, INHBB, KCNJ8, KRT222, KRT27, LCN6, LYVE1, NOVA2, NPR1, PGM5-AS1, PLA1A, RASSF9, ROPN1L, RP11-1024P17.1, RP11-536018.1, SCN3B, SELE, SELP, SNTG2, SOX18, STC1, STC2, TLL1, TSPAN18, KDR, FAM110D, TM4SF18, H19, DARC, MMRN2, C1QTNF9, RAMP3, ZNF833P, FAM167B, PLVAP, BCL6B, AC011526.1, CLDN5, MYCT1, HIGD1B, SHANK3, CXorD6, FLT1, ECSCR, RP11-251M1.1, SLC14A1, ROBO4, VWF, RP11-536O18.2, CYYR1, CDH5, TMEM88, ZNF385D, GPR116, THSD7A, ESAM, APLNR, USHBP1, SOX17, ADM5, SNCG, CD320, RAMP2, ARHGEF15, CD34, CALCRL, EGFL7, GALNT15, NOS3, MADCAM1, FLT4, ANGPT2, ELTD1, THSD1, PODXL, KANK3, GPRC5B, ARAP3, SERPINE1, TNNT1, CYP1B1-AS1, KIAA1462, RP11-23P13.7, TPO, TEK, JAM2, VEGFC, HYAL1, CKMT2, RAPGEF3, MKL2, PALMD, RGS5, CLEC14A, CCL14, NOTCH3, PTPRB, NOSTRIN,

TABLE 7-continued

Stromal Healthy specific markers for indicated cell types
LRRC46, PCDH12, TSPAN7, GPR4, EXOC3L2, SEMA6C, RUNDC3B, S1PR1, CD36, TDRD10, FABP5, ERG, NOTCH4, GRB10, GPR1, EHD4, MAPK11, EXOC3L1, RASIP1, SEMA3F, IGFBP4, PKN3, BTNL9, HSPA12B, RND1, GNG11, ZNF541, FGD5, NUAK1, PKP4, HYAL2, ACE, EVA1C, RP11-473M20.9, SLC35G2, HRC, IPO11, SLC9A3R2, ENPP2, SHE, ARC, MPZL2, ZNF676, RBP7, EPM2A, JAG2, RP11-768F21.1, CD93, SEMA3G, SLC7A2, LINC01013, EPAS1, MASP1, ASB9, ADCY4, MYRIP, RP11-435O5.5, LINC00162, AIF1L, DOCK9, KIF19, SPTBN5, DYSF, CYPIBI, OAZ3, FAM189A2, ENG, PRX, STXBP1, CORT, RAPGEF4, CLIC2, MEOX1, PRSS23, SOX7, SMAD1, CFI, APBB2, ARHGAP29, SH3BP5, FAM84B, ADAM15, TEAD4, CYP26B1, SERPINI1, TGFBR2, HLX, SLC25A25, AC009336.24, MIER2, TIE1, CDC37, ICAM2, CRIP2, CBX2, FILIP1, STOM, EBF1, FZD4, TNFAIP1, EPB41L4A, RIN1, IL33, TMEM255B, HTR2B, BAALC, TACC1, PLLP, CABP1, RP11-830F9.6, PTPN14, RPGR, SLCO2A1, FAM107A, APOLD1, CCDC85B, ALPL, MANSC1, ITGA5, EPHB4, MFAP3, EMCN, MYBBP1A, FAM213A, DOCK4, CX3CL1, PLXND1, CELSR1, SHROOM4, RBP5, TINAGL1, LDB2, C10orf10, RASAL2, TMTC1, ARL15, DGKE, RP11-806H10.4, CSGALNACT1, ACVRL1, C16orf80, BCAM, PDE1C, VAMP5, TNFRSF10D, SLC16A14, MSMP, NES, KLHDC8B F.Endothelial_1
GAS1, RP11-15A1.7, SEMA3G, FCN3, STC1, MASP1, RP11-671J11.4, RP11-105C19.1, ALPL, PRDM16, ARL15, ANO2, BTNL9, RP11-435O5.5, RP11-806H10.4, AC007292.3, EFNB2, C10orf10, RBP7, SOX17, RUNDC3B, C22orf26, MECOM, RTN4R, NOV, HEY1, LCN6, TBC1D13, SSUH2 F.Fibroblast
CFD, FBLN1, PROCR, BMP4, ADAMDEC1, CXCL12, DMKN, CCL8, PLAC9, SPON2, HAAO, CCL13, ADH1B, SCARA5, HAPLN1, PTGDS, CCL11, NSG1, GLT8D2, F3, GADD45G, TMEM119, LRP1, ENHO, VCAM1, FAM150B, VSTM2A, PDGFRA, AGT, SFTA1P, DPT, LOXL1, PDGFD, CXCL1, APOD, PCDH18, FARP1, PRR16, CRISPLD2, TPBG, PXDN, MXRA5, FGF7, CDH11, HTRA3, BAMBI, PLAGL1, TSLP, TDO2, GPC6, TRPA1, FGFR1, ELANE, TNC, LRRN4CL, CP, GLP2R, HSD11B1, LANCL2, SVEP1, NMNAT3, CXCL6, CCL7, REEP2, COL4A5, CIB2, WNT5B, SCUBE2, ALDH1A3, RP11-112H10.4, FZD1, FAM65C, CCL19, PCSK6, LTBP2, C3, SRPX2, FGF9, RP11-1260E13.4, NPY, DACT1, SEMA3E, GPC3, COL4A6, RP11-449D8.1, OBSCN, RP11-93L9.1, SPOCK1, BICC1, BMPER, AC003090.1, RP11-367J11.3, PTGFR, FZD10-AS1, CRABP2, C1QTNF7, WNT5A, LOXL4, FAM19A1, RNF112, C22orf31, HMGCLL1, SAMD14, PDGFRL, AC002511.2, RP11-2E17.1, C3orf55, ATP6V1G2, COL6A5, CLSTN2, PAPLN, FOXL1, KRTDAP, C1QL1, CTB-92J24.3, LRRC15, ADAMTSL3, CTD-2314B22.3, CHODL, RN7SL336P, LCE2A, LRRC18, HS3ST3A1, GSG1L, PGR, RP11-473E2.4, ETNK2, CHI3L1, KIF7, RP11-222A11.1, AC104654.2, OGN, EDAR, MC1R, AMPH, FGF10, RBMS3-AS3, CNNM1, ZNF334, RSPO2, RP11-1008C21.2, AC004538.3, EFCAB1, GALNT9, GS1-18A18.1, RP4-755D9.1, SORCS2, RP11-135D11.2, ADCY2, LPAR3, LRRC8E, RP11-157J24.2 F.Glia
ANGPTL7, CAP2, CDH19, CTD-2325P2.4, CYP27C1, DLX1, DYNC1I1, FAM181B, FGF1, FOXD3, HAND2, LINC00982, LRRC4C, LRRTM1, MGAT4C, NDP, NKAIN3, NRXN3, PCSK2, PMP2, PTPRZ1, RASGEF1C, RORB, RP11-21A7A.4, RP11-713P17.3, RP4-792G4.2, SERPINA5, SHC4, SOX10, SOX2, SRCIN1, STEAP1B, TENM3, TMEM155, VGLL3, CADM2, L1CAM, MYOT, SBSPON, TFAP2A, LINC00632, NRXN1, COL28A1, HPR, TTYH1, TMEM178A, GPM6B, PLP1, SCN7A, MPZ, CMTM5, XKR4, HAND2-AS1, C10orf82, CRYAB, SPP1, TUBB2B, LRAT, NTM, SORCS1, DLX2, NLGN4X, TMEM132B, TSPAN11, BAI3, S100A1, SOX8, ST6GALNAC2, NIM1, AC144449.1, NGFR, KCNMB4, FLRT3, RP11-166D19.1, COL8A1, AATK, SEMA3B, TMOD2, WISP2, KCTD1, TMEM59L, CAPS, CAB39L, COL9A3, SH3BGR, SCN9A, ART3, WDR86, RP11-20J15.3, MMP17, S100B, PRIMA1, GRIK3, MAB21L1, MFAP3L, ALDH1A1, COL21A1, LEPREL1, LINC00882, SNCA, AP001631.9, GPR155, ENTPD2, CPEB1, PRNP, RFTN2, ZNF853, C1orf198, RP11-235E17.4, CNP, RP11-187C18.2, MFSD2A, FST, OLFML2A, ASPA, ABL2, CADM4, SLC16A4, BEX1, CHADL, RCAN1, GFRA3, PCBP4, FXYD1, LGI4, ARHGEF26, CYR61, FGFBP2, EHBP1, RASSF4, COMT, TUBB4A, SECISBP2L, ITPR1, PMP22, SCCPDH, ANK3, SLC22A17, SLC16A8, NCAM1, UCHL1, ARHGAP15, FIBIN, ASTN2, MAL, AP1S2, ENDOD1, POU3F1, GRAMD3, FEZ1, SMIM5, ATL1, SEMA3C, AK5, GFRA1, SREBF1, IL11RA, KDSR, PMEPA1, FBLN2, LINC00894, RBM43, NUP188, NXPH3, ADK, CADM3, USP6, RP4-777D9.2, MATN2, C1orf204, TUBA1A, PDK4, CYP27A1, TPCN2, LAMP5, FADS3, PON2, LINC00263, ANXA2, DKK3, TTLL4, CD9, NDRG2, RTDR1, PEBP1, PAQR6, CNN3, MAPRE2, CLU, SLC15A3, LMBRD2, DEPDC7, MIIP, SPARC, SIPA1L2, ZFYVE1, TIMP3, C8orf4, GNG2, ARHGAP12, ITGB1BP1, NPTX2, CXXC5, PLSCR4, SORBS2, GATM, CRTAC1, TSPAN15, HSPA2, ALCAM, CDC42EP4, TPT1-AS1, ZBTB5, CBR1, RHOB, STARD13, SLC39A6, PLA2G16, PDLIM4 F.Inflammatory
CHI3L1, MMP3, SIRT4, GBP1, TRAFD1, ZCCHC4, BLOC1S5, CDC23, VTA1, PLAU, PSME3, PAQR5, GSTT1, APOL2, CAMKK2, COMMD2, BYSL, UBIAD1, STX5, BCDIN3D, RRP1 F.Microvascular
GABRD, STC2, SPTBN5, F2RL3, PASK, RP11-536O18.2, APLN, MSMP, C11orf95, IVNS1ABP, LYPD5, GIPC3, ME3, PRX, RP11-575F12.1, VWA1, RGCC, PRSS23, SEMA3F, MCPH1, ADARB1, SETD4, AC112693.2, RNF44, PGS1, EXOC3L2, BAALC, TBC1D8, DYSF, NRP1, CIT, TP53I11, WWTR1, NUP43, MICALL1, HSPG2, TBCD, HTRA1, RAPGEF4, ANRD65, SCARB1, RARG, ITGA6, ARHGAP23, JAM3, EGLN3 F.Myofibroblasts
SOGA2, SOSTDC1, HSD17B6, DES, ACTG2, NPNT, AF131217.1, RP11-611D20.2, RAB9B, LUZP2, CNN1, MYLK, TAGLN, RP13-143G15.4, MYH11, SYT10, SNCAIP, LMOD1, DIO2, TMEM158, LINC00595, RP11-356C4.3, HHIP, PDLIM3, C20orf166-AS1, SLC2A4, FBXL22, TGM2, ACTA2, LRRC17, FHL1, SLMAP, NEXN, PDLIM7, LRFN3, BVES-AS1, NAA60, TPM2, SPAG8, LPP, MIR145, KCNMB1, SMTN, MACROD2, SPESP1, TGFB1I1, AOC3, FAT4, DSTN, FLNA, RP11-344E13.3, NDUFA4, TCEAL4, MIR143HG, TRPC6, HMG20B, TES, TTLL7, SLC12A8, PDIA5, LTBP1, TCEAL1, WRN, AKAP6, PLN, SVIL, RP11-196G18.23, VAT1L, TCEAL3, TPM1, TEAD3

TABLE 7-continued

Stromal Healthy specific markers for indicated cell types
F.Pcap_Venules
FOXC1, LYVE1, RASSF9, SCN3B, SELE, TLL1, DARC, MADCAM1, SELP, VEGFC, CCL14, LRRC46, FAM155A, ZNF385D, RAB3C, CELSR1, UBD, LINC01013, C2CD4B, ACKR4, PLA1A, TSPAN18, FAM189A2, RP13-395E19.3, GALNT15, RP5-1021I20.5, CITED4, DUSP23, GPR126, TIAM1, CPE, DTL, ZSCAN31, ICAM1, AMDHD1, ICAM4, KCNMB3, CORT, HTR2B, PMEL, CYP1B1, KLHL3, HESX1, LPCAT4, ZNF521, APLNR, KIAA1683, NR5A2, PRKAR1B, FAM84B, MEOX1, IFIH1, SEMA6A
F.Pericytes
EDNRA, CYP4X1, KCNJ8, COX4I2, STEAP4, RP11-714L20.1, GJC1, CCDC3, HRC, NOTCH3, FAM162B, CDC7, RGS5, ITGA7, PRDM11, BGN, HIGD1B, LDB3, JRKL, NR2F2-AS1, NDUFA4L2, NR1H4, PDGFRB, PGF, ATXN7L2, LINC00883, TEPP, ARHGEF17, UBA2, REM1, ISYNA1, FZD7, TNS1, PLXDC1, CSRP2, OLFM2, GJA4, TMEM38A, NUP133, SERPINI1, TINAGL1, RNF208, EBF1, HES4, SUSD2, CNNM2, ADAMTS1, ATP1B2, EPS8, MCAM, RP11-110I1.12, RP11-349A22.5, ADIRF, TPPP3
F.Stromal
CXCL14, A2M, CALD1, C1S, MFAP4, COL6A2, COL3A1, PLAT, CFD, DCN, TM4SF1, CYGB, TCF21, LUM, FBLN1, SOD3, ADAMDEC1, MMP2, PROCR, COL6A1, BMP4, CXCL12, TPM2, FABP5, MFGE8, CLEC11A, EPHX1, CFH, CTSK, SLC9A3R2, PTN, PPAP2B, SDC2, PCOLCE, CAV1, EMILIN1, DMKN, CCL8, STMN2, LINC01082, POSTN, HAAO, FRZB, FOXF1, ADH1B, PLAU, CCL13, WFDC1, SNAI2, GGT5, PTGDS, SCARA5, CCL11, HAPLN1, ACTA2, EFEMP1, FXYD6, GLT8D2, PITX1, CAV2, FENDRR, RBP5, NKX2-3, NDUFA4L2, EHD2, CTC-276P9.1, RAMP2, CD320, NSG1, MGP, TFPI, THY1, CLEC14A, F3, FILIP1L, TMEM119, FABP4, EDIL3, TMEM204, EMID1, LHFP, TMEM100, VCAN, RCAN2, ENHO, IL34, PLVAP, BMP5, AGT, SFTA1P, FAM150B, COL6A3, LOXL1, VSTM2A, TAGLN, IGFBP5, CCDC80, PDLIM3, CLDN5, CERCAM, PTCH1, FN1, DPT, PDGFD, PDGFRA, MYLK, FGF7, EGFL7, RAMP3, CRISPLD2, PCDH18, TNXB, NEGR1, TAC3, GSTM5, SEPT4, PXDN, PGF, VWF, ESAM, OLFML1, MMP11, TUSC3, ECSCR, VASN, DDR2, SMYD4, EMCN, PRR16, COLEC11, MXRA5, TMEM150C, TMEM88, LRRC32, AC011526.1, C16orf89, FGFR1, VSTM4, RP11-332H18.4, NEXN, PDGFRB, NID1, FOXF2, FAM167B, COLEC12, CYYR1, HTRA3, EVA1A, ADAMTS1, SNCG, CD34, ELANE, FBN1, TDO2, MMP1, CDH11, TRIL, ELTD1, PODXL, PAMR1, RP11-532F6.3, HHIP, RUNX1T1, TRPA1, TBX2, GPC6, TEAD2, TSLP, LAMA5, RP4-665J23.1, LRRN4CL, RP11-514D23.3, HOXA11, AKAP12, TM4SF18, ARHGAP29, NR2F1-AS1, SGCA, RPS6KA2, MIR497HG, MAB21L2, HHIP-AS1, PRKG1, PLEKHH2, NTF3, PDE1A, RASIP1, GPR124, CCL7, APLNR, C7, ACTG2, CCDC102B, EFCC1, EFHD1, CP, LIFR, FAM107A, HOXD11, TFPI2, FLT1, CXCL6, SVEP1, CDH5, CH25H, HOXD8, LOX, MMRN2, SLC14A1, HSPB6, PTGES, MAPK10, ANGPT2, PTGDR2, SPON1, GLP2R, NKD2, LAMC3, CLMP, ROB04, SLIT3, MRVI1, FAM110D, CALCRL, MYCT1, NUAK1, CXorf36, PTPRM, RHOJ, ENPP6, NR2F1, RP11-112H10.4, OSMR, KDR, RGS5, GPR63, COL12A1, COL4A5, MIR143HG, LTBP2, ARHGEF25, HOXD9, C3, DARC, WNT5B, RP11-383H13.1, NXN, SOSTDC1, GPR116, REEP2, RP3-323P13.2, AC131025.8, FZD4, GLI1, TNFRSF10D, SYNDIG1, MIR145, PCDH7, CFHR3, LPHN2, RP11-536O18.2, FGD5, GRB10, SOBP, MADCAM1, PALMD, SULF1, PCSK6, HSPA12B, ZP1, ALPL, AC124789.1, TEK, SOX17, SOX18, VAT1L, FAM162B, USHBP1, DACT1, PTPRG, PDE7B, AC156455.1, CHST1, SALL1, PEAR1, C1orf167, SEMA3E, ASPN, OSR1, CLEC3B, FNDC1, FILIP1, FAM13C, LEPR, AC116035.1, GPRC5B, PREX2, PCDH12, CCL21, CABP1, ROR2, DZIP1, HIGD1B, COL4A6, RSPO3, WDFY3-AS2, PDGFC, LCN6, AMOTL1, HYAL1, KCNE4, TMTC1, NPY, PRX, ADM5, TBXA2R, LRRC17, RBFOX1, GLIS2, SYNPO2, FAM110B, RP11-264B14.1, AP000330.8, GPR4, NTN1, EDA2R, BOC, ISL2, DHRS7C, EXOC3L2, LINC00961, RP11-449D8.1, PCDH19, C16orf46, RBPMS2, NOS3, HOXC9, SEMA3A, BCL6B, KLHL13, SEMA6C, ARHGEF15, ACSS3, HOXC6, PTGFR, WNT5A, IGF2, SPOCK1, ADAMTS4, HSD17B6, CPAMD8, HIF3A, COX4I2, FAM19A1, PPP1R3C, TEKT3, CLSTN2, NPR2, FOXL1, LINC00839, RGMA, MFAP5, PHACTR3, SLCO1C1, LCA5, AC017048.4, BICC1, ZNF423, SLC16A2, AC003090.1, ANGPT1, C1QL1, COL6A5, KRT222, NPR1, MUSK, NOTCH3, THSD1, FMO3, NDNF, SAMD14, APLN, AVPR2, PABPC5, ZNF833P, SCGB1B2P, ZNF385D, GALNT15, AC061992.2, AC002511.2, CRMP1, FAM171B, HOXC8, HMGCLL1, FBXL7, SERPINE1, C22orf31, FGF13, PDGFRL, ADAMTS5, C1QTNF7, GSG1L, KRTDAP, NAP1L3, RP11-2E17.1, ADAMTSL3, FAT4, ARHGAP28, TRPC6, CASP12, RNF112, EVC, FOLR1, CHODL, CTB-92J24.3, LINC00475, OGN, CDO1, ETNK2, PAPLN, IL33, KIF7, DIO2, GJA4, HS3ST3A1, INHBB, KIAA1462, LRRC3B, PTH1R, CORT, C3orf55, C1QTNF9, MMP3, AC116366.6, C10orf107, CHRD, NAALAD2, RP11-572C15.6, RP4-755D9.1, STC1, INMT, BHMT2, SUSD2, CTD-2314B22.3, GLIS1, RP11-774O3.3, AGTR1, CILP, ECM2, FCN3, GRIA4, GRID1, HPSE2, LRRC18, OMG, RAET1G, RP11-54O7.3, RP11-135D11.2, SHANK3, GPR176, RP11-486G15.2, ZDHHC15, RP11-1008C21.2, CNNM1, TTLL11, CCDC178, FAM180A, LRRC15, RP11-395L14.4, SELP, SORCS2, TRPC1, H19, NUDT10, CHI3L1, TRO, MIR503HG, AC092652.1, FGF10, GPIHBP1, LCE2A, LIFR-AS1, MYL3, NOVA2, RBMS3-AS3, RNF150, RP11-710C12.1, RSPO2, GPR133, RP11-251M1.1, LINC00595, ZNF667, CACHD1, AL132709.5, PARD6G, RP11-69I8.3, FLT4, RP11-314C16.1, SLC45A1, C17orf51
F.Villus
DNAI1, F2RL2, GRIN2A, GS1-18A18.1, NEFM, NOTO, RP11-157P1.4, RP11-804A23.4, RP4-755D9.1, RSPO2, REEP2, COL4A6, GLP2R, DLEU7, EDAR, SCN3A, PCSK6, SCUBE2, WNT5B, AC002511.2, RP11-1002K11.1, HS3ST3A1, LPAR3, FGF9, LANCL2, DHRS7C, C22orf31, AC003090.1, ENHO, EGOT, BAMBI, TSLP, SCUBE1, KCNK17, BMP7, VSTM2A, FAM150B, ADAMTS13, MMP11, KREMEN1, SRPX2, RBP4, CBLN2, POSTN, CHST1, NRIP3, NSG1, OBSCN, NMNAT3, TSPAN33, CNTFR, SEMA4D, SEMA3A, FAM218A, C1QL1, EDNRB, PDGFRA, PTGIS, MFAP2, SHANK2, TSHZ2, SDK1, DDHD1, GSG1L, CTD-2334D19.1, ZNF407, LAMC3, GADD45G, TPBG, RP11-449D8.1, WFS1, CNIH3
F.Villus_1
IP6K3, MSX2, NTRK3, TTC25, AC019171.1, MAST1, AC022007.5, ARHGEF33, EGOT, KB-1125A3.11, RP11-473M20.16, AL163953.3, XXbac-BPG252P9.10, EDAR, NHS, CASC14, ADCY2, AC009480.3, CPM, RN7SL336P, FBXW7, BDNF, CTD-3093M3.1, FGF9, HUS1B, RP11-309M23.1, C10orf107

TABLE 7-continued

Stromal Healthy specific markers for indicated cell types
F.Villus_2
GRIN2A, NEFM, VPS37D, F2RL2, LEF1-AS1, DHRS7C, AC096772.6, RP11-86H7.7, RP11-97O12.7, LAMTOR5-AS1, ZNF646, EFHB, RP11-144G6.12

TABLE 8

Stromal UC specific markers for indicated cell types
F.Crypt
AC004538.3, AL132709.8, CILP, COL6A5, FMO2, GRIK4, HHIPL1, MPP2, OMG, RN7SKP295, RP5-1172A22.1, SHISA3, SLC17A7, TEKT3, TMEFF2, CNTN1, CCL13, GAS6-AS2, LPAR4, CCL7, OGN, AL035610.1, ABCA8, ABCA9, CP, CCL11, SVEP1, ELANE, ADAMDEC1, ANGPTL1, RP11-572C15.6, RP11-473E2.4, GPC3, HAPLN1, CFD, SFTA1P, NAALAD2, ADH1B, CCL8, SCGB1B2P, ANKRD13B, CCDC80, FBLN1, ABCA10, ADAMTSL3, CPEB1, DNM1, APOE, PTGDS, SCARA5
F.Crypt_RSPO3
SMAD5-AS1, OGN, CCL19, CAPN6, GREM1, SFRP4, CCL21, C7, PCOLCE2, GREM2, RP11-339B21.13, RP11-195F19.9, PI16, NAALAD2, RP11-572C15.6, CHODL, RSPO3, CCDC80, MAPKAP1, RGMA, NPB, OSR2, GNB3, SFRP1, RP11-597D13.9, FLRT2, ZNF3, C1QTNF9B-AS1, CTC-559E9.6, ADAMTSL3, RNF146, SIMC1, CP, PTGDS, ANGPTL1, DPT, FMR1, SRPX, CXCL12, ADH1B, EFEMP1, COL14A1, IRF2BP1, ZNF398, CFH, COPRS
F.Crypt_hiFos
RP11-173B14.5, TMEFF2, BCDIN3D-AS1, LPAR4, CTD-2651B20.3, RP11-420L9.5, CPEB1
F.Crypt_loFos_1
BPI, AL132709.8, RP11-216B9.6, PNMA2
F.Crpt_loFos_2
RP11-588K22.2, RN7SKP295, PIP4K2B, MAP3K10
F.Endothelial
AC116035.1, C1QTNF9, C1QTNF9B, CASC10, CTD-2536I1.1, CYP1A1, ESM1, FAM69B, GABRD, GALNT15, GJA5, GPIHBP1, GSDMC, KRT222, KRT5, LHX6, LYVE1, MMRN1, NOVA2, NOX4, PDE10A, RASSF9, RP11-286H15.1, RP11-676J12.6, STC2, ZNF541, ZNF833P, ZNF385D, LCN6, KDR, H19, HIGD1B, CXorf36, TM4SF18, AC011526.1, ECSCR, PLVAP, APLNR, SELE, FAM110D, CLDN5, DARC, RP11-251M1.1, VWF, SNCG, FCN3, ESAM, GPR4, FAM167B, COX4I2, MADCAM1, GPR116, SOX17, SHANK3, CDH5, CLEC14A, TLL1, ARHGEF15, EXOC3L2, CORT, RP11-536O18.2, RP11-536O18.1, ROBO4, AVPR2, INHBB, GAS1, MYCT1, BCL6B, THSD1, EGFL7, RAMP2, FLT1, RAMP3, SOX7, CD34, TMEM88, SOX18, TPO, CD320, MMRN2, RP11-23P13.7, KL, FUT1, SLC14A1, RP11-159D12.10, HSPA12B, PODXL, USHBP1, ADM5, CCL14, ANGPT2, ANKRD29, ELTD1, RND1, CCDC3, JAG2, PCDH12, TNFRSF10C, TEK, KCNJ8, KIAA1462, KANK3, ADCY4, RBP7, CYYR1, FOXS1, APLN, SELP, VEGFC, GRB10, CPLX1, JAM2, BFSP1, CALCRL, NPR1, GPRC5B, BTNL9, TSPAN7, C22orf34, PALMD, RP3-473L9.4, RASIP1, IGSF9B, F2RL3, RTN4RL2, RAPGEF3, ERG, ARHGAP29, BAALC, GJA4, EMCN, DYSF, FGD5, FABP5, HYAL2, PKN3, ENG, CTD-2135D7.5, CD36, TIE1, ALPL, SFTA2, SLC9A3R2, EPAS1, RP11-355F16.1, CD93, ACE, NUAK1, TSPAN18, DOCK9, PTPRB, SNTG2, AC009336.24, LEPR, CABP1, RAPGEF4, GPR146, NOSTRIN, EVA1C, ADAMTS4, ICAM2, SEMA3F, TNFAIP1, CSGALNACT1, MIER2, CRIP2, RASA4, MPZL2, KIF26A, SMAD1, SHROOM4, CPXM2, GNG11, EXOC3L1, IFI44L, RP11-830F9.6, SERPINI1, RGS5, DGKE, SHE, LTF, NDST1, LDB2, ADAM15, OAZ3, MYBBP1A, PLA1A, FZD4, C4orf32, SLCO2A1, RP11-92C4.6, AQP1, CACNG8, DLL4, CYP1B1-AS1, TGFBR2, GIMAP8, NOTCH4, IPO11, PCDH17, KCNC4, CUBN, NDUFA4L2, MAPK11, MKL2, PLCB1, APBB2, CFI, C2CD4B, STOM, TMEM204, CASP12, FAM107A, RBP5, SEMA6C, FAM65A, HEG1, PKP4, SLC35G2, PEAR1, SCARF1, EDN1, FAM219A, ARAP3, SYNPO, RAI14, SH2D3C, S1PR1, EHD4, CCDC85B, MTUS1, FAM13C, CLEC3B, RUNDC3B, ENPP2, C11orf95, BCAM, ASB9, IGHV3-64, FKBP1A, TINAGL1, LIFR, PTRF
F.Endothelial_1
FGF12, GJA5, SEMA3G, PDE10A, IGFBP7-AS1, PRODH, RP11-789C17.1, FCN3, TNMD, GPIHBP1, IGF2, SLC6A6, JAG2, ARL15, ALPL, EDN1, HEY1, AQP1, CTD-2035E11.4, RP11-225B17.2, AIF1L, SOX7, RP11-576D8.4, ANKRD29, RBP7, SRP14
F.Fibroblast
AC002511.2, AC004538.3, AKNAD1, AL132709.8, CHRM2, CILP, CLSTN2, COL6A5, CTD-2078B5.2, CTD-2334D19.1, FAM19A1, FAM216B, FGF10, FGF14, FMO2, GLIS1, GREM1, GRIK4, HOXC8, HTR2A, KRTDAP, LIFR-AS1, LRRC15, LRRC18, NACAD, NKX3-2, NPY, OMG, PPAPDC1A, RBMS3-AS3, RN7SKP295, RP11-129B22.1, RP11-395L14.4, RP11-473E2.4, RP11-473L15.2, RP11-7O14.1, RP11-800A3.7, RP3-323P13.2, RP4-530I15.6, RP5-1172A22.1, RSPO2, SHISA3, SLC17A7, STRA6, TCEAL5, TEKT3, WISP1, DPT, SEMA3E, CCL13, CNTN1, FAM19A5, CCL11, AC104654.2, LTBP2, THBS2, ADORA1, HS3ST3A1, IL13RA2, ADAMTSL3, MMP3, VSTM2A, IL11, FAM150B, GLP2R, CHI3L1, GAS6-AS2, SCUBE1, CCL7, RP11-449D8.1, SFTAIP, COL4A5, CHODL, AL035610.1, RP11-112H10.4, DMKN, PDGFRA, RP11-588K22.2, PCOLCE2, NSG1, COL4A6, OXT, WNT5B, SVEP1, OGN, C3, REEP2, CPXM1, SYNDIG1, CYP27C1, F3, LRRN4CL, TNFRSF11B, RP11-572C15.6, SDK1, MMP1, ARL9, ENHO, LRCH2, CP, RNF150, MXRA5, SCARA5, DACT1, FAM65C, ABCA9, TMEM119, RP11-1002K11.1, CYS1, CCL19, SRRM3, COL7A1, SCUBE2, ABCA8, HTRA3, ADH1B, PCSK6, APOD, HAS1, DNM1, FGF7, VCAM1, HMGCLL1, ELANE,

TABLE 8-continued

Stromal UC specific markers for indicated cell types
ADAMTS13, STMN2, BMP4, RP11-69I8.3, PRR16, RP11-152P17.2, BMP7, PIEZO2, CTSK, NPPC, AKR1C1, CTD-2269F5.1, C1QL1, C10orf107, GPC3, FIGN, LOXL1, CCDC71L, CFD, DZIP1L, RP11-204M4.2, FGF9, PI15, DHRS7C, ANGPTL1, GLT8D2, FANCC, BMP5, PROCR, ADAMDEC1, TRPA1, NAALAD2, GPR133, PTGIS, RP11-284F21.8, KB-1125A3.11, GSTM5, LOX, HAPLN1, FBLN1, LAMA2, PLAU, RARRES2, LRP1, CCDC80, PRTG, WNT2 F.Glia
ADAMTS8, ANGPTL7, CADM2, CDH2, CMTM5, CRTAC1, FOXD3, L1CAM, NRXN1, PCSK2, PMP2, RP11-189B4.6, RP4-792G4.2, SERPINA5, SOX10, TENM3, TFAP2A, CDH19, MYOT, GPR17, PLP1, SOX2, LRRTM1, MPZ, COL28A1, XKR4, PPT2-EGFL8, DLX2, PRIMA1, HAND2-AS1, STEAP1B, NTM, GPM6B, AKAP6, LINC00162, SHC4, AC004466.1, CRYAB, DYNC1I1, WISP2, MAB21L1, TMEM59L, ST6GALNAC2, KIRREL3, HAND2, KCNMB4, NRXN3, RP11-262H14.3, TGFB2, SORCS1, NXF3, CADM4, TUBB2B, NGFR, HOXC6, MFAP3L, HOXC9, S100A1, LOXL3, ART3, TTYH1, CAPS, KCTD1, SEMA3B, MMP17, MEGF6, SPP1, COL8A1, RP11-18H7.1, FSTL3, COL9A3, COL21A1, NLGN4X, PMEPA1, DHH, RP4-635E18.6, RP5-1126H10.2, PRNP, TPT1-AS1, UBR4, GAS7, MIA, TSPAN11, GPR155, GFRA3, SLC22A17, SCN7A, SCRG1, EGFL8, TTR, NPTX2, ANKRD53, SNCA, SH3BGR, FHOD3, TIMP4, C1orf198, ITGB8, DEPDC7, GALNT2, LGI4, TSPAN15, RASSF4, TNFAIP6, SCCPDH, NUP188, OLFML2A, LAMP5, ALDH1A1, TMEM17, SEMA3C, RP5-1007M22.2, SCN9A, CNP, CAB39L, DAG1, KCNAB3, RCAN1, SLC15A3, SMIM5, CDKN2A, PMP22, BPGM, MAL, FEZ1, ARHGAP15, GDNF, RIPK4, FBLN2, CHADL, PHLDA3, S100B, SIPA1L2, CYTL1, HSPB2, DKK3, FAM210B, LEPREL1, C12orf43, IMMP2L, FAM124A, SORBS2, ITPR1, ARHGEF26, KCTD11, IER3, BMP8B, COMT, PCDH9, FST, FADS3, TXNRD2, CCL2, VPS52, PON2, CADM3, LPAR1, NRN1, ABL2, LINC00672, SREBF1, ANXA2, FRMD4A, SDC3, PDLIM4, MATN2, SLITRK6, RP11-374M1.5, RXRG, PEBP1, NLRP1, AP1S2, KCNS3, STARD13, JKAMP, GATM, CYR61, CBR1, GPC1, FXYD1, HES1, PCID2, PEPD, ADK, UPB1, CNPY2, MARCH2, S100A3, AP000688.8, B4GALT6, SPARC F.Inflammatory
C22orf15, IL24, SBSN, TMEM215, TRPC4, ZNF295-AS1, TNFRSF11B, IL13RA2, CHRM2, MMP3, PI15, WNT2, CHI3L1, RP1-90J20.8, MMP10, LBP, RP4-530I15.6, STRA6, GALNT16, WISP1, TWIST2, RASL11B, PLAU, STK32B, PTGES, PPAPDC1A, TFPI2, STEAP1, BDNF, MMP1, CXCL6, HGF, RP11-204M4.2, SORCS2, GAL, LINC00944, KIAA1199, PTHLH, PPIL1 F.Microvascular
SCHIP1, MEGF11, RP11-536O18.2, F2RL3, AKR1E2, ME3, FABP5, AK7, CD36, RP11-540B6.6, RIN1, PCDH12, RGCC, SDPR, CTD-2319112.4, PRX, RAPGEF4, PRSS23, BAALC, WWTR1, TSPAN12, CABP1, HLX, VWA1, SEMA3F, C16orf80, ITGA6, MPV17L2, AC116035.1, PLVAP, ANKRD65, SH3BP5, RP11-509E16.1, PASK, PLIN5, FLT1, KIFC3 F.Myofibroblasts
SYT10, SOSTDC1, TRDN, RAB9B, NPNT, HSD17B6, RP11-344E13.3, ACTG2, MYOCD, CTB-47B11.3, AF131217.1, TACR2, CNN1, SPOCD1, HHIP, DES, MYH11, ADAMTS6, KCNMB1, MBNL1-AS1, PDLIM3, MFAP5, LTBP1, FAM150A, MYLK, SLC2A4, LUZP2, FAM74A6, ADCY2, FAM168A, RP11-379B18.5, LPP, TMSB15A, ULK2, SMTN, KANK1, FLNA, TAGLN, LMOD1, ARHGEF25, SLMAP, PDLIM7, CAP2, APCDD1, FHL1, TCEAL1, HFE, HHIP-AS1, TGM2, NDUFA4, GRM7, DPEP2, PLN, NEXN, THSD4, LRRC73, NEO1, CSRP1, RP11-611D20.2, PDIA5, CES1, TGFB1I1, TPM2 F.Pcap_Venules
SELE, DARC, GAS1, MADCAM1, CCL14, MMRN1, RP11-355F16.1, PLA1A, SNTG2, SELP, MEOX2, ZNF385D, C2CD4B, DUSP23, CSF3, RAB3C, LINC00312, SNORA40, LINC01013, RP4-607J23.2, TUBB3, RP11-782C8.5, CPXM2, SMAD1, IL33, PRCP, PKD1L1, TLL1, LHX6, RP11-417J8.6, SYT15, TSPAN7, GABRD, CACNG8, MED24, RASSF9, ICAM1, REM2, TPD52L1, MEOX1 F.Pericytes
FOXS1, NOTCH3, KCNJ8, COX4I2, RGS5, NDUFA4L2, HIGD1B, STEAP4, HEYL, GJC1, CTD-3247F14.2, HRC, LPL, EFHD1, OLFML2B, C1QTNF1, ITGA7, EDNRA, ARVCF, LDB3, FAM162B, RP11-85A1.3, PDGFRB, ENPEP, NR2F2, CTD-3193K9.4, CENPP, HES4, PGF, SEPT4, BGN, AC022007.5, OLFM2, NRIP2, ADCY3, PTGIR, MAP3K7CL, CSRP2, NR1H4, C2orf40, ANO1, SERPINI1, ANGPT2, PLXDC1, LHFP, CYP4X1, HEY2, MEST, TINAGL1, SNAPC3, ADIRF F.Stromal
AC002511.2, AC004538.3, AC092652.1, AC116035.1, AC140912.1, ADAM33, ANGPTL1, AP000525.9, BHLHE22, C1QTNF7, C1QTNF9, C1QTNF9B, C22orf31, CAND2, CCDC178, CCDC8, CDO1, CFHR3, CHRD, CHRDL2, CHRM2, CHST1, CLSTN2, COL6A5, CORO6, CTB-92J24.3, CTD-2135D7.5, CTD-2334D19.1, CTD-2536I1.1, CYP1A1, EDNRA, EGFL6, EXOC3L2, FAM155A, FAM162B, FAM171B, FAM19A1, FAM26E, FAM69B, FBXL7, FGF10, FGF14, FIGN, FLRT2, FMO2, FMO3, FNDC1, FOXL1, FOXS1, GALNT15, GALNT16, GIPC3, GJA4, GJA5, GLI2, GLIS1, GLP2R, GPIHBP1, GREM1, GRIA4, GSG1L, HPSE2, HS3ST3A1, IGDCC4, IGF2, IL17B, ITGB3, KCNJ8, KIAA1755, KIRREL, KRT222, KRTDAP, LAMC3, LBP, LHX6, LIFR-AS1, LOXL4, LPHN3, LRCH2, LRRC15, LRRC3B, LYVE1, MAB21L2, MASP1, MATN3, MEOX2, MMRN1, MUSK, MYOCD, NAALAD2, NKX3-2, NOVA2, NPY, NR2F2-AS1, NUDT11, OGN, OMG, PABPC5, PCDHB4, PCDHB7, PGR, PIEZO2, PKNOX2, PLN, PPAPDC1A, PRRX1, PTGFR, PTH1R, RASSF9, RBMS3-AS3, RGMA, RN7SKP295, RNF112, RP11-129B22.1, RP11-152P17.2, RP11-264B14.1, RP11-395L14.4, RP11-473L15.2, RP11-514D23.3, RP11-536O18.1, RP11-572C15.6, RP11-676J12.6, RP11-710C12.1, RP11-7O14.1, RP11-800A3.7, RP11-804A23.4, RP11-92C4.6, RP3-323P13.2, RSPO2, SALL1, SLC27A6, SLC45A1, SPOCD1, STC2, STRA6, TCEAL5, TEK, TEKT3, TWIST2, VAT1L, VEGFC, WBSCR17, WNT2, ZNF541, ZNF833P, NOTCH3, VSTM2A, CCL21, ASPN, COX4I2, ZNF385D, CTC-276P9.1, CLEC3B, TBX2, DHRS7C, LCN6, KDR, MPDZ, HSPA12B, SFTA1P, MGP, APLNR, PDE1A, SYNDIG1, LMOD1, RAMP3, PAMR1, TNXB, TCF21, FCN3, SRRM3, ZP1, CLDN5, FAM107A, PODN, NTF3, PGM5, RP11-332H18.4, NR2F1, IL13RA2, DCN, RBPMS2, EMCN, H19, HIGD1B, NKX2-3, AC131025.8, TMEM100, SLIT3, ARHGAP28, DPT, TMTC1, POSTN, OLFML1, PRR16, FENDRR, FOXF2, LINC01082, VWF, FILIP1,

TABLE 8-continued

Stromal UC specific markers for indicated cell types
PDGFRA, BMP4, AGT, HSPB6, SEMA3E, PCDH19, RP11-449D8.1, CXorf36, PREX2, CXCL14, AC003090.1, COL4A5, CD34, LUM, STMN2, MMRN2, RAET1G, ACSS3, SOSTDC1, AC011526.1, ECSCR, TM4SF18, SVEP1, LIFR, PLVAP, BCL6B, TDO2, NEXN, FAM110D, MFAP5, ELANE, MFAP4, C1QL1, RGS5, SNCG, SNAI2, FAM150B, KIAA1462, DARC, NTN1, GPR63, ACTG2, ACTA2, RBP5, NXN, MADCAM1, PCOLCE, MRVI1, TRIL, TMEM200B, ADORA1, SCARA5, FAM13C, AC124789.1, SEPT4, SULF1, CLEC14A, CDH11, ESAM, PCDH7, CYGB, PCDH18, PLEKHH2, DNM3OS, ADAMTSL3, TMEM119, CCL13, FOXF1, GPR4, CP, FAM167B, ENPP6, GPR116, CCL7, ITGA11, TLL1, EPHA3, COL4A6, ECM2, RAMP2, LPHN2, MIR145, RP11-251M1.1, LOXL1, SGCD, CFH, RP11-736K20.5, FAM19A5, VASN, MMP3, SULT1C4, CAV1, NID1, SELE, SOX17, EFEMP1, IL11, HSD17B6, PDGFRB, PYGO1, HTRA3, CYS1, SHANK3, LRRC17, RASIP1, ADH1B, ADAMDEC1, BICC1, BMP5, CCDC3, RCAN2, TAGLN, NDNF, TAC3, LRRN4CL, SELP, CCDC74B, DIO2, THBS2, GLIS2, C17orf82, FBLN1, HHIP, SEMA3A, MYH11, CAV2, CDH5, COLEC11, CCL11, MMP2, C16orf89, ARHGEF15, RP11-351D16.3, RP11-536O18.2, SGCA, TRAM1L1, DMKN, LTBP2, OSMR, FJX1, COLEC12, GPRC5B, FGF7, ROBO4, AC100830.3, MIR497HG, GLI1, STC1, EDIL3, USHBP1, COL7A1, KCNE4, EGFL7, THSD1, INHBB, CNTN1, COL6A3, HAPLN1, MAPK10, PRICKLE2, PTCH1, PCDHB10, LOX, RP11-157P1.4, MYCT1, MXRA5, EFHD1, TPO, TRPA1, ARHGAP29, TPM2, AHNAK2, BOC, ABLIM3, ADAMTS5, MFAP2, MYOZ3, DCLK1, SOX7, SNCAIP, DCHS1, HMGCLL1, OSR1, AVPR2, AMPH, C14orf37, FLT1, PPAP2B, SYNPO2, SCARF2, SLC9A3R2, PTGDR2, CRISPLD2, SLC16A2, WNT2B, CHODL, LCA5, CNTNAP3B, ADAMTS12, SNED1, RUSC2, PITX1, CFD, CALD1, THY1, CTHRC1, CCL8, TNFRSF10C, RP11-611D20.2, FGF13, HIF3A, FUT1, RP11-23P13.7, WNT5A, FGD5, FAP, MMP11, TRPC6, DACT1, LAMA5, COX7A1, ARHGEF25, JAM2, GGT5, PEAR1, RPS6KA2, LPL, TMEM88, SCUBE1, IGFBP3, CD320, TCF7L1, CACHD1, HOXD3, TFPI, SOX18, MIR143HG, JAG2, TRPC1, TSPAN9, NDUFA4L2, CTD-2314B22.3, HAS1, ARL9, ACKR3, CD248, HOXA11, AASS, CTSK, EVA1A, TNFRSF11B, CTD-2269F5.1, AL590822.1, A2M, NLGN4Y, DES, CCDC80, GRIP2, WNT5B, P4HA3, FBN2, PLAU, EML1, MMP1, FXYD6, MDFI, COL3A1, TM4SF1, RP11-112H10.4, LAMB1, COL9A1, RP11-204M4.2, ADM5, SOD3, CCL14, CLMP, CCL19, NSG1, PPP1R14A, SLC14A1, ROBO1, EMILIN1, RHOJ, MDGA1, C11orf96, ZC3HAV1L, TMEM150C, RP11-486G15.2, F3, CPXM1, RP11-532F6.3, ANGPT1, FGD1, LPAR3, PRKG1, VCAM1, FZD4, SDK1, SCGB1B2P, IGSF9B
F.Villus
GS1-18A18.1, RP11-804A23.4, REEP2, ENHO, VSTM2A, NPY, PCSK6, FGF9, LPAR3, GSG1L, GLP2R, PTGIS, COL4A5, FAM150B, TTC25, AC002511.2, AC003090.1, CNTFR, AC079779.4, SOX6, BMP5, POSTN, WNT5B, NSG1, PDGFRA, PDGFD, DHRS7C, PTGDR2, RP11-231D20.2, SCUBE1, LANCL2, ZBTB20-AS2, MMP11, DMKN, COL4A6, PTCHD1, EDNRB, C10orf107, RP11-423H2.3, RP4-755D9.1, BMP4, GADD45G, CTC-349C3.1, SEMA3A, KRTDAP, TNFSF15, C1QL1, OBSCN, INSC, F3, APOD
F.Villus_1
EFCAB1, TTC25, TSNAXIP1, FAM178B, GDF15
F.Villus_2
RP11-626G11.3, LGALS8-AS1, CTD-2651B20.1, RP11-231D20.2, LPAR3, RP11-834C11.5, AC079779.4, NPY, RP4-794H19.4, ZC3HAV1L, C14orf23, FOLR1

TABLE 9A

Epithelial						
identE.Absorptive	identE.Absorptive_All	identE.Absorptive_TA	identE.Absorptive_TA_1	identE.Absorptive_TA_2	identE.Best4_Enterocytes	identE.Cycling_TA
CA4	C15orf48	C15orf48	LGALS4	COX4I1	BEST4	TUBA1B
CEACAM5	C19orf33	LGALS4	C15orf48	LGALS4	CA7	H2AFZ
CLDN3	CA2	PHGR1	PIGR	C15orf48	SPIB	GSTP1
CLDN7	CES2	PIGR	KRT8	AGR2	OTOP2	PRDX5
EPCAM	CLDN7	TXN	MT-ND1	TXN	MT1G	UBE2C
FABP1	EPCAM	KRT8	MT-CO3	FABP1	CA4	HMGB2
FTH1	ETHE1	FABP1	EPCAM	ATP5G1	MT2A	RPS2
FXYD3	FABP1	ATP5G1	MT-CYB	MGST1	KRT8	CENPM
GUCA2A	FXYD3	EPCAM	KRT18	ATP5G3	MT1H	RPS3
GUCA2B	KRT19	AGR2	TXN	EPCAM	SDCBP2	RPL36A
KRT20	KRT8	MT1G	MT-ND4	PIGR	MT1E	RPS5
KRT8	LGALS3	GPX2	MT1G	GPX2	KRT19	STMN1
LGALS3	LGALS4	MGST1	MT-CO2	TMSB10	LGALS3	TK1
LYPD8	MT-CO2	MT-ND1	MT-ATP6	COX5B	PHGR1	RPLP0
PHGR1	PHGR1	SELENBP1	MT-ND2	PHGR1	KRT20	RPL8
PLAC8	PIGR	KRT18	AGR2	CYC1	LYPD8	RPS10
SDCBP2	PRSS3	FXYD3	CLDN7	S100A14	NEURL	MIF
SRI	SDCBP2	MT-CO3	SELENBP1	KRT8	FXYD3	RPL36
TSPAN1	SLC26A2	COX5B	GPX2	MT1G	LGALS4	PTTG1
CLDN4	SLC26A3	ATP5G3	ATP5G1	URAD	FABP1	RPS18
CEACAM1	SRI	HMGCS2	PPP1R1B	SELENBP1	HES4	RPS9
CEACAM7	TMEM54	CLDN7	PRDX5	COX5A	CTSE	RPS6
PRSS3	TSPAN1	CHCHD10	COX5B	LGALS3	MT1X	ATP5G1
AQP8	KRT20	MT-CYB	HMGCS2	UGT2B17	EPCAM	C17orf76-AS1
C19orf33	MS4A12	CYC1	MT-ND5	CHCHD10	HRCT1	TMSB10
MISP	GUCA2A	PRDX5	TSPAN8	CA2	S100A10	RPL7A

TABLE 9A-continued

Epithelial						
IFI27	SMIM22	MT-ND4	MT-CO1	COX6C	CKB	RPL35
PRAP1	SELENBP1	PPP1R1B	MT1E	HMGCS2	ITM2C	RPS15
CLCA4	TST	MT-CO2	LGALS3	COX6A1	GUCA2A	BIRC5
HSD17B2	CHP2	COX5A	MGST1	CLDN7	MSLN	RPL12
MUC13	KRT18	TSPAN8	CLDN3	TSPO	CLDN3	RPS8
LGALS4	CYSTM1	S100A14	CHCHD10	TMEM141	CLDN4	COX4I1
CA2	S100A10	TMSB10	KRTCAP3	TSPAN8	TSPAN1	CENPW
CDHR5	CLDN3	COX4I1	ATP5G3	KRT18	SRI	HMGB1
S100A10	CA4	TSPO	S100A14	FXYD3	KRT18	RANBP1
TMEM54	PKIB	LGALS3	KRT19	C10orf99	CLDN7	RPS19
ITM2C	C10orf99	CLDN3	ELF3	UQCR10	S100A6	RPL13
CYSTM1	S100A6	KRTCAP3	MT-ND3	C19orf33	DMBT1	HIST1H4C
PPDPF	TSPAN8	CA2	CA2	SMIM22	MT1M	CDKN3
MYO15B	CA1	COX6C	CYC1	COX6B1	PPDPF	RPL10A
SMIM22	PLAC8	C10orf99	C10orf99	PPP1R1B	C10orf99	AGR2
GPA33	MISP	MT1E	COX5A	UQCRQ	TMEM54	CDC20
AOC1	CDHR5	UGT2B17	KLF5	ATP5D	CYSTM1	RPL37A
S100A6	SLC51B	MT-ATP6	COX6C	CLDN3	ELF3	IGFBP2
TRIM31	CEACAM7	MT-ND2	MT-RNR1	RPL8	PRSS3	RPSA
CDHR2	MT-CO3	TMEM141	ATP5B	KRTCAP3	PCSK1N	TYMS
SPINT2	MT-CO1	ELF3	UGT2B17	KRT19	CEACAM5	AURKB
CFDP1	ANPEP	KRT19	STARD10	UQCRH	C15orf48	RPS21
EMP1	S100A14	ATP5B	TSPO	ATP5B	NOTCH2NL	RPS14
MEPIA	CKB	STARD10	FAM3D	AKR1C3	PIGR	DTYMK

identE.Enterocyte__Immature__1	identE.Enterocyte__Immature__2	identE.Enterocyte__Progenitor
ANPEP	CA1	CA1
AQP8	CA2	CA2
C19orf33	ETHE1	FABP1
CA4	FABP1	FXYD3
CEACAM5	FXYD3	KRT19
CEACAM7	KRT19	KRT8
CLCA4	KRT20	LGALS4
CTD-2228K2.5	KRT8	PHGR1
FABP1	LGALS3	SELENBP1
FXYD3	MS4A12	C15orf48
GUCA2A	PHGR1	CKB
GUCA2B	SLC26A2	PIGR
LYPD8	SLC26A3	LGALS3
MT-CO1	SLC51B	SLC26A2
MT-RNR2	TMEM54	CLDN7
PHGR1	SRI	KRT18
PLAC8	PLAC8	HSD11B2
PRAP1	MALL	CES2
SDCBP2	TSPAN1	ETHE1
SLC26A3	SELENBP1	MT1G
TSPAN1	LGALS4	EPCAM
CDHR5	CTD-2228K2.5	TSPAN1
CLDN7	C19orf33	C19orf33
MISP	PRAP1	UQCRQ
MT-RNR1	CEACAM7	TMEM54
MYO15B	SDCBP2	S100A14
TRIM31	CKB	HMGCS2
IFI27	AKR1B10	MT-CO3
LGALS4	GUCA2A	COX5B
CEACAM1	TST	C10orf99
NEAT1	PKIB	MT-CO2
PIGR	SLC25A5	CHCHD10
KRT8	GCNT3	ADIRF
KRT20	CEACAM1	SMIM22
MT-CO2	MYL6	MT-ND1
CLDN4	CLDN7	CLDN3
SMIM22	CES2	SLC26A3
FTH1	SULT1A2	TST
SFN	FLNB	CHP2
RP11-48O20.4	AQP8	MT-ND4
MS4A12	UQCRQ	AMN
ELF3	CHP2	ATP5G3
HIST1H1C	RP11-48O20.4	MT1E
MUC12	ANPEP	KRT20
PRSS3	C2orf88	SRI
TMEM54	CYSTM1	S100A6
CA2	CDHR5	MT-ND5
SLC51B	BSG	AKR1C3
AMN	IFI27	MT-ATP6
MUC13	COX6A1	MT1M

TABLE 9A-continued

Epithelial					
identE.Enterocytes	identE.Enteroendocrine	identE.Epithelial	identE.Goblet	identE.Immature__Enterocytes	identE.Immature__Goblet
ANPEP	PCSK1N	AGR2	CEACAM5	AQP8	AGR2
APOBEC3B	SCGN	AMN	CLDN4	C15orf48	CLCA1
AQP8	CHGA	C10orf99	FAM3D	C19orf33	FCGBP
C19orf33	CRYBA2	C15orf48	FCGBP	CA1	ITLN1
CA4	PYY	C19orf33	FXYD3	CA2	KLK1
CEACAM1	FEV	CA2	GSN	CDHR5	KRT18
CEACAM5	SCG5	CDHR5	IFI27	CEACAM7	LRRC26
CEACAM7	GCG	CKB	LYPD8	CES2	MUC2
CFDP1	TTR	CLDN3	MUC1	CKB	REP15
CLCA4	MS4A8	CLDN4	MUC2	CLDN7	RETNLB
CLDN23	NEUROD1	CLDN7	TFF1	CTD-2228K2.5	RNASE1
CLDN7	CACNA1A	COX5B	TFF3	EPCAM	SERPINA1
CTD-2228K2.5	STARD10	ELF3	TSPAN1	ETHE1	SPINK1
EMP1	HOXB9	EPCAM	ZG16	FABP1	SPINK4
FTH1	MLXIPL	FABP1	MUC13	FXYD3	ST6GALNAC1
FXYD3	PRDX5	FAM3D	REP15	GUCA2A	TFF3
GPRC5A	RAB26	FCGBP	S100P	KRT18	WFDC2
GUCA2A	CPE	FXYD3	PHGR1	KRT19	ZG16
GUCA2B	KIF12	HMGCS2	MT-RNR2	KRT20	LGALS4
HIST1H1C	SLC29A4	IFI27	CLDN7	KRT8	TPSG1
HPGD	FXYD3	KRT18	ENTPD8	LGALS3	PHGR1
IFI27	CHGB	KRT19	ELF3	LGALS4	FXYD3
IL32	SCT	KRT20	NEAT1	MALL	STARD10
KRT20	VWA5B2	KRT8	KRT18	MISP	GMDS
LYPD8	MDK	LGALS3	MALAT1	MS4A12	KRT8
MISP	CES1	LGALS4	SERPINA1	MT-CO2	FAM3D
MS4A12	KIAA1324	MT-ATP6	VSIG2	PHGR1	HEPACAM2
MYO15B	C15orf48	MT-CO1	PLAC8	PIGR	MT-ND1
NLN	DDC	MT-CO2	LGALS4	PLAC8	RPL36
PKIB	HOXB8	MT-CO3	SDCBP2	PRAP1	NPDC1
PLAC8	LGALS4	MT-CYB	KLK1	PRSS3	EPCAM
PRAP1	ERI3	MT-ND1	TM4SF5	SDCBP2	MB
RP11-48020.4	SOX4	MT-ND2	MT-RNR1	SELENBP1	C15orf48
SDCBP2	MARCKSL1	MT-ND4	BCAS1	SLC26A2	SMIM22
SLC26A3	REG4	MT-RNR1	KRT8	SLC26A3	ANG
SLC51B	TFF3	MT-RNR2	AMN	SLC51B	ANXA13
SRI	KRT8	MT1E	CLDN3	SMIM22	MT-CO3
TMEM37	RTN1	MT1G	SPATS2L	SRI	TSPAN13
TRIM31	CXXC4	PHGR1	GUCA2B	TMEM54	NANS
TSPAN1	TPH1	PIGR	SMIM6	TSPAN1	IFI27
TMIGD1	C19orf77	PRSS3	TPSG1	TST	CREB3L1
MALL	RAMP1	S100A14	CREB3L1	IFI27	COX6C
MUC13	SPINK1	S100A6	C19orf33	AMN	PRDX5
HSD17B2	ARX	SELENBP1	CLTB	S100A6	C2orf82
FABP1	DNAJC12	SMIM22	MT-CO1	PKIB	RP11-234B24.2
SFN	RAB3B	SPINT2	MLPH	ANPEP	SPDEF
NEAT1	RP11-279F6.1	TMEM54	SMIM22	CA4	TMEM141
PRSS3	NPDC1	TSPAN1	ZG16B	CHP2	TCEA3
MEP1A	TMEM141	TSPAN8	CAPN8	MT-CO1	CLDN7
CDA	CLDN7	STAP2	EPCAM	CYSTM1	URAD

identE.Secretory	identE.Secretory__AII	identE.Secretory__TA	identE.Stern	identE.Tuft
FCGBP	CLCA1	TFF3	PRDX5	KRT18
KRT18	FCGBP	ITLN1	LEFTY1	AZGP1
MUC2	FXYD3	RPL36	ASCL2	SH2D6
TFF1	ITLN1	KLK1	GPX2	MARCKSL1
TFF3	KLK1	PRDX5	C17orf76-AS1	BIK
ZG16	KRT18	SPINK4	RPLP0	LRMP
ELF3	KRT8	CLCA1	CDCA7	HCK
KRT8	LGALS4	LRRC26	RGMB	PTPN18
MT-RNR2	MUC2	MUC2	RPS18	ANXA13
CLDN4	REP15	RETNLB	RPL12	KRT8
MUC1	SERPINA1	RPL12	SMOC2	ATP2A3
GSN	SPINK1	RPS18	RPS6	AVIL
MALAT1	SPINK4	WFDC2	RPS3	IL17RB
FXYD3	TFF3	FCGBP	PPP1R1B	TRPM5
LGALS4	WFDC2	RPL8	GAS5	ALOX5
CEACAM5	ZG16	AGR2	GNB2L1	SH2D7
LYPD8	LRRC26	RPS9	RPS2	BMX
MT-CO1	PHGR1	GPX2	MARCKSL1	PTGS1
IFI27	AGR2	RPS2	LGALS4	ELF3
FAM3D	TPSG1	RPS3	NUPR1	PPDPF
S100P	RNASE1	SPINK1	RPS5	EIF1B
MT-RNR1	RETNLB	RPS15	ETS2	TPM1
TSPAN1	STARD10	ZG16	PIGR	GNG13

TABLE 9A-continued

Epithelial				
REP15	MT-ND1	RPS14	RPL29	PSTPIP2
MUC13	FAM3D	TMSB10	SLC25A6	MALAT1
S100A6	SMIM22	RPS5	CLDN7	HOTAIRM1
CLDN7	EPCAM	PIGR	RPL31	SPIB
TM4SF5	MT-CO3	C17orf76-AS1	RPS9	TFF3
CLDN3	C15orf48	RPL35	RPL8	CC2D1A
PHGR1	MT-ND4	STARD10	EPHB3	HTR3E
SERPINA1	ELF3	CLDN7	RPL36A	IFT172
SMIM22	CLDN7	RPS8	RPL3	PLCG2
SPATS2L	CLDN3	RNASE1	RPL10A	DEFB1
ENTPD8	IFI27	LGALS4	RPL5	RASSF6
MT-CO3	NPDC1	RPL18	RPL36	HPGDS
MARCKSL1	PIGR	RPL37A	RPS4X	MATK
MT-ND4	ST6GALNAC1	RPL13	RPS24	MT-CO3
TPM1	CLDN4	URAD	RPL14	MT-CO1
KLK1	MT-CYB	MT-ND1	IMPDH2	ANXA4
MT-CO2	MT-ATP6	RPL13A	EPCAM	PPAP2C
BCAS1	MT-ND2	C15orf48	RPL7A	AOC1
EPCAM	MT-CO1	RPL7A	RPL13	OGDHL
AZGP1	MT-CO2	REP15	RPS3A	ATPIF1
MT-ND5	MARCKSL1	RPS6	RPL13A	EPS8L3
PRSS3	MB	MT1G	ALDH1B1	S100A6
NEAT1	CREB3L1	EPCAM	RPS8	FURIN
SMIM6	S100A6	RPL32	SLC12A2	H2AFJ
ZG16B	ANG	COX4I1	C15orf48	TMEM63A
MT-ND1	MUC1	RPL29	RPS19	IFI6
VSIG2	SPINT2	RPL18A	SPINK1	EHF

TABLE 9B

Fibroblast				
identF.Crypt	identF.Crypt__RSPO3	identF.Crypt__hiFos	identF.Crypt__loFos__1	identF.Crypt__loFos__2
A2M	DCN	A2M	A2M	APOE
ABCA8	LUM	ABCA8	ABCA8	CFD
ADAM28	EFEMP1	ADAMDEC1	ADAMDEC1	IGFBP7
ADAMDEC1	FBLN1	APOE	APOE	IFITM3
ADH1B	CFH	C1R	C1R	DCN
APOE	CFD	C1S	C1S	ADAMDEC1
BMP4	CCDC80	CCL2	CALD1	TMEM176B
C1R	C1R	CCL8	CCL13	FBLN1
C1S	C1S	CFD	CCL2	MFAP4
CALD1	CCL11	COL1A1	CCL8	LUM
CCL11	ADH1B	COL1A2	CFD	SOD3
CCL13	COL1A2	COL3A1	CFH	CXCL14
CCL2	CXCL12	COL6A2	CLEC11A	A2M
CCL8	GSN	CTSC	COL1A1	C1S
CD63	MFAP4	CXCL12	COL1A2	GSN
CFD	IGFBP7	CXCL14	COL3A1	C1R
CFH	SOD3	CYGB	COL6A2	RARRES2
CLEC11A	C7	DCN	CTSC	LGALS1
COL1A1	SERPINF1	FBLN1	CTSK	COL1A2
COL1A2	PLAC9	GPX3	CXCL12	COL3A1
COL3A1	MGP	GSN	CXCL14	RNA28S5
COL6A1	ADAMDEC1	HAPLN1	CYGB	TCF21
COL6A2	SERPING1	IFITM3	DCN	CCL13
CTSC	TCF21	IGFBP7	DKK3	CTSC
CTSK	CTSK	LUM	FBLN1	CCL8
CXCL12	PTGDS	MFAP4	GGT5	LTBP4
CXCL14	IFITM3	PPAP2B	GPX3	CCL11
CYGB	LTBP4	PROCR	GSN	COL6A2
DCN	THY1	RBP1	IFITM3	CD63
DKK3	COL3A1	SERPINF1	IGFBP7	CD81
EFEMP1	RSPO3	SOD3	LGALS1	NGFRAP1
EFEMP2	PMP22	TCF21	LINC01082	RBP1
EMILIN1	VIM	TMEM176B	LUM	TMEM176A
FABP4	RARRES2	VIM	MFAP4	SELM
FBLN1	C3	CALD1	MMP2	PTGDS
GGT5	APOE	STMN2	PLAC9	CALD1
GNG11	LGALS1	PTN	PMP22	COL1A1
GPX3	TMEM176B	LINC01082	PPAP2B	CCL2
GSN	ASPN	CTSK	PROCR	TIMP1
HAAO	COL6A2	CCL13	PTN	QSOX1
HAPLN1	CALD1	CFH	RARRES2	PLAC9

TABLE 9B-continued

Fibroblast				
IFITM3	CCL2	PMP22	RBP1	RAB13
IGFBP6	TIMP1	CCL11	SERPINF1	S100A13
IGFBP7	A2M	DKK3	SERPING1	CYGB
LAPTM4A	GPX3	LGALS1	SOD3	GPX3
LGALS1	LAPTM4A	SEPP1	SPARC	ABCA8
LINC01082	COL14A1	PLAC9	TCF21	PPAP2B
LTBP4	PCOLCE	GGT5	TIMP1	CST3
LUM	DPT	RARRES2	TMEM176A	CLEC11A
MATN2	CD63	SERPING1	TMEM176B	VKORC1

identF.Endothelial	identF.Endothelial__1	identF.Fibroblast	identF.Glia
BCAM	CD320	A2M	ALDH1A1
CAV1	CLDN5	ABCA8	CD9
CCDC85B	FABP5	ADAMDEC1	CLU
CD320	GNG11	APOE	CRYAB
CD36	IGFBP4	BMP4	S100B
CD59	PLVAP	BST2	TUBA1A
CLDN5	RAMP2	C1R	GPM6B
CLEC14A	SLC9A3R2	C1S	PMP22
CRIP2	CRIP2	CALD1	PLP1
ECSCR	SPARCL1	CCL11	SPARC
EGFL7	ESAM	CCL13	SPP1
ENG	EGFL7	CCL2	PRNP
ESAM	IFITM3	CCL8	SEMA3B
FABP5	VAMP5	CD63	JUN
FKBP1A	GSN	CFD	MATN2
GIMAP7	TMEM88	CFH	FOS
GNG11	CD36	CLEC11A	CYR61
HLA-C	CLEC14A	COL1A1	CD59
HLA-E	CAV1	COL1A2	COMT
IFITM3	RAMP3	COL3A1	IGFBP7
IGFBP4	HLA-E	COL6A1	CALM2
IGFBP7	ENPP2	COL6A2	HES1
ITM2B	TXNIP	CTSC	MPZ
JAM2	JAM2	CTSK	LGALS1
MGP	ECSCR	CXCL12	ANXA2
NPDC1	SEPW1	CXCL14	LGI4
PLVAP	IGFBP7	CYGB	GFRA3
RAMP2	CD59	DCN	TUBB2B
RAMP3	MGP	DKK3	CNN3
RBP5	TM4SF1	DMKN	C8orf4
SEPW1	BCAM	ECM1	PEBP1
SLC9A3R2	NPDC1	EFEMP2	TIMP3
SNCG	CCDC85B	EID1	DKK3
SPARCL1	VWF	EMILIN1	NRXN1
TM4SF1	CD74	FBLN1	IFITM3
TMEM88	GIMAP7	GGT5	TMEM176B
VWF	ICAM2	GPX3	CCL2
FAM167B	FKBP1A	GSN	IER2
AC011526.1	RBP7	HAAO	JUNB
SDPR	IFITM2	HAPLN1	VIM
IFITM2	SDPR	IFITM3	EGR1
ENPP2	HLA-C	IGFBP6	NDRG2
CYYR1	HLA-DRB1	IGFBP7	RGS16
PRSS23	CYYR1	LAMA4	PMEPA1
GSN	ENG	LAPTM4A	SOCS3
HSPB1	ITM2B	LGALS1	RHOB
CTGF	IFI27	LGALS3BP	CBR1
SPARC	A2M	LINC01082	S100A4
CD34	RBP5	LTBP4	SORBS2
TSPAN7	HES1	LUM	AP1S2

identF.Inflammatory	identF.Microvascular	identF.Myofibrobiasts	identF.Pcap__Venules	identF.Pericytes
NNMT	CD320	ACTA2	CLDN5	RGS5
LUM	FABP5	TAGLN	NPC2	MYL9
C1S	PLVAP	MYL9	DARC	TINAGL1
MMP2	GNG11	TPM2	CLU	CSRP2
COL3A1	PRSS23	ACTG2	TSPAN7	NDUFA4L2
IFITM3	CD36	PDLIM3	GNG11	IGFBP7
CXCL14	GSN	TPM1	VWF	HIGD1B
C1R	SLC9A3R2	MYLK	FABP5	BGN
DCN	RAMP2	SOSTDC1	RAMP3	COX4I2
IGFBP7	CRIP2	DSTN	CPE	ADIRF
RARRES2	RAMP3	NDUFA4	IGFBP4	FRZB
COL1A2	ESAM	MYH11	PLVAP	TSC22D1
LGALS1	SPARCL1	MYL6	RAMP2	CD36

TABLE 9B-continued

Fibroblast				
SPARC	VWF	FHL1	LY6E	SOD3
PLAT	VWA1	HHIP	ECSCR	PDGFRB
FBLN1	RGCC	PRKCDBP	JAM2	TPPP3
TIMP1	ECSCR	SELM	ITM2B	MGP
COL1A1	ITM2B	LGALS1	EGFL7	NOTCH3
MFGE8	EGFL7	TGFB1I1	SPARCL1	MFGE8
TSPAN4	ENG	IGFBP7	CD320	HSPB1
COL6A2	RBP5	CXCL14	MADCAM1	ACTA2
MFAP4	SDPR	HSPB1	IGFBP7	IFITM3
COL6A1	VAMP5	TM4SF1	HLA-E	EGR1
SERPING1	TMEM88	HSD17B6	APLNR	BCAM
TMEM176B	IGFBP4	DCN	CLEC14A	GPX3
LY6E	FKBP1A	FLNA	IFITM3	HLA-C
PROCR	CLEC14A	CNN1	DUSP23	CALD1
RBP1	IGFBP7	PPIC	HHEX	LGALS1
CCL2	CAV1	NPNT	CTGF	PKIG
SOD3	MGP	PDLIM7	NNMT	HES4
DMKN	BCAM	COL1A2	NPDC1	CAV1
PLAU	SPARC	CES1	TM4SF1	PRKCDBP
SELM	CCDC85B	CSRP1	ICAM1	GEM
APOE	PLAT	ILK	GIMAP7	ZFP36L1
CALD1	IFITM3	ADAMDEC1	AC011526.1	FAM162B
F3	CA4	CAV1	SNCG	PGF
CTSK	TM4SF18	COL3A1	CD74	NR2F2
PKIG	TMEM204	LUM	CRIP2	TPM2
TPM2	HLA-E	PPP1R14A	FAM167B	MAP1LC3A
CTSC	HSPG2	SPARC	FAM213A	EPHX1
A2M	EMCN	SMTN	SDCBP	PRSS23
TMEM176A	PASK	APOE	CAV1	CALM2
TCF21	FAM167B	C1S	TNFSF10	MCAM
GPX3	ELTD1	C1R	CTNNAL1	STEAP4
PCOLCE	SLC14A1	NBL1	HLA-DRB1	GADD45B
MYL9	SNCG	TMEM176B	FKBP1A	STOM
CYGB	PODXL	WFDC1	HLA-DRA	LHFP
WARS	FLT1	NEXN	GIMAP4	NDUFAF4
RNA28S5	CAV2	SPARCL1	BCAM	COL18A1
STMN2	CLDN5	LINC01082	CD34	EPAS1

identF.Stromal	identF.Villus	identF.Villus__1	identF.Villus__2
A2M	AGT	CXCL14	BMP4
ADAMDEC1	BMP4	FRZB	COL6A2
APOE	C1S	PLAT	CXCL14
BMP4	CALD1	POSTN	DMKN
BST2	CAV1	DMKN	F3
C1R	COL1A2	NSG1	FRZB
C1S	COL3A1	NBL1	MMP2
CALD1	COL6A1	MMP2	NSG1
CCL2	COL6A2	COL6A1	PLAT
CCL8	CXCL14	FOS	RARRES2
CD63	CYGB	CAV1	LGALS1
CFD	DMKN	VSTM2A	COL6A1
CFH	EDNRB	COL6A2	TMEM176B
CLEC11A	ENHO	TMEM176B	POSTN
COL1A1	F3	BMP4	ENHO
COL1A2	FRZB	IGFBP7	IGFBP3
COL3A1	GPX3	F3	IGFBP7
COL6A1	HSD17B2	ENHO	IFITM3
COL6A2	IFITM3	CYGB	CALD1
CRIP2	IGFBP3	LGALS1	CAV1
CTSC	IGFBP7	SDC2	VSTM2A
CTSK	LGALS1	EDNRB	COL3A1
CXCL12	MFAP4	MFAP4	GPX3
CXCL14	MMP2	CALD1	MFGE8
CYGB	NBL1	IGFBP3	TPM2
DCN	NSG1	RARRES2	TIMP1
ECM1	PLAT	GADD45B	SDC2
EFEMP2	POSTN	GPX3	CYGB
EID1	RARRES2	JUNB	SPARC
EMILIN1	SDC2	TPM2	COL1A2
FBLN1	SERPINF1	SERPINF1	MFAP4
GNG11	SPARC	EGR1	HSD17B2
GPX3	TIMP1	HSD17B2	NBL1
GSN	TMEM176B	IER2	AGT
HSPB1	TPM2	SPARC	EDNRB
IFITM1	VSTM2A	IFITM3	FENDRR
IFITM3	FOXF1	COL3A1	S100A13
IGFBP6	FENDRR	C1S	FOXF1

TABLE 9B-continued

Fibroblast			
IGFBP7	COL1A1	COL1A2	COL1A1
LAPTM4A	SCPEP1	MYL9	C1S
LGALS1	MFGE8	HSPA1A	SERPINF1
LINC01082	C1R	JUN	LGALS3BP
LTBP4	PPP1R14A	AGT	SCPEP1
LUM	LAPTM4A	PDGFD	ECM1
MFAP4	ECM1	FOXF1	APLP2
MFGE8	MYL9	ID1	WFDC1
MMP2	PKIG	C11orf96	PPP1R14A
MYL9	TMEM176A	PKIG	PKIG
NGFRAP1	TMEM119	LAPTM4A	C1R
NNMT	S100A13	FENDRR	LTBP4

TABLE 9C

Immune				
identB.Bcells	identB.Cycling	identB.FO	identB.GC	identB.Plasma
AC096579.7	IGHA1	CD74	CD79A	AC096579.7
AL928768.3	IGJ	CD79A	CD79B	AL928768.3
CCR10	CD79A	HLA-DRA	AL928768.3	CCR10
CD27	AL928768.3	MS4A1	TCL1A	CD27
CD74	MZB1	VPREB3	SMIM14	CD79A
CD79A	DERL3	HLA-DPB1	MS4A1	CHPF
DERL3	EAF2	HLA-DRB1	CD74	CRELD2
DNAJB9	IGKC	HLA-DPA1	LIMD2	CYTIP
EAF2	IGHA2	HLA-DQA1	C7orf10	DERL3
FAM46C	TNFRSF17	HLA-DQB1	MARCKSL1	DNAJB9
FCRL5	HERPUD1	CD79B	VPREB3	DPP7
FKBP11	UBE2J1	CD37	FCRLA	DUSP5
GNG7	SSR4	HERPUD1	IRF8	EAF2
HERPUD1	SEC11C	CXCR4	SERPINA9	EVI2B
ICAM2	AC096579.7	RPS27	EAF2	FAM46C
IGHA1	IGLC2	LTB	CD53	FCRL5
IGHA2	DNAJB9	AL928768.3	RGS13	FGF23
IGJ	CD74	BANK1	NCF1	FKBP11
IGKC	CD27	CD52	BCAS4	GNG7
IGLC2	CCR10	CD83	CD40	GYPC
IGLC3	XBP1	LINC00926	SNX29P2	HERPUD1
IGLL5	SDF2L1	RPS23	PTPRCAP	ICAM2
MEI1	POU2AF1	IGKC	ISG20	IFNAR2
MZB1	FKBP11	RPS25	RHOH	IGHA1
PIM2	IGLC3	IGHM	CD37	IGHA2
POU2AF1	CYTIP	RPL23A	POU2AF1	IGJ
PTPRCAP	MANF	RPLP2	LTB	IGKC
SEC11C	GNG7	RPL21	HTR3A	IGLC2
SSR4	SPCS3	RP5-887A10.1	HMCES	IGLC3
TNFRSF17	PNOC	CD19	AC023590.1	IGLL5
UBE2J1	FAM46C	FCRLA	GPR18	IGLV3-1
SPAG4	DUSP5	SMIM14	CD72	ISG20
CYTIP	SSR3	BTG1	HERPUD1	LMAN1
CD79B	ISG20	HLA-DMA	LAPTM5	MANF
EVI2B	RGS2	LY86	UBE2J1	MEI1
GYPC	IGLL5	RPS8	HMGN1	MZB1
DUSP5	LSP1	PTPRCAP	CD22	NUCB2
IGLC7	TRAM1	HLA-DRB5	CD19	PABPC4
TRAM1	CD79B	RPS27A	LRMP	PDIA4
SPCS3	SPCS2	RPS20	NEIL1	PIM2
LSP1	GYPC	RPS5	HLA-DMA	PPAPDC1B
XBP1	PIM2	RPL18A	LY86	PRDX4
TPST2	RGS1	RPL32	TPD52	RGCC
TXNDC15	CD38	RPL3	IGKC	RGS1
CHPF	PDIA4	RPL13A	HLA-DQA1	SDF2L1
SLAMF7	IFNAR2	FAU	CD27	SEC11C
PPAPDC1B	TPST2	CYBA	P2RX5	SLAMF7
PNOC	ARHGDIB	SELL	HLA-DRA	SPAG4
IGLV3-1	TSC22D3	HVCN1	HLA-DOB	SPCS3
ISG20	CRELD2	RPS3A	BASP1	SSR3

identI.Immune	identI.Lymphoid	identM.CD69neg__Mast	identM.CD69pos__Mast	identM.Cycling
ARHGDIB	ARHGDIB	TPSAB1	H3F3B	TUBA1B
CCL5	CCL5	VWA5A	NFKBIA	AIF1
CD37	CD2	CAPG	PPP1R15A	FTL

TABLE 9C-continued

Immune				
CD3D	CD3D	LTC4S	TPSAB1	GPX1
CD3E	CD3E	KRT1	VWA5A	CST3
CD48	CD52	MAOB	ANXA1	CD74
CD52	CD69	HPGDS	JUN	C1QC
CD53	CD7	CTSG	CTSG	HLA-DRB1
CD69	CORO1A	GATA2	GLUL	LYZ
CD7	CYTIP	CLU	CAPG	HLA-DPA1
CORO1A	EVL	SAMSN1	DNAJA1	MS4A6A
CYBA	IL32	RP11-354E11.2	UBB	C1QA
CYTIP	LTB	FCER1G	LMNA	HLA-DPB1
EVL	PTPRCAP	ALOX5AP	NFKBIZ	HLA-DRA
HCST	RAC2	SLC18A2	LTC4S	C1QB
LAPTM5	TRAC	FCER1A	FTH1	TYROBP
LTB	TRBC2	NSMCE1	LAPTM4A	PSAP
PTPRCAP	SRGN	ANXA1	C1orf186	DNASE1L3
RAC2	IL2RG	ADRB2	FCER1G	HLA-DQA1
RGS1	LCK	BTK	HSP90AB1	HLA-DRB5
SRGN	CD27	C1orf186	HPGDS	NPC2
TRBC2	CD79A	GMPR	CLU	H2AFZ
ALOX5AP	NKG7	CPA3	DUSP1	FCER1G
TRAC	HCST	ATP6V1F	GATA2	HLA-DMA
NCF1	CD37	GLUL	DDX5	STMN1
TMSB4X	SEPT1	TSC22D1	SERPINB1	LST1
COTL1	HOPX	SLC45A3	ASAH1	MS4A7
DUSP2	GZMA	HS3ST1	BTG2	IGSF6
LCK	CD53	SVOPL	HSPA1B	HLA-DQB1
IL2RG	ACAP1	MITF	FCER1A	TUBB
EVI2B	RGS1	TYROBP	HSPA8	CTSB
CKLF	PCED1B-AS1	CD9	RPL36AL	IL1B
IL32	CD48	ALOX5	DNAJB1	HLA-DMB
HCLS1	AL928768.3	SDPR	HPGD	SPI1
CD2	BTG1	LMO4	IER2	CPVL
SAMSN1	RPS19	CD44	HDC	FAM26F
NKG7	TNFRSF17	NCOA4	MAOB	VSIG4
PTPRC	CTSW	FAM212A	KRT1	MS4A4A
GPSM3	B2M	VIM	LMO4	RNASE6
HOPX	ICAM3	MLPH	HSPA5	SAT1
ARPC1B	FKBP11	FXYD5	EIF1	CCL3
ACAP1	TSC22D3	S100A11	JUNB	AP2S1
ARPC2	RHOH	RGS10	EGR1	RNASET2
PCED1B-AS1	TBC1D10C	ARHGDIB	SLC45A3	NCF4
RHOH	IGHV1OR15-1	QPCT	RPL7	FGL2
ITGB7	CXCR4	S100A4	DYNLL1	CYBA
LIMD2	RPLP1	CATSPER1	MALAT1	LAPTM5
CD27	STK17A	ASAH1	SELK	CTSH
GZMA	RPL10	PKM	MIR24-2	HLA-DQB2
LCP1	RPL3	LAPTM4A	FOSB	COTL1

identM.DCs	identM.Macrophages	identM.Mast	identM.Monocytes	identM.Myeloid
AIF1	ACP5	CAPG	ACP5	AIF1
CD74	AIF1	H3F3B	AIF1	C1QA
CPVL	C1QA	NFKBIA	AMICA1	C1QB
CST3	C1QB	PPP1R15A	C1QA	C1QC
HLA-DMA	C1QC	TPSAB1	C1QB	CD74
HLA-DMB	CD74	VWA5A	C1QC	CLEC10A
HLA-DPA1	CST3	ANXA1	C1orf162	CPVL
HLA-DPB1	CTSB	GLUL	CD74	CST3
HLA-DQA1	CTSD	CTSG	CLEC10A	CTSB
HLA-DQB1	CTSZ	JUN	COTL1	CYBA
HLA-DRA	CYBA	LTC4S	CPVL	DNASE1L3
HLA-DRB1	DNASE1L3	DNAJA1	CST3	FAM26F
HLA-DRB5	FCER1G	UBB	CTSB	FCER1G
LST1	FCGRT	LMNA	CYBA	FGL2
LYZ	FTL	CLU	DNASE1L3	FTH1
SPI1	FUCA1	GATA2	FAM26F	FTL
CLEC10A	GPX1	NFKBIZ	FCER1G	GLUL
HLA-DQB2	HLA-DMA	LAPTM4A	FGL2	GPX1
LGALS2	HLA-DMB	FTH1	FTL	HLA-DMA
AMICA1	HLA-DPA1	C1orf186	GPX1	HLA-DMB
COTL1	HLA-DPB1	HSP90AB1	GRN	HLA-DPA1
TYROBP	HLA-DQA1	HPGDS	HLA-DMA	HLA-DPB1
FCER1G	HLA-DQB1	FCER1G	HLA-DMB	HLA-DQA1
FCER1A	HLA-DRA	KRT1	HLA-DPA1	HLA-DQA2
IL1B	HLA-DRB1	MAOB	HLA-DPB1	HLA-DQB1
HLA-DQA2	HLA-DRB5	ASAH1	HLA-DQA1	HLA-DQB2
MS4A6A	IGSF6	FCER1A	HLA-DQA2	HLA-DRA
CD83	LGMN	SERPINB1	HLA-DQB1	HLA-DRB1

TABLE 9C-continued

Immune				
DNASE1L3	LST1	DUSP1	HLA-DQB2	HLA-DRB5
GPX1	LYZ	BTG2	HLA-DRA	IFI30
FGL2	MS4A4A	DDX5	HLA-DRB1	IGSF6
SRGN	MS4A6A	RP11-354E11.2	HLA-DRB5	IL1B
C1orf162	MS4A7	HDC	IFI30	LST1
ACTB	NPC2	SLC45A3	IGSF6	LYZ
ITGB2	PSAP	IER2	IL1B	MPEG1
FAM26F	RNASE1	CPA3	ITGB2	MS4A4A
MNDA	RNASET2	LMO4	LAPTM5	MS4A6A
SGK1	S100A11	HSPA8	LGALS1	MS4A7
CFP	SAT1	HSPA1B	LST1	NPC2
SAT1	SEPP1	HSPA5	LYZ	PSAP
PLAUR	STAB1	HPGD	MPEG1	RNASE6
IFI30	TMSB4X	SLC18A2	MS4A4A	RNASET2
GPR183	TYROBP	RPL7	MS4A6A	S100A11
RNASET2	CD14	EGR1	MS4A7	SAT1
MPEG1	SDS	DNAJB1	NPC2	SPI1
IGSF6	GRN	RPL36AL	PLAUR	SRGN
RGS2	CTSS	ATP6V1F	PSAP	TMSB4X
LSP1	APOC1	MALAT1	RGS10	TYROBP
LY86	SPI1	MIR24-2	RNASE6	VSIG4
RNASE6	AP2S1	CLIC1	RNASET2	SDS

identM.Neutrophils	identM.Tissue__DCs	identM.Tolerogenic__DCs	identT.Activated__CD4__hiFos	identT.Activated__CD4__loFos
CST3	AIF1	CST3	TRBC2	ANXA1
LYZ	CD74	CPVL	TRAC	TRAC
AIF1	CLEC10A	IDO1	CD69	CD3D
LST1	CST3	CD74	ANXA1	LTB
HLA-DRB1	HLA-DMA	SNX3	CD3D	S100A4
HLA-DRA	HLA-DPA1	HLA-DPB1	IL32	TRBC2
FTL	HLA-DPB1	CLEC9A	S100A4	IL32
HLA-DPB1	HLA-DQA1	HLA-DPA1	CD52	CD52
IL1B	HLA-DQB1	DNASE1L3	LTB	RPLP1
PLAUR	HLA-DRA	HLA-DRB1	CD2	EEF1A1
TYROBP	HLA-DRB1	LGALS2	TSC22D3	ARHGDIB
SOD2	LST1	HLA-DRA	DNAJA1	RPL10
CD74	LYZ	HLA-DQB1	CD3E	RPS27A
HLA-DPA1	FCER1A	HLA-DQA1	ARHGDIB	RPS25
FCER1G	TYROBP	CTD-2319I12.1	KLF6	RPL21
HLA-DQB1	CPVL	LYZ	BTG1	CD3E
GPX1	HLA-DRB5	HLA-DRB5	EIF1	CXCR4
HLA-DRB5	IL1B	Clorf54	RPLP1	RPS19
HLA-DMA	HLA-DMB	HLA-DQB2	HSPA8	RPL32
G0S2	AMICA1	COTL1	SRGN	CD2
HLA-DQA1	FCER1G	SPI1	CORO1A	RPL3
TYMP	MS4A6A	LSP1	EEF1A1	RPS3
MS4A6A	SPI1	IRF8	CCL5	RPS15A
SAT1	HLA-DQB2	HLA-DQA2	DUSP1	RPL13
CLEC10A	PLAUR	AIF1	B2M	BTG1
FCN1	LGALS2	MPEG1	YPEL5	RPLP2
SPI1	HLA-DQA2	HLA-DMA	TNFAIP3	RPS12
S100A9	GPX1	ACTB	TMEM66	RPL9
LGALS2	IGSF6	BATF3	TMSB4X	RPS3A
CFP	CD83	CD83	CXCR4	TMEM66
COTL1	SRGN	HLA-DMB	ID2	RPS6
CYBA	COTL1	SGK1	RGCC	CORO1A
HLA-DMB	CFP	FGL2	RPS27A	RPS27
NPC2	IFI30	C1orf162	RPL10	TMSB4X
SRGN	MNDA	LST1	PTPRCAP	RPL23A
IGSF6	DNASE1L3	RGCC	H3F3B	TPT1
C1orf162	FGL2	RGS10	RPL21	SRGN
FAM26F	FAM26F	CADM1	RPS19	RPL11
CPVL	C1orf162	HLA-DOB	MYL12A	RPSA
STX11	ITGB2	PLEK	RPS3	RPL19
C1QA	RGS2	PPT1	EVL	RPS4X
FTH1	CD1C	HCK	DNAJB1	RPS14
FGL2	SAT1	BASP1	IL7R	RPL4
ITGB2	RNASE6	PTPRE	ACTB	GPR183
CTSS	GPR183	ITGB2	ZFP36L2	RPS2
OAZ1	CTSH	S100B	DDX5	B2M
MS4A7	SGK1	CST7	RPS25	RPL30

TABLE 9C-continued

Immune						
PSAP	ACTB	GLIPR1	RPL32	RPL28		
S100A11	RNASET2	ASB2	SH3BGRL3	RPL31		
IFI30	C1QA	LY86	JUNB	IL7R		
identT.CD4	identT.CD8	identT.CD8__IELs	identT.CD8__LP	identT.CXCRB__Th17	identT.Cycling__T	identT.ILCs
ARHGDIB	ACTB	CCL5	CCL5	CD2	CD52	LST1
B2M	ARHGDIB	CD3D	NKG7	CD52	STMN1	LTB
BTG1	B2M	CD52	IL32	CD3D	CCL5	KRT86
CD2	CCL5	CD7	DUSP2	LTB	CD3D	FXYD5
CD3D	CD3D	HOPX	GZMA	TRAC	CORO1A	NFKBIA
CD3E	CD3E	IL32	CD3D	TRBC2	IL32	IL4I1
CD52	CD52	NKG7	CCL4	IL32	CD3E	ID2
EEF1A1	CD7	TMSB4X	B2M	S100A4	ARHGDIB	CASP3
IL32	CORO1A	PTPRCAP	TRBC2	CD3E	GZMA	DUSP1
LTB	CTSW	GZMA	GZMK	ID2	TRBC2	ZFP36L1
RPL10	GZMA	TRDC	BTG1	ARHGDIB	HMGB2	TYROBP
RPL21	HCST	HCST	CD8A	CXCR6	TUBB	EIF1
RPLP1	HOPX	CORO1A	TRAC	KLRB1	TRAC	CD52
RPS19	IL32	CD3E	TMSB4X	ACTB	CD2	H2AFY
RPS25	NKG7	ACTB	CD52	CORO1A	ACTB	FOS
RPS27	PTPRCAP	ARHGDIB	CXCR4	TMSB4X	TYMS	HSPA8
RPS27A	TMSB4X	TRBC2	ARHGDIB	CKLF	EVL	ZFP36
RPS3	TRAC	TRGC2	HCST	TNFRSF25	KIAA0101	HNRNPA0
TMEM66	TRBC2	CKLF	CD8B	B2M	HMGN2	SPINK2
TMSB4X	EVL	EVL	ZFP36L2	LCK	TMSB4X	BTG1
TRAC	SH3BGRL3	CD160	CD3E	SH3BGRL3	LCK	BTG2
TRBC2	GZMB	RAC2	CD2	CD69	TUBA1B	CXCR4
RPL32	CKLF	TRAC	CST7	GZMA	COTL1	IL2RG
CORO1A	RAC2	CTSW	PTPRCAP	AC092580.4	PFN1	OTUD5
RPL3	CST7	TMIGD2	HLA-C	PTPRCAP	RAC2	DDIT4
RPLP2	CD8A	KLRC2	CORO1A	ARPCIB	NKG7	TNFRSF25
RPS15A	ID2	GZMB	SH3BGRL3	RPS19	TK1	KRT81
RPL13	MYL12A	SH3BGRL3	CD7	OSTF1	PTMA	ARL4A
S100A4	CD8B	LCK	CD69	HCST	CD69	JUNB
PTPRCAP	CCL4	ABI3	TMEM66	IL2RG	PTPRCAP	SRGN
RPL28	LCK	ID2	YPEL5	MYL12A	ARPC2	DNAJA1
EIF1	RPS19	ARPC2	EIF1	BTG1	DUT	MAFF
RPL23A	CD160	TRGC1	CTSW	PCBP1	H2AFV	MIR24-2
RPL19	TRGC2	XCL1	SRGN	CACYBP	ASF1B	TMIGD2
RPS6	CD2	RARRES3	RGCC	SPOCK2	HOPX	CD69
RPS3A	ARPC2	CD96	ACTB	GIMAP7	CD7	ALDOC
RPL11	CD69	PRF1	HLA-B	RPLP1	SRGN	LTA4H
RPL3O	SRGN	RPS19	MYL12A	SEPT1	B2M	FOSB
LCK	PFN1	AC092580.4	HOPX	ODF2L	SH3BGRL3	AMICA1
RPL13A	RARRES3	STK17A	GZMH	PFN1	HCST	IL7R
CXCR4	XCL1	ALOX5AP	ID2	CCL5	ARPC1B	H3F3B
RPS4X	ALOX5AP	MYL12A	H3F3B	SLAMF1	SLBP	PRMT10
RPL9	TRDC	B2M	NR4A2	CCL20	H2AFZ	IER2
SRGN	BTG1	CD247	ANXA1	AMICA1	CKLF	SRSF2
RPL4	ZFP36L2	GNLY	GZMB	CALM1	SRSF7	NR4A2
ANXA1	PRF1	PFN1	EVL	CD6	RGS1	EEF1A1
CD69	HLA-C	CST7	IL2RG	EVL	HSPA8	HMGN3
RPSA	RPS27	ACTG1	RPS27	ABRACL	RRM2	NCOA7
RPL31	DUSP2	TBC1D10C	MCL1	EEF1A1	CLSPN	YPEL5
RPS2	IL2RG	GIMAP7	LCK	ARPC2	CTSW	NR4A1

identT.MT	identT.Memory__CD4	identT.NK	identT.PD1__CD4	identT.Tcells	identT.Tregs
MALAT1	RPS27	NKG7	TRBC2	ACTB	IL32
CCL5	RPL21	FCER1G	CD3D	ARHGDIB	TRBC2
MT-CYB	BTG1	TYROBP	ARHGDIB	B2M	TRAC
SON	RPS3	CCL4	TRAC	BTG1	BTG1
MT-ND2	RPS25	XCL1	LTB	CCL5	ARHGDIB
IL32	RPL32	CTSW	ITM2A	CD2	CD3D
MT-ND4	TMEM66	GNLY	RP5-1028K7.2	CD3D	LTB
SF1	RPS27A	GZMA	CORO1B	CD3E	B2M
VAMP2	RPS15A	CD7	ICA1	CD3G	RGS1
ARHGEF1	RPL10	GZMK	SRGN	CD52	SRGN
C1orf63	EEF1A1	IL2RB	BTG1	CD7	ARPC1B
ZFP36L2	RPL3	XCL2	TIGIT	CKLF	IL2RG
FUS	RPL13	CLIC3	PTPN7	CORO1A	ACTB
MT-ATP6	RPLP2	TRDC	RPL21	EVL	CORO1A
ILF3	RPS4X	KLRC1	JUNB	GZMA	CD2
C9orf142	RPS19	GZMB	CD200	HCST	PFN1
MYH9	RPL9	SRGN	LDHB	HOPX	PTPRCAP
SRSF2	RPL19	HCST	RPS15A	IL2RG	CD52
TRABD	TRBC2	CCL5	EEF1D	IL32	BATF

TABLE 9C-continued

Immune					
KLF6	RPS20	IFITM2	CD52	LCK	CD27
MT-ND5	ARHGDIB	KLRD1	COTL1	LTB	CREM
TSC22D4	RPL31	APOBEC3G	RPS4X	MYL12A	UBC
MT-CO3	RPL30	BTG1	CD2	NKG7	RGCC
DDX5	RPL23A	PRF1	CD27	PTPRCAP	TIGIT
SSU72	TRAC	CST7	RPS15	RAC2	CORO1B
ANKRD12	CD52	EIF3G	B2M	RPLP1	CARD16
SRSF7	RPS3A	CCL3	RPS27	RPS19	CD3E
TRAPPC1	RPL11	DUSP2	RPL32	RPS27	LCK
RBM39	RPL13A	HOPX	ARPC1B	RPS27A	UCP2
PPP2R5C	RPS6	H3F3B	CD3E	SH3BGRL3	EIF1
TMEM66	RPS13	CORO1A	PTPRCAP	TMEM66	RPS27
MIR24-2	RPS14	NR4A2	GIMAP7	TMSB4X	S100A4
FOSB	RPS12	STK17A	CD37	TRAC	TMEM66
BTG1	CD3D	ZFP36	C9orf16	TRBC2	SPOCK2
ICAM3	LDHB	PFN1	LCK	PFN1	HLA-A
HNRNPK	RPL27A	ZFP36L2	H3F3B	RPL21	TNFRSF4
MT-CO1	RPL4	DUSP1	RPS25	RPS3	RAP1A
SUN2	RPL28	CD160	PDCD1	ARPC2	TMSB4X
PNISR	ZFP36L2	TMSB4X	RPL6	SRGN	C9orf16
EIF4G2	LTB	MATK	RPS13	RPLP2	CD44
ABRACL	RPL18A	CD69	RPL3	SEPT1	RAC2
MRPL20	RPL35A	KLRF1	ACTB	CD69	BIRC3
HLA-F	RPLP1	CD97	RPS27A	CD247	TSC22D3
BUB3	RPL41	ARHGDIB	RPS3A	EEF1A1	EEF1D
PRPF38B	RPL14	FGR	RPL28	ID2	ARPC2
MT-CO2	IL32	ARPC5L	RPL7	RPL13	DUSP4
IDS	TMSB4X	ID2	IL32	ARPC1B	HSPA8
PPP1R2	RPS15	MYL12A	TMSB4X	GIMAP7	PBXIP1
KMT2E	RPS18	B2M	FXYD5	RPL10	PCBP1
HLA-E	RPL7	FAM46C	GPSM3	CST7	CALM3

TABLE 10

GWAS Gene List and Cell Subtype	
MEI1	identB.Plasma
SLC26A3	identE.Absorptive__All
ITLN1	identE.Immature__Goblet
ITLN1	identE.Secretory__All
CCL11	identF.Crypt
CCDC85B	identF.Endothelial
CCL11	identF.Fibroblast
PROCR	identF.Fibroblast
CCL2	identF.Stromal
EFEMP2	identF.Stromal
PROCR	identF.Stromal
GPX1	identM.Monocytes
MXRA8	identF.Stromal
SLC26A3	identE.Epithelial
PTPRC	identI.Immune
SEMA3B	identF.Glia
NKX2-3	identF.Stromal
PKIG	identF.Stromal
FCGR2A	identM.Myeloid
PLAU	identF.Stromal
FCGR2A	identM.Monocytes
CCL11	identF.Stromal
VWA1	identF.Microvascular
CTSW	identI.Immune
SULT1A1	identE.Absorptive__All
GPR183	identI.Immune
SLAMF8	identM.Myeloid
SLAMF8	identM.Monocytes
HYAL2	identF.Endothelial
TAGAP	identI.Immune
CXCL1	identF.Fibroblast
PDLIM4	identF.Stromal
SULT1A2	identE.Epithelial
ITLN1	identE.Epithelial
C1orf106	identE.Epithelial
CTSW	identT.NK
CD6	identT.Tcells
LPXN	identI.Immune
CCL7	identF.Crypt

TABLE 10-continued

GWAS Gene List and Cell Subtype	
IL10RA	identI.Immune
RNF186	identE.Epithelial
CD19	identB.Bcells
MEI1	identI.Immune
CREM	identI.Immune
CXCL1	identF.Stromal
TTYH3	identM.Monocytes
FUT2	identE.Epithelial
ESRRA	identE.Epithelial
CHP1	identE.Epithelial
LY9	identI.Immune
HNF4A	identE.Epithelial
NEU4	identE.Epithelial
GSDMB	identE.Epithelial
PLCG2	identE.Tuft
VDR	identE.Epithelial
CCL7	identF.Fibroblast
NEXN	identF.Myofibroblasts
NEXN	identF.Stromal
GPR65	identI.Immune
SCNN1A	identE.Epithelial
TNNI2	identM.Myeloid
LAMB2	identF.Stromal
OVOL1	identE.Epithelial
PTPN22	identI.Immune
CXCL6	identF.Fibroblast
SP140	identI.Immune
RSPO3	identF.Crypt__RSPO3
RAPGEF3	identF.Endothelial
IKZF1	identI.Immune
ANKRD65	identF.Stromal
CCL7	identF.Stromal
SLC26A6	identE.Epithelial
THEMIS	identT.Tcells
GRB7	identE.Epithelial
NLRP7	identB.Bcells
CD6	identI.Lymphoid
CD28	identT.Tcells
MST1R	identE.Epithelial

TABLE 10-continued

GWAS Gene List and Cell Subtype	
CD19	identI.Lymphoid
CD6	identI.Immune
FADS3	identF.Glia
ANKRD65	identF.Microvascular
SLAMF8	identI.Immune
TAS1R3	identE.Tuft
STAT4	identI.Lymphoid
TNNI2	identM.Tolerogenic__DCs
CXCL6	identF.Stromal
SNX20	identI.Immune
IFNG	identI.Lymphoid
SEMA3F	identF.Microvascular
CD40	identB.GC
CD244	identI.Immune
CD244	identI.Lymphoid
CD19	identI.Immune
IFNG	identI.Immune
HYAL1	identF.Endothelial
STAT4	identI.Immune
OSMR	identF.Stromal
SEMA3F	identF.Endothelial
IRF4	identI.Immune
MMEL1	identE.Best4__Enterocytes
CIT	identF.Microvascular
NLRP7	identI.Lymphoid
RSPO3	identF.Stromal
ITGAL	identI.Immune
CCR5	identI.Immune
TNNI2	identI.Immune
DGKE	identF.Endothelial
IL23R	identT.ILCs
THEMIS	identI.Lymphoid
CSF2	identT.ILCs
TAS1R3	identE.Secretory
THEMIS	identI.Immune
FAM212A	identM.CD69neg__Mast
CD28	identI.Immune

TABLE 10-continued

GWAS Gene List and Cell Subtype	
CD28	identI.Lymphoid
TNFRSF9	identT.Tregs
CXCR5	identI.Lymphoid
MYRF	identE.Epithelial
BACH2	identB.GC
CCR2	identI.Immune
NLRP7	identI.Immune
CARD11	identI.Immune
IL2RA	identI.Immune
PRKCB	identI.Immune
RASGRP1	identI.Lymphoid
CD226	identI.Immune
KIR3DL2	identI.Lymphoid
CXCR5	identI.Immune
TNFRSF9	identI.Immune
CARD11	identI.Lymphoid
KIR3DL2	identI.Immune
C0L7A1	identF.Stromal
CCRL2	identM.Neutrophils
IL10	identI.Immune
RASGRP1	identI.Immune
IKZF3	identI.Lymphoid
ACSL6	identT.Tcells
RFTN2	identF.Stromal
IL27	identM.Monocytes
PF4	identE.Epithelial
IKZF3	identI.Immune
ZMYND10	identM.Cycling
IL27	identM.Neutrophils
TNFSF8	identI.Immune
IL2	identT.Tcells
IL23R	identI.Lymphoid
IL2	identI.Lymphoid
CELSR3	identE.Enteroendocrine

Table 11. Specific Cell Gene Lists

TABLE 11A

Epithelial						
identE.Absorptive	identE.Absorptive__All	identE.Absorptive__TA	identE.Absorptive__TA__1	identE.Absorptive__TA__2	identE.Best4__Enterocytes	identE.Cycling__TA
CLDN3	C15orf48	TXN	MT-ND3	COX4I1	BEST4	MIF
CLDN7	CA2	MGST1	SUCLG2	TXN	CA7	HIST1H4C
EPCAM	CES2	UQCRFS1	LCN2	MGST1	OTOP2	IGFBP2
GUCA2A	ETHE1	PLA2G2A	NGEF	ATP5G3	MT1G	TUBB4B
GUCA2B	FABP1	LCN2	DEFA6	CYC1	MT2A	RPSAP58
LYPD8	KRT19	ATP5O	AC092620.2	TMEM141	MT1H	STRA13
PLAC8	LGALS3	SUCLG2	#N/A	UQCR10	MT1E	CTD-2090113.1
SDCBP2	MT-CO2	CTD-2228K2.7	#N/A	ATP5D	NEURL	CCDC34
CEACAM1	PIGR	TLN2	#N/A	UQCRH	CTSE	REG1A
ITM2C	SLC26A2	PITPNM3	#N/A	DBI	MT1X	RP11-519G16.5
CEACAM6	SLC26A3	XXyac-YM21GA2.4	#N/A	COX7C	HRCT1	SAPCD2
CLDN23	SRI	RP1-102H19.8	#N/A	ATP5EP2	MSLN	GMNN
CA7	KRT20	AC013268.5	#N/A	UQCRFS1	DMBT1	C18orf56
TMEM171	MS4A12	CTA-363E6.2	#N/A	MESP1	MT1M	MZT2B
BEST4	GUCA2A	AL133245.2	#N/A	ATP5O	NOTCH2NL	NUDT8
NLN	SELENBP1	RN7SL485P	#N/A	BOLA3	MT1F	GGCT
PRR15L	TST	RP11-7K24.3	#N/A	MRPS33	MYOM1	FOXP1
OTOP2	CHP2	RP11-57H14.4	#N/A	CTD-2228K2.7	STAP2	F12
APOBEC3B	CYSTM1	CTD-2256P15.4	#N/A	GJB1	NBPF10	TOMM40
TMPRSS2	C10orf99	SNORD3B-1	#N/A	GOT1	OTOP3	TSFM
C12orf36	CA1	FITM1	#N/A	MFSD3	GPRC5C	CTC-524C5.2
SCIN	SLC51B	AC007255.8	#N/A	APEH	CDX1	CDC25C
CELA3B	CEACAM7	RP11-214N9.1	#N/A	LINC00668	SCIN	GCAT
TDP2	ANPEP	RP11-31506.1	#N/A	UBAC1	ADCY5	KIF4A
CHMP4B	S100A14	REG3A	#N/A	MRPL21	RHOV	ATAD3A
PTTG1IP	CTD-2228K2.5	PLCH1	#N/A	SH2D4A	TDP2	EMC9
RP11-680F8.1	PRAP1	ATP13A4	#N/A	TLN2	CDK18	SNRPF
PTPRR	PPP1R14D	ZSCAN20	#N/A	XRCC6BP1	C2orf54	TCOF1
APOBEC1	HMGCS2	CTD-2619J13.14	#N/A	C1orf53	CRYL1	NDUFA7
CTSE	TMEM45B	RP11-192H23.8	#N/A	SPRYD4	ALDH2	CECR5
GNG12	SFN	#N/A	#N/A	RP1-102H19.8	CEACAM3	HPDL

TABLE 11A-continued

Epithelial						
TRIM15	DHRS11	#N/A	#N/A	XXyac-YM21GA2.4	NOTCH2	YBX2
MT1H	CEACAM1	#N/A	#N/A	PITPNM3	MEIS1	RCC1
MSLN	AKR1B10	#N/A	#N/A	YY2	CCNYL1	MYO19
TMCC3	AGPAT2	#N/A	#N/A	ATP13A4	MMEL1	WDR90
B3GNT3	UQCRQ	#N/A	#N/A	RP11-50E11.3	A1CF	CTB-175P5.4
CHMP2B	SULT1A1	#N/A	#N/A	CTA-363E6.2	SMPDL3B	HMBS
HSD17B11	SULT1A2	#N/A	#N/A	LL22NC03-86G7.1	SULT1E1	SERPINA6
CELA3A	STAP2	#N/A	#N/A	RP11-52112.3	RP11-44N21.1	PTBP1
CTC-490G23.2	AKR1C3	#N/A	#N/A	RP11-7K24.3	CPA6	PLEK2
DMBT1	MT1G	#N/A	#N/A	UNC79	NBPF14	ACAD9
PARP4	SLC22A18	#N/A	#N/A	RP11-73M18.9	HR	ICT1
RHPN2	TMEM171	#N/A	#N/A	SNORD3B-1	REN	MCM8
MYOM1	ACAA2	#N/A	#N/A	RP1-80N2.2	RP11-771K4.1	RP11-304L19.1
MT1G	TMIGD1	#N/A	#N/A	RN7SL485P	SAMD13	C12orf54
VDAC2	MPST	#N/A	#N/A	RP5-914P20.5	NPY1R	RAC3
CEBPA	LINC00483	#N/A	#N/A	HTR4	TNFRSF11A	NMRAL1
IL10RB	GNA11	#N/A	#N/A	PLCH1	AGXT	TONSL
GPRC5C	MT1E	#N/A	#N/A	CTD-2256P15.4	TLDC2	C9orf24
C2orf54	SLC22A18AS	#N/A	#N/A	RP11-57H14.4	AC069277.2	POLE

	identE.Enterocyte__Immature__1	identE.Enterocyte__Immature__2	identE.Enterocyte__Progenitor	identE.Enterocytes
	MT-CO1	ETHE1	SELENBP1	ANPEP
	MT-RNR1	FABP1	AKR7A3	APOBEC3B
	MT-CO2	KRT19	GOLM1	AQP8
	MT-ND2	KRT20	ACADS	C19orf33
	MT-ATP6	KRT8	CMBL	CEACAM1
	MT-ND5	LGALS3	SLC39A5	CEACAM5
	MT-ND4L	PHGR1	CKMT1B	CEACAM7
	SIRT6	SLC26A2	CKMT1A	CFDP1
	VPS13A	TMEM54	ASL	CLCA4
	RP11-747D18.1	LGALS4	TRPM4	CLDN23
	SIRT7	AKR1B10	HADH	CLDN7
	PHYKPL	TST	SDHA	CTD-2228K2.5
	BAIAP2L2	SLC25A5	LIMA1	EMP1
	MT-TL1	CES2	NAPRT1	FTH1
	TAC1	FLNB	UGDH	GPRC5A
	KRTAP13-2	UQCRQ	BCL2L15	GUCA2A
	HIST1H3F	CHP2	ACO2	HIST1H1C
	MT-TN	BSG	AIFM3	IFI27
	RP11-505E24.2	COX6A1	PKP2	LYPD8
	STAB2	S100A14	MOGAT2	MISP
	RNU1-134P	AHCYL2	ETFA	MS4A12
	#N/A	COX5B	OPLAH	NLN
	#N/A	SULT1A1	CAPN1	PKIB
	#N/A	PLCD3	OSBPL7	PLAC8
	#N/A	MGST3	TTLL12	PRAP1
	#N/A	SLC22A18AS	LPIN3	RP11-48020.4
	#N/A	UQCR11	VPS9D1	SDCBP2
	#N/A	SGK2	SLC23A1	SLC26A3
	#N/A	TPRN	EME2	SLC51B
	#N/A	TP53I3	TRIM66	SRI
	#N/A	ACAA1	GLDN	TMEM37
	#N/A	ATP1A1	AF127936.7	TRIM31
	#N/A	ETNK1	C21orf88	TSPAN1
	#N/A	IGSF9	#N/A	TMIGD1
	#N/A	NDUFA1	#N/A	MALL
	#N/A	TNNC2	#N/A	SFN
	#N/A	CYP4F12	#N/A	PRSS3
	#N/A	ATP5J	#N/A	MEP1A
	#N/A	TMEM82	#N/A	CDA
	#N/A	LDHD	#N/A	RHOC
	#N/A	SHD	#N/A	SMIM22
	#N/A	ZBTB7B	#N/A	SULT1A2
	#N/A	PPARG	#N/A	ASS1
	#N/A	RAPGEFL1	#N/A	C11orf86
	#N/A	AXDND1	#N/A	SLC6A8
	#N/A	ITPKA	#N/A	TMEM171
	#N/A	MPST	#N/A	SPINT2
	#N/A	LETM1	#N/A	RHOF
	#N/A	CYCS	#N/A	GCNT3
	#N/A	GDPD2	#N/A	GPA33

identE.Enteroendocrine	identE.Epithelial	identE.Goblet	identE.Immature__Enterocytes	identE.Immature__Goblet
PCSK1N	AGR2	FAM3D	CA1	AGR2
SCGN	AMN	FCGBP	CES2	CLCA1
CHGA	C10orf99	MUC1	ETHE1	ITLN1

TABLE 11A-continued

Epithelial				
CRYBA2	C15orf48	MUC2	KRT19	KLK1
PYY	C19orf33	TFF1	MT-CO2	LRRC26
FEV	CA2	ZG16	PIGR	RETNLB
SCG5	CDHR5	MUC13	SELENBP1	SERPINA1
GCG	CLDN3	REP15	SLC26A2	SPINK1
MS4A8	CLDN4	S100P	TST	SPINK4
NEUROD1	CLDN7	ENTPD8	CHP2	ST6GALNAC1
CACNA1A	COX5B	MALAT1	HSD11B2	TFF3
HOXB9	ELF3	VSIG2	FLNB	WFDC2
MLXIPL	EPCAM	TM4SF5	AKR1B10	TPSG1
RAB26	FABP1	BCAS1	SULT1A1	GMDS
KIF12	FAM3D	AMN	MVP	HEPACAM2
SLC29A4	FCGBP	SPATS2L	MGAT4B	MB
CHGB	FXYD3	SMIM6	SLC22A18AS	ANG
VWA5B2	HMGCS2	CREB3L1	MYO1A	TSPAN13
KIAA1324	KRT18	ZG16B	PLCD3	NANS
DDC	KRT19	CAPN8	ATP1A1	RP11-234B24.2
HOXB8	KRT20	FFAR4	GPT	TCEA3
ERI3	KRT8	GDPD3	ABCC3	URAD
CXXC4	LGALS3	SYTL2	PAPSS2	IL1R2
TPH1	LGALS4	PARM1	CMBL	CDC42EP5
C19orf77	MT-ATP6	TBX10	PPARG	TSTA3
ARX	MT-CO1	FOXA3	SHD	RAP1GAP
RP11-279F6.1	MT-CO2	LGALS9B	IGSF9	TMEM61
ABCC8	MT-CO3	PLA2G10	VIL1	HES6
CADPS	MT-ND1	SCNN1A	TMPRSS4	FABP2
ETV1	MT-ND4	TP53INP2	CYP4F12	CREB3L4
LCN15	MT-RNR1	BEST2	ACADVL	EFCAB4A
PELI3	MT1E	MLLT3	LETM1	AC011523.2
SST	MT1G	GALE	DGAT1	RAB15
NKX2-2	PHGR1	GPR153	LDHD	ERGIC1
PEMT	PIGR	SPDEF	SHROOM1	DYRK4
CYP2W1	PRSS3	SCGB2A1	MAP2K2	CTD-2547H18.1
PAX6	S100A14	AC009133.21	MOGAT3	SNHG18
QDPR	SELENBP1	NEDD4L	RAPGEFL1	LINC00261
C6orf141	SMIM22	VILL	LIMA1	KLK15
COL2A1	SPINT2	RAB27A	NAPRT1	PYCR1
BRAT1	TMEM54	DNM2	PACSIN2	C9orf152
SYT13	TSPAN1	FAM101A	ITPKA	ZNF511
SSTR5-AS1	TSPAN8	GPRIN2	VDR	ABLIM1
SEZ6L2	STAP2	FUT3	PFKL	KLK4
RXFP4	TFF3	MTMR11	ACO2	GNE
PSCA	SLC44A4	ACSS2	MMP15	HDLBP
KIAA1456	GUCA2A	KCNK1	ZBTB7A	HES2
MNX1	ETHE1	VIPR1	AXDND1	KDELR2
STX1A	TST	DST	ITGA3	FOXA2
INSL5	PRAP1	RASEF	SLC27A4	TRPT1

	identE.Secretory	identE.Secretory__All	identE.Secretory__TA	identE.Stem	identE.Tuft
	FCGBP	CLCA1	RPL36	PRDX5	KRT18
	MUC2	FCGBP	RPL35	LEFTY1	AZGP1
	TFF1	ITLN1	RPL37A	ASCL2	SH2D6
	ZG16	KLK1	AC112229.7	GPX2	MARCKSL1
	ELF3	KRT18	ANKS6	C17orf76-AS1	BIK
	MUC1	MUC2	KCNJ12	RPLP0	LRMP
	MALAT1	REP15	ZSCAN22	CDCA7	HCK
	S100P	SPINK1	FAM183A	RGMB	PTPN18
	TM4SF5	SPINK4	TTC4	RPS18	ANXA13
	ENTPD8	TFF3	RP4-610C12.3	RPL12	ATP2A3
	BCAS1	WFDC2	KRTAP4-1	SMOC2	AVIL
	AZGP1	ZG16	RGMB-AS1	RPS6	IL17RB
	SMIM6	LRRC26	RP11-884K10.7	PPP1R1B	TRPM5
	ZG16B	AGR2	RP11-199F11.2	GNB2L1	ALOX5
	SH2D6	TPSG1	SLC25A30-AS1	RPS2	SH2D7
	FFAR4	RETNLB	B4GALT6	RPS5	BMX
	CAPN8	STARD10	CTA-797E19.1	RPL29	PTGS1
	FOXA3	FAM3D	CACNA1F	SLC25A6	ELF3
	ATP2A3	ST6GALNAC1	AP001462.6	EPHB3	EIF1B
	TBX10	MB	RP11-548H3.1	RPS24	GNG13
	SYTL2	CREB3L1	KIAA1875	IMPDH2	PSTPIP2
	GALE	ANG	CITF22-1A6.3	RPL7A	HOTAIRM1
	LGALS9B	MUC1	RP4-565E6.1	ALDH1B1	SPIB
	GPR153	GMDS	SLC35G5	OLFM4	CC2D1A
	HCK	BEST2	RNVU1-14	FERMT1	HTR3E
	ANXA13	ANXA13	CTD-2196E14.4	AP003774.1	IFT172
	AVIL	SPDEF	CTC-360G5.1	KCNN4	PLCG2
	H1F0	FOXA3	ZNF334	EPHB2	DEFB1

TABLE 11A-continued

Epithelial				
RASSF7	ZG16B	RP11-677M14.2	GPR160	RASSF6
SCNN1A	TFF1	RP11-391M1.4	APEX1	MATK
IL17RB	CDC42EP5	AP001619.2	PTPRO	ANXA4
MLLT3	RP11-234B24.2	LINC00959	RNF186	PPAP2C
TRPM5	KIAA1324	ANKUB1	CDK6	AOC1
NEDD4L	REG4	CTD-2196E14.6	EXOSC5	OGDHL
AC009133.21	TMEM61	RP11-188P20.3	ADCK3	ATPIF1
BMX	RAP1GAP	CTB-75G16.3	ARSE	EPS8L3
SH2D7	S100P	AC073133.2	REPIN1	FURIN
GNG13	BCAS1	FAM221B	ZNF814	TMEM63A
FAM101A	CAPN9	RP11-932O9.9	NOX1	EHF
IFT172	SCGB2A1	HP	CDHR1	C2orf82
GPRIN2	TM4SF5	RP11-361F15.2	MACROD1	ESPN
HOTAIRM1	AZGP1	OTUB2	SH3YL1	POU2F3
CBFA2T2	ERN2	LRRC16B	LGR5	SPTLC2
KCNK1	FFAR4	RP11-163N6.2	UGT2A3	CDH17
EHF	ERI3	RP11-13K12.1	SLC39A2	NT5C
PSTPIP2	AC009133.21	#N/A	ACSM3	BLOC1S1
HTR3E	ATP2A3	#N/A	SFXN4	IL13RA1
SCGN	SH2D6	#N/A	LRIG1	CENPV
DDR1	TSTA3	#N/A	TSPAN6	ASMTL
SYT7	ANO7	#N/A	CRLS1	FYB

TABLE 11B

Fibroblast				
identF.Crypt	identF.Crypt__RSPO3	identF.Crypt__hiFos	identF.Crypt__loFos__1	identF.Crypt__loFos__2
A2M	DCN	ADAMDEC1	APOE	IFI27L2
ABCA8	LUM	CCL8	SCARA5	PKDCC
ADAM28	EFEMP1	HAPLN1	COLEC11	DTX4
ADAMDEC1	FBLN1	STMN2	RP11-54O7.3	ABCA6
APOE	CFH	CCL7	ANKRD53	C1RL
CCL11	CCDC80	IL7	RP11-107N15.1	TEKT3
CCL13	CCL11	EPHA7	LNP1	ROBO1
CCL8	ADH1B	PHACTR3	MFI2-AS1	LINC00663
CFD	CXCL12	BPI	C17orf51	#N/A
CFH	MFAP4	GALNT9	AC144449.1	#N/A
CXCL12	C7	AL117190.3	PNMA2	#N/A
DCN	SERPINF1	RP11-374M1.5	RN7SKP295	#N/A
FABP4	PLAC9	LINC00309	RP11-422P24.11	#N/A
FBLN1	SERPING1	LRRC8E	L3MBTL1	#N/A
HAPLN1	PTGDS	ZKSCAN7	FLNC	#N/A
MFAP4	RSPO3	RP11-556N21.1	ZNF510	#N/A
PLTP	C3	RP11-88H9.2	LPP-AS2	#N/A
PTGDS	ASPN	RP11-774O3.3	BVES	#N/A
PTN	COL14A1	RP11-353B9.1	DNHD1	#N/A
SCARA5	DPT	ATP6V0E2-AS1	ZC3H12B	#N/A
SFTA1P	GSTM3	ZNF114	MARK1	#N/A
TCF21	GSTM5	MAATS1	RP11-112L6.4	#N/A
SNAI2	PRELP	C9orf96	RP3-510D11.2	#N/A
EDIL3	ANGPTL1	LIN7A	SEC24B-AS1	#N/A
CXCL1	C16orf89	NBPF15	RP11-267N12.3	#N/A
C6orf48	CXCL6	ZNF660	#N/A	#N/A
TNXB	CHODL	RP11-326C3.11	#N/A	#N/A
PROS1	SERPINE2	ANKRD6	#N/A	#N/A
SERPINE2	OGN	CMYA5	#N/A	#N/A
ABCA6	NFIA	PRTG	#N/A	#N/A
IFI27L2	GREM2	RP11-475I24.3	#N/A	#N/A
CP	CCL19	CNTNAP1	#N/A	#N/A
CCL7	CP	WASF1	#N/A	#N/A
ELANE	GPC6	FAM184B	#N/A	#N/A
ANGPTL1	CCL21	DNM3OS	#N/A	#N/A
HOXB-AS3	PAM	RP11-173B14.5	#N/A	#N/A
NR2F1-AS1	RGMA	#N/A	#N/A	#N/A
GPC6	APOD	#N/A	#N/A	#N/A
CXCL6	RP11-135D11.2	#N/A	#N/A	#N/A
FMOD	GPC3	#N/A	#N/A	#N/A
SLIT3	TMEM59	#N/A	#N/A	#N/A
BCL3	PTGER1	#N/A	#N/A	#N/A
CRYBG3	FAIM2	#N/A	#N/A	#N/A
PRCD	MAPKAP1	#N/A	#N/A	#N/A
FNDC1	PTGFR	#N/A	#N/A	#N/A
EPHA7	SFRP2	#N/A	#N/A	#N/A

TABLE 11B-continued

Fibroblast				
CCL19	CAPN6	#N/A	#N/A	#N/A
ADAMTS2	OSR2	#N/A	#N/A	#N/A
RP3-323P13.2	SFRP4	#N/A	#N/A	#N/A
CFHR3	CDO1	#N/A	#N/A	#N/A

identF.Endothelial	identF.Endothelial__1	identF.Fibroblast	identF.Glia
BCAM	CD320	ABCA8	ALDH1A1
CCDC85B	IGFBP4	ADAMDEC1	CD9
CD320	ENPP2	APOE	CLU
CD36	TXNIP	BMP4	CRYAB
CLDN5	ICAM2	C1R	S100B
CLEC14A	RBP7	CIS	TUBA1A
CRIP2	CYYR1	CCL11	GPM6B
ECSCR	CD34	CCL13	PMP22
EGFL7	MMRN2	CCL8	PLP1
ENG	GPR146	CFD	SPARC
ESAM	IL3RA	CFH	SPP1
FABP5	SOX17	CLEC11A	PRNP
FKBP1A	SRP14	COL6A1	SEMA3B
GIMAP7	FAM107A	COL6A2	JUN
GNG11	OAZ2	CTSK	MATN2
HLA-C	C10orf54	CXCL12	FOS
HLA-E	SYNPO	CYGB	CYR61
IGFBP4	C10orf10	DCN	CD59
ITM2B	HEY1	DMKN	COMT
JAM2	LPAR6	ECM1	CALM2
NPDC1	TIE1	EMILIN1	HES1
PLVAP	KLF2	FBLN1	MPZ
RAMP2	AIF1L	GGT5	ANXA2
RAMP3	ADAM15	HAAO	LGI4
RBP5	COL15A1	HAPLN1	GFRA3
SEPW1	NOV	LAMA4	TUBB2B
SLC9A3R2	PLLP	LTBP4	CNN3
SNCG	ALPL	LUM	C8orf4
SPARCL1	SEMA3G	MFAP4	PEBP1
TMEM88	BTNL9	MMP2	TIMP3
VWF	EFNB2	PCOLCE	DKK3
FAM167B	MECOM	PLAC9	NRXN1
AC011526.1	SHE	PROCR	CCL2
ENPP2	STC1	PTN	IER2
CYYR1	RUNDC3B	RARRES2	JUNB
PRSS23	C1QTNF9	RBP1	VIM
CTGF	INHBB	SCARA5	EGR1
CD34	FCN3	SERPINF1	NDRG2
TSPAN7	ARL15	SPON2	RGS16
ICAM2	GPIHBP1	STMN2	PMEPA1
PTRF	OAZ3	TCF21	SOCS3
VAMP5	RP11-536O18.1	SNAI2	RHOB
TGFBR2	SSUH2	ADH1B	CBR1
CAV2	PRDM16	PTGDS	S100A4
FAM213A	FGF12	PLTP	SORBS2
EMCN	RP11-105C19.1	ADAM28	AP1S2
ELTD1	RP11-1379J22.5	GLT8D2	FXYD1
TM4SF18	SNORA7	TMEM119	ANXA5
HLA-A	AC007161.5	VCAM1	S100A1
TXNIP	RP4-569M23.2	CTC-276P9.1	PLEKHB1

identF.Inflammatory	identF.Microvascular	identF.Myofibrobiasts	identF.Pcap__Venules	identF.Pericytes
CHI3L1	FABP5	ACTA2	CLDN5	RGS5
RHBDD3	PLVAP	TAGLN	NPC2	TINAGL1
RCVRN	GNG11	MYL9	DARC	CSRP2
MMP3	PRSS23	TPM2	TSPAN7	NDUFA4L2
RP11-676J12.7	CD36	ACTG2	CPE	IGFBP7
LRCH2	GSN	PDLIM3	LY6E	HIGD1B
MMP10	RAMP3	TPM1	MADCAM1	BGN
AP000688.29	SPARCL1	MYLK	APLNR	COX4I2
ZC3HAV1L	VWF	SOSTDC1	DUSP23	ADIRF
#N/A	VWA1	DSTN	HHEX	PDGFRB
#N/A	RGCC	NDUFA4	ICAM1	TPPP3
#N/A	ITM2B	MYH11	TNFSF10	NOTCH3
#N/A	ENG	MYL6	LINC01013	HES4
#N/A	RBP5	FHL1	GPR126	GEM
#N/A	SDPR	HHIP	ZNF385D	FAM162B
#N/A	TMEM88	PRKCDBP	KCTD12	PGF
#N/A	FKBP1A	TGFB1I1	CCL14	NR2F2
#N/A	TM4SF18	HSD17B6	CYP1B1	MCAM

TABLE 11B-continued

Fibroblast				
#N/A	TMEM204	FLNA	RPS28	STEAP4
#N/A	HSPG2	CNN1	ADM5	STOM
#N/A	EMCN	PPIC	PIR	LHFP
#N/A	PASK	NPNT	LPCAT4	EPS8
#N/A	ELTD1	PDLIM7	IL33	SERPINI1
#N/A	SLC14A1	CES1	KRT222	REM1
#N/A	PODXL	CSRP1	SELP	ISYNA1
#N/A	FLT1	ILK	MEOX1	TNS1
#N/A	CAV2	SMTN	MTUS1	UBA2
#N/A	C16orf80	NEXN	SEMA6A	PLXDC1
#N/A	SH3BP5	LINC01082	SMAD1	ADAMTS1
#N/A	KDR	TCEAL4	GALNT15	ITGA7
#N/A	ARHGAP29	HHIP-AS1	VGLL4	NFATC4
#N/A	CDC37	C9orf3	ENY2	MEST
#N/A	APP	RBPMS	TNFRSF10D	EDNRA
#N/A	RP11-536O18.2	KCNMB1	LEPR	NR1H4
#N/A	HTRA1	LMOD1	ICAM4	EBF1
#N/A	EHD4	CD151	FAM84B	OLFM2
#N/A	KANK3	PDIA5	RAB3C	KCNE4
#N/A	CXorf36	UBE2E3	C2CD4B	LDB3
#N/A	BAALC	LPP	ZNF521	HEY2
#N/A	HLX	AOC3	PLA1A	HRC
#N/A	ROBO4	TTLL7	MMP28	RASL12
#N/A	NQO1	RCN1	SLC41A3	ARHGEF17
#N/A	GAS6	HMG20B	FAM155A	GJC1
#N/A	LXN	MIR145	CORT	KCNJ8
#N/A	SLCO2A1	MFAP5	VEGFC	LINC00883
#N/A	WWTR1	AC131025.8	CA8	HEYL
#N/A	GALNT18	PARVA	KLK10	C1QTNF1
#N/A	MGLL	TCEAL1	PRKAR1B	FZD7
#N/A	PTPRB	CALU	BCAT1	NTF3
#N/A	NRP1	CCDC107	TIAM1	GJA4

identF.Stromal	identF.Villus	identF.Villus__1	identF.Villus__2
A2M	BMP4	POSTN	BMP4
ADAMDEC1	COL6A1	NSG1	F3
APOE	EDNRB	NBL1	IGFBP3
BMP4	ENHO	MMP2	APLP2
C1R	F3	VSTM2A	MMP11
C1S	HSD17B2	GADD45B	BMP5
CALD1	IGFBP3	PDGFD	BAMBI
CCL2	MMP2	C11orf96	LANCL2
CCL8	NBL1	LAMA4	TSPAN33
CFD	NSG1	PLK2	ITGA8
CFH	POSTN	CPM	NKD2
CLEC11A	VSTM2A	RBP4	GBGT1
COL1A1	FOXF1	PROM1	BMP7
COL1A2	SCPEP1	SOX6	C22orf31
COL3A1	APLP2	FGF9	RP11-2E17.1
COL6A1	BMP5	TSHZ2	NEFM
COL6A2	FAM150B	GLP2R	LEF1-AS1
CRIP2	PDGFD	CRISPLD2	F2RL2
CTSK	MMP11	MAFB	GRIN2A
CXCL12	LAMA4	KLF10	LPAR3
CXCL14	MRPS6	PCSK6	FZD8
CYGB	PITX1	FAM92A1	RP11-157P1.4
DCN	ISCU	SCUBE2	POU6F1
ECM1	C1orf21	NMNAT3	SOX5
EFEMP2	INSC	DDHD1	EFHB
EMILIN1	RBP4	FRY	ARL10
FBLN1	GLP2R	RN7SL832P	AGAP10
GNG11	GLT8D2	CCDC68	KDM8
GPX3	TSHZ2	FBXO21	RSG1
HSPB1	BAMBI	POLA2	RP11-298J20.3
IFITM1	TSLP	ADAMTS13	ISPD
IFITM3	KREMEN1	AC061992.2	KANSL1L
IGFBP6	CRISPLD2	CTD-2035E11.3	#N/A
IGFBP7	REEP2	C10orf107	#N/A
LINC01082	FGF9	RP11-108M9.6	#N/A
LTBP4	TPBG	WBSCR17	#N/A
LUM	LANCL2	HUS1B	#N/A
MFAP4	PLBD1	EDAR	#N/A
MFGE8	PCSK6	AP000769.1	#N/A
MMP2	SCUBE2	EFCAB1	#N/A
MYL9	WNT5B	EGOT	#N/A
NGFRAP1	SEMA4D	NOTO	#N/A
NNMT	MFAP2	SRPK3	#N/A

TABLE 11B-continued

Fibroblast			
PCOLCE	LAMA5	RP11-473M20.16	#N/A
PLAC9	COL4A6	KCNK17	#N/A
PLAT	WFS1	ZCCHC18	#N/A
PMP22	CCDC68	ZNF410	#N/A
PPAP2A	SRPX2	BDNF	#N/A
PPAP2B	CNTFR	COLGALT2	#N/A
PPP1R14A	RP11-449D8.1	ZNF594	#N/A

TABLE 11C

Immune						
identB.Bcells	identB.Cycling	identB.FO	identB.GC	identB.Plasma	identI.Immune	identI.Lymphoid
AC096579.7	PBK	BANK1	CD79A	AC096579.7	ARHGDIB	CCL5
AL928768.3	SEC23B	RP5-887A10.1	CD79B	AL928768.3	CCL5	CD2
CCR10	NDC1	SELL	TCL1A	CCR10	CD37	CD3D
CD79A	ZBTB8OS	ARHGAP24	SMIM14	CHPF	CD3D	CD3E
DERL3	HBD	TNFRSF13B	MS4A1	CRELD2	CD3E	CD52
DNAJB9	ZFAT	CCDC50	LIMD2	DERL3	CD48	CD7
EAF2	IGLV3-9	RALGPS2	C7orf10	DNAJB9	CD52	CYTIP
FCRL5	KIF14	SIDT1	VPREB3	DUSP5	CD53	EVL
GNG7	ZNF264	OSTN-AS1	FCRLA	FCRL5	CD69	LTB
HERPUD1	ZNF215	FCRL4	SERPINA9	FGF23	CD7	PTPRCAP
IGHA1	ZNF66	GYLTL1B	EAF2	FKBP11	CORO1A	TRAC
IGHA2	HIST1H1B	CLECL1	CD53	HERPUD1	CYBA	TRBC2
IGJ	AP000569.9	IGHE	NCF1	IFNAR2	CYTIP	IL2RG
IGKC	RP11-166B2.5	DENND5B	BCAS4	IGHA1	EVL	LCK
IGLC2	C4orf21	AP001046.5	CD40	IGHA2	HCST	CD27
IGLC3	RP11-382J12.1	BEND4	SNX29P2	IGJ	LAPTM5	CD79A
IGLL5	HIST1H2AH	C2ORF15	ISG20	IGKC	LTB	NKG7
MEI1	AC090587.5	SMKR1	POU2AF1	IGLC2	PTPRCAP	SEPT1
MZB1	CECR7	ZBED2	HTR3A	IGLC3	RAC2	HOPX
POU2AF1	ACSBG1	KCNIP2	HMCES	IGLL5	RGS1	GZMA
SEC11C	UBE2NL	RP11-861A13.4	AC023590.1	IGLV3-1	TRBC2	ACAP1
SSR4	RP4-536B24.3	#N/A	CD72	LMAN1	TRAC	PCED1B-AS1
TNFRSF17	TTF2	#N/A	UBE2J1	MANF	NCF1	AL928768.3
UBE2J1	MDH1B	#N/A	HMGN1	MEI1	COTL1	BTG1
SPAG4	RP11-46H11.12	#N/A	NEIL1	MZB1	DUSP2	TNFRSF17
CD79B	RP11-266K4.9	#N/A	TPD52	PDIA4	LCK	CTSW
EVI2B	DNMT3B	#N/A	P2RX5	PPAPDC1B	IL2RG	ICAM3
DUSP5	RP11-347C18.3	#N/A	HLA-DOB	PRDX4	EVI2B	FKBP11
IGLC7	#N/A	#N/A	BFSP2	SDF2L1	CKLF	TSC22D3
SPCS3	#N/A	#N/A	HVCN1	SEC11C	HCLS1	TBC1D10C
XBP1	#N/A	#N/A	GNG7	SPAG4	CD2	IGHV1OR15-1
PPAPDC1B	#N/A	#N/A	EZR	SPCS3	SAMSN1	STK17A
PNOC	#N/A	#N/A	MTMR14	SSR3	NKG7	POU2AF1
IGLV3-1	#N/A	#N/A	AICDA	SSR4	PTPRC	TNFRSF18
FGF23	#N/A	#N/A	TCEA1	TNFRSF17	GPSM3	FCRL5
CRELD2	#N/A	#N/A	MBD4	TRAM1	HOPX	CD247
TNFRSF13B	#N/A	#N/A	CYB561A3	TXNDC15	ACAP1	MZB1
IGLV6-57	#N/A	#N/A	RP11-138118.2	WT1-AS	ARPC2	DERL3
RP11-290F5.1	#N/A	#N/A	CD180	XBP1	PCED1B-AS1	CD3G
WT1-AS	#N/A	#N/A	CCDC144A	IGKV4-1	RHOH	CD96
IGHM	#N/A	#N/A	GGA2	IGLV6-57	ITGB7	PIM2
IGKV4-1	#N/A	#N/A	SEL1L3	IGLC7	LIMD2	GZMB
PDIA4	#N/A	#N/A	BCL7A	DNAJB11	CD27	TRDC
C16orf74	#N/A	#N/A	LSM10	SPCS2	GZMA	TRGC2
MANF	#N/A	#N/A	TMEM156	ANKRD37	LCP1	TMIGD2
SSR3	#N/A	#N/A	RP11-164H13.1	ERLEC1	CTSW	MEI1
TPD52	#N/A	#N/A	BACH2	ALG5	TMEM66	TAGAP
ANKRD37	#N/A	#N/A	ZNF581	RP11-290F5.1	FCER1G	FAM46C
PRDX4	#N/A	#N/A	CD38	UAP1	CST7	AC092580.4
SPCS2	#N/A	#N/A	STX7	SPCS1	TBC1D10C	GZMM

	identM.CD69neg__Mast	identM.CD69pos__Mast	identM.Cycling	identM.DCs
	CAPG	H3F3B	TUBA1B	CD74
	LTC4S	NFKBIA	H2AFZ	CPVL
	KRT1	PPP1R15A	STMN1	CST3
	MAOB	ANXA1	AP2S1	HLA-DPA1
	HPGDS	GLUL	UBE2C	HLA-DPB1
	SAMSN1	DNAJA1	CENPM	HLA-DQA1
	ALOX5AP	UBB	CKS1B	HLA-DQB1
	SLC18A2	LMNA	YWHAH	HLA-DRA

TABLE 11C-continued

Immune			
NSMCE1	NFKBIZ	CDK1	HLA-DRB1
ADRB2	C1orf186	ATP6V0B	HLA-DRB5
BTK	HSP90AB1	KPNA2	CLEC10A
GMPR	DDX5	NUDT1	HLA-DQB2
SVOPL	HDC	TOP2A	LGALS2
CD44	HSPA5	SNRNP25	AMICA1
NCOA4	FAM46A	TROAP	FCER1A
FAM212A	HSP90AA1	EIF4EBP1	HLA-DQA2
CATSPER1	STXBP6	LSM4	SGK1
LYL1	HSPH1	COMMD4	CD1C
ARL6IP5	IL1RAPL1	SYCE2	PLD4
HSD17B12	ELF1	GGH	CD1E
BEX4	UBBP4	NCAPD3	CLEC9A
MAML1	AC020571.3	FAM64A	PHACTR1
AJ271736.10	DNAJB4	AC009005.2	CD1D
NTRK1	RP11-620J15.3	FAM72C	IFNGR1
SLC43A3	IL1RL1	ZMYND10	CACNA2D3
PABPC4	EGR3	C20orf201	IDO1
ABCB8	CALB2	SIGLEC15	CTD-2319112.1
IL9R	ADCYAP1	GPR42	TNNI2
PSMD1	IL13	RP11-327F22.2	FLT3
CASS4	ARL5B-AS1	INCENP	C12orf5
RN7SL243P	FER	RP11-1100L3.8	SERPINF2
ADAM22	RP11-293M10.2	PIPOX	CD207
ASIC4	RP4-794H19.2	RP11-421L21.2	NABP1
RP4-669L17.10	TPSD1	#N/A	GHRL
RP5-1013A22.5	DKFZP434E1119	#N/A	TBC1D9
ACAD11	HIST1H2AG	#N/A	CLEC4F
RP11-336K24.12	#N/A	#N/A	TATDN3
ST8SIA6	#N/A	#N/A	DGAT2
ZNF709	#N/A	#N/A	ELAVL4
#N/A	#N/A	#N/A	XCR1
#N/A	#N/A	#N/A	TOMM34
#N/A	#N/A	#N/A	SLAMF9
#N/A	#N/A	#N/A	UPK3A
#N/A	#N/A	#N/A	CD1B
#N/A	#N/A	#N/A	SFTPD
#N/A	#N/A	#N/A	RFPL4A
#N/A	#N/A	#N/A	CEACAM4
#N/A	#N/A	#N/A	AP003774.6
#N/A	#N/A	#N/A	CTD-2514K5.2
#N/A	#N/A	#N/A	CLCN4

identM.Macrophages	identM.Mast	identM.Monocytes	identM.Myeloid	identM.Neutrophils	identM.Tissue_DCs
ACP5	CAPG	ACP5	AIF1	IL1B	CLEC10A
C1QA	H3F3B	AIF1	C1QA	PLAUR	FCER1A
C1QB	NFKBIA	C1QA	C1QB	SOD2	AMICA1
C1QC	PPP1R15A	C1QB	C1QC	G0S2	RGS2
CTSB	TPSAB1	C1QC	CLEC10A	TYMP	CD1C
CTSD	VWA5A	C1orf162	CPVL	FCN1	GPR183
CTSZ	ANXA1	CD74	CST3	S100A9	PLD4
FCGRT	GLUL	CLEC10A	CTSB	CYBA	CD1E
FTL	CTSG	CPVL	CYBA	STX11	CXCL16
FUCA1	LTC4S	CST3	DNASE1L3	OAZ1	CD1D
HLA-DMB	DNAJA1	CTSB	FAM26F	C5AR1	PHACTR1
IGSF6	UBB	CYBA	FTL	EREG	CACNA2D3
LGMN	LMNA	DNASE1L3	GLUL	CXCL2	LITAF
MS4A4A	GATA2	FAM26F	GPX1	NCF2	P2RY13
MS4A7	NFKBIZ	FTL	HLA-DPA1	LILRB2	CD207
PSAP	C1orf186	GPX1	HLA-DPB1	IL1RN	GHRL
RNASE1	HSP90AB1	GRN	HLA-DQA1	GLRX	TBC1D9
RNASET2	HPGDS	HLA-DMA	HLA-DQA2	CSTA	CLEC4F
SEPP1	KRT1	HLA-DMB	HLA-DQB1	RAB20	ELAVL4
STAB1	MAOB	HLA-DPA1	HLA-DQB2	ASGR1	PLB1
TYROBP	ASAH1	HLA-DPB1	HLA-DRA	S100A8	SLAMF9
CD14	SERPINB1	HLA-DQA1	HLA-DRB1	UBE2D1	CD1B
SDS	DDX5	HLA-DQA2	HLA-DRB5	ATF5	CEACAM4
GRN	RP11-354E11.2	HLA-DQB1	IFI30	JUND	RFPL4A
APOC1	HDC	HLA-DQB2	IGSF6	FCGR1A	AP003774.6
SLC40A1	SLC45A3	HLA-DRA	IL1B	CXCL3	CTD-2514K5.2
GPNMB	CPA3	HLA-DRB1	LYZ	LILRA2	RP11-667K14.3
PLD3	LMO4	HLA-DRB5	MPEG1	APOBEC3A	RASGRF1
FOLR2	HSPA5	IFI30	MS4A4A	EMILIN2	TBX19
CD68	HPGD	IGSF6	MS4A6A	FPR1	RP11-196G11.2
ADORA3	SLC18A2	IL1B	MS4A7	SCO2	RUFY4
LIPA	RPL36AL	LYZ	PSAP	NLRP3	RP11-13811.2
IGF1	CLIC1	MPEG1	RNASE6	CCRL2	MS4A14

TABLE 11C-continued

Immune					
CD163L1	CTNNBL1	MS4A4A	RNASET2	ARL8B	TMEM170B
CSTB	DAD1	MS4A6A	S100A11	LILRA3	RP11-117D22.2
CREG1	ADRB2	MS4A7	SAT1	RNF19B	ZDHHC19
TREM2	ALOX5AP	PLAUR	SPI1	FCGR1B	ANKRD55
MMP12	PLIN2	PSAP	TYROBP	RP11-701P16.5	RP11-248J18.2
GM2A	STX3	RNASE6	VSIG4	IL27	NAMPTL
ATOX1	HS3ST1	RNASET2	SDS	LILRA5	CTC-428H11.2
CD4	PRKAR1A	SAT1	C1orf162	RP11-686D22.8	GRAMD1B
ATP6V0D2	HNRNPM	SDS	ATP6V1F	#N/A	RP11-147L13.2
CD209	FAM46A	SPI1	FCER1A	#N/A	LEKR1
BRI3	CD44	TYMP	TYMP	#N/A	CTD-2619J13.17
ADAP2	CMA1	TYROBP	GRN	#N/A	LUCAT1
CD163	STXBP6	VSIG4	STAB1	#N/A	RP11-73K9.2
DAB2	BTK	STAB1	PLAUR	#N/A	RN7SL605P
LILRB5	EIF3D	OAZ1	RNF130	#N/A	AC144652.1
OTOA	SAMSN1	AP2S1	CTSS	#N/A	RP11-128M1.1
NPL	GMPR	CTSZ	CTSD	#N/A	#N/A

identM.Tolerogenic__DCs	identT.Activated__CD4__hiFos	identT.Activated__CD4__loFos	identT.CD4	identT.CD8
CST3	TSC22D3	RPLP1	RPL10	CCL5
CPVL	KLF6	ZDBF2	RPL21	CD8A
IDO1	TNFAIP3	AC006369.2	RPLP1	CD8B
CD74	CITED2	#N/A	RPS25	TRGC2
SNX3	RP11-302B13.5	#N/A	RPS27A	TRGC1
HLA-DPB1	#N/A	#N/A	TRAC	LYAR
CLEC9A	#N/A	#N/A	RPL32	RP11-291B21.2
HLA-DPA1	#N/A	#N/A	RPS15A	NCR2
DNASE1L3	#N/A	#N/A	RPL19	RP11-713M15.1
LGALS2	#N/A	#N/A	RPL30	AC131056.3
CTD-2319112.1	#N/A	#N/A	RPL9	RP11-305L7.3
C1orf54	#N/A	#N/A	CD40LG	SLC25A5-AS1
HLA-DQB2	#N/A	#N/A	RORA	CACNA1C-AS2
COTL1	#N/A	#N/A	CD5	GSG2
LSP1	#N/A	#N/A	FLT3LG	CCR9
HLA-DQA2	#N/A	#N/A	CTLA4	#N/A
MPEG1	#N/A	#N/A	PDCD1	#N/A
ACTB	#N/A	#N/A	LAIR2	#N/A
BATF3	#N/A	#N/A	RP11-664D1.1	#N/A
SGK1	#N/A	#N/A	SUSD4	#N/A
PPT1	#N/A	#N/A	IL26	#N/A
PTPRE	#N/A	#N/A	RP11-265P11.2	#N/A
GLIPR1	#N/A	#N/A	CDKL2	#N/A
ASB2	#N/A	#N/A	HAR1A	#N/A
KIAA0226L	#N/A	#N/A	AC006369.2	#N/A
TMSB4X	#N/A	#N/A	RP4-594110.3	#N/A
SERPINF2	#N/A	#N/A	F5	#N/A
TNNI2	#N/A	#N/A	CCDC157	#N/A
SLAMF7	#N/A	#N/A	LA16c-431H6.6	#N/A
FLT3	#N/A	#N/A	C15orf53	#N/A
WDFY4	#N/A	#N/A	#N/A	#N/A
SMCO4	#N/A	#N/A	#N/A	#N/A
VMO1	#N/A	#N/A	#N/A	#N/A
CPNE3	#N/A	#N/A	#N/A	#N/A
CKS2	#N/A	#N/A	#N/A	#N/A
RAB32	#N/A	#N/A	#N/A	#N/A
GSTP1	#N/A	#N/A	#N/A	#N/A
FKBP1B	#N/A	#N/A	#N/A	#N/A
TACSTD2	#N/A	#N/A	#N/A	#N/A
CCND1	#N/A	#N/A	#N/A	#N/A
C12orf5	#N/A	#N/A	#N/A	#N/A
NABP1	#N/A	#N/A	#N/A	#N/A
FNIP2	#N/A	#N/A	#N/A	#N/A
KIAA1598	#N/A	#N/A	#N/A	#N/A
VAC14	#N/A	#N/A	#N/A	#N/A
LSM6	#N/A	#N/A	#N/A	#N/A
XCR1	#N/A	#N/A	#N/A	#N/A
PPM1M	#N/A	#N/A	#N/A	#N/A
PPM1J	#N/A	#N/A	#N/A	#N/A
IER5	#N/A	#N/A	#N/A	#N/A

identT.CD8__IELs	identT.CD8__LP	identT.CXCR6__Th17	identT.Cycling__T	identT.ILCs	identT.MT
CCL5	CD8A	CD2	TYMS	LST1	ACAP1
HOPX	CD8B	CXCR6	KIAA0101	LTB	PAK6
GZMA	ZFP36L2	KLRB1	DUT	KRT86	CTD-2035E11.5
TRDC	GZMH	AC092580.4	GINS2	FXYD5	RN7SL55P

TABLE 11C-continued

Immune					
TRGC2	LYAR	SLAMF1	PCNA	IL4I1	#N/A
KLRC2	IFNG	CCL20	DNAJC9	ID2	#N/A
ABI3	CRTAM	IL12RB1	SMC4	CASP3	#N/A
TRGC1	RP11-291B21.2	ZNRD1	MCM3	H2AFY	#N/A
RARRES3	RP11-305L7.3	ZFYVE28	CENPF	HNRNPA0	#N/A
CD96	ZNF80	RP11-403A21.1	YEATS4	SPINK2	#N/A
CD244	ATP1A3	RP11-85K15.2	NRM	OTUD5	#N/A
NCR2	#N/A	RP11-415F23.2	RAD51	DDIT4	#N/A
KIR2DL3	#N/A	RP11-401F2.3	CDCA5	ARL4A	#N/A
RP11-713M15.1	#N/A	OVCH1-AS1	TCTEX1D2	ALDOC	#N/A
DRAXIN	#N/A	#N/A	MTFR2	LTA4H	#N/A
URB2	#N/A	#N/A	ACAT2	PRMT10	#N/A
RP11-535A5.1	#N/A	#N/A	VSIG1	SRSF2	#N/A
SEC14L6	#N/A	#N/A	ABCD2	HMGN3	#N/A
RP11-104L21.3	#N/A	#N/A	A1BG	MAP3K8	#N/A
AL590452.1	#N/A	#N/A	C5orf17	AREG	#N/A
ADAMTS17	#N/A	#N/A	AC027307.3	MPG	#N/A
SEMA4F	#N/A	#N/A	#N/A	IL23R	#N/A
LRRIQ3	#N/A	#N/A	#N/A	CD164	#N/A
KLRC4	#N/A	#N/A	#N/A	CSF2	#N/A
ALG11	#N/A	#N/A	#N/A	HINT3	#N/A
CCDC7	#N/A	#N/A	#N/A	MED30	#N/A
#N/A	#N/A	#N/A	#N/A	LINC00299	#N/A
#N/A	#N/A	#N/A	#N/A	OSTC	#N/A
#N/A	#N/A	#N/A	#N/A	DLL1	#N/A
#N/A	#N/A	#N/A	#N/A	TNFSF11	#N/A
#N/A	#N/A	#N/A	#N/A	TCTN3	#N/A
#N/A	#N/A	#N/A	#N/A	SLC4A10	#N/A
#N/A	#N/A	#N/A	#N/A	TEX30	#N/A
#N/A	#N/A	#N/A	#N/A	FXYD7	#N/A
#N/A	#N/A	#N/A	#N/A	SAMD10	#N/A
#N/A	#N/A	#N/A	#N/A	PLEKHN1	#N/A
#N/A	#N/A	#N/A	#N/A	ZNF724P	#N/A
#N/A	#N/A	#N/A	#N/A	ZNF385C	#N/A
#N/A	#N/A	#N/A	#N/A	RP11-403113.5	#N/A
#N/A	#N/A	#N/A	#N/A	RP11-77P16.4	#N/A
#N/A	#N/A	#N/A	#N/A	SYDE2	#N/A
#N/A	#N/A	#N/A	#N/A	RNU2-63P	#N/A
#N/A	#N/A	#N/A	#N/A	RP11-53019.3	#N/A
#N/A	#N/A	#N/A	#N/A	FAM169A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A
#N/A	#N/A	#N/A	#N/A	#N/A	#N/A

identT.Memory__CD4	identT.NK	identT.PD1__CD4	identT .Tcells	identT .Tregs
RPS27	NKG7	RP5-1028K7.2	CD2	IL32
RPL21	CCL4	CORO1B	CD3D	TRBC2
RPS25	XCL1	ICA1	CD3E	RGS1
RPL32	CTSW	PTPN7	CD3G	BATF
TMEM66	GNLY	CD200	LCK	CREM
RPLP2	IL2RB	PDCD1	RPS19	TNFRSF4
RPL9	XCL2	KIF2A	TRAC	CTLA4
RPL19	CLIC3	RP11-455F5.5	TRBC2	GBP2
RPS20	KLRC1	GNG4	AC092580.4	TNFRSF1B
RPL31	GZMB	RP11-566E18.3	ACAP1	FOXP3
RPL30	HCST	RP11-479G22.8	SIRPG	LAIR2
RPL11	KLRD1	RP11-126K1.2	TRGC2	MIR4435-1HG
RPL13A	APOBEC3G	IQSEC3	ICAM3	NINJ2
RPL27A	PRF1	NTRK3	RGL4	LINC00649
RPL35A	EIF3G	#N/A	CYTIP	TNFRSF9
RPS29	CCL3	#N/A	CD8A	CUL9
CCR7	STK17A	#N/A	TIGIT	DUSP16
NOSIP	CD160	#N/A	CXCR6	CDKL2
LEF1	KLRF1	#N/A	TRAT1	ANKS1B
RP11-664D1.1	FGR	#N/A	C9orf78	TRAV36DV7
AC013264.2	VPS37B	#N/A	CD8B	RN7SL443P
RP11-166B2.3	CMC1	#N/A	CD6	C15orf53
#N/A	CHST12	#N/A	GPR171	TRAV13-2
#N/A	LINC00996	#N/A	LAG3	TRAV8-2
#N/A	SH2D1B	#N/A	LYAR	RP11-53B2.6
#N/A	BCO2	#N/A	OXNAD1	#N/A
#N/A	SLC35E1	#N/A	DDX24	#N/A
#N/A	FCRL6	#N/A	IGHV1OR15-1	#N/A
#N/A	RP11-222K16.2	#N/A	SSBP4	#N/A

TABLE 11C-continued

Immune				
#N/A	AC017104.6	#N/A	RCAN3	#N/A
#N/A	EOMES	#N/A	CD40LG	#N/A
#N/A	IL12RB2	#N/A	THEMIS	#N/A
#N/A	TRIM54	#N/A	RGS14	#N/A
#N/A	PADI4	#N/A	FLT3LG	#N/A
#N/A	RP11-449P15.2	#N/A	CD28	#N/A
#N/A	RP11-24B19.3	#N/A	CISH	#N/A
#N/A	KIF21B	#N/A	CD5	#N/A
#N/A	#N/A	#N/A	CA10	#N/A
#N/A	#N/A	#N/A	CHRM3-AS2	#N/A
#N/A	#N/A	#N/A	BCL11B	#N/A
#N/A	#N/A	#N/A	UBASH3A	#N/A
#N/A	#N/A	#N/A	LRRN3	#N/A
#N/A	#N/A	#N/A	RP11-291B21.2	#N/A
#N/A	#N/A	#N/A	CTLA4	#N/A
#N/A	#N/A	#N/A	CCR5	#N/A
#N/A	#N/A	#N/A	TNIP3	#N/A
#N/A	#N/A	#N/A	MIAT	#N/A
#N/A	#N/A	#N/A	LINC00649	#N/A
#N/A	#N/A	#N/A	AC013264.2	#N/A
#N/A	#N/A	#N/A	AC104820.2	#N/A

Tables 12-15

Column	Description
ident	cell subset ID
gene	gene name
contrast	DE comparison
coefD	discrete coefficient of model
pvalD	discrete p-value
coefC	continuous coefficient of model
pvalC	continuous p-value
mastfc	fold-change of gene estimated by MAST
pvalH	combined p-value (discrete and continuous)
ref	name of reference group
n	number of expressing cells
ref__n	for reference group
	alpha fraction of expressing cells
	ref__alpha for reference group
mu	mean expression level within expressing cells

-continued

Tables 12-15

Column	Description
ref__mu	for reference group
	mean mean expression
	ref__mean for reference group
total	fraction of total expression within group
ref__total	for reference group
	log2fc log2(fold-change) re1ative to reference group
	padjD adjusted p-value for discrete term
	padjC adjusted p-value for continuous term
	padjH adjusted p-value (combined)
	contam.res residual from contamination fit
	contam fraction of total expression within group
	nsamps number of samples gene is expressed in

TABLE 12

Additional Cell Type Markers

ident	gene	coefD	pvalD	coefC	pvalC	mastfc
B.Bcells	AC096579.7	3.268	0.00E+00	2.04E+00	2.22E−31	2.073248198
B.Bcells	AL928768.3	6.364	0.00E+00	9.39E−01	2.47E−04	1.917529901
B.Bcells	CD27	3.202	0.00E+00	−5.04E−01	4.30E−13	1.454640372
B.Bcells	CD74	4.682	0.00E+00	6.43E−01	1.98E−18	3.951093813
B.Bcells	CD79A	7.006	0.00E+00	8.64E−01	3.04E−04	2.727051658
B.Bcells	CFL1	−0.738	1.34E−20	−1.64E+00	0.00E+00	−1.184421042
B.Bcells	DERL3	4.997	0.00E+00	1.27E+00	1.40E−26	1.221885789
B.Bcells	DNAJB9	2.666	0.00E+00	1.02E−01	3.58E−02	1.403867423
B.Bcells	FKBP11	2.607	0.00E+00	8.26E−01	1.12E−69	1.333818231
B.Bcells	HERPUD1	2.593	0.00E+00	1.74E+00	0.00E+00	2.631118963
B.Bcells	IGHA1	2.237	1.67E−211	4.66E+00	0.00E+00	5.929899096
B.Bcells	IGHA2	2.087	4.56E−255	4.18E+00	0.00E+00	4.806875561
B.Bcells	IGJ	2.338	5.24E−289	4.55E+00	0.00E+00	5.565921598
B.Bcells	IGKC	2.917	0.00E+00	4.37E+00	4.37E−196	5.440840209
B.Bcells	IGLC2	2.701	0.00E+00	2.24E+00	1.28E−34	2.653469053
B.Bcells	IGLC3	2.590	0.00E+00	2.07E+00	3.89E−31	2.686736798
B.Bcells	MZB1	4.212	0.00E+00	1.98E+00	3.72E−74	2.231289984
B.Bcells	PTPRCAP	2.259	3.03E−294	−9.81E−01	5.62E−61	1.530286416
B.Bcells	SEC11C	2.343	8.29E−272	1.01E+00	7.87E−140	1.081174331
B.FO	CD74	4.460	2.85E−280	2.49E+00	3.51E−181	5.354121926
B.FO	CD79A	3.737	0.00E+00	7.69E−01	1.09E−17	2.695535941
B.FO	HLA-DRA	3.473	0.00E+00	1.31E+00	2.57E−31	4.584234603
B.Plasma	AC096579.7	4.338	0.00E+00	1.87E+00	1.20E−28	4.119453937
B.Plasma	AL928768.3	6.031	0.00E+00	−3.82E−01	4.82E−03	2.80561746
B.Plasma	CCR10	5.264	0.00E+00	−3.53E−01	6.29E−03	1.099736317
B.Plasma	CD27	4.354	0.00E+00	−6.00E−01	3.05E−17	2.032701947

TABLE 12-continued

Additional Cell Type Markers						
B.Plasma	CD79A	6.105	0.00E+00	−6.42E−01	8.21E−10	2.569609064
B.Plasma	CRELD2	3.642	0.00E+00	−7.49E−02	7.62E−02	1.521987695
B.Plasma	CYTIP	2.801	8.56E−287	−1.12E+00	4.40E−108	1.172161746
B.Plasma	DERL3	7.160	0.00E+00	1.06E+00	1.28E−27	3.432708536
B.Plasma	DNAJB9	4.516	0.00E+00	2.31E−01	1.13E−06	2.751694035
B.Plasma	DUSP5	3.550	0.00E+00	−5.31E−01	8.87E−15	1.084131907
B.Plasma	EAF2	4.763	0.00E+00	−3.45E−01	1.57E−06	1.626266352
B.Plasma	EMP3	2.523	1.73E−240	−1.18E+00	4.28E−175	1.039438032
B.Plasma	EVI2B	2.894	3.61E−279	−9.89E−01	4.61E−76	1.091108309
B.Plasma	FAM46C	3.600	0.00E+00	−6.89E−01	3.30E−41	1.056523747
B.Plasma	FGF23	4.651	0.00E+00	−2.47E−01	4.23E−02	1.271037067
B.Plasma	FKBP11	5.774	0.00E+00	9.52E−01	3.02E−96	3.37615678
B.Plasma	GNG7	4.228	0.00E+00	−5.70E−01	3.94E−21	1.273964782
B.Plasma	GYPC	2.905	0.00E+00	−9.97E−01	2.47E−119	1.374166018
B.Plasma	HERPUD1	5.656	0.00E+00	1.96E+00	0.00E+00	4.539832048
B.Plasma	IGHA1	5.916	8.02E−264	6.74E+00	0.00E+00	8.832840744
B.Plasma	IGHA2	5.673	0.00E+00	5.34E+00	0.00E+00	8.005763853
B.Plasma	IGJ	6.775	0.00E+00	5.95E+00	0.00E+00	8.446894928
B.Plasma	IGKC	4.405	0.00E+00	5.28E+00	2.45E−275	7.801070323
B.Plasma	IGLC2	3.773	0.00E+00	2.28E+00	4.98E−32	4.275847217
B.Plasma	IGLC3	3.401	0.00E+00	2.02E+00	6.17E−26	3.981855127
B.Plasma	IGLL5	4.075	0.00E+00	5.73E−01	6.19E−02	2.106667448
B.Plasma	IL2RG	2.386	1.07E−225	−9.48E−01	1.03E−106	1.018567961
B.Plasma	ISG20	3.760	0.00E+00	−2.47E−01	5.63E−09	2.1133028
B.Plasma	MANF	3.944	0.00E+00	1.73E−01	1.39E−05	2.022112695
B.Plasma	MZB1	8.081	0.00E+00	1.70E+00	2.09E−87	4.636645997
B.Plasma	NUCB2	2.932	4.18E−299	−4.76E−01	4.17E−31	1.121345488
B.Plasma	PDIA4	3.344	0.00E+00	−1.51E−01	2.50E−04	1.089626914
B.Plasma	PIM2	3.954	0.00E+00	−6.11E−01	4.80E−16	1.249090523
B.Plasma	PPAPDC1B	3.473	0.00E+00	−1.84E−01	9.65E−06	1.180769265
B.Plasma	PRDX4	3.794	0.00E+00	2.13E−01	2.49E−08	1.908367774
B.Plasma	RGCC	2.955	0.00E+00	−1.39E+00	3.65E−86	1.671612761
B.Plasma	RGS1	2.958	0.00E+00	−6.46E−01	3.21E−24	2.027928073
B.Plasma	SDF2L1	3.816	0.00E+00	2.29E−01	7.68E−09	2.12000614
B.Plasma	SEC11C	5.065	0.00E+00	1.06E+00	1.35E−157	3.257253887
B.Plasma	SPCS3	3.550	0.00E+00	−2.48E−01	6.75E−09	1.303454494
B.Plasma	SSR3	3.937	0.00E+00	2.78E−01	1.50E−14	1.985908248
B.Plasma	SSR4	5.407	2.05E−119	2.36E+00	0.00E+00	4.875540628
B.Plasma	TNFRSF17	7.053	0.00E+00	3.55E−01	2.28E−03	2.775933525
B.Plasma	TRAM1	3.600	0.00E+00	−3.83E−01	2.34E−25	1.594121993
B.Plasma	TXNDC15	3.410	0.00E+00	−3.88E−01	1.71E−18	1.24259521
B.Plasma	UBE2J1	4.889	0.00E+00	3.20E−02	5.13E−01	2.040155386
B.Plasma	WT1-AS	3.838	0.00E+00	7.54E−01	2.19E−08	1.850996813
B.Plasma	XBP1	5.257	0.00E+00	9.96E−01	1.20E−110	3.416010759
E.Absorptive	CA4	3.869	0.00E+00	2.23E+00	5.83E−168	4.966152183
E.Absorptive	CEACAM5	3.040	0.00E+00	1.32E+00	4.22E−101	2.471517978
E.Absorptive	CLDN3	3.520	2.44E−265	7.28E−01	1.38E−70	2.849876849
E.Absorptive	CLDN7	3.451	3.17E−254	9.20E−01	2.72E−114	3.239205689
E.Absorptive	EPCAM	3.611	8.10E−263	8.16E−01	3.65E−76	3.498387043
E.Absorptive	FABP1	4.261	3.07E−269	2.02E+00	1.43E−129	5.705513317
E.Absorptive	FTH1	1.212	4.19E−02	2.26E+00	0.00E+00	2.904022981
E.Absorptive	FXYD3	4.139	9.84E−269	1.43E+00	1.68E−142	4.637026365
E.Absorptive	GUCA2A	3.019	0.00E+00	2.71E+00	2.07E−158	5.019707907
E.Absorptive	GUCA2B	2.911	0.00E+00	2.15E+00	2.49E−91	3.832151794
E.Absorptive	KRT20	3.141	0.00E+00	9.79E−01	2.09E−53	3.027566969
E.Absorptive	KRT8	4.729	1.42E−270	1.04E+00	9.65E−86	4.383298523
E.Absorptive	LGALS3	3.504	1.18E−100	1.55E+00	9.06E−244	3.952510867
E.Absorptive	LYPD8	3.338	0.00E+00	1.55E+00	2.72E−88	3.510660931
E.Absorptive	PHGR1	5.683	1.10E−267	1.69E+00	9.76E−127	5.833162008
E.Absorptive	PLAC8	2.520	5.24E−261	1.32E+00	1.29E−80	2.780344753
E.Absorptive	SDCBP2	3.592	0.00E+00	1.25E+00	1.13E−118	3.146564742
E.Absorptive	SRI	2.653	1.32E−117	1.49E+00	1.05E−263	3.080149952
E.Absorptive	TSPAN1	3.255	3.14E−288	1.28E+00	8.98E−120	3.449336247
E.Absorptive_All	C15orf48	3.617	0.00E+00	9.36E−01	1.72E−112	3.001269361
E.Absorptive_All	C19orf33	2.845	0.00E+00	1.00E+00	5.63E−118	1.314768165
E.Absorptive_All	CA2	3.138	0.00E+00	1.71E+00	2.24E−195	2.609090429
E.Absorptive_All	CLDN7	3.105	0.00E+00	7.51E−01	4.22E−84	2.010379557
E.Absorptive_All	EPCAM	3.213	0.00E+00	4.23E−01	3.37E−23	2.504645735
E.Absorptive_All	ETHE1	2.302	2.35E−221	1.03E+00	1.66E−142	1.039913635
E.Absorptive_All	FABP1	3.780	0.00E+00	3.21E+00	0.00E+00	5.586554967
E.Absorptive_All	FXYD3	3.402	0.00E+00	1.63E+00	9.61E−216	3.576992003
E.Absorptive_All	KRT19	2.755	0.00E+00	1.55E+00	8.44E−143	1.818399526
E.Absorptive_All	KRT8	3.698	0.00E+00	1.16E+00	6.91E−128	3.836768245
E.Absorptive_All	LGALS3	2.848	3.50E−188	1.60E+00	0.00E+00	3.461283056
E.Absorptive_All	LGALS4	4.384	0.00E+00	7.03E−01	3.02E−50	4.211537187
E.Absorptive_All	PHGR1	5.445	0.00E+00	2.14E+00	9.74E−280	5.851633306
E.Absorptive_All	PIGR	3.492	0.00E+00	9.55E−01	5.70E−99	2.40099232
E.Absorptive_All	SDCBP2	2.672	5.76E−306	7.80E−01	1.60E−30	1.124968887

TABLE 12-continued

Additional Cell Type Markers

E.Absorptive_All	SLC26A3	2.567	5.04E−296	1.53E+00	9.49E−54	1.462101925
E.Absorptive_All	SRI	2.120	2.05E−168	1.20E+00	2.42E−223	1.743839617
E.Absorptive_All	TMEM54	2.793	0.00E+00	9.67E−01	1.34E−104	1.077198575
E.Absorptive_All	TSPAN1	2.599	2.92E−308	9.87E−01	1.25E−67	1.638371845
E.Absorptive_TA_1	LGALS4	3.972	0.00E+00	−2.12E−01	4.36E−04	3.560085632
E.Best4_Enterocytes	BEST4	5.329	0.00E+00	1.91E+00	8.10E−12	2.425352878
E.Best4_Enterocytes	CA7	5.258	0.00E+00	1.69E+00	9.89E−17	2.608165149
E.Best4_Enterocytes	SPIB	4.611	0.00E+00	5.00E−01	4.09E−06	1.727259355
E.Enterocyte_Immature_1	ANPEP	3.273	0.00E+00	4.23E−01	3.34E−10	2.255957196
E.Enterocyte_Immature_1	AQP8	5.529	0.00E+00	2.22E+00	6.64E−104	5.678449028
E.Enterocyte_Immature_1	C19orf33	3.309	3.92E−279	7.66E−01	4.51E−54	2.553397084
E.Enterocyte_Immature_1	CA4	4.624	0.00E+00	9.84E−01	2.85E−28	4.39738035
E.Enterocyte_Immature_1	CEACAM5	3.877	0.00E+00	7.92E−01	1.17E−33	2.717411561
E.Enterocyte_Immature_1	CEACAM7	3.601	0.00E+00	2.86E−01	6.89E−05	2.272494617
E.Enterocyte_Immature_1	CLCA4	3.608	0.00E+00	5.71E−01	5.87E−10	1.903154797
E.Enterocyte_Immature_1	CTD-2228K2.5	3.928	0.00E+00	2.35E−01	3.99E−04	2.663088343
E.Enterocyte_Immature_1	FABP1	6.525	1.00E−301	1.58E+00	1.78E−63	5.694861283
E.Enterocyte_Immature_1	FXYD3	5.069	0.00E+00	1.02E+00	1.47E−58	4.485597281
E.Enterocyte_Immature_1	GUCA2A	4.903	0.00E+00	1.94E+00	1.25E−79	5.559428295
E.Enterocyte_Immature_1	GUCA2B	3.889	0.00E+00	8.26E−01	3.33E−16	3.558658878
E.Enterocyte_Immature_1	LYPD8	3.820	0.00E+00	6.53E−01	1.07E−15	3.082198702
E.Enterocyte_Immature_1	MT-RNR2	2.292	2.30E−14	2.71E+00	0.00E+00	4.854022399
E.Enterocyte_Immature_1	PHGR1	5.718	2.20E−275	1.58E+00	1.98E−86	5.828514036
E.Enterocyte_Immature_1	PLAC8	3.821	0.00E+00	9.36E−01	8.51E−43	3.344273115
E.Enterocyte_Immature_1	PRAP1	3.639	0.00E+00	6.96E−01	3.88E−21	2.616769997
E.Enterocyte_Immature_1	SDCBP2	3.416	0.00E+00	5.58E−01	4.57E−22	2.47146566
E.Enterocyte_Immature_1	SLC26A3	3.960	0.00E+00	5.28E−01	9.36E−11	3.105329195
E.Enterocyte_Immature_1	TSPAN1	4.105	0.00E+00	8.49E−01	3.42E−44	3.553346713
E.Enterocyte_Immature_2	CA1	3.617	7.44E−271	1.90E+00	2.14E−95	4.022433153
E.Enterocyte_Immature_2	CA2	6.076	2.56E−210	1.82E+00	5.16E−196	5.018877036
E.Enterocyte_Immature_2	ETHE1	3.172	2.56E−107	1.61E+00	2.65E−288	3.031843788
E.Enterocyte_Immature_2	FABP1	6.700	3.73E−169	3.54E+00	0.00E+00	7.466412634
E.Enterocyte_Immature_2	FXYD3	6.468	3.46E−163	2.11E+00	5.90E−304	5.521904327
E.Enterocyte_Immature_2	KRT19	4.212	5.25E−177	2.29E+00	3.79E−280	4.943887282
E.Enterocyte_Immature_2	KRT20	4.317	0.00E+00	1.31E+00	3.19E−87	3.976800169
E.Enterocyte_Immature_2	KRT8	5.494	7.38E−149	2.01E+00	2.61E−259	5.358446529
E.Enterocyte_Immature_2	LGALS3	3.960	5.85E−49	2.24E+00	0.00E+00	4.773676172
E.Enterocyte_Immature_2	MS4A12	4.243	0.00E+00	1.01E+00	4.80E−42	3.534180442
E.Enterocyte_Immature_2	PHGR1	6.551	1.19E−151	2.63E+00	7.99E−271	6.710120779
E.Enterocyte_Immature_2	SLC26A2	4.441	1.25E−277	1.03E+00	1.22E−65	2.835807204
E.Enterocyte_Immature_2	SLC26A3	4.350	0.00E+00	9.07E−01	2.06E−30	3.660394983
E.Enterocyte_Immature_2	SLC51B	3.934	0.00E+00	4.63E−01	1.35E−17	2.37432504
E.Enterocyte_Immature_2	TMEM54	4.061	8.68E−165	1.39E+00	1.73E−199	3.480691951
E.Enterocyte_Progenitor	CA1	3.386	0.00E+00	1.50E+00	8.58E−55	3.281612499
E.Enterocyte_Progenitor	CA2	3.952	0.00E+00	8.98E−01	5.54E−42	3.742427108
E.Enterocyte_Progenitor	FABP1	6.816	0.00E+00	2.32E+00	2.12E−145	6.384233482
E.Enterocyte_Progenitor	FXYD3	4.646	0.00E+00	9.74E−01	2.64E−57	4.403240028
E.Enterocyte_Progenitor	KRT19	4.065	0.00E+00	1.24E+00	4.89E−73	3.955605149
E.Enterocyte_Progenitor	KRT8	4.971	0.00E+00	1.07E+00	3.04E−69	4.573460965
E.Enterocyte_Progenitor	LGALS4	5.934	0.00E+00	1.03E+00	1.02E−70	4.817857244
E.Enterocyte_Progenitor	PHGR1	7.475	0.00E+00	1.88E+00	8.07E−133	6.100770415
E.Enterocyte_Progenitor	SELENBP1	4.211	0.00E+00	1.33E+00	4.51E−136	3.135115956
E.Enterocytes	ANPEP	4.276	0.00E+00	9.70E−01	4.37E−49	3.4334963
E.Enterocytes	APOBEC3B	3.764	0.00E+00	6.10E−01	1.70E−21	1.781460279
E.Enterocytes	AQP8	7.060	0.00E+00	3.38E+00	2.11E−268	7.177138737
E.Enterocytes	C19orf33	5.584	3.11E−198	1.36E+00	2.22E−188	4.137577174
E.Enterocytes	CA4	6.565	0.00E+00	2.15E+00	2.95E−149	5.939432428
E.Enterocytes	CEACAM1	4.695	0.00E+00	7.73E−01	9.35E−25	3.045247994
E.Enterocytes	CEACAM5	6.519	0.00E+00	1.84E+00	4.95E−199	4.700907519
E.Enterocytes	CEACAM7	5.715	0.00E+00	9.49E−01	4.29E−43	3.622341305
E.Enterocytes	CFDP1	4.497	6.15E−231	1.06E+00	1.38E−132	3.245164922
E.Enterocytes	CLCA4	5.018	0.00E+00	1.15E+00	1.95E−32	3.503102339
E.Enterocytes	CLDN23	4.089	0.00E+00	5.26E−01	2.60E−16	2.160346928
E.Enterocytes	CLDN7	5.365	2.79E−173	1.42E+00	9.21E−207	4.427110007
E.Enterocytes	CTD-2228K2.5	5.362	0.00E+00	1.21E+00	9.92E−83	3.877284229
E.Enterocytes	EMP1	4.123	0.00E+00	4.12E−01	1.24E−09	2.047517041
E.Enterocytes	FTH1	1.916	1.32E−01	3.29E+00	0.00E+00	4.290842634
E.Enterocytes	FXYD3	6.057	2.22E−164	1.91E+00	5.88E−195	5.426847174
E.Enterocytes	GPRC5A	4.048	0.00E+00	5.24E−01	1.70E−19	1.525511114
E.Enterocytes	GUCA2A	6.907	0.00E+00	3.09E+00	6.58E−220	7.354492732
E.Enterocytes	GUCA2B	6.330	0.00E+00	1.83E+00	4.32E−82	5.559777218
E.Enterocytes	HIST1H1C	4.085	0.00E+00	7.94E−01	2.15E−36	2.894643396
E.Enterocytes	HPGD	4.238	0.00E+00	5.12E−01	2.25E−16	2.509509481
E.Enterocytes	IFI27	6.392	3.05E−125	2.53E+00	0.00E+00	5.895091164
E.Enterocytes	IL32	5.937	3.27E−218	1.59E+00	1.14E−139	4.756889198
E.Enterocytes	KRT20	5.007	0.00E+00	8.96E−01	8.40E−40	3.876747723
E.Enterocytes	LYPD8	5.363	0.00E+00	1.79E+00	1.38E−122	4.928965265
E.Enterocytes	MISP	4.804	3.19E−301	7.87E−01	4.27E−65	2.937076305

TABLE 12-continued

Additional Cell Type Markers						
E.Enterocytes	MS4A12	4.286	0.00E+00	9.91E−01	6.77E−37	3.637728367
E.Enterocytes	MY015B	4.284	0.00E+00	3.86E−01	5.87E−14	2.331334816
E.Enterocytes	NLN	3.914	0.00E+00	5.51E−01	5.98E−17	1.748615136
E.Enterocytes	PKIB	3.969	1.63E−252	1.03E+00	3.43E−94	2.846373547
E.Enterocytes	PLAC8	6.696	0.00E+00	2.10E+00	6.90E−230	5.029379735
E.Enterocytes	PRAP1	5.954	0.00E+00	1.34E+00	1.28E−81	4.30079732
E.Enterocytes	RP11-48020.4	3.959	0.00E+00	5.85E−01	4.40E−29	2.478995999
E.Enterocytes	SDCBP2	5.657	0.00E+00	1.52E+00	7.07E−168	4.352042706
E.Enterocytes	SLC26A3	5.722	0.00E+00	1.77E+00	1.86E−111	4.84897002
E.Enterocytes	SLC51B	3.996	0.00E+00	4.22E−01	1.66E−15	2.404698069
E.Enterocytes	SRI	4.171	7.04E−80	1.82E+00	5.05E−295	4.265517134
E.Enterocytes	TMEM37	3.713	1.33E−299	6.67E−01	5.75E−41	2.013255733
E.Enterocytes	TRIM31	4.538	0.00E+00	4.75E−01	1.39E−11	2.802587786
E.Enterocytes	TSPAN1	6.413	1.57E−228	1.94E+00	2.82E−237	5.148729385
E.Epithelial	AGR2	3.949	0.00E+00	1.01E+00	8.09E−10	1.253081377
E.Epithelial	ANXA1	−4.217	0.00E+00	−1.04E+00	7.40E−07	−1.710241201
E.Epithelial	BTG1	−1.582	1.48E−130	−1.36E+00	2.91E−239	−1.367126527
E.Epithelial	C15orf48	4.669	0.00E+00	1.59E+00	8.27E−80	2.960253603
E.Epithelial	C19orf33	4.647	0.00E+00	9.18E−01	1.35E−10	1.134930377
E.Epithelial	CA2	3.288	0.00E+00	1.19E+00	2.03E−32	2.331379028
E.Epithelial	CKB	3.289	0.00E+00	8.62E−01	2.47E−12	1.146140076
E.Epithelial	CLDN3	4.663	0.00E+00	9.77E−01	1.82E−24	1.215653124
E.Epithelial	CLDN4	4.347	0.00E+00	7.77E−01	6.52E−13	1.15526912
E.Epithelial	CLDN7	4.624	0.00E+00	1.00E+00	6.15E−31	1.876200849
E.Epithelial	COX5B	2.214	5.36E−161	1.11E+00	8.18E−267	1.799641559
E.Epithelial	DUSP1	−1.288	2.69E−97	−1.53E+00	2.48E−242	−1.135839708
E.Epithelial	EIF1	−1.762	2.34E−66	−1.40E+00	0.00E+00	−2.021194885
E.Epithelial	ELF3	4.803	0.00E+00	7.95E−01	2.09E−12	1.239636169
E.Epithelial	EPCAM	4.613	0.00E+00	1.62E+00	1.40E−82	2.59722632
E.Epithelial	FABP1	3.453	0.00E+00	2.94E+00	3.19E−179	4.955159628
E.Epithelial	FCGBP	3.946	0.00E+00	1.37E+00	2.63E−10	1.688693541
E.Epithelial	FXYD3	4.263	0.00E+00	2.08E+00	2.40E−125	3.385670825
E.Epithelial	H3F3B	−1.872	3.49E−99	−1.42E+00	0.00E+00	−1.851301465
E.Epithelial	HMGCS2	4.819	0.00E+00	2.68E−01	7.29E−02	1.305286854
E.Epithelial	IFI27	2.816	0.00E+00	6.65E−01	1.44E−17	2.137897548
E.Epithelial	IFITM2	−2.952	0.00E+00	−1.39E+00	2.78E−77	−1.263956467
E.Epithelial	JUNB	−1.448	3.67E−98	−1.77E+00	0.00E+00	−1.744661197
E.Epithelial	KRT18	4.848	0.00E+00	1.75E+00	9.68E−103	3.014353055
E.Epithelial	KRT19	3.783	0.00E+00	1.05E+00	1.11E−15	1.678360125
E.Epithelial	KRT20	3.500	0.00E+00	9.49E−01	1.35E−09	1.692310998
E.Epithelial	KRT8	4.853	0.00E+00	2.26E+00	2.77E−200	4.101240322
E.Epithelial	LGALS1	−3.516	0.00E+00	−1.95E+00	2.98E−52	−1.780792681
E.Epithelial	LGALS3	2.748	1.14E−241	1.69E+00	9.68E−287	3.079368421
E.Epithelial	LGALS4	5.445	0.00E+00	2.59E+00	5.11E−274	4.781743305
E.Epithelial	MT-ATP6	0.934	7.28E−19	2.05E+00	0.00E+00	2.293028029
E.Epithelial	MT-ND2	0.492	5.82E−05	1.81E+00	0.00E+00	1.625662978
E.Epithelial	MT-RNR1	1.652	3.50E−62	2.20E+00	0.00E+00	3.082297281
E.Epithelial	MT1G	3.638	0.00E+00	7.00E−01	7.15E−06	1.243604189
E.Epithelial	PIGR	4.870	0.00E+00	1.44E+00	1.80E−40	2.220870574
E.Epithelial	RPL21	−2.431	6.34E−73	−1.21E+00	1.28E−260	−3.027643271
E.Epithelial	S100A6	2.947	4.26E−150	1.71E+00	0.00E+00	3.608164898
E.Epithelial	SMIM22	6.002	0.00E+00	5.78E−01	3.52E−04	1.024792323
E.Epithelial	SPINT2	3.019	0.00E+00	7.90E−01	1.76E−51	1.075499988
E.Epithelial	TSPAN1	4.132	0.00E+00	1.01E+00	2.20E−11	1.756588332
E.Epithelial	ZFP36	−1.608	8.96E−149	−1.59E+00	3.30E−285	−1.438143355
E.Goblet	CEACAM5	4.002	0.00E+00	1.03E+00	4.78E−45	2.968738633
E.Goblet	CLDN4	3.623	3.64E−260	9.79E−01	4.81E−70	2.991613153
E.Goblet	FAM3D	3.571	1.62E−260	8.96E−01	3.82E−68	2.437979965
E.Goblet	FCGBP	5.018	0.00E+00	2.85E+00	2.31E−219	5.921268619
E.Goblet	FXYD3	4.708	3.13E−259	1.30E+00	6.86E−74	4.686719039
E.Goblet	GSN	4.114	1.01E−263	1.45E+00	1.95E−107	4.26091539
E.Goblet	IFI27	5.113	2.73E−240	1.79E+00	3.67E−134	5.086890298
E.Goblet	LYPD8	4.063	0.00E+00	8.87E−01	2.31E−25	3.43572456
E.Goblet	MUC1	3.744	2.28E−303	1.06E+00	8.46E−49	1.779435114
E.Goblet	MUC2	6.322	0.00E+00	3.25E+00	1.13E−201	6.142438491
E.Goblet	TFF1	5.714	0.00E+00	2.47E+00	3.84E−54	4.455223547
E.Goblet	TFF3	5.667	0.00E+00	3.29E+00	5.07E−166	6.864284391
E.Goblet	TSPAN1	4.367	0.00E+00	1.20E+00	8.68E−69	4.020758556
E.Goblet	ZG16	6.895	0.00E+00	5.45E+00	0.00E+00	9.067037516
E.Immature_Enterocytes	AQP8	2.562	0.00E+00	1.17E+00	3.17E−29	2.608741765
E.Immature_Enterocytes	C15orf48	3.540	0.00E+00	4.76E−01	3.03E−29	3.057877917
E.Immature_Enterocytes	C19orf33	3.153	0.00E+00	7.95E−01	4.84E−85	2.007697328
E.Immature_Enterocytes	CA1	2.744	0.00E+00	1.90E+00	4.64E−101	2.192458205
E.Immature_Enterocytes	CA2	3.825	0.00E+00	1.35E+00	3.12E−132	3.555364117
E.Immature_Enterocytes	CDHR5	2.788	0.00E+00	4.38E−01	4.00E−25	1.143355387
E.Immature_Enterocytes	CEACAM7	2.742	0.00E+00	3.30E−01	1.42E−05	1.247437806
E.Immature_Enterocytes	CKB	2.424	1.57E−270	1.35E+00	1.05E−108	1.574412494
E.Immature_Enterocytes	CLDN7	3.489	0.00E+00	5.32E−01	2.73E−47	2.705758523

TABLE 12-continued

Additional Cell Type Markers

E.Immature_Enterocytes	CTD-2228K2.5	2.752	0.00E+00	3.71E−01	9.67E−09	1.49783796
E.Immature_Enterocytes	EPCAM	2.955	0.00E+00	−1.17E−02	7.87E−01	2.427057509
E.Immature_Enterocytes	ETHE1	2.453	4.30E−258	9.99E−01	1.05E−132	1.482997692
E.Immature_Enterocytes	FABP1	7.054	0.00E+00	3.05E+00	0.00E+00	6.557149922
E.Immature_Enterocytes	FXYD3	4.961	0.00E+00	1.70E+00	1.42E−287	4.711504101
E.Immature_Enterocytes	GUCA2A	2.653	0.00E+00	1.35E+00	9.17E−43	2.839818034
E.Immature_Enterocytes	KRT18	3.119	0.00E+00	2.67E−01	6.93E−10	2.756402712
E.Immature_Enterocytes	KRT19	3.054	0.00E+00	1.74E+00	3.42E−197	2.892412398
E.Immature_Enterocytes	KRT20	3.095	0.00E+00	8.75E−01	2.59E−40	2.309331115
E.Immature_Enterocytes	KRT8	4.742	0.00E+00	1.46E+00	1.61E−217	4.522895646
E.Immature_Enterocytes	LGALS3	3.227	6.30E−211	1.53E+00	3.05E−290	3.780959158
E.Immature_Enterocytes	LGALS4	4.998	0.00E+00	6.64E−01	1.01E−44	4.280123818
E.Immature_Enterocytes	MS4A12	3.085	0.00E+00	7.42E−01	4.17E−20	1.717936251
E.Immature_Enterocytes	PHGR1	6.879	0.00E+00	2.49E+00	0.00E+00	6.287397388
E.Immature_Enterocytes	PIGR	3.423	0.00E+00	6.49E−01	5.35E−50	2.774586468
E.Immature_Enterocytes	PLAC8	2.738	0.00E+00	5.60E−01	2.45E−18	2.073305121
E.Immature_Enterocytes	PRAP1	2.623	0.00E+00	4.30E−01	3.61E−10	1.510711869
E.Immature_Enterocytes	SDCBP2	2.707	0.00E+00	3.15E−01	1.19E−09	1.418862701
E.Immature_Enterocytes	SELENBP1	2.469	8.53E−272	1.20E+00	7.94E−130	1.298087006
E.Immature_Enterocytes	SLC26A2	3.134	0.00E+00	9.92E−01	3.09E−61	1.123729159
E.Immature_Enterocytes	SLC26A3	3.427	0.00E+00	8.97E−01	7.27E−31	2.292018359
E.Immature_Enterocytes	SLC51B	3.063	0.00E+00	3.81E−01	8.85E−11	1.024945086
E.Immature_Enterocytes	SMIM22	2.809	0.00E+00	5.17E−01	4.28E−49	1.685183951
E.Immature_Enterocytes	SRI	2.507	5.04E−209	1.08E+00	3.30E−176	2.332610674
E.Immature_Enterocytes	TMEM54	2.975	0.00E+00	9.87E−01	2.95E−121	1.645157143
E.Immature_Enterocytes	TSPAN1	3.329	0.00E+00	7.60E−01	1.30E−51	2.602637796
E.Immature_Goblet	AGR2	3.431	1.31E−304	1.75E+00	4.76E−122	3.413884158
E.Immature_Goblet	CLCA1	4.350	0.00E+00	2.34E+00	1.17E−98	3.288406852
E.Immature_Goblet	FCGBP	4.495	0.00E+00	2.12E+00	8.68E−176	4.957987636
E.Immature_Goblet	ITLN1	5.156	0.00E+00	2.32E+00	3.48E−92	4.367175216
E.Immature_Goblet	KLK1	5.385	0.00E+00	1.96E+00	2.94E−163	3.739014763
E.Immature_Goblet	KRT18	3.877	1.01E−269	8.78E−01	9.19E−60	3.753416847
E.Immature_Goblet	LRRC26	4.285	0.00E+00	8.34E−01	8.76E−29	1.36967859
E.Immature_Goblet	MUC2	4.313	0.00E+00	4.61E−01	2.10E−06	3.154373567
E.Immature_Goblet	REP15	3.858	0.00E+00	4.12E−01	3.84E−08	1.607019236
E.Immature_Goblet	RETNLB	4.214	0.00E+00	1.69E+00	7.13E−42	1.929546104
E.Immature_Goblet	RNASE1	4.048	0.00E+00	8.71E−01	3.95E−38	2.827005292
E.Immature_Goblet	SERPINA1	3.421	0.00E+00	8.22E−01	3.24E−31	1.633161619
E.Immature_Goblet	SPINK1	3.753	0.00E+00	1.08E+00	1.84E−48	1.913114833
E.Immature_Goblet	SPINK4	3.885	0.00E+00	1.57E+00	1.52E−19	2.475188133
E.Immature_Goblet	TFF3	6.904	0.00E+00	4.93E+00	0.00E+00	8.29841861
E.Immature_Goblet	WFDC2	4.563	0.00E+00	1.82E+00	1.43E−85	2.003880612
E.Immature_Goblet	ZG16	3.631	0.00E+00	2.46E+00	4.56E−78	5.239192724
E.Secretory	FCGBP	2.255	1.76E−180	2.51E+00	2.12E−170	2.685649637
E.Secretory	KRT18	3.797	0.00E+00	9.56E−01	2.03E−60	3.870979692
E.Secretory	MUC2	3.090	8.90E−300	2.88E+00	1.05E−153	2.97529401
E.Secretory	TFF1	3.677	0.00E+00	2.22E+00	2.45E−45	2.433519046
E.Secretory	TFF3	3.887	0.00E+00	2.43E+00	7.95E−106	5.096886913
E.Secretory	ZG16	2.414	1.69E−209	4.64E+00	6.23E−264	4.51896634
E.Secretory_All	CLCA1	3.005	0.00E+00	1.59E+00	1.20E−45	1.398794545
E.Secretory_All	FCGBP	3.151	0.00E+00	2.22E+00	4.83E−247	3.402013896
E.Secretory_All	FXYD3	2.648	7.25E−302	−6.63E−01	6.00E−37	2.27714686
E.Secretory_All	ITLN1	3.479	0.00E+00	1.50E+00	5.99E−33	1.898258706
E.Secretory_All	KLK1	4.279	0.00E+00	1.28E+00	5.36E−62	1.43230919
E.Secretory_All	KRT18	3.810	0.00E+00	8.00E−01	1.08E−74	3.69599281
E.Secretory_All	KRT8	3.729	0.00E+00	−1.29E−01	7.04E−03	3.307698873
E.Secretory_All	LGALS4	3.259	0.00E+00	3.38E−02	4.74E−01	3.402953324
E.Secretory_All	MUC2	3.811	0.00E+00	1.65E+00	7.54E−54	2.531118742
E.Secretory_All	REP15	3.631	0.00E+00	5.12E−01	1.68E−07	1.007908306
E.Secretory_All	SPINK4	3.264	0.00E+00	7.97E−01	2.70E−05	1.333729761
E.Secretory_All	TFF3	4.523	0.00E+00	4.34E+00	0.00E+00	6.403931399
E.Secretory_All	ZG16	2.819	0.00E+00	3.35E+00	1.31E−190	4.477100018
E.Tuft	KRT18	5.434	7.28E−158	2.62E+00	1.91E−209	5.752838414
F.Crypt	A2M	4.284	0.00E+00	1.17E+00	1.85E−72	3.492074115
F.Crypt	ABCA8	5.496	0.00E+00	7.50E−01	5.75E−06	1.688536779
F.Crypt	ADAM28	3.648	0.00E+00	7.34E−01	1.73E−17	1.3316427
F.Crypt	ADAMDEC1	5.668	0.00E+00	4.47E+00	0.00E+00	5.70918829
F.Crypt	ADH1B	3.617	0.00E+00	1.26E+00	1.14E−43	1.243902457
F.Crypt	APOE	6.298	0.00E+00	3.31E+00	0.00E+00	6.688838049
F.Crypt	BMP4	3.215	0.00E+00	−5.22E−01	6.37E−13	1.570952671
F.Crypt	C1R	5.051	0.00E+00	1.27E+00	6.77E−60	3.743899141
F.Crypt	C1S	5.165	0.00E+00	1.18E+00	2.98E−50	3.879547488
F.Crypt	CALD1	3.961	0.00E+00	1.27E−01	7.55E−02	2.800815759
F.Crypt	CCL11	5.288	0.00E+00	2.77E+00	9.04E−12	3.068255858
F.Crypt	CCL13	5.690	0.00E+00	3.29E+00	1.88E−14	2.738743783
F.Crypt	CCL2	4.486	0.00E+00	1.01E+00	7.78E−15	3.492339648
F.Crypt	CCL8	5.709	0.00E+00	2.86E+00	1.14E−33	2.701919577
F.Crypt	CD63	2.718	4.96E−122	1.43E+00	0.00E+00	3.486481313

TABLE 12-continued

Additional Cell Type Markers						
F.Crypt	CFD	6.712	0.00E+00	4.21E+00	0.00E+00	6.838074558
F.Crypt	CFH	4.252	0.00E+00	6.33E−01	7.26E−09	1.853771933
F.Crypt	CLEC11A	3.606	0.00E+00	5.62E−01	1.03E−18	1.895949104
F.Crypt	COL1A1	4.065	0.00E+00	1.86E−01	3.22E−02	2.600863122
F.Crypt	COL1A2	4.802	0.00E+00	5.71E−01	1.78E−13	3.478176115
F.Crypt	COL3A1	4.651	0.00E+00	6.79E−01	1.20E−13	3.464081884
F.Crypt	COL6A1	3.150	0.00E+00	−4.52E−01	3.79E−10	1.63183674
F.Crypt	COL6A2	4.071	0.00E+00	−1.23E−01	1.12E−01	2.870797734
F.Crypt	CTSC	3.442	0.00E+00	2.00E+00	0.00E+00	3.77792912
F.Crypt	CTSK	4.270	0.00E+00	6.12E−01	9.43E−11	2.07068938
F.Crypt	CXCL12	4.295	0.00E+00	8.91E−01	2.89E−17	2.357940547
F.Crypt	CXCL14	3.894	0.00E+00	2.81E+00	0.00E+00	5.192128961
F.Crypt	CYGB	4.307	0.00E+00	3.91E−02	6.32E−01	2.398157949
F.Crypt	DCN	6.004	0.00E+00	2.79E+00	2.10E−201	4.989098789
F.Crypt	DKK3	4.247	0.00E+00	−2.46E−01	1.45E−02	1.25655402
F.Crypt	EFEMP1	4.062	0.00E+00	3.40E−01	2.66E−02	1.037851843
F.Crypt	EFEMP2	3.540	0.00E+00	−4.70E−02	5.51E−01	1.084607071
F.Crypt	EMILIN1	3.650	0.00E+00	6.55E−02	4.18E−01	1.522259058
F.Crypt	FABP4	5.111	0.00E+00	2.30E−01	5.01E−01	1.194045652
F.Crypt	FBLN1	5.764	0.00E+00	1.54E+00	1.40E−46	3.438001639
F.Crypt	GGT5	5.016	0.00E+00	4.02E−01	5.03E−03	1.343247026
F.Crypt	GNG11	3.200	0.00E+00	−8.10E−01	2.01E−23	1.5347982
F.Crypt	GPX3	4.218	0.00E+00	5.13E−01	4.53E−11	2.829560076
F.Crypt	GSN	3.608	0.00E+00	1.86E+00	0.00E+00	4.01570815
F.Crypt	HAAO	3.538	0.00E+00	4.78E−01	1.81E−09	1.117489226
F.Crypt	IFITM3	4.587	0.00E+00	1.81E+00	2.24E−305	4.693229283
F.Crypt	IGFBP6	3.447	0.00E+00	2.88E−01	2.45E−03	1.802560823
F.Crypt	IGFBP7	6.374	0.00E+00	2.12E+00	1.07E−150	6.278605
F.Crypt	LAPTM4A	2.172	1.00E−225	1.15E+00	9.11E−216	1.650359625
F.Crypt	LGALS1	4.361	0.00E+00	1.20E+00	2.63E−129	4.014277197
F.Crypt	LINC01082	4.891	0.00E+00	3.90E−01	1.26E−03	1.832126089
F.Crypt	LTBP4	2.845	0.00E+00	7.67E−01	5.61E−53	1.55451071
F.Crypt	LUM	5.474	0.00E+00	2.63E+00	5.18E−131	4.610864086
F.Crypt	MFAP4	5.218	0.00E+00	1.51E+00	8.79E−64	4.233927469
F.Crypt	MFGE8	2.986	0.00E+00	−2.47E−01	1.09E−03	1.347363767
F.Crypt	MMP2	3.597	0.00E+00	−2.95E−01	9.94E−05	1.902455796
F.Crypt	MYL9	2.778	0.00E+00	−5.15E−01	1.34E−11	1.502286202
F.Crypt	NGFRAP1	2.528	0.00E+00	6.10E−01	5.49E−56	1.354437953
F.Crypt	NNMT	3.431	0.00E+00	−2.14E−01	1.54E−02	1.388286729
F.Crypt	PCOLCE	3.816	0.00E+00	1.40E−01	1.41E−01	1.520934896
F.Crypt	PLAC9	4.658	0.00E+00	3.18E−01	7.56E−03	2.119682525
F.Crypt	PLAT	2.836	0.00E+00	−9.77E−01	1.02E−31	1.714357364
F.Crypt	PLTP	3.245	0.00E+00	4.97E−01	2.42E−12	1.128031708
F.Crypt	PMP22	3.549	0.00E+00	4.10E−01	5.72E−09	1.968640894
F.Crypt	PPAP2A	2.665	0.00E+00	8.91E−01	1.70E−84	1.654665665
F.Crypt	PPAP2B	4.323	0.00E+00	8.74E−01	8.59E−24	1.672913736
F.Crypt	PPP1R14A	2.882	0.00E+00	3.39E−01	7.24E−09	2.075006444
F.Crypt	PRKCDBP	3.358	0.00E+00	−1.01E−01	1.34E−01	1.868623908
F.Crypt	PROCR	4.040	0.00E+00	6.40E−01	2.77E−18	2.45588358
F.Crypt	PTGDS	4.801	0.00E+00	1.38E+00	3.35E−07	2.157176738
F.Crypt	PTN	4.436	0.00E+00	4.86E−01	3.27E−05	1.90716397
F.Crypt	RARRES2	3.704	0.00E+00	7.23E−01	1.11E−43	2.949004193
F.Crypt	RBP1	4.222	0.00E+00	6.90E−01	1.61E−19	2.667468
F.Crypt	S100A13	2.452	2.98E−301	5.56E−01	1.24E−40	1.18901627
F.Crypt	SELM	2.910	0.00E+00	7.91E−01	8.90E−74	2.662116539
F.Crypt	SEPPI	2.702	0.00E+00	8.41E−01	1.07E−55	2.690236454
F.Crypt	SERPINF1	3.865	0.00E+00	3.20E−01	1.08E−05	2.625543209
F.Crypt	SERPING1	3.525	0.00E+00	3.51E−01	1.15E−07	2.202321285
F.Crypt	SGCE	3.394	0.00E+00	9.98E−02	1.93E−01	1.318068281
F.Crypt	SOD3	4.535	0.00E+00	1.32E+00	1.26E−57	2.867761402
F.Crypt	SPARC	3.291	0.00E+00	−2.81E−01	8.62E−05	2.178834875
F.Crypt	SPARCL1	2.885	0.00E+00	−7.17E−01	2.83E−19	1.289030226
F.Crypt	SPON2	3.311	0.00E+00	4.11E−01	2.88E−08	1.109871188
F.Crypt	STMN2	4.214	0.00E+00	7.72E−01	9.69E−10	1.298791061
F.Crypt	TCF21	5.007	0.00E+00	9.02E−01	3.64E−21	3.133263086
F.Crypt	TIMP1	3.158	0.00E+00	8.42E−01	7.64E−62	3.071014624
F.Crypt	TM4SF1	2.743	0.00E+00	1.77E−02	7.98E−01	1.620288745
F.Crypt	TMEM176A	2.953	0.00E+00	1.16E+00	1.88E−195	2.275110559
F.Crypt	TMEM176B	3.878	0.00E+00	1.81E+00	0.00E+00	4.09743926
F.Crypt	TPM2	2.939	0.00E+00	−6.77E−01	5.60E−19	1.538165952
F.Crypt	TSPAN4	3.028	0.00E+00	−1.37E−02	8.11E−01	1.529585907
F.Crypt	VIM	3.222	0.00E+00	1.35E+00	8.69E−224	3.162898723
F.Crypt_hiFos	A2M	4.512	0.00E+00	8.15E−01	3.22E−33	3.676893205
F.Crypt_hiFos	ABCA8	4.194	0.00E+00	−4.76E−02	6.20E−01	2.649916107
F.Crypt_hiFos	ADAMDEC1	7.088	0.00E+00	2.83E+00	4.26E−106	7.218882666
F.Crypt_hiFos	APOE	6.567	0.00E+00	2.01E+00	3.43E−76	6.615669035
F.Crypt_hiFos	C1R	5.565	0.00E+00	8.50E−01	2.64E−30	4.216039635
F.Crypt_hiFos	C1S	5.634	0.00E+00	9.16E−01	5.97E−39	4.521134396

TABLE 12-continued

Additional Cell Type Markers

F.Crypt_hiFos	CCL2	6.150	0.00E+00	1.27E+00	1.29E−30	5.123848379
F.Crypt_hiFos	CCL8	4.875	0.00E+00	9.76E−01	3.13E−13	4.529100706
F.Crypt_hiFos	CFD	6.860	0.00E+00	2.89E+00	9.60E−176	7.220630374
F.Crypt_hiFos	COL1A1	4.013	0.00E+00	−1.52E−01	6.42E−02	2.82946601
F.Crypt_hiFos	COL1A2	5.086	0.00E+00	2.94E−02	6.96E−01	3.494207311
F.Crypt_hiFos	COL3A1	4.638	0.00E+00	1.50E−01	7.55E−02	3.596814435
F.Crypt_hiFos	COL6A2	3.948	0.00E+00	−3.21E−01	2.07E−05	2.806908085
F.Crypt_hiFos	CTSC	4.500	6.34E−256	1.89E+00	1.98E−199	4.569762818
F.Crypt_hiFos	CXCL12	4.235	0.00E+00	3.80E−01	1.02E−06	3.1951176
F.Crypt_hiFos	CXCL14	5.349	1.31E−258	2.52E+00	3.41E−138	5.763443334
F.Crypt_hiFos	CYGB	4.188	0.00E+00	9.68E−02	1.58E−01	2.819846584
F.Crypt_hiFos	DCN	6.287	0.00E+00	1.31E+00	1.48E−43	5.283090907
F.Crypt_hiFos	FBLN1	5.461	0.00E+00	4.82E−01	5.93E−10	3.726786119
F.Crypt_hiFos	GPX3	4.276	0.00E+00	2.55E−01	4.12E−04	3.3265932
F.Crypt_hiFos	GSN	4.198	3.26E−202	1.61E+00	1.66E−141	4.426932662
F.Crypt_hiFos	HAPLN1	4.502	0.00E+00	4.15E−01	2.32E−05	2.524390098
F.Crypt_hiFos	IFITM3	4.767	2.69E−230	1.50E+00	3.30E−120	4.706261067
F.Crypt_hiFos	IGFBP7	7.507	0.00E+00	1.40E+00	9.36E−43	6.303383638
F.Crypt_hiFos	LUM	6.169	0.00E+00	1.29E+00	9.03E−34	5.351962011
F.Crypt_hiFos	MFAP4	5.988	0.00E+00	7.99E−01	5.26E−23	4.555224313
F.Crypt_hiFos	PPAP2B	3.920	0.00E+00	3.93E−01	9.26E−09	2.394203067
F.Crypt_hiFos	PROCR	4.081	0.00E+00	2.87E−01	1.61E−05	3.077806433
F.Crypt_hiFos	RBP1	4.194	0.00E+00	4.28E−01	5.10E−10	3.130240169
F.Crypt_hiFos	SERPINF1	4.010	0.00E+00	4.87E−02	4.85E−01	3.045950154
F.Crypt_hiFos	SOD3	4.488	0.00E+00	7.24E−01	1.16E−19	3.463482129
F.Crypt_hiFos	TCF21	4.584	0.00E+00	2.38E−01	1.31E−03	3.283744234
F.Crypt_hiFos	TMEM176B	4.410	7.82E−165	1.71E+00	1.08E−197	4.527681262
F.Crypt_hiFos	VIM	4.984	3.19E−214	1.39E+00	1.13E−121	3.48544695
F.Crypt_loFos_1	A2M	4.566	0.00E+00	5.85E−01	2.88E−20	3.471644048
F.Crypt_loFos_1	ABCA8	4.248	0.00E+00	2.03E−01	4.13E−02	2.55026446
F.Crypt_loFos_1	ADAMDEC1	7.160	0.00E+00	3.05E+00	9.68E−134	6.568413627
F.Crypt_loFos_1	APOE	8.389	0.00E+00	2.58E+00	2.82E−151	7.136783921
F.Crypt_loFos_1	C1R	5.496	0.00E+00	7.93E−01	1.24E−30	4.131494165
F.Crypt_loFos_1	C1S	5.837	0.00E+00	6.91E−01	4.03E−22	4.237252058
F.Crypt_loFos_1	CALD1	4.220	0.00E+00	9.82E−03	8.86E−01	3.150459876
F.Crypt_loFos_1	CCL13	3.859	0.00E+00	7.60E−01	1.35E−04	3.58486718
F.Crypt_loFos_1	CCL2	4.141	0.00E+00	2.30E−01	4.37E−02	3.733752357
F.Crypt_loFos_1	CCL8	4.449	0.00E+00	2.59E−01	5.58E−02	3.576080936
F.Crypt_loFos_1	CFD	7.081	0.00E+00	3.01E+00	2.68E−209	7.152385774
F.Crypt_loFos_1	CFH	3.783	0.00E+00	1.85E−01	2.47E−02	2.220815228
F.Crypt_loFos_1	CLEC11A	3.494	0.00E+00	2.04E−01	4.21E−04	2.258975783
F.Crypt_loFos_1	COL1A1	4.014	0.00E+00	7.08E−02	3.52E−01	2.963298302
F.Crypt_loFos_1	COL1A2	5.242	0.00E+00	3.40E−01	2.62E−06	3.602018387
F.Crypt_loFos_1	COL3A1	4.942	0.00E+00	5.30E−01	7.50E−11	3.873803804
F.Crypt_loFos_1	COL6A2	3.984	0.00E+00	−2.72E−01	1.28E−04	2.837098282
F.Crypt_loFos_1	CTSC	4.685	0.00E+00	1.83E+00	1.10E−208	4.520244292
F.Crypt_loFos_1	CTSK	4.130	0.00E+00	2.49E−01	1.66E−03	2.620660286
F.Crypt_loFos_1	CXCL12	3.721	0.00E+00	3.29E−01	9.35E−05	2.775507108
F.Crypt_loFos_1	CXCL14	5.123	0.00E+00	2.51E+00	6.71E−163	5.704823079
F.Crypt_loFos_1	CYGB	4.375	0.00E+00	−5.80E−03	9.33E−01	2.860992966
F.Crypt_loFos_1	DCN	7.822	0.00E+00	1.52E+00	2.00E−63	5.238131885
F.Crypt_loFos_1	DKK3	3.769	0.00E+00	−2.18E−01	4.21E−03	1.908342802
F.Crypt_loFos_1	FBLN1	5.573	0.00E+00	3.66E−01	7.01E−06	3.461190649
F.Crypt_loFos_1	GGT5	3.900	0.00E+00	2.03E−01	9.92E−03	1.851084854
F.Crypt_loFos_1	GPX3	4.330	0.00E+00	4.80E−01	7.17E−13	3.458058087
F.Crypt_loFos_1	GSN	3.859	1.47E−254	1.60E+00	6.27E−159	4.263567086
F.Crypt_loFos_1	IFITM3	6.560	0.00E+00	1.77E+00	2.23E−192	5.166646778
F.Crypt_loFos_1	IGFBP7	7.514	0.00E+00	1.59E+00	6.62E−66	6.290186933
F.Crypt_loFos_1	LGALS1	5.430	1.44E−306	1.08E+00	1.33E−67	3.918497227
F.Crypt_loFos_1	LINC01082	4.011	0.00E+00	−2.52E−03	9.74E−01	2.466725414
F.Crypt_loFos_1	LUM	6.948	0.00E+00	1.46E+00	2.78E−44	5.224703375
F.Crypt_loFos_1	MFAP4	5.686	0.00E+00	9.07E−01	5.35E−29	4.455406471
F.Crypt_loFos_1	MMP2	3.547	0.00E+00	−3.40E−01	2.88E−07	2.36769262
F.Crypt_loFos_1	PLAC9	3.828	0.00E+00	1.85E−02	8.08E−01	2.327666003
F.Crypt_loFos_1	PMP22	3.692	0.00E+00	8.69E−02	2.23E−01	2.538680468
F.Crypt_loFos_1	PPAP2B	3.844	0.00E+00	3.25E−01	2.22E−06	2.317632739
F.Crypt_loFos_1	PROCR	4.373	0.00E+00	3.95E−01	6.81E−09	3.195637587
F.Crypt_loFos_1	PTN	3.804	0.00E+00	7.31E−02	3.62E−01	2.563456235
F.Crypt_loFos_1	RARRES2	3.874	0.00E+00	5.14E−01	2.99E−18	3.294341143
F.Crypt_loFos_1	RBP1	4.074	0.00E+00	3.93E−01	7.33E−10	3.101702956
F.Crypt_loFos_1	SERPINF1	3.726	0.00E+00	2.23E−01	6.29E−04	2.970864106
F.Crypt_loFos_1	SERPING1	3.431	0.00E+00	2.52E−01	4.68E−05	2.610215112
F.Crypt_loFos_1	SOD3	4.177	0.00E+00	7.64E−01	1.37E−23	3.282749538
F.Crypt_loFos_1	SPARC	3.802	0.00E+00	−1.66E−01	2.29E−02	2.730098195
F.Crypt_loFos_1	TCF21	4.897	0.00E+00	2.46E−01	9.84E−04	3.412667084
F.Crypt_loFos_1	TIMP1	4.084	0.00E+00	8.14E−01	5.04E−42	3.536639892
F.Crypt_loFos_1	TMEM176A	3.351	4.02E−211	1.10E+00	2.76E−128	2.998762433
F.Crypt_loFos_1	TMEM176B	4.864	8.48E−225	1.74E+00	1.12E−245	4.741101922

TABLE 12-continued

Additional Cell Type Markers						
F.Crypt_loFos_1	VIM	5.295	5.46E−276	1.18E+00	1.88E−108	3.248254715
F.Crypt_loFos_2	APOE	5.899	0.00E+00	1.76E+00	1.67E−43	6.466993305
F.Crypt_loFos_2	CFD	5.299	0.00E+00	2.35E+00	3.36E−92	6.443773934
F.Endothelial	BCAM	4.293	0.00E+00	1.23E+00	9.84E−42	1.212070381
F.Endothelial	CAV1	4.086	0.00E+00	7.55E−01	1.03E−14	2.963859243
F.Endothelial	CCDC85B	2.406	2.79E−184	1.30E+00	1.32E−165	1.989479948
F.Endothelial	CD320	3.689	0.00E+00	3.25E+00	0.00E+00	3.29103572
F.Endothelial	CD36	4.135	0.00E+00	1.90E+00	4.90E−39	2.182349023
F.Endothelial	CD59	2.172	1.73E−130	1.53E+00	2.54E−236	1.506163126
F.Endothelial	CLDN5	6.137	0.00E+00	3.07E+00	1.45E−25	3.338557396
F.Endothelial	CLEC14A	5.319	0.00E+00	9.66E−01	3.87E−12	1.451043092
F.Endothelial	CRIP2	4.642	0.00E+00	1.27E+00	2.67E−42	3.236897944
F.Endothelial	EGFL7	6.013	0.00E+00	1.41E+00	5.14E−12	1.84382156
F.Endothelial	ENG	3.721	0.00E+00	1.00E+00	3.27E−30	1.859620568
F.Endothelial	ESAM	5.913	0.00E+00	1.59E+00	1.49E−18	1.438464574
F.Endothelial	FABP5	3.117	1.32E−228	3.41E+00	0.00E+00	4.374347395
F.Endothelial	FKBP1A	2.022	2.10E−112	1.50E+00	1.63E−264	1.788766568
F.Endothelial	GIMAP7	3.221	1.42E−300	7.65E−01	2.55E−28	2.842038719
F.Endothelial	GNG11	4.738	0.00E+00	1.85E+00	1.78E−120	4.14121094
F.Endothelial	HLA-C	1.469	1.65E−11	1.59E+00	0.00E+00	2.645174636
F.Endothelial	HLA-E	1.845	1.35E−74	1.66E+00	0.00E+00	2.607209735
F.Endothelial	IFITM3	3.985	1.50E−298	1.75E+00	2.69E−201	4.533520832
F.Endothelial	IGFBP4	3.576	0.00E+00	1.85E+00	8.00E−222	1.952179734
F.Endothelial	IGFBP7	4.755	0.00E+00	1.67E+00	1.53E−71	5.974854235
F.Endothelial	ITM2B	1.752	3.79E−56	1.97E+00	0.00E+00	2.756111513
F.Endothelial	JAM2	5.981	0.00E+00	1.15E+00	3.42E−05	1.121967689
F.Endothelial	MGP	4.392	0.00E+00	8.05E−01	8.10E−07	1.998657704
F.Endothelial	NPDC1	3.004	3.12E−242	1.16E+00	6.47E−87	1.254551441
F.Endothelial	PLVAP	6.365	0.00E+00	3.94E+00	8.19E−45	4.167360966
F.Endothelial	RAMP2	5.270	0.00E+00	2.14E+00	8.66E−61	2.914625288
F.Endothelial	RAMP3	8.188	0.00E+00	2.19E+00	5.51E−05	1.424899143
F.Endothelial	RBP5	4.299	0.00E+00	5.14E−01	2.73E−05	1.573217657
F.Endothelial	SEPW1	2.111	5.35E−106	1.47E+00	3.05E−269	2.044916625
F.Endothelial	SLC9A3R2	3.082	2.77E−266	1.84E+00	1.69E−126	2.09792238
F.Endothelial	SPARCL1	4.167	0.00E+00	1.32E+00	1.29E−55	3.33841819
F.Endothelial	TM4SF1	3.406	0.00E+00	1.01E+00	7.43E−40	2.817273257
F.Endothelial	TMEM88	5.627	0.00E+00	1.27E+00	3.57E−06	1.415444312
F.Endothelial	VWF	8.023	0.00E+00	2.22E+00	2.29E−02	1.464896788
F.Endothelial_1	CD320	4.615	3.19E−220	3.53E+00	0.00E+00	4.954668807
F.Endothelial_1	CLDN5	5.988	0.00E+00	5.24E−01	1.28E−02	4.442027574
F.Endothelial_1	FABP5	4.513	1.86E−151	3.03E+00	2.87E−248	5.598134063
F.Endothelial_1	GNG11	4.944	2.31E−270	1.61E+00	5.47E−66	4.383616677
F.Endothelial_1	IGFBP4	3.758	3.71E−187	1.85E+00	3.16E−146	2.636215458
F.Endothelial_1	PLVAP	6.417	0.00E+00	1.88E+00	3.88E−21	5.305889624
F.Fibroblast	A2M	3.869	0.00E+00	1.17E+00	1.10E−57	2.858008192
F.Fibroblast	ADAMDEC1	3.583	0.00E+00	4.98E+00	1.90E−267	3.594023618
F.Fibroblast	APOE	4.039	0.00E+00	3.22E+00	3.38E−168	4.921162902
F.Fibroblast	BMP4	5.864	0.00E+00	1.00E+00	6.50E−07	1.42480642
F.Fibroblast	C1R	5.580	0.00E+00	2.31E+00	7.05E−71	2.692699318
F.Fibroblast	C1S	5.850	0.00E+00	2.13E+00	3.11E−49	2.913093084
F.Fibroblast	CALD1	5.259	0.00E+00	6.73E−01	1.84E−07	2.814729165
F.Fibroblast	CCL11	4.991	0.00E+00	2.97E+00	7.98E−08	1.681673822
F.Fibroblast	CCL13	4.265	0.00E+00	3.42E+00	6.41E−26	1.449036254
F.Fibroblast	CCL2	3.541	0.00E+00	1.41E+00	1.38E−22	2.112347447
F.Fibroblast	CCL8	4.674	0.00E+00	2.67E+00	2.49E−26	1.387750615
F.Fibroblast	CD63	2.229	2.01E−114	1.43E+00	0.00E+00	2.975250752
F.Fibroblast	CFD	3.800	0.00E+00	4.03E+00	1.33E−289	4.028336506
F.Fibroblast	CFH	5.163	0.00E+00	8.04E−01	2.06E−05	1.034054406
F.Fibroblast	CLEC11A	4.337	0.00E+00	7.52E−01	1.23E−16	1.281757763
F.Fibroblast	COL1A1	5.087	0.00E+00	1.51E+00	2.53E−25	2.075687041
F.Fibroblast	COL1A2	5.820	0.00E+00	1.32E+00	1.22E−19	2.962132038
F.Fibroblast	COL3A1	5.960	0.00E+00	2.06E+00	3.13E−30	2.867219098
F.Fibroblast	COL6A1	4.892	0.00E+00	1.29E+00	1.08E−20	1.674302912
F.Fibroblast	COL6A2	5.960	0.00E+00	1.49E+00	1.19E−17	2.844489178
F.Fibroblast	CTSC	2.217	6.04E−280	1.78E+00	5.98E−242	2.19902085
F.Fibroblast	CXCL12	4.276	0.00E+00	1.52E+00	1.55E−32	1.645919137
F.Fibroblast	CXCL14	4.288	0.00E+00	4.13E+00	0.00E+00	5.862818394
F.Fibroblast	CYGB	6.236	0.00E+00	1.22E+00	4.60E−12	1.721814926
F.Fibroblast	DCN	5.155	0.00E+00	3.87E+00	3.97E−112	3.204355181
F.Fibroblast	DMKN	3.898	0.00E+00	1.59E+00	1.34E−20	1.008034114
F.Fibroblast	EID1	1.941	2.83E−209	9.60E−01	2.83E−165	1.465413201
F.Fibroblast	EMILIN1	5.819	0.00E+00	1.04E+00	1.19E−07	1.055725268
F.Fibroblast	FBLN1	6.416	0.00E+00	2.15E+00	1.21E−20	1.654953126
F.Fibroblast	GNG11	2.966	3.60E−305	−1.21E+00	4.11E−46	1.064901305
F.Fibroblast	GPX3	4.875	0.00E+00	1.03E+00	3.28E−22	2.355348742
F.Fibroblast	GSN	2.553	0.00E+00	1.45E+00	9.12E−168	2.612701254
F.Fibroblast	IFITM3	4.287	0.00E+00	1.91E+00	0.00E+00	4.209536056
F.Fibroblast	IGFBP6	4.030	0.00E+00	4.48E−01	3.06E−04	1.420392445

TABLE 12-continued

Additional Cell Type Markers						
F.Fibroblast	IGFBP7	5.423	0.00E+00	1.92E+00	1.34E−86	5.704163002
F.Fibroblast	LAMA4	4.389	0.00E+00	1.00E−01	4.76E−01	1.039331541
F.Fibroblast	LAPTM4A	2.132	3.25E−223	1.30E+00	7.56E−280	1.339834069
F.Fibroblast	LGALS1	4.316	0.00E+00	1.63E+00	7.62E−267	4.303949742
F.Fibroblast	LGALS3BP	2.142	2.57E−224	1.08E+00	2.12E−204	1.091162389
F.Fibroblast	LTBP4	3.130	0.00E+00	1.18E+00	5.17E−104	1.309909843
F.Fibroblast	LUM	5.009	0.00E+00	3.79E+00	7.61E−97	2.964227078
F.Fibroblast	MFAP4	6.497	0.00E+00	3.15E+00	4.74E−64	3.285006765
F.Fibroblast	MFGE8	4.113	0.00E+00	9.42E−01	1.57E−13	1.289214426
F.Fibroblast	MMP2	6.500	0.00E+00	1.66E+00	3.72E−12	1.747981548
F.Fibroblast	MYL9	3.785	0.00E+00	4.76E−01	2.51E−04	1.942377438
F.Fibroblast	NGFRAP1	2.546	0.00E+00	7.85E−01	3.46E−78	1.005472029
F.Fibroblast	NNMT	4.284	0.00E+00	−6.65E−02	6.52E−01	1.043271273
F.Fibroblast	PLAC9	5.422	0.00E+00	6.10E−01	6.25E−03	1.166274382
F.Fibroblast	PLAT	3.585	0.00E+00	7.36E−01	4.31E−11	2.298300837
F.Fibroblast	PMP22	3.499	0.00E+00	3.66E−01	2.39E−05	1.310460807
F.Fibroblast	PPP1R14A	3.624	0.00E+00	8.61E−01	8.44E−31	2.050855445
F.Fibroblast	PRKCDBP	3.972	0.00E+00	2.19E−01	2.86E−02	1.653768965
F.Fibroblast	PROCR	5.144	0.00E+00	1.17E+00	2.40E−19	1.662380716
F.Fibroblast	PTN	5.707	0.00E+00	5.65E−01	1.10E−02	1.06748513
F.Fibroblast	RARRES2	4.164	0.00E+00	1.33E+00	4.13E−118	2.422426722
F.Fibroblast	RBP1	4.610	0.00E+00	1.05E+00	1.54E−21	1.771585228
F.Fibroblast	S100A13	2.664	0.00E+00	8.65E−01	3.26E−84	1.068941824
F.Fibroblast	SDC2	4.548	0.00E+00	6.00E−01	2.34E−05	1.04905118
F.Fibroblast	SELM	2.801	0.00E+00	1.18E+00	4.03E−158	2.474691328
F.Fibroblast	SERPINF1	4.562	0.00E+00	1.04E+00	2.49E−24	2.265134228
F.Fibroblast	SERPING1	3.893	0.00E+00	6.95E−01	1.18E−17	1.766270888
F.Fibroblast	SOD3	4.119	0.00E+00	1.79E+00	1.53E−81	1.7043373
F.Fibroblast	SPARC	3.920	0.00E+00	−5.69E−02	5.24E−01	2.258898195
F.Fibroblast	TCF21	6.571	0.00E+00	1.33E+00	1.05E−10	1.816207729
F.Fibroblast	TIMP1	3.012	0.00E+00	1.16E+00	1.19E−104	2.839662172
F.Fibroblast	TM4SF1	3.104	0.00E+00	2.91E−01	8.34E−04	1.581472528
F.Fibroblast	TMEM176A	2.830	0.00E+00	1.40E+00	1.16E−277	1.769196047
F.Fibroblast	TMEM176B	3.791	0.00E+00	2.20E+00	0.00E+00	3.832911655
F.Fibroblast	TPM2	4.664	0.00E+00	9.64E−01	4.00E−09	1.939714308
F.Fibroblast	TSPAN4	3.186	0.00E+00	2.44E−01	2.05E−04	1.26975591
F.Fibroblast	VIM	2.603	0.00E+00	1.23E+00	1.46E−198	2.867719694
F.Glia	ALDH1A1	4.071	2.33E−198	2.62E+00	2.02E−201	3.761789138
F.Glia	CD9	4.124	2.25E−110	2.31E+00	2.70E−220	4.789181961
F.Glia	CLU	6.270	0.00E+00	2.13E+00	1.12E−48	5.703214125
F.Glia	CRYAB	7.727	0.00E+00	3.82E+00	1.03E−142	6.612674122
F.Glia	S100B	6.472	0.00E+00	2.20E+00	2.22E−23	4.64832577
F.Microvascular	CD320	5.109	3.81E−136	3.11E+00	9.49E−225	5.155185625
F.Microvascular	FABP5	5.789	1.22E−94	4.26E+00	0.00E+00	7.141626843
F.Microvascular	PLVAP	8.376	5.02E−296	2.99E+00	2.61E−58	6.877072514
F.Myofibroblasts	ACTA2	6.853	1.08E−258	3.42E+00	1.21E−118	6.872108933
F.Myofibroblasts	TAGLN	6.260	1.93E−256	3.28E+00	2.29E−94	6.533966568
F.Stromal	A2M	4.108	0.00E+00	1.73E+00	3.25E−93	2.420855705
F.Stromal	ADAMDEC1	2.954	0.00E+00	4.68E+00	1.14E−198	2.910515351
F.Stromal	APOE	2.975	0.00E+00	3.07E+00	1.74E−148	3.827897438
F.Stromal	BMP4	5.111	0.00E+00	1.74E+00	3.18E−15	1.30003534
F.Stromal	BST2	2.012	3.45E−242	9.82E−01	4.04E−122	1.935227746
F.Stromal	C1R	5.080	0.00E+00	2.41E+00	1.09E−47	2.145519647
F.Stromal	CIS	5.202	0.00E+00	2.60E+00	5.03E−47	2.33056005
F.Stromal	CALD1	6.181	0.00E+00	1.95E+00	7.99E−15	1.966047523
F.Stromal	CCL2	3.734	0.00E+00	2.05E+00	1.56E−30	1.986582677
F.Stromal	CCL8	4.304	0.00E+00	2.83E+00	1.77E−24	1.144580585
F.Stromal	CD63	1.819	1.79E−89	1.29E+00	0.00E+00	2.406521128
F.Stromal	CFD	2.806	0.00E+00	4.00E+00	2.05E−268	2.868892416
F.Stromal	CLEC11A	3.739	0.00E+00	9.36E−01	1.75E−24	1.025199717
F.Stromal	COL1A1	5.431	0.00E+00	2.03E+00	7.75E−16	1.75794711
F.Stromal	COL1A2	5.603	0.00E+00	2.25E+00	4.89E−26	2.478102984
F.Stromal	COL3A1	5.196	0.00E+00	2.72E+00	2.58E−39	2.355722526
F.Stromal	COL6A1	5.454	0.00E+00	1.47E+00	1.18E−09	1.375024981
F.Stromal	COL6A2	5.503	0.00E+00	1.70E+00	9.14E−15	2.21250568
F.Stromal	CTSC	1.583	3.43E−152	1.64E+00	1.13E−199	1.629643567
F.Stromal	CXCL12	4.310	0.00E+00	1.60E+00	9.03E−26	1.242570645
F.Stromal	CXCL14	2.342	0.00E+00	3.87E+00	0.00E+00	4.433021518
F.Stromal	CYGB	5.565	0.00E+00	1.80E+00	1.20E−19	1.380616503
F.Stromal	DCN	3.977	0.00E+00	3.86E+00	5.63E−126	2.624796179
F.Stromal	EID1	1.833	2.53E−189	1.04E+00	1.08E−203	1.386022122
F.Stromal	FBLN1	5.291	0.00E+00	2.51E+00	6.46E−23	1.542104205
F.Stromal	GNG11	5.522	0.00E+00	2.03E+00	6.87E−16	1.024915045
F.Stromal	GPX3	5.203	0.00E+00	2.14E+00	7.78E−41	1.908920129
F.Stromal	GSN	2.806	0.00E+00	1.85E+00	1.20E−258	2.671887439
F.Stromal	HSPB1	2.089	9.10E−212	1.13E+00	6.26E−190	1.97223964
F.Stromal	IFITM1	2.098	3.42E−252	9.15E−01	3.94E−101	1.630880521
F.Stromal	IFITM3	4.606	0.00E+00	2.62E+00	0.00E+00	4.057873527

TABLE 12-continued

Additional Cell Type Markers

F.Stromal	IGFBP6	4.614	0.00E+00	1.46E+00	9.98E−16	1.209098122
F.Stromal	IGFBP7	6.204	0.00E+00	4.58E+00	0.00E+00	5.88712189
F.Stromal	LAPTM4A	2.041	3.57E−211	1.29E+00	5.86E−279	1.268032666
F.Stromal	LGALS1	3.180	0.00E+00	1.70E+00	5.11E−250	4.001715701
F.Stromal	LTBP4	2.655	1.13E−299	1.25E+00	5.14E−109	1.044916065
F.Stromal	LUM	3.968	0.00E+00	3.64E+00	9.21E−91	2.418426911
F.Stromal	MFAP4	4.998	0.00E+00	3.05E+00	1.99E−66	2.65491401
F.Stromal	MMP2	6.151	0.00E+00	1.66E+00	1.03E−06	1.45210403
F.Stromal	MYL9	4.791	0.00E+00	1.68E+00	1.22E−14	1.659548772
F.Stromal	PLAT	4.548	0.00E+00	1.94E+00	1.74E−28	2.167799271
F.Stromal	PMP22	3.820	0.00E+00	1.13E+00	6.81E−21	1.283005003
F.Stromal	PPP1R14A	3.223	0.00E+00	1.01E+00	2.56E−39	1.700199238
F.Stromal	PRKCDBP	5.658	0.00E+00	1.34E+00	3.79E−10	1.243717165
F.Stromal	PROCR	4.810	0.00E+00	1.12E+00	6.77E−15	1.252978763
F.Stromal	RARRES2	3.237	0.00E+00	1.40E+00	2.15E−110	1.838084217
F.Stromal	RBP1	4.332	0.00E+00	1.30E+00	2.48E−27	1.423203449
F.Stromal	SELM	2.476	0.00E+00	1.14E+00	4.80E−134	2.053452374
F.Stromal	SERPINF1	3.472	0.00E+00	1.01E+00	1.47E−27	1.720141644
F.Stromal	SERPING1	4.471	0.00E+00	1.20E+00	1.82E−26	1.455173755
F.Stromal	SOD3	3.747	0.00E+00	2.28E+00	7.79E−96	1.301466108
F.Stromal	SPARC	6.089	0.00E+00	2.11E+00	1.77E−23	2.08492746
F.Stromal	SPARCL1	5.397	0.00E+00	2.19E+00	3.29E−18	1.157334608
F.Stromal	TCF21	5.231	0.00E+00	1.98E+00	9.17E−25	1.514343398
F.Stromal	TIMP1	2.749	0.00E+00	1.17E+00	1.48E−91	2.447949478
F.Stromal	TM4SF1	3.823	0.00E+00	1.34E+00	1.41E−32	1.422652756
F.Stromal	TMEM176A	1.962	3.88E−209	1.38E+00	9.94E−242	1.2868717
F.Stromal	TMEM176B	2.318	1.97E−286	2.07E+00	0.00E+00	2.548034924
F.Stromal	TPM2	4.510	0.00E+00	1.38E+00	1.36E−12	1.570324457
F.Stromal	TSPAN4	3.521	0.00E+00	7.00E−01	8.16E−21	1.059144752
F.Stromal	VIM	2.599	0.00E+00	1.27E+00	2.09E−203	2.963469114
F.Villus	AGT	5.191	0.00E+00	7.61E−01	2.86E−03	1.565337446
F.Villus	BMP4	4.133	0.00E+00	9.55E−01	3.23E−35	3.04641886
F.Villus	C1S	3.052	0.00E+00	−6.76E−01	9.73E−21	2.265592255
F.Villus	CALD1	3.626	0.00E+00	3.40E−01	8.31E−07	3.076513343
F.Villus	CAV1	3.940	0.00E+00	3.44E−01	6.33E−04	2.679407949
F.Villus	COL1A2	3.222	0.00E+00	−2.45E−01	7.00E−04	2.508175055
F.Villus	COL3A1	3.337	0.00E+00	−3.69E−02	6.47E−01	2.699343963
F.Villus	COL6A1	4.045	0.00E+00	9.09E−01	5.49E−33	3.105851972
F.Villus	COL6A2	4.186	0.00E+00	8.33E−01	1.96E−28	3.587072611
F.Villus	CXCL14	5.331	0.00E+00	3.87E+00	0.00E+00	6.639737212
F.Villus	CYGB	3.575	0.00E+00	2.25E−01	6.46E−04	2.448508799
F.Villus	DMKN	4.682	0.00E+00	1.76E+00	2.36E−49	3.100766685
F.Villus	EDNRB	4.259	0.00E+00	6.52E−01	5.45E−10	1.964731755
F.Villus	ENHO	5.765	0.00E+00	5.60E−01	5.06E−03	2.037996647
F.Villus	F3	5.091	0.00E+00	1.41E+00	9.73E−25	2.111992756
F.Villus	FRZB	4.758	0.00E+00	1.68E+00	4.91E−58	3.163962402
F.Villus	GPX3	3.409	0.00E+00	2.34E−01	1.77E−04	2.723044038
F.Villus	HSD17B2	2.813	2.90E−286	1.07E+00	4.46E−80	1.978660202
F.Villus	IFITM3	3.410	0.00E+00	8.60E−01	6.14E−52	3.534780337
F.Villus	IGFBP3	4.041	0.00E+00	1.30E+00	1.17E−25	2.513313933
F.Villus	IGFBP7	4.072	0.00E+00	−3.70E−01	7.67E−05	4.395528895
F.Villus	LGALS1	4.297	0.00E+00	1.49E+00	2.96E−146	4.260881439
F.Villus	MFAP4	3.452	0.00E+00	−4.94E−01	6.77E−11	2.767660733
F.Villus	MMP2	3.936	0.00E+00	7.39E−01	1.11E−27	3.105311214
F.Villus	NBL1	2.298	8.07E−190	1.43E+00	2.84E−212	1.288462163
F.Villus	NSG1	5.310	0.00E+00	1.17E+00	1.93E−16	2.688454505
F.Villus	PLAT	4.548	0.00E+00	1.53E+00	4.34E−75	4.300004313
F.Villus	POSTN	4.627	0.00E+00	1.79E+00	1.11E−35	3.366108575
F.Villus	RARRES2	3.600	0.00E+00	9.47E−01	7.40E−62	3.155237799
F.Villus	SDC2	3.610	0.00E+00	6.90E−01	1.47E−19	2.172949162
F.Villus	SERPINF1	3.086	0.00E+00	3.73E−01	2.39E−08	2.484627191
F.Villus	SPARC	3.176	0.00E+00	1.08E−01	1.27E−01	2.582445259
F.Villus	TIMP1	2.751	2.30E−277	1.00E+00	1.07E−62	2.948613606
F.Villus	TMEM176B	3.213	2.56E−272	1.64E+00	3.08E−240	3.649384031
F.Villus	TPM2	3.507	0.00E+00	6.95E−01	1.29E−16	2.708057439
F.Villus	VSTM2A	6.302	0.00E+00	1.17E+00	3.87E−05	1.94824354
F.Villus_1	CXCL14	5.215	1.74E−209	3.59E+00	4.77E−225	6.731692814
F.Villus_1	FRZB	4.374	0.00E+00	1.21E+00	1.92E−33	3.44591024
F.Villus_1	PLAT	4.344	2.06E−300	1.19E+00	6.68E−41	4.3838881
F.Villus_1	POSTN	4.774	0.00E+00	1.43E+00	4.92E−25	4.224144974
F.Villus_2	BMP4	4.055	0.00E+00	7.81E−01	1.46E−21	3.18144352
F.Villus_2	COL6A2	4.047	0.00E+00	7.36E−01	1.95E−22	3.663402198
F.Villus_2	CXCL14	5.188	1.56E−257	3.53E+00	1.21E−262	6.468476855
F.Villus_2	DMKN	4.194	0.00E+00	1.14E+00	1.96E−25	3.122402938
F.Villus_2	F3	4.600	0.00E+00	8.82E−01	1.40E−13	2.378018518
F.Villus_2	FRZB	4.341	0.00E+00	1.31E+00	1.27E−36	3.273271947
F.Villus_2	MMP2	3.863	0.00E+00	5.82E−01	1.14E−15	3.004724044
F.Villus_2	NSG1	4.447	0.00E+00	4.64E−01	1.67E−05	2.733631613

TABLE 12-continued

Additional Cell Type Markers						
F.Villus_2	PLAT	4.234	0.00E+00	1.42E+00	9.20E−57	4.328991007
F.Villus_2	RARRES2	3.647	4.28E−284	9.70E−01	4.92E−50	3.333240445
I.Immune	ARHGDIB	4.207	0.00E+00	7.82E−01	6.32E−22	3.181654331
I.Immune	CCL5	3.713	0.00E+00	2.86E+00	5.61E−41	3.227650679
I.Immune	CD37	5.394	0.00E+00	2.57E−01	2.73E−01	1.385527254
I.Immune	CD3D	4.743	0.00E+00	1.63E+00	1.37E−11	2.656028184
I.Immune	CD3E	5.114	0.00E+00	1.25E+00	4.63E−06	2.008260655
I.Immune	CD52	5.341	0.00E+00	1.58E+00	2.86E−13	3.098900803
I.Immune	CD69	3.468	0.00E+00	9.81E−01	7.45E−15	2.209932935
I.Immune	CD7	4.101	0.00E+00	2.28E+00	1.90E−27	1.902035143
I.Immune	CORO1A	5.181	0.00E+00	1.37E+00	1.40E−16	2.294753907
I.Immune	CST3	−3.303	0.00E+00	5.57E−01	1.48E−17	−2.400189989
I.Immune	CYBA	1.716	1.86E−131	1.11E+00	2.74E−244	1.660237626
I.Immune	EVL	3.462	0.00E+00	6.54E−01	2.05E−11	1.493950621
I.Immune	HCST	5.437	0.00E+00	7.94E−01	6.19E−04	1.609957297
I.Immune	LAPTM5	5.136	0.00E+00	8.70E−01	3.17E−05	1.184622899
I.Immune	LTB	4.541	0.00E+00	1.46E+00	5.87E−07	1.551222258
I.Immune	PTPRCAP	5.120	0.00E+00	1.23E+00	1.08E−11	2.166023611
I.Immune	RAC2	4.648	0.00E+00	6.56E−01	5.34E−07	1.313198
I.Immune	RGS1	3.798	0.00E+00	1.15E+00	3.62E−22	2.015574355
I.Immune	SRGN	3.581	0.00E+00	3.14E−01	1.61E−04	2.825816153
I.Immune	TRBC2	4.401	0.00E+00	1.45E+00	5.26E−12	2.825938206
I.Lymphoid	ARHGDIB	3.161	0.00E+00	2.32E−01	4.47E−05	3.051707434
I.Lymphoid	CCL5	4.003	0.00E+00	2.91E+00	4.01E−44	3.723272334
I.Lymphoid	CD2	4.995	0.00E+00	7.92E−01	5.47E−03	2.213341168
I.Lymphoid	CD3D	4.827	0.00E+00	1.84E+00	1.44E−17	3.248239337
I.Lymphoid	CD3E	5.611	0.00E+00	1.26E+00	2.42E−05	2.497000932
I.Lymphoid	CD52	3.726	0.00E+00	1.10E+00	2.79E−32	3.478443808
I.Lymphoid	CD69	2.848	0.00E+00	5.09E−02	5.93E−01	2.43959911
I.Lymphoid	CD7	4.040	0.00E+00	2.42E+00	1.15E−39	2.231958553
I.Lymphoid	CORO1A	3.316	0.00E+00	7.40E−01	7.28E−22	2.580002303
I.Lymphoid	CYTIP	3.486	0.00E+00	2.17E−01	1.62E−02	1.083215597
I.Lymphoid	EVL	3.009	2.49E−308	8.04E−01	1.35E−25	1.719868351
I.Lymphoid	IL32	1.886	7.28E−217	1.53E+00	1.65E−150	2.754297032
I.Lymphoid	LTB	3.458	0.00E+00	1.22E+00	6.33E−15	1.960757541
I.Lymphoid	PTPRCAP	5.483	0.00E+00	9.99E−01	1.59E−11	2.664468478
I.Lymphoid	RAC2	3.576	0.00E+00	4.91E−01	2.55E−09	1.619586858
I.Lymphoid	TRAC	3.277	0.00E+00	9.75E−01	4.22E−23	2.970592688
I.Lymphoid	TRBC2	4.628	0.00E+00	1.31E+00	8.72E−12	3.495017388
M.CD69pos Mast	H3F3B	3.540	1.14E−70	2.04E+00	0.00E+00	4.709127236
M.CD69pos Mast	NFKBIA	2.588	4.21E−135	2.26E+00	3.68E−261	3.816864413
M.CD69pos Mast	PPP1R15A	2.241	4.32E−119	1.88E+00	3.12E−235	2.716247642
M.CD69pos Mast	TPSAB1	8.102	0.00E+00	5.34E+00	1.96E−81	8.759937866
M.CD69pos Mast	VWA5A	4.147	4.01E−306	2.24E+00	2.67E−153	2.804667246
M.DCs	AIF1	5.554	0.00E+00	6.91E−02	5.32E−01	4.109607894
M.DCs	CD74	6.686	1.89E−172	4.31E+00	0.00E+00	7.361182144
M.DCs	CPVL	5.451	0.00E+00	9.74E−01	1.72E−13	3.259858496
M.DCs	CST3	5.077	1.81E−84	3.22E+00	0.00E+00	6.239191066
M.DCs	HLA-DMA	5.034	0.00E+00	1.19E+00	1.06E−60	3.949279865
M.DCs	HLA-DMB	4.713	0.00E+00	2.68E−02	7.46E−01	2.996355003
M.DCs	HLA-DPA1	7.499	0.00E+00	3.16E+00	3.81E−219	6.620670842
M.DCs	HLA-DPB1	7.613	0.00E+00	3.30E+00	1.84E−212	7.191760426
M.DCs	HLA-DQA1	7.085	0.00E+00	1.57E+00	3.77E−47	5.548948208
M.DCs	HLA-DQB1	6.326	0.00E+00	1.65E+00	9.64E−76	4.944199971
M.DCs	HLA-DRA	7.705	0.00E+00	3.77E+00	2.22E−196	7.875311998
M.DCs	HLA-DRB1	7.430	4.72E−272	3.62E+00	5.06E−285	7.13770053
M.DCs	HLA-DRB5	4.876	0.00E+00	1.85E+00	3.04E−68	4.910951864
M.DCs	LST1	5.039	0.00E+00	2.99E−01	1.74E−03	3.486090838
M.DCs	LYZ	5.747	0.00E+00	2.04E+00	1.56E−44	5.88694392
M.Macrophages	ACP5	3.187	4.27E−303	1.34E+00	6.76E−73	2.590818222
M.Macrophages	AIF1	5.576	0.00E+00	1.04E+00	1.07E−22	4.307976358
M.Macrophages	C1QA	6.150	0.00E+00	2.87E+00	1.46E−84	5.300031996
M.Macrophages	C1QB	6.052	0.00E+00	2.86E+00	7.25E−75	4.677009635
M.Macrophages	C1QC	6.172	0.00E+00	2.57E+00	1.21E−69	4.762331438
M.Macrophages	CD74	5.009	7.44E−287	3.39E+00	0.00E+00	6.179449074
M.Macrophages	CST3	3.100	2.80E−150	2.47E+00	0.00E+00	4.680553349
M.Macrophages	CTSB	2.952	8.47E−251	1.92E+00	7.20E−294	2.192366953
M.Macrophages	CTSD	2.222	5.30E−145	1.99E+00	0.00E+00	2.293098548
M.Macrophages	CTSZ	2.801	8.27E−225	1.20E+00	1.03E−124	1.283964758
M.Macrophages	CYBA	1.691	7.98E−52	1.72E+00	0.00E+00	2.742799342
M.Macrophages	DNASE1L3	5.106	0.00E+00	9.20E−01	3.60E−09	2.994302955
M.Macrophages	FCER1G	4.663	0.00E+00	9.35E−01	2.28E−28	4.105822052
M.Macrophages	FCGRT	2.078	1.29E−112	1.35E+00	1.21E−221	1.42923146
M.Macrophages	FTL	4.189	2.32E−26	4.10E+00	0.00E+00	6.501041387
M.Macrophages	FUCA1	2.678	3.03E−209	1.80E+00	1.44E−157	1.444883944
M.Macrophages	GPX1	3.408	1.48E−239	2.08E+00	0.00E+00	3.660866748
M.Macrophages	HLA-DMA	3.705	0.00E+00	1.27E+00	2.39E−89	2.908577367
M.Macrophages	HLA-DMB	3.933	0.00E+00	8.50E−01	4.73E−26	2.265503073

TABLE 12-continued

Additional Cell Type Markers						
M.Macrophages	HLA-DPA1	4.231	0.00E+00	2.53E+00	1.04E−207	5.115407151
M.Macrophages	HLA-DPB1	5.213	0.00E+00	2.35E+00	5.56E−166	5.724454744
M.Macrophages	HLA-DQA1	4.701	0.00E+00	1.18E+00	3.01E−30	4.031618355
M.Macrophages	HLA-DQB1	3.829	0.00E+00	9.39E−01	1.29E−31	3.050844971
M.Macrophages	HLA-DRA	5.837	0.00E+00	2.84E+00	4.85E−170	6.499764955
M.Macrophages	HLA-DRB1	5.097	0.00E+00	2.83E+00	1.57E−257	5.910780843
M.Macrophages	HLA-DRB5	3.390	0.00E+00	1.74E+00	1.88E−77	3.498438452
M.Macrophages	IGSF6	5.196	0.00E+00	5.53E−01	2.67E−04	1.625886678
M.Macrophages	LGMN	2.996	7.35E−263	1.72E+00	2.49E−165	1.837166624
M.Macrophages	LST1	4.287	0.00E+00	−1.14E−01	2.10E−01	2.582366499
M.Macrophages	LYZ	4.983	0.00E+00	1.99E+00	1.85E−41	4.35619307
M.Macrophages	MS4A4A	5.392	0.00E+00	7.67E−01	3.65E−05	1.044712017
M.Macrophages	MS4A6A	5.055	0.00E+00	8.89E−01	1.94E−13	2.624760555
M.Macrophages	MS4A7	5.211	0.00E+00	7.97E−01	2.20E−07	1.824855194
M.Macrophages	NPC2	2.844	1.41E−177	2.19E+00	0.00E+00	2.979535936
M.Macrophages	PSAP	2.931	2.19E−193	2.40E+00	0.00E+00	3.379791933
M.Macrophages	RNASE1	2.869	2.01E−246	2.02E+00	4.73E−141	2.33910545
M.Macrophages	RNASET2	2.002	5.77E−127	1.47E+00	1.81E−255	1.746194062
M.Macrophages	S100A11	2.110	1.58E−119	1.51E+00	1.50E−219	2.530747738
M.Macrophages	SAT1	3.003	8.08E−149	2.35E+00	0.00E+00	4.071450542
M.Macrophages	SEPP1	2.949	9.84E−254	1.64E+00	5.90E−136	3.60554335
M.Macrophages	STAB1	5.244	0.00E+00	4.85E−01	3.14E−03	1.299766554
M.Macrophages	TMSB4X	3.375	2.03E−05	2.11E+00	0.00E+00	2.573438479
M.Macrophages	TYROBP	5.234	0.00E+00	1.63E+00	7.88E−86	4.732860448
M.Mast	CAPG	2.432	4.98E−146	1.70E+00	6.15E−192	2.17915183
M.Mast	H3F3B	3.313	3.21E−65	1.93E+00	0.00E+00	4.47755371
M.Mast	NFKBIA	2.271	1.45E−118	2.20E+00	2.86E−255	3.455658808
M.Mast	PPP1R15A	2.033	2.06E−108	1.87E+00	1.26E−240	2.476327326
M.Mast	TPSAB1	8.512	0.00E+00	6.42E+00	4.45E−163	8.639427859
M.Mast	VWA5A	4.283	0.00E+00	2.45E+00	7.39E−197	2.846401762
M.Monocytes	ACP5	2.724	8.51E−303	9.53E−01	3.39E−33	1.882241762
M.Monocytes	AIF1	6.739	0.00E+00	2.17E+00	9.08E−46	4.232871977
M.Monocytes	AMICA1	3.065	0.00E+00	8.74E−02	2.31E−01	1.677961646
M.Monocytes	C1QA	5.492	0.00E+00	4.03E+00	2.99E−69	4.155816971
M.Monocytes	C1QB	5.282	0.00E+00	3.70E+00	7.83E−53	3.441937672
M.Monocytes	C1QC	5.400	0.00E+00	3.19E+00	9.69E−45	3.642706749
M.Monocytes	C1orf162	3.733	0.00E+00	−1.04E−01	2.85E−01	1.170437832
M.Monocytes	CD74	5.291	0.00E+00	3.98E+00	0.00E+00	6.598762611
M.Monocytes	COTL1	2.597	7.05E−307	9.03E−01	5.44E−85	2.212565365
M.Monocytes	CPVL	5.896	0.00E+00	1.33E+00	3.40E−11	1.189459222
M.Monocytes	CST3	3.513	6.58E−239	2.90E+00	0.00E+00	5.233170493
M.Monocytes	CTSB	2.202	2.93E−211	1.55E+00	9.60E−204	1.356719163
M.Monocytes	CYBA	1.897	2.10E−81	1.50E+00	0.00E+00	2.769627973
M.Monocytes	DNASE1L3	6.099	0.00E+00	2.45E+00	9.24E−18	2.563358103
M.Monocytes	FAM26F	4.957	0.00E+00	2.28E−01	1.99E−01	1.145484272
M.Monocytes	FCER1G	4.804	0.00E+00	7.06E−01	9.51E−13	3.864097586
M.Monocytes	FGL2	3.941	0.00E+00	9.35E−01	4.92E−21	1.291638448
M.Monocytes	FTL	3.690	6.14E−25	3.33E+00	0.00E+00	5.135226719
M.Monocytes	GPX1	3.523	0.00E+00	1.94E+00	0.00E+00	3.477841098
M.Monocytes	HLA-DMA	4.277	0.00E+00	1.60E+00	7.42E−148	3.137660058
M.Monocytes	HLA-DMB	4.587	0.00E+00	8.74E−01	1.14E−22	2.298238533
M.Monocytes	HLA-DPA1	4.926	0.00E+00	3.06E+00	0.00E+00	5.55420434
M.Monocytes	HLA-DPB1	5.650	0.00E+00	3.21E+00	0.00E+00	6.141157002
M.Monocytes	HLA-DQA1	5.332	0.00E+00	2.21E+00	8.84E−99	4.355634178
M.Monocytes	HLA-DQA2	3.920	0.00E+00	8.37E−01	3.45E−10	1.7733194
M.Monocytes	HLA-DQB1	4.715	0.00E+00	1.86E+00	4.05E−100	3.47409069
M.Monocytes	HLA-DQB2	4.951	0.00E+00	3.95E−01	2.47E−02	1.429331185
M.Monocytes	HLA-DRA	6.364	0.00E+00	3.77E+00	0.00E+00	6.90336385
M.Monocytes	HLA-DRB1	5.624	0.00E+00	3.53E+00	0.00E+00	6.291170635
M.Monocytes	HLA-DRB5	4.212	0.00E+00	2.13E+00	2.24E−103	3.906936969
M.Monocytes	IL1B	5.314	0.00E+00	2.02E+00	1.23E−09	1.362160979
M.Monocytes	ITGB2	3.243	0.00E+00	1.26E−01	7.84E−02	1.46825593
M.Monocytes	LAPTM5	2.698	0.00E+00	1.33E−01	1.19E−02	2.055128002
M.Monocytes	LGALS1	3.002	0.00E+00	8.09E−01	9.54E−44	3.344243506
M.Monocytes	LST1	5.286	0.00E+00	6.40E−01	1.30E−07	2.821686152
M.Monocytes	LYZ	5.942	0.00E+00	3.45E+00	2.44E−87	4.680781408
M.Monocytes	MS4A6A	6.354	0.00E+00	1.78E+00	9.88E−17	2.246168647
M.Monocytes	MS4A7	5.854	0.00E+00	1.02E+00	6.74E−05	1.332493787
M.Monocytes	NPC2	2.814	2.22E−246	1.78E+00	0.00E+00	2.574957856
M.Monocytes	PLAUR	2.657	3.67E−283	1.12E+00	3.46E−56	1.648644174
M.Monocytes	PSAP	2.534	5.30E−224	1.91E+00	0.00E+00	2.503500359
M.Monocytes	RGS10	2.565	0.00E+00	4.82E−01	4.78E−31	2.150189084
M.Monocytes	RNASE6	4.098	0.00E+00	9.94E−01	4.50E−21	1.036740582
M.Monocytes	RNASET2	2.270	2.04E−218	1.30E+00	6.18E−257	1.751116723
M.Monocytes	S100A11	2.204	3.20E−179	1.28E+00	2.47E−222	2.369494044
M.Monocytes	SAT1	3.237	2.41E−232	2.09E+00	0.00E+00	3.959712325
M.Monocytes	SPI1	4.890	0.00E+00	1.01E+00	2.42E−17	1.592825824
M.Monocytes	TMSB4X	3.136	8.25E−06	2.05E+00	0.00E+00	2.614405699

TABLE 12-continued

Additional Cell Type Markers						
M.Monocytes	TYMP	2.489	3.09E−282	9.52E−01	2.47E−101	1.861697922
M.Monocytes	TYROBP	5.333	0.00E+00	1.66E+00	1.01E−62	4.513467018
M.Myeloid	AIF1	5.813	0.00E+00	2.02E+00	1.09E−33	2.305919495
M.Myeloid	C1QA	4.690	0.00E+00	3.98E+00	1.50E−84	2.293597851
M.Myeloid	C1QB	4.688	0.00E+00	4.01E+00	5.78E−68	1.93454735
M.Myeloid	C1QC	5.203	0.00E+00	3.75E+00	2.68E−46	1.994680241
M.Myeloid	CD74	1.729	2.70E−174	3.83E+00	0.00E+00	3.96445085
M.Myeloid	CST3	1.583	1.20E−114	2.55E+00	0.00E+00	2.496545122
M.Myeloid	CYBA	0.845	3.74E−30	1.30E+00	0.00E+00	1.355375364
M.Myeloid	DNASE1L3	5.938	0.00E+00	2.54E+00	5.07E−17	1.357649186
M.Myeloid	FCER1G	5.155	0.00E+00	7.53E−01	6.05E−10	3.351878581
M.Myeloid	FTH1	2.972	6.58E−17	1.58E+00	0.00E+00	3.161764242
M.Myeloid	FTL	3.481	2.47E−46	2.81E+00	0.00E+00	5.143530637
M.Myeloid	GLUL	2.625	9.29E−308	1.05E+00	2.08E−81	1.104516091
M.Myeloid	GPX1	2.294	7.45E−245	1.92E+00	0.00E+00	1.892173705
M.Myeloid	HLA-DMA	3.140	0.00E+00	1.61E+00	8.42E−166	1.804731204
M.Myeloid	HLA-DMB	4.269	0.00E+00	1.05E+00	1.83E−26	1.310971013
M.Myeloid	HLA-DPA1	2.822	0.00E+00	3.07E+00	0.00E+00	3.603351858
M.Myeloid	HLA-DPB1	3.000	0.00E+00	3.42E+00	0.00E+00	3.960321522
M.Myeloid	HLA-DQA1	4.043	0.00E+00	2.04E+00	1.83E−73	2.645131811
M.Myeloid	HLA-DQA2	3.981	0.00E+00	7.23E−01	8.78E−06	1.096108771
M.Myeloid	HLA-DQB1	3.588	0.00E+00	1.90E+00	8.14E−107	2.070477499
M.Myeloid	HLA-DRA	3.065	0.00E+00	3.69E+00	0.00E+00	4.339804481
M.Myeloid	HLA-DRB1	2.879	0.00E+00	3.40E+00	0.00E+00	3.753125817
M.Myeloid	HLA-DRB5	3.170	0.00E+00	2.12E+00	1.23E−103	2.390321388
M.Myeloid	LST1	4.767	0.00E+00	4.39E−01	7.52E−04	1.650785876
M.Myeloid	LYZ	4.702	0.00E+00	3.68E+00	7.62E−110	2.556327471
M.Myeloid	MS4A6A	6.737	0.00E+00	1.99E+00	1.24E−17	1.009965999
M.Myeloid	NPC2	2.140	6.05E−205	1.71E+00	0.00E+00	1.557639793
M.Myeloid	PSAP	1.917	4.55E−178	1.82E+00	0.00E+00	1.557168286
M.Myeloid	S100A11	1.592	1.63E−131	1.21E+00	1.01E−219	1.623417727
M.Myeloid	SAT1	1.885	4.03E−151	2.00E+00	0.00E+00	2.378322556
M.Myeloid	SRGN	2.346	3.11E−303	6.68E−01	2.24E−51	2.663800303
M.Myeloid	TMSB4X	3.924	1.08E−11	1.61E+00	0.00E+00	2.455257638
M.Myeloid	TYROBP	4.999	0.00E+00	1.22E+00	2.51E−22	3.317457944
M.Tissue_DCs	AIF1	5.733	0.00E+00	3.04E−01	6.77E−03	4.343902986
M.Tissue_DCs	CD74	6.537	8.69E−147	4.22E+00	0.00E+00	7.317250586
M.Tissue_DCs	CLEC10A	5.783	0.00E+00	1.04E+00	4.56E−13	3.638767911
M.Tissue_DCs	CST3	4.913	7.85E−72	3.17E+00	0.00E+00	6.099017935
M.Tissue_DCs	HLA-DMA	5.111	5.40E−280	1.36E+00	1.87E−71	4.010642012
M.Tissue_DCs	HLA-DPA1	7.274	3.20E−256	3.23E+00	2.20E−206	6.561614831
M.Tissue_DCs	HLA-DPB1	7.476	3.55E−290	3.09E+00	4.68E−164	7.139900132
M.Tissue_DCs	HLA-DQA1	6.883	0.00E+00	1.65E+00	1.64E−46	5.545865153
M.Tissue_DCs	HLA-DQB1	6.394	0.00E+00	1.75E+00	1.37E−75	4.964711147
M.Tissue_DCs	HLA-DRA	7.540	1.52E−267	3.88E+00	3.58E−183	7.91753476
M.Tissue_DCs	HLA-DRB1	7.352	5.21E−243	3.50E+00	5.44E−237	7.1857139
M.Tissue_DCs	LST1	5.239	0.00E+00	4.97E−01	7.18E−08	3.72542232
M.Tissue_DCs	LYZ	5.579	0.00E+00	2.14E+00	3.62E−44	5.80083893
T.CD4	ARHGDIB	2.714	0.00E+00	6.95E−01	5.09E−60	2.948999621
T.CD4	B2M	2.524	4.10E−11	1.31E+00	0.00E+00	3.181207891
T.CD4	BTG1	2.081	8.64E−201	1.29E+00	3.42E−241	2.666942355
T.CD4	CD2	3.325	0.00E+00	−4.30E−02	5.70E−01	2.361888134
T.CD4	CD3D	3.865	0.00E+00	−1.53E−01	3.12E−02	3.285517157
T.CD4	CD3E	3.298	0.00E+00	−1.03E−01	9.38E−02	2.441937608
T.CD4	CD52	3.093	0.00E+00	4.27E−01	6.58E−15	3.285206277
T.CD4	EEF1A1	1.811	1.44E−18	1.29E+00	0.00E+00	2.913519854
T.CD4	IL32	3.257	0.00E+00	9.29E−01	7.35E−73	3.875940105
T.CD4	LTB	3.303	0.00E+00	5.68E−01	2.19E−11	2.960038975
T.CD4	RPL10	1.878	5.33E−17	1.19E+00	0.00E+00	2.933302608
T.CD4	RPL21	2.075	2.43E−43	1.20E+00	0.00E+00	3.077829574
T.CD4	RPLP1	2.061	3.31E−25	1.22E+00	0.00E+00	2.97564638
T.CD4	RPS19	2.122	1.71E−40	1.24E+00	0.00E+00	3.029170811
T.CD4	RPS25	1.749	4.46E−50	1.10E+00	0.00E+00	2.510200315
T.CD4	RPS27	1.969	2.14E−30	1.29E+00	0.00E+00	3.052783949
T.CD4	RPS27A	1.880	5.73E−50	1.22E+00	0.00E+00	2.910333285
T.CD4	RPS3	1.822	1.75E−33	1.14E+00	0.00E+00	2.909904991
T.CD4	TMEM66	1.634	1.36E−148	9.77E−01	2.12E−191	1.516743632
T.CD4	TMSB4X	2.596	3.91E−08	1.50E+00	0.00E+00	2.234471623
T.CD4	TRAC	3.572	0.00E+00	6.66E−01	7.52E−26	3.57637506
T.CD4	TRBC2	3.692	0.00E+00	4.12E−01	1.65E−08	3.684828708
T.CD8	ACTB	2.475	3.60E−42	1.50E+00	0.00E+00	3.50971244
T.CD8	ARHGDIB	2.865	0.00E+00	6.08E−01	1.44E−49	2.982840619
T.CD8	B2M	3.216	1.13E−08	1.43E+00	0.00E+00	2.404427044
T.CD8	CCL5	5.160	0.00E+00	2.00E+00	4.92E−151	5.905248855
T.CD8	CD3D	3.462	0.00E+00	4.53E−01	6.24E−15	3.394691814
T.CD8	CD3E	3.001	0.00E+00	2.17E−01	1.56E−05	2.761361085
T.CD8	CD52	3.267	0.00E+00	7.59E−01	2.58E−46	3.532187537
T.CD8	CD7	3.358	0.00E+00	9.13E−01	2.79E−31	3.042456161

TABLE 12-continued

Additional Cell Type Markers

T.CD8	CORO1A	2.680	0.00E+00	6.16E−01	3.12E−38	2.743977822	
T.CD8	EVL	2.487	2.00E−302	5.33E−01	1.11E−29	2.184459445	
T.CD8	GZMA	3.738	0.00E+00	1.48E+00	1.48E−21	3.352055654	
T.CD8	HCST	2.860	0.00E+00	5.95E−01	1.90E−34	2.695248321	
T.CD8	HOPX	3.414	0.00E+00	5.97E−01	1.12E−13	2.402446002	
T.CD8	IL32	3.922	0.00E+00	1.20E+00	3.71E−150	4.279234249	
T.CD8	NKG7	4.290	0.00E+00	6.17E−01	7.86E−08	3.272826393	
T.CD8	PTPRCAP	2.633	0.00E+00	8.49E−01	1.44E−69	2.810217158	
T.CD8	SH3BGRL3	1.886	5.60E−118	1.05E+00	5.36E−212	2.458584789	
T.CD8	TMSB4X	4.143	4.19E−11	1.88E+00	0.00E+00	2.661426524	
T.CD8	TRAC	2.825	0.00E+00	2.81E−01	2.77E−07	3.041416989	
T.CD8	TRBC2	3.074	0.00E+00	1.88E−01	1.58E−03	3.233102921	
T.CD8_IELs	CCL5	6.114	0.00E+00	1.88E+00	2.57E−123	6.194585882	
T.CD8_IELs	CD3D	3.256	0.00E+00	5.35E−01	1.20E−18	3.441592568	
T.CD8_IELs	CD52	3.451	1.72E−306	7.40E−01	1.11E−37	3.498103129	
T.CD8_IELs	CD7	3.988	0.00E+00	1.24E+00	4.14E−68	4.046757488	
T.CD8_IELs	HOPX	3.762	0.00E+00	5.68E−01	3.21E−13	3.314436098	
T.CD8_IELs	IL32	4.020	2.09E−271	1.38E+00	4.88E−124	4.322274876	
T.CD8_IELs	NKG7	3.841	0.00E+00	−3.01E−02	7.46E−01	3.446184383	
T.CD8 LP	CCL5	5.676	0.00E+00	1.27E+00	5.56E−57	5.633700535	
T.CD8 LP	NKG7	3.722	0.00E+00	4.11E−01	3.52E−05	3.486023674	
T.Tcells	ACTB	2.020	4.86E−40	1.65E+00	0.00E+00	3.316981313	
T.Tcells	ARHGDIB	3.191	0.00E+00	1.10E+00	3.46E−131	3.341126137	
T.Tcells	B2M	2.272	1.17E−09	1.50E+00	0.00E+00	3.065937757	
T.Tcells	BTG1	1.763	8.44E−157	1.26E+00	2.58E−229	2.123789859	
T.Tcells	CCL5	4.279	0.00E+00	2.74E+00	1.64E−83	4.302419639	
T.Tcells	CD2	5.172	0.00E+00	6.17E−01	7.82E−05	2.052746914	
T.Tcells	CD3D	6.166	0.00E+00	2.08E+00	5.91E−46	3.397618572	
T.Tcells	CD3E	6.421	0.00E+00	7.92E−01	4.38E−07	2.370389625	
T.Tcells	CD52	4.108	0.00E+00	1.20E+00	1.58E−68	3.95478922	
T.Tcells	CD7	4.693	0.00E+00	9.36E−01	1.78E−11	2.221062807	
T.Tcells	CKLF	2.025	3.39E−207	1.20E+00	2.90E−176	1.080775129	
T.Tcells	CORO1A	3.262	0.00E+00	1.09E+00	7.57E−77	2.860991596	
T.Tcells	EVL	3.434	0.00E+00	9.82E−01	1.41E−49	2.035932542	
T.Tcells	GZMA	3.945	0.00E+00	2.12E+00	1.82E−18	1.960681705	
T.Tcells	HCST	3.243	0.00E+00	7.05E−01	4.60E−27	2.173769075	
T.Tcells	HOPX	4.032	0.00E+00	6.86E−01	5.98E−07	1.726884514	
T.Tcells	IL2RG	2.193	7.47E−228	1.17E+00	1.41E−136	1.152000617	
T.Tcells	IL32	4.161	0.00E+00	1.81E+00	8.41E−260	4.656688606	
T.Tcells	LCK	4.921	0.00E+00	6.42E−01	8.05E−07	1.507134026	
T.Tcells	LTB	3.053	0.00E+00	3.90E−01	3.13E−04	2.116429025	
T.Tcells	MYL12A	1.681	2.24E−123	1.06E+00	3.94E−231	1.746942368	
T.Tcells	NKG7	4.103	0.00E+00	2.56E−01	1.48E−01	1.791038239	
T.Tcells	PTPRCAP	3.216	0.00E+00	1.41E+00	4.57E−128	2.773769069	
T.Tcells	RAC2	2.651	0.00E+00	1.13E+00	2.04E−99	1.676182044	
T.Tcells	RPLP1	1.843	1.24E−20	1.12E+00	0.00E+00	2.762677204	
T.Tcells	RPS19	2.379	6.55E−43	1.34E+00	0.00E+00	3.222843513	
T.Tcells	RPS27	2.047	1.14E−31	1.22E+00	0.00E+00	3.079388618	
T.Tcells	RPS27A	1.878	5.06E−50	1.19E+00	0.00E+00	2.82253802	
T.Tcells	SH3BGRL3	1.894	7.78E−139	1.22E+00	1.42E−266	2.177941405	
T.Tcells	TMEM66	1.554	3.21E−135	1.03E+00	2.83E−211	1.23170526	
T.Tcells	TMSB4X	3.485	6.22E−17	2.01E+00	0.00E+00	3.017818451	
T.Tcells	TRAC	4.649	0.00E+00	1.34E+00	9.50E−47	3.593010994	
T.Tcells	TRBC2	5.165	0.00E+00	1.21E+00	3.55E−24	3.838266308	

	ident	pvalH	n	ref_n	mu	ref_mu	total	ref_total
	B.Bcells	0	2578	359	5.641	2.160	0.988	0.012
	B.Bcells	0	2871	54	3.440	2.038	0.993	0.007
	B.Bcells	0	2822	654	2.141	3.245	0.667	0.333
	B.Bcells	0	4698	3412	6.225	5.422	0.706	0.294
	B.Bcells	0	4236	96	3.539	2.601	0.988	0.012
	B.Bcells	0	3975	6433	3.404	4.208	0.261	0.739
	B.Bcells	0	2866	202	3.310	1.484	0.980	0.020
	B.Bcells	0	2886	1147	2.490	2.410	0.727	0.273
	B.Bcells	0	2838	1234	3.073	2.136	0.815	0.185
	B.Bcells	0	4045	2898	4.309	2.510	0.829	0.171
	B.Bcells	0	4090	3927	10.531	4.627	0.984	0.016
	B.Bcells	0	3316	1856	8.718	3.178	0.988	0.012
	B.Bcells	0	3809	2394	8.956	3.375	0.987	0.013
	B.Bcells	0	4051	2015	9.672	3.306	0.994	0.006
	B.Bcells	0	3141	970	9.006	2.698	0.996	0.004
	B.Bcells	0	3104	1057	8.945	2.694	0.996	0.004
	B.Bcells	0	3236	327	4.523	2.282	0.979	0.021
	B.Bcells	0	3514	1633	3.061	3.806	0.562	0.438
	B.Bcells	0	3115	1862	3.082	2.014	0.778	0.222
	B.FO	0	1636	3662	7.169	5.408	0.602	0.398
	B.FO	0	1329	611	4.069	3.148	0.805	0.195

TABLE 12-continued

Additional Cell Type Markers							
B.FO	0	1424	1964	6.368	5.807	0.517	0.483
B.Plasma	0	1938	476	5.757	3.326	0.956	0.044
B.Plasma	0	1952	187	3.086	3.582	0.881	0.119
B.Plasma	0	1446	67	1.049	1.739	0.930	0.070
B.Plasma	0	1965	694	1.883	3.067	0.555	0.445
B.Plasma	0	2232	415	2.837	3.768	0.738	0.262
B.Plasma	0	2047	1483	1.669	1.866	0.546	0.454
B.Plasma	0	1614	1080	0.998	2.928	0.282	0.718
B.Plasma	0	2257	308	3.404	2.046	0.949	0.051
B.Plasma	0	2175	1211	2.502	2.401	0.658	0.342
B.Plasma	0	1575	464	1.118	2.147	0.625	0.375
B.Plasma	0	1896	390	1.327	2.039	0.748	0.252
B.Plasma	0	1938	2367	1.332	3.351	0.168	0.832
B.Plasma	0	1464	743	0.806	2.612	0.360	0.640
B.Plasma	0	1743	692	0.998	1.926	0.570	0.430
B.Plasma	0	987	57	0.872	1.673	0.909	0.091
B.Plasma	0	2264	1310	3.132	2.155	0.773	0.227
B.Plasma	0	1711	310	0.885	1.806	0.745	0.255
B.Plasma	0	1812	1347	1.099	2.730	0.303	0.697
B.Plasma	0	2289	2972	4.600	2.649	0.749	0.251
B.Plasma	0	2277	3971	11.091	6.041	0.950	0.050
B.Plasma	0	2191	1943	9.110	4.205	0.971	0.029
B.Plasma	0	2276	2508	9.345	5.235	0.940	0.060
B.Plasma	0	2236	2285	10.236	5.820	0.954	0.046
B.Plasma	0	2004	1122	9.451	5.412	0.967	0.033
B.Plasma	0	1949	1188	9.318	5.456	0.960	0.040
B.Plasma	0	1489	229	7.071	4.038	0.982	0.018
B.Plasma	0	1665	1897	0.949	2.751	0.201	0.799
B.Plasma	0	2132	1910	1.991	2.682	0.409	0.591
B.Plasma	0	2167	1989	2.174	2.088	0.536	0.464
B.Plasma	0	2288	444	4.708	3.157	0.938	0.062
B.Plasma	0	1847	1542	1.330	2.140	0.406	0.594
B.Plasma	0	1994	1742	1.575	1.818	0.492	0.508
B.Plasma	0	1754	530	1.437	2.396	0.630	0.370
B.Plasma	0	1913	1076	1.259	1.678	0.571	0.429
B.Plasma	0	2173	1824	2.321	2.002	0.598	0.402
B.Plasma	0	1876	1532	2.366	4.316	0.241	0.759
B.Plasma	0	1935	1939	3.018	4.263	0.296	0.704
B.Plasma	0	2188	2170	2.399	2.306	0.518	0.482
B.Plasma	0	2257	1916	3.186	2.059	0.720	0.280
B.Plasma	0	1997	1374	1.537	1.815	0.545	0.455
B.Plasma	0	2186	2124	2.197	2.042	0.534	0.466
B.Plasma	0	2304	4597	5.264	3.048	0.700	0.300
B.Plasma	0	2144	159	2.368	2.270	0.935	0.065
B.Plasma	0	2074	1697	1.437	2.029	0.448	0.552
B.Plasma	0	1851	906	1.197	1.820	0.570	0.430
B.Plasma	0	2142	1136	1.859	1.783	0.665	0.335
B.Plasma	0	1182	181	3.150	2.281	0.923	0.077
B.Plasma	0	2269	2366	3.808	2.402	0.718	0.282
E.Absorptive	0	2419	1210	5.657	4.012	0.862	0.138
E.Absorptive	0	2368	1676	4.134	3.090	0.744	0.256
E.Absorptive	0	2543	2453	3.920	3.230	0.626	0.374
E.Absorptive	0	2538	2572	4.215	3.389	0.636	0.364
E.Absorptive	0	2569	2856	4.828	4.237	0.575	0.425
E.Absorptive	0	2586	3229	7.343	6.378	0.610	0.390
E.Absorptive	0	2636	7360	8.704	6.761	0.579	0.421
E.Absorptive	0	2604	2999	5.836	4.833	0.635	0.365
E.Absorptive	0	2291	1543	6.851	4.898	0.852	0.148
E.Absorptive	0	1915	864	6.005	3.687	0.917	0.083
E.Absorptive	0	2319	1549	3.931	3.630	0.648	0.352
E.Absorptive	0	2625	3403	5.557	5.034	0.526	0.474
E.Absorptive	0	2615	4913	5.677	4.600	0.529	0.471
E.Absorptive	0	2255	1042	4.595	3.340	0.838	0.162
E.Absorptive	0	2629	3625	7.680	6.559	0.612	0.388
E.Absorptive	0	2235	1712	4.390	3.443	0.716	0.284
E.Absorptive	0	2413	1313	3.557	2.644	0.776	0.224
E.Absorptive	0	2552	3904	4.571	3.259	0.619	0.381
E.Absorptive	0	2510	2308	4.466	3.800	0.633	0.367
E.Absorptive_All	0	6268	2463	4.694	3.733	0.832	0.168
E.Absorptive_All	0	5395	1757	3.378	2.208	0.874	0.126
E.Absorptive_All	0	5581	1642	4.383	2.304	0.935	0.065
E.Absorptive_All	0	5855	2149	3.753	2.912	0.830	0.170
E.Absorptive_All	0	6196	2409	4.475	3.788	0.805	0.195
E.Absorptive_All	0	5203	2380	3.467	2.281	0.833	0.167
E.Absorptive_All	0	6288	2771	7.262	4.198	0.950	0.050
E.Absorptive_All	0	6280	2556	5.411	4.074	0.861	0.139
E.Absorptive_All	0	5846	2079	4.970	3.024	0.915	0.085
E.Absorptive_All	0	6520	2928	5.497	4.207	0.845	0.155

TABLE 12-continued

Additional Cell Type Markers							
E.Absorptive_All	0	6456	4467	5.441	3.867	0.811	0.189
E.Absorptive_All	0	6540	2740	5.707	4.974	0.799	0.201
E.Absorptive_All	0	6653	3203	7.396	5.409	0.892	0.108
E.Absorptive_All	0	6008	2284	5.037	3.789	0.862	0.138
E.Absorptive_All	0	4148	778	2.897	2.025	0.907	0.093
E.Absorptive_All	0	4088	681	4.251	1.773	0.971	0.029
E.Absorptive_All	0	5736	3566	3.994	2.566	0.812	0.188
E.Absorptive_All	0	5391	1861	3.459	2.234	0.871	0.129
E.Absorptive_All	0	5464	1809	4.071	2.982	0.865	0.135
E.Absorptive_TA_1	0	1888	3219	5.228	5.469	0.332	0.668
E.Best4_Enterocytes	0	883	79	4.152	1.316	0.988	0.012
E.Best4_Enterocytes	0	1008	159	4.234	2.208	0.963	0.037
E.Best4_Enterocytes	0	998	312	2.542	2.166	0.806	0.194
E.Enterocyte_Immature_1	0	1208	986	3.636	2.657	0.707	0.293
E.Enterocyte_Immature_1	0	1509	1055	6.138	4.740	0.790	0.210
E.Enterocyte_Immature_1	0	1448	2202	3.934	2.974	0.561	0.439
E.Enterocyte_Immature_1	0	1541	1211	5.270	4.437	0.694	0.306
E.Enterocyte_Immature_1	0	1469	1685	4.045	3.252	0.602	0.398
E.Enterocyte_Immature_1	0	1355	926	3.502	3.047	0.667	0.333
E.Enterocyte_Immature_1	0	1160	562	3.641	2.825	0.784	0.216
E.Enterocyte_Immature_1	0	1245	791	3.305	2.625	0.716	0.284
E.Enterocyte_Immature_1	0	1649	3213	7.297	6.450	0.480	0.520
E.Enterocyte_Immature_1	0	1624	2958	5.587	4.929	0.464	0.536
E.Enterocyte_Immature_1	0	1576	1563	6.327	5.274	0.677	0.323
E.Enterocyte_Immature_1	0	1375	869	4.845	4.491	0.669	0.331
E.Enterocyte_Immature_1	0	1397	1101	4.274	3.659	0.660	0.340
E.Enterocyte_Immature_1	0	1636	7064	9.382	7.272	0.500	0.500
E.Enterocyte_Immature_1	0	1650	3582	7.715	6.569	0.505	0.495
E.Enterocyte_Immature_1	0	1508	1743	4.271	3.450	0.604	0.396
E.Enterocyte_Immature_1	0	1303	988	3.838	2.743	0.738	0.262
E.Enterocyte_Immature_1	0	1364	1389	3.484	2.750	0.620	0.380
E.Enterocyte_Immature_1	0	1511	1278	4.441	3.959	0.623	0.377
E.Enterocyte_Immature_1	0	1585	2292	4.562	3.771	0.545	0.455
E.Enterocyte_Immature_2	0	1613	1448	5.329	4.259	0.700	0.300
E.Enterocyte_Immature_2	0	1733	2294	4.949	3.991	0.595	0.405
E.Enterocyte_Immature_2	0	1706	2741	4.217	2.898	0.608	0.392
E.Enterocyte_Immature_2	0	1742	3229	8.185	6.228	0.677	0.323
E.Enterocyte_Immature_2	0	1741	2988	6.218	4.786	0.611	0.389
E.Enterocyte_Immature_2	0	1728	2665	5.773	4.442	0.620	0.380
E.Enterocyte_Immature_2	0	1686	1570	4.051	3.624	0.591	0.409
E.Enterocyte_Immature_2	0	1740	3405	6.253	4.952	0.557	0.443
E.Enterocyte_Immature_2	0	1739	4853	6.280	4.541	0.545	0.455
E.Enterocyte_Immature_2	0	1651	1026	3.644	3.194	0.687	0.313
E.Enterocyte_Immature_2	0	1742	3640	8.382	6.389	0.656	0.344
E.Enterocyte_Immature_2	0	1657	1239	3.473	2.556	0.716	0.284
E.Enterocyte_Immature_2	0	1681	1257	4.082	3.996	0.587	0.413
E.Enterocyte_Immature_2	0	1563	722	2.284	2.256	0.688	0.312
E.Enterocyte_Immature_2	0	1721	2289	4.045	3.026	0.604	0.396
E.Enterocyte_Progenitor	0	1449	1447	5.583	4.128	0.733	0.267
E.Enterocyte_Progenitor	0	1666	2312	5.128	3.860	0.634	0.366
E.Enterocyte_Progenitor	0	1775	3197	7.585	6.413	0.556	0.444
E.Enterocyte_Progenitor	0	1750	2962	5.506	4.937	0.467	0.533
E.Enterocyte_Progenitor	0	1732	2698	5.418	4.421	0.562	0.438
E.Enterocyte_Progenitor	0	1788	3407	5.829	4.994	0.483	0.517
E.Enterocyte_Progenitor	0	1794	3248	6.231	5.312	0.511	0.489
E.Enterocyte_Progenitor	0	1805	3625	7.738	6.539	0.533	0.467
E.Enterocyte_Progenitor	0	1571	2085	4.310	2.747	0.690	0.310
E.Enterocytes	0	1208	975	3.631	2.639	0.711	0.289
E.Enterocytes	0	917	355	1.979	1.221	0.814	0.186
E.Enterocytes	0	1300	1081	6.579	4.568	0.829	0.171
E.Enterocytes	0	1399	2198	4.012	2.940	0.572	0.428
E.Enterocytes	0	1373	1236	5.591	4.360	0.723	0.277
E.Enterocytes	0	1332	890	3.427	2.674	0.716	0.284
E.Enterocytes	0	1401	1679	4.545	3.150	0.687	0.313
E.Enterocytes	0	1365	915	3.753	2.942	0.724	0.276
E.Enterocytes	0	1357	1984	3.033	2.101	0.566	0.434
E.Enterocytes	0	1246	523	3.893	2.827	0.833	0.167
E.Enterocytes	0	1138	521	2.204	1.612	0.767	0.233
E.Enterocytes	0	1400	2545	4.586	3.458	0.546	0.454
E.Enterocytes	0	1287	769	3.495	2.429	0.778	0.222
E.Enterocytes	0	1163	628	2.203	2.004	0.680	0.320
E.Enterocytes	0	1407	7359	9.255	6.746	0.521	0.479
E.Enterocytes	0	1406	2957	6.072	4.857	0.525	0.475
E.Enterocytes	0	1245	840	2.147	1.559	0.690	0.310
E.Enterocytes	0	1360	1569	6.764	5.134	0.728	0.272
E.Enterocytes	0	1323	842	5.194	4.497	0.718	0.282
E.Enterocytes	0	1312	1210	3.191	2.445	0.645	0.355
E.Enterocytes	0	1273	867	2.494	2.449	0.602	0.398

TABLE 12-continued

Additional Cell Type Markers							
E.Enterocytes	0	1407	3535	6.492	4.715	0.577	0.423
E.Enterocytes	0	1396	3426	4.999	4.657	0.341	0.659
E.Enterocytes	0	1370	1546	3.900	3.754	0.495	0.505
E.Enterocytes	0	1329	1109	4.750	3.508	0.739	0.261
E.Enterocytes	0	1367	1283	2.746	2.110	0.623	0.377
E.Enterocytes	0	1296	1000	3.998	3.267	0.683	0.317
E.Enterocytes	0	1269	765	2.116	1.954	0.650	0.350
E.Enterocytes	0	1004	338	1.924	1.388	0.812	0.188
E.Enterocytes	0	1318	1256	3.092	2.264	0.651	0.349
E.Enterocytes	0	1400	1769	4.877	3.398	0.688	0.312
E.Enterocytes	0	1271	976	3.950	2.808	0.742	0.258
E.Enterocytes	0	1269	906	2.510	2.150	0.643	0.357
E.Enterocytes	0	1383	1375	3.797	2.739	0.677	0.323
E.Enterocytes	0	1361	1268	5.029	3.857	0.708	0.292
E.Enterocytes	0	1252	769	2.441	2.197	0.659	0.341
E.Enterocytes	0	1396	3893	4.751	3.276	0.499	0.501
E.Enterocytes	0	1189	699	2.159	1.498	0.729	0.271
E.Enterocytes	0	1282	561	2.649	2.497	0.718	0.282
E.Enterocytes	0	1405	2295	4.950	3.765	0.582	0.418
E.Epithelial	0	5973	612	4.662	2.328	0.980	0.020
E.Epithelial	0	307	3272	3.229	4.267	0.044	0.956
E.Epithelial	0	3989	5281	1.787	4.098	0.132	0.868
E.Epithelial	0	6692	739	4.464	2.690	0.969	0.031
E.Epithelial	0	5641	162	3.091	1.879	0.988	0.012
E.Epithelial	0	5315	529	4.057	2.477	0.968	0.032
E.Epithelial	0	5479	542	4.053	2.368	0.970	0.030
E.Epithelial	0	6025	324	3.331	2.067	0.978	0.022
E.Epithelial	0	5725	313	3.030	1.789	0.977	0.023
E.Epithelial	0	6329	341	3.514	2.357	0.976	0.024
E.Epithelial	0	6657	3899	3.928	2.819	0.787	0.213
E.Epithelial	0	2953	4393	1.575	4.053	0.108	0.892
E.Epithelial	0	6291	7064	3.410	4.852	0.247	0.753
E.Epithelial	0	5939	220	2.986	1.950	0.982	0.018
E.Epithelial	0	6749	538	4.356	2.299	0.981	0.019
E.Epithelial	0	6503	1475	6.761	2.996	0.984	0.016
E.Epithelial	0	4839	273	4.634	2.143	0.990	0.010
E.Epithelial	0	6836	736	5.030	2.380	0.983	0.017
E.Epithelial	0	6115	6812	3.156	4.678	0.238	0.762
E.Epithelial	0	4232	77	2.454	2.392	0.983	0.017
E.Epithelial	0	6506	1536	4.979	4.205	0.879	0.121
E.Epithelial	0	1130	3867	1.024	3.483	0.050	0.950
E.Epithelial	0	4787	5723	2.296	4.826	0.127	0.873
E.Epithelial	0	6932	773	4.516	2.208	0.978	0.022
E.Epithelial	0	6214	504	4.638	2.285	0.984	0.016
E.Epithelial	0	3967	188	3.602	2.227	0.982	0.018
E.Epithelial	0	7212	1063	5.228	2.254	0.982	0.018
E.Epithelial	0	536	4026	1.750	4.763	0.016	0.984
E.Epithelial	0	6974	3280	5.112	3.428	0.872	0.128
E.Epithelial	0	7167	943	5.524	2.568	0.983	0.017
E.Epithelial	0	6851	6095	6.555	4.769	0.795	0.205
E.Epithelial	0	6938	6665	6.706	4.903	0.784	0.216
E.Epithelial	0	6912	5562	6.655	5.153	0.779	0.221
E.Epithelial	0	4403	256	3.945	2.516	0.979	0.021
E.Epithelial	0	6432	562	4.723	2.396	0.983	0.017
E.Epithelial	0	6606	7339	4.757	5.640	0.328	0.672
E.Epithelial	0	7408	5397	6.193	4.281	0.838	0.162
E.Epithelial	0	6127	139	3.183	2.235	0.988	0.012
E.Epithelial	0	5976	1086	2.970	2.252	0.900	0.100
E.Epithelial	0	5745	240	3.827	2.062	0.988	0.012
E.Epithelial	0	3260	4585	1.622	4.032	0.118	0.882
E.Goblet	0	1014	1738	4.280	3.261	0.542	0.458
E.Goblet	0	1028	2386	4.238	2.967	0.510	0.490
E.Goblet	0	1019	2318	3.786	2.986	0.434	0.566
E.Goblet	0	1130	1888	6.958	3.952	0.828	0.172
E.Goblet	0	1139	2993	5.805	4.876	0.420	0.580
E.Goblet	0	1116	2845	5.250	3.470	0.574	0.426
E.Goblet	0	1144	3565	5.970	4.780	0.423	0.577
E.Goblet	0	1013	1161	4.358	3.537	0.606	0.394
E.Goblet	0	901	980	3.415	1.838	0.733	0.267
E.Goblet	0	1147	1035	6.701	3.303	0.921	0.079
E.Goblet	0	1047	874	5.978	3.644	0.858	0.142
E.Goblet	0	1155	2699	8.105	6.062	0.638	0.362
E.Goblet	0	1112	2295	4.690	3.832	0.468	0.532
E.Goblet	0	1152	1799	9.543	5.487	0.914	0.086
E.Immature_Enterocytes	0	2770	974	5.397	4.780	0.814	0.186
E.Immature_Enterocytes	0	4103	2842	4.682	4.247	0.661	0.339
E.Immature_Enterocytes	0	3737	2024	3.594	2.779	0.765	0.235
E.Immature_Enterocytes	0	3209	1234	5.279	3.343	0.909	0.091

TABLE 12-continued

Additional Cell Type Markers							
E.Immature_Enterocytes	0	3984	2104	4.839	3.403	0.837	0.163
E.Immature_Enterocytes	0	3148	1205	2.557	1.970	0.797	0.203
E.Immature_Enterocytes	0	2795	702	3.278	2.891	0.839	0.161
E.Immature_Enterocytes	0	3495	2259	4.787	3.428	0.799	0.201
E.Immature_Enterocytes	0	3987	2429	3.904	3.355	0.706	0.294
E.Immature_Enterocytes	0	2467	682	2.970	2.406	0.842	0.158
E.Immature_Enterocytes	0	4002	2792	4.364	4.240	0.610	0.390
E.Immature_Enterocytes	0	3518	2703	3.810	2.732	0.733	0.267
E.Immature_Enterocytes	0	4306	3066	7.752	5.616	0.861	0.139
E.Immature_Enterocytes	0	4259	2804	5.786	4.542	0.783	0.217
E.Immature_Enterocytes	0	3313	1399	5.742	5.195	0.776	0.224
E.Immature_Enterocytes	0	4043	3078	4.457	4.346	0.586	0.414
E.Immature_Enterocytes	0	3925	2492	5.394	3.918	0.814	0.186
E.Immature_Enterocytes	0	3478	1272	3.920	3.183	0.820	0.180
E.Immature_Enterocytes	0	4298	3250	5.891	4.632	0.760	0.240
E.Immature_Enterocytes	0	4231	4762	5.744	4.378	0.696	0.304
E.Immature_Enterocytes	0	4267	3099	5.988	5.204	0.703	0.297
E.Immature_Enterocytes	0	3067	767	3.589	2.881	0.867	0.133
E.Immature_Enterocytes	0	4339	3536	7.965	5.941	0.833	0.167
E.Immature_Enterocytes	0	3955	2610	4.983	4.291	0.710	0.290
E.Immature_Enterocytes	0	3423	1503	3.872	3.325	0.769	0.231
E.Immature_Enterocytes	0	2621	844	3.295	2.782	0.816	0.184
E.Immature_Enterocytes	0	3107	1191	2.956	2.634	0.765	0.235
E.Immature_Enterocytes	0	3242	1926	3.977	2.504	0.824	0.176
E.Immature_Enterocytes	0	3097	1082	3.413	2.109	0.876	0.124
E.Immature_Enterocytes	0	3549	972	4.198	3.576	0.849	0.151
E.Immature_Enterocytes	0	2613	579	2.414	1.908	0.865	0.135
E.Immature_Enterocytes	0	3743	2268	3.484	2.977	0.701	0.299
E.Immature_Enterocytes	0	3919	3787	4.221	3.085	0.695	0.305
E.Immature_Enterocytes	0	3721	2131	3.735	2.740	0.777	0.223
E.Immature_Enterocytes	0	3931	2068	4.145	3.590	0.736	0.264
E.Immature_Goblet	0	1551	2662	5.765	4.313	0.615	0.385
E.Immature_Goblet	0	1359	695	5.136	2.744	0.911	0.089
E.Immature_Goblet	0	1573	1880	5.942	4.318	0.720	0.280
E.Immature_Goblet	0	1565	966	5.946	3.560	0.894	0.106
E.Immature_Goblet	0	1530	954	4.467	2.127	0.890	0.110
E.Immature_Goblet	0	1605	3182	4.941	4.379	0.427	0.573
E.Immature_Goblet	0	1175	381	2.500	0.954	0.900	0.100
E.Immature_Goblet	0	1480	1003	4.504	4.612	0.578	0.422
E.Immature_Goblet	0	1191	439	2.826	1.954	0.832	0.168
E.Immature_Goblet	0	1193	409	4.378	1.993	0.938	0.062
E.Immature_Goblet	0	1408	1494	3.866	3.130	0.611	0.389
E.Immature_Goblet	0	1224	828	3.130	2.242	0.732	0.268
E.Immature_Goblet	0	1382	1364	3.880	2.933	0.661	0.339
E.Immature_Goblet	0	1236	768	6.140	4.371	0.846	0.154
E.Immature_Goblet	0	1658	2739	8.816	5.512	0.857	0.143
E.Immature_Goblet	0	1370	959	4.276	2.274	0.851	0.149
E.Immature_Goblet	0	1449	1816	7.937	6.485	0.686	0.314
E.Secretory	0	1291	1951	6.784	3.914	0.829	0.171
E.Secretory	0	1845	3181	5.589	4.243	0.596	0.404
E.Secretory	0	1231	1080	6.606	3.313	0.918	0.082
E.Secretory	0	1131	920	5.885	3.694	0.849	0.151
E.Secretory	0	1794	2690	7.582	6.100	0.651	0.349
E.Secretory	0	1349	1854	9.323	5.425	0.916	0.084
E.Secretory_All	0	2517	603	4.459	1.756	0.965	0.035
E.Secretory_All	0	3656	1746	5.947	2.828	0.948	0.052
E.Secretory_All	0	3924	2945	4.548	5.087	0.478	0.522
E.Secretory_All	0	3044	802	5.231	2.741	0.955	0.045
E.Secretory_All	0	3200	755	3.709	1.530	0.950	0.050
E.Secretory_All	0	4218	3113	5.026	4.144	0.714	0.286
E.Secretory_All	0	4234	3340	4.732	5.151	0.487	0.513
E.Secretory_All	0	4111	3186	5.379	5.488	0.545	0.455
E.Secretory_All	0	3391	817	5.311	1.951	0.977	0.023
E.Secretory_All	0	2389	240	2.570	0.913	0.969	0.031
E.Secretory_All	0	2326	612	5.647	3.504	0.944	0.056
E.Secretory_All	0	4234	2580	8.009	4.159	0.959	0.041
E.Secretory_All	0	3449	1682	8.247	3.561	0.981	0.019
E.Tuft	0	552	3208	6.765	4.217	0.502	0.498
F.Crypt	0	3156	920	4.099	3.199	0.865	0.135
F.Crypt	0	2386	78	3.398	2.781	0.979	0.021
F.Crypt	0	1779	316	2.763	1.870	0.913	0.087
F.Crypt	0	3497	556	7.247	3.992	0.984	0.016
F.Crypt	0	2123	327	3.330	1.894	0.946	0.054
F.Crypt	0	3623	868	7.043	5.086	0.942	0.058
F.Crypt	0	2087	487	2.812	3.595	0.713	0.287
F.Crypt	0	3308	639	4.365	3.670	0.893	0.107
F.Crypt	0	3341	614	4.536	3.693	0.907	0.093
F.Crypt	0	2951	718	3.608	3.828	0.779	0.221

TABLE 12-continued

Additional Cell Type Markers							
F.Crypt	0	2221	119	5.921	3.852	0.987	0.013
F.Crypt	0	1919	48	5.837	2.060	0.998	0.002
F.Crypt	0	2986	445	4.944	4.651	0.892	0.108
F.Crypt	0	2149	64	5.018	1.983	0.996	0.004
F.Crypt	0	3624	5585	5.307	4.208	0.582	0.418
F.Crypt	0	3596	926	6.711	3.192	0.978	0.022
F.Crypt	0	2375	360	3.327	2.554	0.919	0.081
F.Crypt	0	2375	500	2.948	2.424	0.872	0.128
F.Crypt	0	2949	618	3.768	3.722	0.831	0.169
F.Crypt	0	3310	671	4.189	3.910	0.857	0.143
F.Crypt	0	3281	671	4.522	4.262	0.854	0.146
F.Crypt	0	2324	591	3.038	3.498	0.741	0.259
F.Crypt	0	3069	706	3.715	3.901	0.793	0.207
F.Crypt	0	3322	2236	4.673	2.996	0.826	0.174
F.Crypt	0	2564	397	3.253	2.783	0.899	0.101
F.Crypt	0	2503	333	3.720	2.966	0.927	0.073
F.Crypt	0	3542	2197	6.261	5.187	0.772	0.228
F.Crypt	0	2782	488	3.451	3.339	0.860	0.140
F.Crypt	0	3546	596	5.853	4.297	0.946	0.054
F.Crypt	0	1979	213	2.670	3.009	0.880	0.120
F.Crypt	0	1732	188	3.131	2.839	0.919	0.081
F.Crypt	0	1789	319	2.403	2.658	0.825	0.175
F.Crypt	0	2102	375	2.752	2.686	0.854	0.146
F.Crypt	0	1146	42	3.718	3.221	0.975	0.025
F.Crypt	0	3283	344	4.242	2.792	0.963	0.037
F.Crypt	0	1902	156	2.727	2.171	0.947	0.053
F.Crypt	0	2145	630	2.846	3.905	0.620	0.380
F.Crypt	0	2755	567	3.695	3.335	0.862	0.138
F.Crypt	0	3351	2620	4.812	3.347	0.779	0.221
F.Crypt	0	1671	350	2.744	1.965	0.891	0.109
F.Crypt	0	3564	2640	4.917	3.851	0.739	0.261
F.Crypt	0	2196	511	3.312	3.323	0.810	0.190
F.Crypt	0	3646	1406	6.519	5.994	0.789	0.211
F.Crypt	0	3006	3294	3.700	2.735	0.641	0.359
F.Crypt	0	3604	2719	5.252	4.673	0.664	0.336
F.Crypt	0	2245	167	2.910	2.829	0.934	0.066
F.Crypt	0	2549	1084	3.174	2.069	0.835	0.165
F.Crypt	0	3454	597	5.922	4.575	0.936	0.064
F.Crypt	0	3320	521	4.843	3.536	0.940	0.060
F.Crypt	0	2033	554	2.858	3.439	0.710	0.290
F.Crypt	0	2459	506	3.042	3.445	0.786	0.214
F.Crypt	0	2088	727	2.818	4.133	0.536	0.464
F.Crypt	0	2587	1685	3.046	2.198	0.734	0.266
F.Crypt	0	2032	506	2.896	3.270	0.756	0.244
F.Crypt	0	2260	449	3.014	3.247	0.811	0.189
F.Crypt	0	2329	276	3.061	2.836	0.908	0.092
F.Crypt	0	2063	698	3.375	4.421	0.589	0.411
F.Crypt	0	1794	389	2.610	2.032	0.873	0.127
F.Crypt	0	2512	640	3.163	2.978	0.817	0.183
F.Crypt	0	2523	1293	3.135	2.224	0.786	0.214
F.Crypt	0	2286	337	3.137	1.894	0.941	0.059
F.Crypt	0	2383	721	3.249	3.040	0.793	0.207
F.Crypt	0	2258	647	2.978	3.157	0.755	0.245
F.Crypt	0	2622	560	3.322	2.862	0.866	0.134
F.Crypt	0	1947	119	4.614	3.985	0.962	0.038
F.Crypt	0	2273	250	3.298	3.244	0.904	0.096
F.Crypt	0	3290	1485	4.071	3.414	0.777	0.223
F.Crypt	0	2670	421	3.435	2.749	0.911	0.089
F.Crypt	0	2562	1770	3.036	2.263	0.712	0.288
F.Crypt	0	3087	1931	3.545	2.881	0.717	0.283
F.Crypt	0	2953	2154	4.010	3.961	0.586	0.414
F.Crypt	0	2780	656	3.501	3.499	0.809	0.191
F.Crypt	0	2554	666	3.133	3.021	0.806	0.194
F.Crypt	0	1797	361	2.604	2.770	0.816	0.184
F.Crypt	0	3091	938	4.135	2.948	0.882	0.118
F.Crypt	0	2800	943	3.632	4.166	0.672	0.328
F.Crypt	0	1879	588	2.948	3.943	0.616	0.384
F.Crypt	0	2024	517	2.767	2.396	0.835	0.165
F.Crypt	0	1997	215	3.327	2.866	0.928	0.072
F.Crypt	0	2985	366	3.792	2.967	0.935	0.065
F.Crypt	0	3299	2614	4.083	4.024	0.568	0.432
F.Crypt	0	2007	948	3.037	3.560	0.596	0.404
F.Crypt	0	3150	2348	3.853	2.738	0.744	0.256
F.Crypt	0	3498	2880	4.789	3.365	0.765	0.235
F.Crypt	0	2180	660	2.906	4.096	0.591	0.409
F.Crypt	0	2111	714	2.713	2.627	0.758	0.242
F.Crypt	0	3478	3224	5.026	4.148	0.665	0.335
F.Crypt_hiFos	0	1049	1083	4.022	3.446	0.591	0.409

TABLE 12-continued

Additional Cell Type Markers							
F.Crypt_hiFos	0	844	278	3.112	3.507	0.698	0.302
F.Crypt_hiFos	0	1134	794	7.597	5.955	0.817	0.183
F.Crypt_hiFos	0	1134	1087	6.856	5.919	0.666	0.334
F.Crypt_hiFos	0	1105	818	4.389	3.853	0.662	0.338
F.Crypt_hiFos	0	1111	784	4.675	3.976	0.697	0.303
F.Crypt_hiFos	0	1108	687	5.225	4.744	0.692	0.308
F.Crypt_hiFos	0	795	197	5.246	4.437	0.876	0.124
F.Crypt_hiFos	0	1136	1213	6.608	5.024	0.737	0.263
F.Crypt_hiFos	0	997	782	3.471	3.886	0.489	0.511
F.Crypt_hiFos	0	1083	826	3.970	4.166	0.534	0.466
F.Crypt_hiFos	0	1080	848	4.301	4.422	0.539	0.461
F.Crypt_hiFos	0	1001	860	3.368	3.938	0.440	0.560
F.Crypt_hiFos	0	1120	2480	4.771	3.249	0.565	0.435
F.Crypt_hiFos	0	936	514	3.479	3.169	0.693	0.307
F.Crypt_hiFos	0	1136	2226	6.269	5.371	0.487	0.513
F.Crypt_hiFos	0	985	628	3.315	3.356	0.604	0.396
F.Crypt_hiFos	0	1131	817	5.879	5.050	0.711	0.289
F.Crypt_hiFos	0	1089	606	4.156	3.697	0.712	0.288
F.Crypt_hiFos	0	965	715	3.482	3.394	0.589	0.411
F.Crypt_hiFos	0	1090	2798	4.676	3.594	0.452	0.548
F.Crypt_hiFos	0	867	214	3.125	2.672	0.847	0.153
F.Crypt_hiFos	0	1126	2791	4.687	3.886	0.413	0.587
F.Crypt_hiFos	0	1141	1517	6.456	6.170	0.478	0.522
F.Crypt_hiFos	0	1126	788	6.057	5.403	0.692	0.308
F.Crypt_hiFos	0	1110	725	4.771	4.184	0.697	0.303
F.Crypt_hiFos	0	863	519	3.017	2.422	0.715	0.285
F.Crypt_hiFos	0	946	706	3.151	2.989	0.600	0.400
F.Crypt_hiFos	0	952	550	3.255	3.030	0.669	0.331
F.Crypt_hiFos	0	981	742	3.297	3.443	0.544	0.456
F.Crypt_hiFos	0	1060	1107	4.028	3.266	0.619	0.381
F.Crypt_hiFos	0	1014	526	3.617	3.403	0.691	0.309
F.Crypt_hiFos	0	1131	3028	4.716	3.536	0.458	0.542
F.Crypt_hiFos	0	1134	3268	5.166	4.234	0.398	0.602
F.Crypt_loFos_1	0	1250	1134	3.901	3.480	0.596	0.404
F.Crypt_loFos_1	0	1022	281	3.158	3.451	0.748	0.252
F.Crypt_loFos_1	0	1366	818	7.306	6.044	0.800	0.200
F.Crypt_loFos_1	0	1376	1174	7.234	5.806	0.759	0.241
F.Crypt_loFos_1	0	1327	881	4.308	3.896	0.667	0.333
F.Crypt_loFos_1	0	1332	858	4.445	4.073	0.668	0.332
F.Crypt_loFos_1	0	1216	918	3.499	3.798	0.518	0.482
F.Crypt_loFos_1	0	787	185	5.923	5.332	0.865	0.135
F.Crypt_loFos_1	0	1183	727	4.634	4.814	0.590	0.410
F.Crypt_loFos_1	0	916	204	4.830	4.778	0.823	0.177
F.Crypt_loFos_1	0	1358	1240	6.713	5.016	0.780	0.220
F.Crypt_loFos_1	0	1001	520	3.080	2.914	0.684	0.316
F.Crypt_loFos_1	0	1009	676	2.746	2.685	0.609	0.391
F.Crypt_loFos_1	0	1199	837	3.662	3.906	0.547	0.453
F.Crypt_loFos_1	0	1317	883	4.130	4.085	0.606	0.394
F.Crypt_loFos_1	0	1307	902	4.577	4.438	0.615	0.385
F.Crypt_loFos_1	0	1211	903	3.424	3.976	0.478	0.522
F.Crypt_loFos_1	0	1343	2404	4.706	3.355	0.588	0.412
F.Crypt_loFos_1	0	1090	562	3.120	3.084	0.665	0.335
F.Crypt_loFos_1	0	1023	543	3.627	3.278	0.706	0.294
F.Crypt_loFos_1	0	1364	2359	6.358	5.403	0.528	0.472
F.Crypt_loFos_1	0	1197	671	3.404	3.343	0.651	0.349
F.Crypt_loFos_1	0	1371	874	5.894	5.057	0.737	0.263
F.Crypt_loFos_1	0	898	359	2.565	2.894	0.666	0.334
F.Crypt_loFos_1	0	1301	618	4.125	3.797	0.725	0.275
F.Crypt_loFos_1	0	853	286	2.556	2.363	0.773	0.227
F.Crypt_loFos_1	0	1182	796	3.740	3.357	0.659	0.341
F.Crypt_loFos_1	0	1310	2894	4.812	3.611	0.510	0.490
F.Crypt_loFos_1	0	1370	2857	4.959	3.939	0.493	0.507
F.Crypt_loFos_1	0	1374	1612	6.526	6.130	0.529	0.471
F.Crypt_loFos_1	0	1365	2794	5.146	4.733	0.394	0.606
F.Crypt_loFos_1	0	960	350	2.743	2.988	0.698	0.302
F.Crypt_loFos_1	0	1365	826	5.956	5.358	0.714	0.286
F.Crypt_loFos_1	0	1323	795	4.867	4.057	0.745	0.255
F.Crypt_loFos_1	0	1044	692	2.856	3.290	0.528	0.472
F.Crypt_loFos_1	0	958	475	2.702	2.874	0.642	0.358
F.Crypt_loFos_1	0	1069	779	3.034	3.129	0.562	0.438
F.Crypt_loFos_1	0	1015	529	3.017	2.494	0.734	0.266
F.Crypt_loFos_1	0	1182	710	3.305	2.950	0.680	0.320
F.Crypt_loFos_1	0	996	438	3.197	3.275	0.683	0.317
F.Crypt_loFos_1	0	1300	1739	3.944	3.565	0.493	0.507
F.Crypt_loFos_1	0	1136	595	3.285	3.027	0.695	0.305
F.Crypt_loFos_1	0	1156	851	3.365	3.538	0.546	0.454
F.Crypt_loFos_1	0	1088	846	3.023	3.037	0.560	0.440
F.Crypt_loFos_1	0	1227	1199	4.022	3.296	0.629	0.371

TABLE 12-continued

Additional Cell Type Markers							
F.Crypt_loFos_1	0	1208	1128	3.689	4.066	0.452	0.548
F.Crypt_loFos_1	0	1223	588	3.747	3.373	0.729	0.271
F.Crypt_loFos_1	0	1325	2772	4.035	4.051	0.321	0.679
F.Crypt_loFos_1	0	1294	2583	3.807	2.807	0.500	0.500
F.Crypt_loFos_1	0	1365	3132	4.845	3.565	0.514	0.486
F.Crypt_loFos_1	0	1368	3268	4.997	4.262	0.411	0.589
F.Crypt_loFos_2	0	949	1084	7.101	5.953	0.660	0.340
F.Crypt_loFos_2	0	916	1243	6.828	5.015	0.721	0.279
F.Endothelial	0	1219	273	2.908	0.994	0.944	0.056
F.Endothelial	0	1559	618	3.985	3.482	0.781	0.219
F.Endothelial	0	1441	1881	3.510	2.125	0.667	0.333
F.Endothelial	0	1556	1426	5.383	1.472	0.943	0.057
F.Endothelial	0	951	148	4.156	1.856	0.969	0.031
F.Endothelial	0	1604	2782	4.064	2.214	0.675	0.325
F.Endothelial	0	1414	49	5.228	1.567	0.997	0.003
F.Endothelial	0	1281	59	3.399	2.168	0.981	0.019
F.Endothelial	0	1643	444	4.115	2.641	0.911	0.089
F.Endothelial	0	1351	58	3.331	1.770	0.986	0.014
F.Endothelial	0	1245	368	3.311	1.973	0.895	0.105
F.Endothelial	0	1282	78	3.259	0.870	0.989	0.011
F.Endothelial	0	1635	2518	6.400	3.120	0.863	0.137
F.Endothelial	0	1644	3414	4.059	2.462	0.593	0.407
F.Endothelial	0	1334	849	3.624	3.301	0.663	0.337
F.Endothelial	0	1722	601	4.684	2.860	0.910	0.090
F.Endothelial	0	1928	6769	5.707	4.574	0.384	0.616
F.Endothelial	0	1718	4543	4.333	3.002	0.488	0.512
F.Endothelial	0	1893	2711	5.196	3.748	0.656	0.344
F.Endothelial	0	1500	1206	3.811	1.626	0.850	0.150
F.Endothelial	0	1914	1455	6.984	5.874	0.739	0.261
F.Endothelial	0	1805	5038	5.020	3.334	0.536	0.464
F.Endothelial	0	1054	47	3.046	1.581	0.984	0.016
F.Endothelial	0	1345	206	4.033	2.843	0.937	0.063
F.Endothelial	0	1289	996	3.201	1.726	0.782	0.218
F.Endothelial	0	1579	72	5.687	1.269	0.998	0.002
F.Endothelial	0	1528	143	4.279	1.597	0.986	0.014
F.Endothelial	0	1331	15	3.868	0.963	0.998	0.002
F.Endothelial	0	1006	128	3.109	2.540	0.921	0.079
F.Endothelial	0	1676	3525	4.151	2.590	0.584	0.416
F.Endothelial	0	1305	906	4.166	1.802	0.881	0.119
F.Endothelial	0	1602	512	4.493	3.167	0.887	0.113
F.Endothelial	0	1513	909	4.155	3.150	0.770	0.230
F.Endothelial	0	905	47	3.234	1.512	0.985	0.015
F.Endothelial	0	1244	15	3.544	1.783	0.996	0.004
F.Endothelial_1	0	652	1575	5.796	2.413	0.812	0.188
F.Endothelial_1	0	585	172	5.192	4.948	0.801	0.199
F.Endothelial_1	0	654	2665	6.229	3.695	0.587	0.413
F.Endothelial_1	0	676	750	4.828	3.440	0.702	0.298
F.Endothelial_1	0	586	1320	4.051	2.045	0.641	0.359
F.Endothelial_1	0	666	217	5.705	5.102	0.823	0.177
F.Fibroblast	0	4029	635	3.832	3.104	0.913	0.087
F.Fibroblast	0	3456	408	6.974	2.269	0.995	0.005
F.Fibroblast	0	4106	607	6.605	4.675	0.963	0.037
F.Fibroblast	0	3267	73	3.344	1.646	0.993	0.007
F.Fibroblast	0	4326	213	4.183	2.021	0.989	0.011
F.Fibroblast	0	4410	163	4.300	2.446	0.990	0.010
F.Fibroblast	0	4239	261	3.842	3.442	0.955	0.045
F.Fibroblast	0	1873	92	5.972	1.932	0.997	0.003
F.Fibroblast	0	1422	59	5.806	1.785	0.997	0.003
F.Fibroblast	0	2929	351	4.833	4.585	0.908	0.092
F.Fibroblast	0	1563	61	4.966	2.517	0.993	0.007
F.Fibroblast	0	5111	5338	5.197	4.037	0.681	0.319
F.Fibroblast	0	3949	704	6.211	2.064	0.990	0.010
F.Fibroblast	0	2740	114	3.128	2.120	0.980	0.020
F.Fibroblast	0	2962	197	2.886	1.903	0.967	0.033
F.Fibroblast	0	4125	199	3.894	2.397	0.983	0.017
F.Fibroblast	0	4518	186	4.169	2.996	0.982	0.018
F.Fibroblast	0	4579	172	4.539	2.685	0.990	0.010
F.Fibroblast	0	3657	165	3.437	2.078	0.983	0.017
F.Fibroblast	0	4478	190	4.006	2.265	0.987	0.013
F.Fibroblast	0	3827	2143	4.427	2.818	0.845	0.155
F.Fibroblast	0	2679	184	3.600	2.643	0.966	0.034
F.Fibroblast	0	5077	1724	6.700	2.109	0.986	0.014
F.Fibroblast	0	3686	97	3.433	2.581	0.986	0.014
F.Fibroblast	0	4311	182	5.480	1.697	0.997	0.003
F.Fibroblast	0	2121	249	3.980	1.133	0.984	0.016
F.Fibroblast	0	3905	2725	3.376	2.406	0.737	0.263
F.Fibroblast	0	2953	59	2.846	1.676	0.991	0.009
F.Fibroblast	0	3645	58	3.945	1.554	0.997	0.003

TABLE 12-continued

Additional Cell Type Markers							
F.Fibroblast	0	2584	465	2.863	4.368	0.662	0.338
F.Fibroblast	0	3550	254	3.635	2.703	0.964	0.036
F.Fibroblast	0	4136	2346	4.358	3.393	0.775	0.225
F.Fibroblast	0	4971	2195	4.744	3.624	0.831	0.169
F.Fibroblast	0	3046	212	3.466	2.742	0.960	0.040
F.Fibroblast	0	5121	933	6.266	6.102	0.860	0.140
F.Fibroblast	0	2401	139	2.800	2.555	0.953	0.047
F.Fibroblast	0	4228	3014	3.706	2.526	0.761	0.239
F.Fibroblast	0	5158	2426	5.537	4.140	0.848	0.152
F.Fibroblast	0	3920	2336	3.479	2.320	0.789	0.211
F.Fibroblast	0	3415	811	3.148	1.349	0.936	0.064
F.Fibroblast	0	4072	234	5.743	1.786	0.996	0.004
F.Fibroblast	0	4268	103	4.481	1.355	0.997	0.003
F.Fibroblast	0	2988	230	3.363	2.578	0.957	0.043
F.Fibroblast	0	3714	77	3.343	1.563	0.994	0.006
F.Fibroblast	0	3349	331	3.886	3.831	0.913	0.087
F.Fibroblast	0	3281	1352	3.054	1.920	0.842	0.158
F.Fibroblast	0	2747	228	3.114	2.952	0.931	0.069
F.Fibroblast	0	2564	75	2.996	2.370	0.981	0.019
F.Fibroblast	0	3283	345	4.326	3.405	0.947	0.053
F.Fibroblast	0	2891	416	3.084	3.061	0.876	0.124
F.Fibroblast	0	3402	334	3.328	2.179	0.958	0.042
F.Fibroblast	0	2975	375	3.145	3.035	0.895	0.105
F.Fibroblast	0	3329	204	3.271	2.174	0.972	0.028
F.Fibroblast	0	2585	54	3.301	2.573	0.988	0.012
F.Fibroblast	0	4613	988	4.226	2.277	0.947	0.053
F.Fibroblast	0	3032	169	3.280	2.058	0.977	0.023
F.Fibroblast	0	3516	1433	3.177	1.918	0.855	0.145
F.Fibroblast	0	2875	151	3.076	2.437	0.967	0.033
F.Fibroblast	0	4317	1602	3.686	2.347	0.872	0.128
F.Fibroblast	0	3857	273	3.650	2.531	0.968	0.032
F.Fibroblast	0	3417	364	3.186	2.451	0.940	0.060
F.Fibroblast	0	3733	634	4.046	2.123	0.957	0.043
F.Fibroblast	0	4160	540	3.881	4.055	0.872	0.128
F.Fibroblast	0	3510	61	3.541	2.220	0.993	0.007
F.Fibroblast	0	4636	2280	4.656	3.474	0.822	0.178
F.Fibroblast	0	2901	671	3.427	3.580	0.795	0.205
F.Fibroblast	0	4235	1927	3.787	2.310	0.859	0.141
F.Fibroblast	0	4918	2415	4.735	2.770	0.888	0.112
F.Fibroblast	0	3694	196	3.854	3.302	0.965	0.035
F.Fibroblast	0	2773	496	2.761	2.469	0.873	0.127
F.Fibroblast	0	4853	3142	4.876	3.992	0.740	0.260
F.Glia	0	348	875	5.078	1.800	0.794	0.206
F.Glia	0	412	3823	5.854	3.599	0.340	0.660
F.Glia	0	380	452	5.884	3.738	0.788	0.212
F.Glia	0	422	256	6.580	2.417	0.967	0.033
F.Glia	0	377	118	5.034	3.083	0.925	0.075
F.Microvascular	0	395	1567	5.613	2.622	0.667	0.333
F.Microvascular	0	403	2618	7.296	3.566	0.671	0.329
F.Microvascular	0	405	241	6.509	4.671	0.857	0.143
F.Myofibroblasts	0	594	552	6.751	3.937	0.883	0.117
F.Myofibroblasts	0	586	486	6.561	3.942	0.881	0.119
F.Stromal	0	4699	323	3.769	2.021	0.980	0.020
F.Stromal	0	3224	434	6.862	2.089	0.995	0.005
F.Stromal	0	3873	667	6.467	4.709	0.952	0.048
F.Stromal	0	2981	52	3.325	1.280	0.996	0.004
F.Stromal	0	4083	1908	3.402	2.549	0.794	0.206
F.Stromal	0	4219	125	4.112	1.466	0.995	0.005
F.Stromal	0	4206	92	4.244	1.369	0.997	0.003
F.Stromal	0	4456	52	3.803	1.491	0.998	0.002
F.Stromal	0	3138	223	4.997	3.309	0.978	0.022
F.Stromal	0	1341	40	4.975	2.629	0.994	0.006
F.Stromal	0	6062	5255	5.051	3.987	0.707	0.293
F.Stromal	0	3536	750	6.157	1.994	0.988	0.012
F.Stromal	0	2758	202	2.865	1.552	0.971	0.029
F.Stromal	0	3999	99	3.904	0.760	0.997	0.003
F.Stromal	0	4386	98	4.164	1.264	0.997	0.003
F.Stromal	0	4396	114	4.521	1.678	0.996	0.004
F.Stromal	0	3587	69	3.430	1.068	0.996	0.004
F.Stromal	0	4371	87	3.975	1.532	0.996	0.004
F.Stromal	0	3962	2146	4.285	2.821	0.836	0.164
F.Stromal	0	2689	96	3.499	1.539	0.991	0.009
F.Stromal	0	5009	1743	6.560	2.060	0.985	0.015
F.Stromal	0	3480	42	3.414	1.739	0.996	0.004
F.Stromal	0	3982	197	5.413	1.504	0.997	0.003
F.Stromal	0	4636	2608	3.343	2.255	0.791	0.209
F.Stromal	0	3294	56	3.917	1.115	0.998	0.002
F.Stromal	0	3587	86	3.720	1.424	0.995	0.005

TABLE 12-continued

Additional Cell Type Markers							
F.Stromal	0	3544	121	3.603	0.980	0.994	0.006
F.Stromal	0	4983	2076	4.421	2.935	0.871	0.129
F.Stromal	0	5515	3101	4.283	2.766	0.836	0.164
F.Stromal	0	3508	1426	3.269	2.276	0.830	0.170
F.Stromal	0	6010	1863	4.863	2.442	0.945	0.055
F.Stromal	0	3172	92	3.461	1.376	0.993	0.007
F.Stromal	0	6201	540	6.457	1.796	0.997	0.003
F.Stromal	0	4943	2914	3.611	2.444	0.792	0.208
F.Stromal	0	5847	2307	5.474	3.855	0.886	0.114
F.Stromal	0	3341	737	3.113	1.004	0.951	0.049
F.Stromal	0	3754	257	5.716	1.713	0.996	0.004
F.Stromal	0	3881	115	4.406	1.112	0.997	0.003
F.Stromal	0	3445	45	3.320	1.498	0.996	0.004
F.Stromal	0	3697	112	3.933	1.190	0.995	0.005
F.Stromal	0	3599	159	4.283	2.060	0.991	0.009
F.Stromal	0	3125	275	3.367	1.958	0.968	0.032
F.Stromal	0	3323	277	3.311	1.743	0.973	0.027
F.Stromal	0	3562	99	3.208	1.151	0.993	0.007
F.Stromal	0	3247	133	3.161	2.329	0.978	0.022
F.Stromal	0	4497	900	4.201	1.891	0.961	0.039
F.Stromal	0	2947	118	3.219	1.504	0.988	0.012
F.Stromal	0	4640	1511	3.613	2.214	0.890	0.110
F.Stromal	0	3498	279	3.641	2.437	0.967	0.033
F.Stromal	0	3728	181	3.137	1.846	0.981	0.019
F.Stromal	0	3590	561	4.073	1.321	0.977	0.023
F.Stromal	0	5071	127	4.105	1.102	0.997	0.003
F.Stromal	0	3314	63	3.793	1.337	0.997	0.003
F.Stromal	0	3169	39	3.500	0.992	0.998	0.002
F.Stromal	0	5320	2150	4.570	3.528	0.836	0.164
F.Stromal	0	3633	337	3.716	2.230	0.968	0.032
F.Stromal	0	4059	1930	3.743	2.244	0.856	0.144
F.Stromal	0	4772	2353	4.676	2.747	0.885	0.115
F.Stromal	0	3627	105	3.869	1.411	0.995	0.005
F.Stromal	0	3246	314	2.721	2.032	0.943	0.057
F.Stromal	0	5801	3009	4.853	3.850	0.794	0.206
F.Villus	0	1118	113	3.482	3.031	0.931	0.069
F.Villus	0	1755	429	3.858	2.664	0.903	0.097
F.Villus	0	1620	749	3.772	4.170	0.621	0.379
F.Villus	0	1785	760	3.998	3.616	0.754	0.246
F.Villus	0	1634	619	3.845	3.580	0.760	0.240
F.Villus	0	1701	774	3.820	4.191	0.630	0.370
F.Villus	0	1799	792	4.333	4.445	0.678	0.322
F.Villus	0	1785	592	3.789	3.151	0.824	0.176
F.Villus	0	1952	738	4.298	3.740	0.796	0.204
F.Villus	0	2185	2158	7.330	4.679	0.864	0.136
F.Villus	0	1641	565	3.540	3.345	0.769	0.231
F.Villus	0	1599	390	4.467	2.254	0.950	0.050
F.Villus	0	1319	208	3.234	2.430	0.917	0.083
F.Villus	0	1354	66	3.310	2.408	0.975	0.025
F.Villus	0	1575	269	3.591	1.921	0.949	0.051
F.Villus	0	1792	403	4.335	2.595	0.937	0.063
F.Villus	0	1669	662	3.683	3.272	0.770	0.230
F.Villus	0	1624	1098	3.742	2.252	0.806	0.194
F.Villus	0	2046	2669	4.561	3.963	0.537	0.463
F.Villus	0	1420	317	4.194	3.145	0.903	0.097
F.Villus	0	2089	1461	5.894	6.223	0.532	0.468
F.Villus	0	2165	2685	5.737	4.614	0.637	0.363
F.Villus	0	1608	676	3.810	4.416	0.610	0.390
F.Villus	0	1738	548	3.702	3.101	0.828	0.172
F.Villus	0	1617	2123	3.864	2.021	0.732	0.268
F.Villus	0	1545	159	3.557	2.182	0.962	0.038
F.Villus	0	1979	606	5.011	3.416	0.908	0.092
F.Villus	0	1771	333	4.989	3.348	0.943	0.057
F.Villus	0	1988	1564	4.363	3.326	0.723	0.277
F.Villus	0	1508	496	3.401	2.790	0.823	0.177
F.Villus	0	1642	703	3.859	3.280	0.777	0.223
F.Villus	0	1738	991	3.973	4.056	0.624	0.376
F.Villus	0	1939	2612	4.926	3.772	0.623	0.377
F.Villus	0	2050	2924	4.861	3.433	0.654	0.346
F.Villus	0	1657	632	3.869	3.723	0.744	0.256
F.Villus	0	1203	24	3.408	2.581	0.989	0.011
F.Villus_1	0	982	2294	7.382	5.226	0.656	0.344
F.Villus_1	0	836	564	4.269	3.244	0.751	0.249
F.Villus_1	0	886	791	4.923	3.822	0.706	0.294
F.Villus_1	0	858	467	5.104	3.865	0.813	0.187
F.Villus_2	0	969	549	3.899	2.999	0.767	0.233
F.Villus_2	0	1084	884	4.389	3.824	0.645	0.355
F.Villus_2	0	1203	2333	7.286	5.180	0.690	0.310

TABLE 12-continued

Additional Cell Type Markers							
F.Villus_2	0	884	511	4.521	3.079	0.825	0.175
F.Villus_2	0	864	374	3.665	2.638	0.825	0.175
F.Villus_2	0	956	509	4.390	3.149	0.816	0.184
F.Villus_2	0	947	645	3.695	3.037	0.698	0.302
F.Villus_2	0	813	275	3.551	2.916	0.821	0.179
F.Villus_2	0	1093	757	5.078	3.833	0.774	0.226
F.Villus_2	0	1105	1727	4.490	3.435	0.571	0.429
I.Immune	0	6020	912	4.060	2.685	0.945	0.055
I.Immune	0	2923	198	5.993	1.342	0.997	0.003
I.Immune	0	3578	85	3.206	1.336	0.994	0.006
I.Immune	0	3612	91	4.454	1.223	0.997	0.003
I.Immune	0	3063	50	3.608	1.035	0.997	0.003
I.Immune	0	5000	160	4.518	1.339	0.996	0.004
I.Immune	0	3952	245	4.383	1.564	0.991	0.009
I.Immune	0	2831	115	4.230	1.067	0.995	0.005
I.Immune	0	4900	234	3.876	1.264	0.992	0.008
I.Immune	0	1786	6623	5.707	4.195	0.435	0.565
I.Immune	0	6213	4853	4.296	3.229	0.728	0.272
I.Immune	0	3302	276	3.332	1.746	0.973	0.027
I.Immune	0	3552	79	3.464	0.713	0.997	0.003
I.Immune	0	3745	128	3.391	1.254	0.992	0.008
I.Immune	0	3265	181	4.581	1.703	0.993	0.007
I.Immune	0	4538	170	3.795	0.812	0.995	0.005
I.Immune	0	3824	294	3.168	0.746	0.986	0.014
I.Immune	0	4472	331	4.275	2.045	0.984	0.016
I.Immune	0	5777	805	4.342	3.298	0.937	0.063
I.Immune	0	3800	145	4.546	1.690	0.995	0.005
I.Lymphoid	0	6125	1705	4.081	3.443	0.848	0.152
I.Lymphoid	0	3441	211	5.946	1.275	0.998	0.002
I.Lymphoid	0	3474	55	3.773	1.342	0.997	0.003
I.Lymphoid	0	4459	84	4.452	1.570	0.997	0.003
I.Lymphoid	0	3794	36	3.590	1.424	0.998	0.002
I.Lymphoid	0	5543	633	4.577	3.224	0.957	0.043
I.Lymphoid	0	4340	623	4.262	4.865	0.821	0.179
I.Lymphoid	0	3425	123	4.186	1.085	0.996	0.004
I.Lymphoid	0	5360	766	3.943	2.738	0.942	0.058
I.Lymphoid	0	3266	302	2.824	1.917	0.953	0.047
I.Lymphoid	0	3701	469	3.393	1.843	0.959	0.041
I.Lymphoid	0	5118	2541	5.374	3.490	0.881	0.119
I.Lymphoid	0	3944	330	4.659	3.021	0.974	0.026
I.Lymphoid	0	5618	178	3.758	1.359	0.994	0.006
I.Lymphoid	0	4248	586	3.189	2.168	0.936	0.064
I.Lymphoid	0	4692	364	4.507	2.525	0.981	0.019
I.Lymphoid	0	4741	147	4.535	1.971	0.995	0.005
M.CD69pos Mast	0	1123	6490	6.312	4.300	0.411	0.589
M.CD69pos Mast	0	993	3547	5.806	3.295	0.615	0.385
M.CD69pos Mast	0	813	2506	4.718	2.379	0.621	0.379
M.CD69pos Mast	0	1124	144	9.027	7.355	0.961	0.039
M.CD69pos Mast	0	835	630	4.462	1.515	0.911	0.089
M.DCs	0	751	463	4.164	4.386	0.582	0.418
M.DCs	0	794	3651	8.113	5.410	0.586	0.414
M.DCs	0	690	242	3.712	2.844	0.839	0.161
M.DCs	0	792	4441	7.237	4.407	0.559	0.441
M.DCs	0	759	1369	3.847	2.861	0.523	0.477
M.DCs	0	705	637	3.162	3.124	0.532	0.468
M.DCs	0	793	1729	6.636	4.414	0.681	0.319
M.DCs	0	792	1535	6.940	4.638	0.718	0.282
M.DCs	0	785	775	5.480	4.250	0.704	0.296
M.DCs	0	781	1025	4.857	3.358	0.683	0.317
M.DCs	0	794	1950	7.880	5.598	0.665	0.335
M.DCs	0	794	2305	6.995	4.605	0.644	0.356
M.DCs	0	727	1079	5.291	3.724	0.666	0.334
M.DCs	0	713	452	3.452	3.275	0.641	0.359
M.DCs	0	761	779	6.025	4.610	0.723	0.277
M.Macrophages	0	1259	981	4.367	2.516	0.822	0.178
M.Macrophages	0	1604	315	4.880	3.984	0.905	0.095
M.Macrophages	0	1604	193	6.399	4.403	0.971	0.029
M.Macrophages	0	1551	182	6.180	4.112	0.973	0.027
M.Macrophages	0	1591	168	5.922	4.068	0.972	0.028
M.Macrophages	0	1779	3605	7.519	5.211	0.710	0.290
M.Macrophages	0	1706	4504	6.494	4.310	0.632	0.368
M.Macrophages	0	1350	2231	4.318	2.083	0.740	0.260
M.Macrophages	0	1380	2970	4.750	2.506	0.688	0.312
M.Macrophages	0	1138	1656	3.421	1.644	0.702	0.298
M.Macrophages	0	1616	5507	5.357	3.728	0.476	0.524
M.Macrophages	0	1356	167	4.750	3.405	0.954	0.046
M.Macrophages	0	1529	569	4.931	4.204	0.816	0.184
M.Macrophages	0	1354	3286	4.180	2.604	0.551	0.449

TABLE 12-continued

Additional Cell Type Markers							
M.Macrophages	0	1792	7034	9.465	5.572	0.791	0.209
M.Macrophages	0	1114	1352	4.300	1.573	0.845	0.155
M.Macrophages	0	1628	3460	4.771	2.665	0.669	0.331
M.Macrophages	0	1398	1302	4.047	2.615	0.743	0.257
M.Macrophages	0	1249	553	3.713	2.569	0.833	0.167
M.Macrophages	0	1696	1686	6.184	4.077	0.813	0.187
M.Macrophages	0	1741	1435	6.354	4.449	0.820	0.180
M.Macrophages	0	1587	646	5.108	3.988	0.842	0.158
M.Macrophages	0	1440	922	4.304	3.316	0.756	0.244
M.Macrophages	0	1770	1877	7.374	5.256	0.804	0.196
M.Macrophages	0	1741	2216	6.563	4.333	0.787	0.213
M.Macrophages	0	1331	1031	5.158	3.414	0.812	0.188
M.Macrophages	0	1000	96	3.324	2.648	0.943	0.057
M.Macrophages	0	1129	1343	3.886	1.713	0.791	0.209
M.Macrophages	0	1271	364	3.376	3.304	0.786	0.214
M.Macrophages	0	1511	670	5.912	4.114	0.887	0.113
M.Macrophages	0	890	68	2.914	1.915	0.963	0.037
M.Macrophages	0	1342	175	4.006	3.216	0.930	0.070
M.Macrophages	0	1099	121	3.368	2.594	0.940	0.060
M.Macrophages	0	1572	3624	4.921	2.750	0.661	0.339
M.Macrophages	0	1546	3595	5.063	2.492	0.719	0.281
M.Macrophages	0	1008	1558	5.248	2.858	0.772	0.228
M.Macrophages	0	1245	2803	3.727	2.193	0.563	0.437
M.Macrophages	0	1527	4245	4.435	3.320	0.438	0.562
M.Macrophages	0	1671	4532	5.541	3.360	0.626	0.374
M.Macrophages	0	1471	2221	5.315	3.691	0.671	0.329
M.Macrophages	0	898	90	2.765	1.742	0.953	0.047
M.Macrophages	0	1801	7464	8.586	7.077	0.407	0.593
M.Macrophages	0	1631	568	5.310	4.061	0.872	0.128
M.Mast	0	892	2099	4.344	2.247	0.645	0.355
M.Mast	0	1265	6569	6.234	4.296	0.425	0.575
M.Mast	0	1076	3546	5.738	3.286	0.624	0.376
M.Mast	0	869	2424	4.659	2.349	0.640	0.360
M.Mast	0	1269	116	9.035	3.446	0.998	0.002
M.Mast	0	965	593	4.446	0.972	0.948	0.052
M.Monocytes	0	1897	874	4.019	2.490	0.862	0.138
M.Monocytes	0	2857	156	4.719	2.195	0.991	0.009
M.Monocytes	0	1815	508	2.944	3.082	0.764	0.236
M.Monocytes	0	2307	114	6.165	2.078	0.997	0.003
M.Monocytes	0	2133	103	5.989	2.142	0.997	0.003
M.Monocytes	0	2209	95	5.739	2.159	0.996	0.004
M.Monocytes	0	1463	275	2.488	2.625	0.829	0.171
M.Monocytes	0	3091	3493	7.652	4.889	0.857	0.143
M.Monocytes	0	2424	2140	3.732	2.793	0.685	0.315
M.Monocytes	0	1908	80	3.354	1.253	0.990	0.010
M.Monocytes	0	3008	4313	6.722	4.040	0.817	0.183
M.Monocytes	0	2157	2153	3.992	1.897	0.811	0.189
M.Monocytes	0	2909	5455	5.153	3.680	0.597	0.403
M.Monocytes	0	2106	64	4.561	1.775	0.996	0.004
M.Monocytes	0	1712	141	2.960	2.399	0.947	0.053
M.Monocytes	0	2662	401	4.673	4.038	0.912	0.088
M.Monocytes	0	1818	292	2.889	2.044	0.918	0.082
M.Monocytes	0	3110	7054	9.015	5.357	0.848	0.152
M.Monocytes	0	2856	3292	4.577	2.548	0.780	0.220
M.Monocytes	0	2563	1179	3.945	2.455	0.859	0.141
M.Monocytes	0	2288	465	3.482	2.480	0.908	0.092
M.Monocytes	0	2982	1495	6.259	3.531	0.930	0.070
M.Monocytes	0	3026	1289	6.486	3.739	0.940	0.060
M.Monocytes	0	2772	544	5.172	3.422	0.945	0.055
M.Monocytes	0	1395	205	3.329	2.362	0.930	0.070
M.Monocytes	0	2620	767	4.448	2.817	0.914	0.086
M.Monocytes	0	1336	110	2.684	2.345	0.939	0.061
M.Monocytes	0	3082	1688	7.493	4.610	0.931	0.069
M.Monocytes	0	3046	2056	6.647	3.831	0.913	0.087
M.Monocytes	0	2468	850	5.151	2.923	0.932	0.068
M.Monocytes	0	1602	70	4.341	1.876	0.992	0.008
M.Monocytes	0	1725	547	2.594	2.639	0.754	0.246
M.Monocytes	0	2208	1427	3.181	3.343	0.580	0.420
M.Monocytes	0	2760	2651	5.009	4.777	0.550	0.450
M.Monocytes	0	2437	224	3.487	2.716	0.949	0.051
M.Monocytes	0	2709	513	5.972	2.582	0.982	0.018
M.Monocytes	0	2287	51	3.900	2.227	0.993	0.007
M.Monocytes	0	1745	54	3.150	2.092	0.985	0.015
M.Monocytes	0	2775	3440	4.601	2.716	0.749	0.251
M.Monocytes	0	1744	855	3.547	2.139	0.844	0.156
M.Monocytes	0	2672	3468	4.656	2.351	0.792	0.208
M.Monocytes	0	2279	1706	3.213	2.735	0.651	0.349
M.Monocytes	0	1651	203	2.735	1.357	0.955	0.045

TABLE 12-continued

Additional Cell Type Markers							
M.Monocytes	0	2301	2679	3.514	2.173	0.685	0.315
M.Monocytes	0	2739	4164	4.264	3.231	0.574	0.426
M.Monocytes	0	2962	4464	5.344	3.186	0.748	0.252
M.Monocytes	0	2057	196	2.895	1.824	0.957	0.043
M.Monocytes	0	3122	7474	8.491	7.064	0.529	0.471
M.Monocytes	0	2380	2020	3.528	2.135	0.756	0.244
M.Monocytes	0	2822	362	5.067	3.625	0.955	0.045
M.Myeloid	0	2919	140	4.702	2.218	0.992	0.008
M.Myeloid	0	2321	124	6.159	1.666	0.998	0.002
M.Myeloid	0	2150	125	5.980	1.824	0.997	0.003
M.Myeloid	0	2223	93	5.732	1.822	0.997	0.003
M.Myeloid	0	3288	3628	7.571	4.821	0.859	0.141
M.Myeloid	0	3580	4368	6.509	4.044	0.819	0.181
M.Myeloid	0	3625	5451	4.985	3.677	0.622	0.378
M.Myeloid	0	2111	81	4.559	1.796	0.994	0.006
M.Myeloid	0	3593	235	4.604	3.771	0.965	0.035
M.Myeloid	0	4393	7356	7.972	6.710	0.589	0.411
M.Myeloid	0	4387	7036	8.638	5.278	0.865	0.135
M.Myeloid	0	2545	1392	3.591	1.731	0.869	0.131
M.Myeloid	0	3403	3404	4.467	2.435	0.804	0.196
M.Myeloid	0	2644	1244	3.926	2.383	0.861	0.139
M.Myeloid	0	2300	439	3.484	2.295	0.923	0.077
M.Myeloid	0	3135	1526	6.198	3.482	0.931	0.069
M.Myeloid	0	3111	1304	6.454	3.554	0.947	0.053
M.Myeloid	0	2798	529	5.165	3.338	0.949	0.051
M.Myeloid	0	1400	208	3.331	2.234	0.935	0.065
M.Myeloid	0	2648	787	4.439	2.881	0.908	0.092
M.Myeloid	0	3181	1708	7.454	4.571	0.932	0.068
M.Myeloid	0	3202	2024	6.585	3.810	0.915	0.085
M.Myeloid	0	2535	866	5.121	2.926	0.931	0.069
M.Myeloid	0	2494	230	3.483	3.035	0.937	0.063
M.Myeloid	0	2749	527	5.960	2.455	0.983	0.017
M.Myeloid	0	2300	48	3.900	1.788	0.995	0.005
M.Myeloid	0	3387	3537	4.481	2.615	0.777	0.223
M.Myeloid	0	3206	3517	4.532	2.297	0.811	0.189
M.Myeloid	0	3391	4180	4.220	3.215	0.620	0.380
M.Myeloid	0	3745	4510	5.191	3.125	0.777	0.223
M.Myeloid	0	3737	2618	4.753	4.074	0.696	0.304
M.Myeloid	0	4407	7468	8.202	7.029	0.571	0.429
M.Myeloid	0	3501	255	4.897	3.573	0.972	0.028
M.Tissue_DCs	0	643	481	4.281	4.460	0.541	0.459
M.Tissue_DCs	0	672	3634	8.013	5.364	0.537	0.463
M.Tissue_DCs	0	578	146	3.803	3.080	0.867	0.133
M.Tissue_DCs	0	670	4472	7.124	4.451	0.489	0.511
M.Tissue_DCs	0	643	1368	3.884	2.767	0.505	0.495
M.Tissue_DCs	0	671	1759	6.577	4.420	0.630	0.370
M.Tissue_DCs	0	670	1484	6.863	4.773	0.658	0.342
M.Tissue_DCs	0	663	738	5.457	4.290	0.669	0.331
M.Tissue_DCs	0	662	1000	4.815	3.367	0.644	0.356
M.Tissue_DCs	0	672	1937	7.874	5.574	0.631	0.369
M.Tissue_DCs	0	672	2279	6.984	4.587	0.608	0.392
M.Tissue_DCs	0	622	462	3.581	3.366	0.610	0.390
M.Tissue_DCs	0	640	782	6.080	4.547	0.703	0.297
T.CD4	0	5187	2552	4.312	3.578	0.772	0.228
T.CD4	0	6115	7425	7.908	6.955	0.615	0.385
T.CD4	0	5262	4406	4.793	3.354	0.764	0.236
T.CD4	0	4067	522	3.823	3.702	0.894	0.106
T.CD4	0	5156	643	4.361	4.376	0.888	0.112
T.CD4	0	4233	549	3.570	3.491	0.891	0.109
T.CD4	0	5137	1523	4.538	4.307	0.798	0.202
T.CD4	0	6074	7227	6.822	5.836	0.625	0.375
T.CD4	0	5533	2804	5.278	4.263	0.800	0.200
T.CD4	0	4588	886	4.766	4.230	0.883	0.117
T.CD4	0	6079	7288	7.129	6.260	0.604	0.396
T.CD4	0	5989	6942	6.135	5.158	0.629	0.371
T.CD4	0	6061	7192	6.695	5.717	0.624	0.376
T.CD4	0	6034	7017	6.324	5.430	0.615	0.385
T.CD4	0	5855	6596	5.349	4.369	0.637	0.363
T.CD4	0	6030	7028	6.381	5.184	0.663	0.337
T.CD4	0	5927	6769	5.913	4.944	0.631	0.369
T.CD4	0	5988	6999	6.052	5.244	0.600	0.400
T.CD4	0	4285	3675	3.757	2.468	0.740	0.260
T.CD4	0	6122	7459	7.932	7.047	0.602	0.398
T.CD4	0	5232	948	4.671	3.876	0.905	0.095
T.CD4	0	5075	837	4.719	4.066	0.905	0.095
T.CD8	0	4141	7129	6.459	5.447	0.540	0.460
T.CD8	0	3679	2662	4.342	3.756	0.675	0.325
T.CD8	0	4167	7446	8.044	7.029	0.531	0.469

TABLE 12-continued

Additional Cell Type Markers

T.CD8	0	3896	699	6.285	4.684	0.944	0.056
T.CD8	0	3622	1088	4.617	4.237	0.812	0.188
T.CD8	0	3183	896	3.706	3.503	0.804	0.196
T.CD8	0	3668	1773	4.811	4.187	0.761	0.239
T.CD8	0	3012	783	4.335	3.569	0.867	0.133
T.CD8	0	3458	1801	4.144	3.610	0.735	0.265
T.CD8	0	2775	1166	3.555	2.976	0.780	0.220
T.CD8	0	2956	344	5.852	4.682	0.951	0.049
T.CD8	0	3117	1132	3.782	3.025	0.823	0.177
T.CD8	0	2194	318	3.874	3.303	0.911	0.089
T.CD8	0	4007	3265	5.519	4.367	0.732	0.268
T.CD8	0	3166	315	4.585	4.231	0.928	0.072
T.CD8	0	3384	1619	4.095	3.450	0.766	0.234
T.CD8	0	3856	5624	4.736	3.749	0.576	0.424
T.CD8	0	4168	7463	8.386	7.040	0.587	0.413
T.CD8	0	3505	1405	4.545	4.333	0.743	0.257
T.CD8	0	3498	1277	4.549	4.496	0.740	0.260
T.CD8_IELs	0	1582	1004	6.549	5.273	0.792	0.208
T.CD8_IELs	0	1364	1360	4.702	4.376	0.557	0.443
T.CD8_IELs	0	1486	1995	4.865	4.341	0.517	0.483
T.CD8_IELs	0	1414	1003	4.790	3.630	0.759	0.241
T.CD8_IELs	0	1211	424	4.054	3.412	0.817	0.183
T.CD8_IELs	0	1552	3461	5.772	4.518	0.517	0.483
T.CD8_IELs	0	1311	593	4.406	4.614	0.657	0.343
T.CD8 LP	0	1849	931	6.222	5.372	0.782	0.218
T.CD8 LP	0	1523	544	4.793	4.225	0.806	0.194
T.Tcells	0	7176	7092	6.254	5.363	0.652	0.348
T.Tcells	0	6214	2208	4.290	3.309	0.847	0.153
T.Tcells	0	7263	7424	7.915	6.800	0.679	0.321
T.Tcells	0	6125	4331	4.691	3.042	0.816	0.184
T.Tcells	0	4168	350	5.968	3.879	0.981	0.019
T.Tcells	0	4718	126	3.815	2.607	0.989	0.011
T.Tcells	0	6220	143	4.461	1.922	0.996	0.004
T.Tcells	0	5275	90	3.603	2.457	0.992	0.008
T.Tcells	0	6205	1100	4.606	3.906	0.902	0.098
T.Tcells	0	4463	217	4.085	3.492	0.969	0.031
T.Tcells	0	3661	2127	3.412	1.851	0.835	0.165
T.Tcells	0	5641	1278	4.004	3.324	0.876	0.124
T.Tcells	0	4420	669	3.464	2.212	0.940	0.060
T.Tcells	0	2751	189	5.826	4.113	0.979	0.021
T.Tcells	0	4351	749	3.584	2.617	0.919	0.081
T.Tcells	0	2136	218	3.775	3.224	0.935	0.065
T.Tcells	0	3819	1590	3.287	1.717	0.877	0.123
T.Tcells	0	6717	2386	5.388	3.569	0.909	0.091
T.Tcells	0	3982	177	3.294	2.299	0.978	0.022
T.Tcells	0	4454	687	4.631	4.205	0.897	0.103
T.Tcells	0	5665	5265	4.016	3.130	0.665	0.335
T.Tcells	0	2809	225	4.479	4.344	0.932	0.068
T.Tcells	0	5519	1057	3.917	2.940	0.911	0.089
T.Tcells	0	4119	1178	3.375	2.293	0.881	0.119
T.Tcells	0	7206	7197	6.564	5.647	0.654	0.346
T.Tcells	0	7191	7013	6.286	5.318	0.667	0.333
T.Tcells	0	7181	7033	6.297	5.052	0.708	0.292
T.Tcells	0	7057	6748	5.806	4.867	0.667	0.333
T.Tcells	0	6212	5466	4.504	3.586	0.682	0.318
T.Tcells	0	4941	3660	3.646	2.209	0.785	0.215
T.Tcells	0	7271	7444	8.103	6.826	0.703	0.297
T.Tcells	0	6163	451	4.592	2.553	0.983	0.017
T.Tcells	0	6049	358	4.642	2.673	0.985	0.015

TABLE 13

Inflamed vs Healthy Markers

ident	gene	coefD	pvalD	coefC	pvalC	mastfc
B.Bcells	AC009501.4	–0.840	3.95E–34	2.53E–01	2.55E–07	–0.741
B.Bcells	ACAP1	1.066	1.15E–42	6.23E–01	2.91E–34	0.707
B.Bcells	ACP5	0.764	2.94E–22	8.02E–01	9.84E–33	0.540
B.Bcells	ACTG1	0.518	8.84E–07	1.33E+00	2.04E–185	1.239
B.Bcells	ACTR3	0.992	1.10E–43	6.71E–01	2.51E–48	0.544
B.Bcells	ALOX5AP	1.429	5.97E–60	4.36E–01	1.73E–10	1.430
B.Bcells	ARHGDIB	0.800	1.93E–23	8.96E–01	1.64E–90	1.398
B.Bcells	ARPC1B	0.824	2.50E–30	9.25E–01	1.70E–84	1.086
B.Bcells	ARPC2	0.596	1.17E–08	9.73E–01	2.29E–138	0.656

TABLE 13-continued

Inflamed vs Healthy Markers						
B.Bcells	ARPC5	1.043	3.72E–46	7.81E–01	3.25E–61	0.815
B.Bcells	ATP5E	0.560	6.15E–08	7.70E–01	4.66E–104	0.767
B.Bcells	BATF	2.091	1.33E–43	5.98E–01	8.77E–06	0.637
B.Bcells	CAP1	0.816	9.89E–29	5.78E–01	6.04E–39	0.511
B.Bcells	CAPZB	0.616	1.83E–16	7.46E–01	2.09E–66	0.575
B.Bcells	CD37	0.709	1.90E–24	8.98E–01	7.79E–70	0.856
B.Bcells	CD52	0.831	1.88E–32	1.34E+00	1.78E–101	1.800
B.Bcells	CD53	0.836	1.56E–32	9.36E–01	3.51E–91	0.723
B.Bcells	CFL1	0.552	6.13E–07	9.86E–01	2.82E–121	1.185
B.Bcells	CORO1A	1.217	3.24E–65	1.17E+00	4.13E–96	1.971
B.Bcells	COTL1	1.254	1.98E–62	6.23E–01	4.95E–23	1.044
B.Bcells	DHRS9	2.923	1.56E–85	5.75E–01	3.94E–04	1.495
B.Bcells	DUOXA2	4.226	3.70E–21		1.00E+00	2.568
B.Bcells	EVL	1.158	1.79E–47	6.17E–01	1.75E–27	1.267
B.Bcells	GAPDH	0.738	9.52E–08	1.03E+00	3.18E–140	1.167
B.Bcells	GBP1	1.930	1.69E–33	6.71E–01	2.07E–07	0.656
B.Bcells	GBP2	1.390	1.19E–22	9.89E–01	1.58E–21	0.920
B.Bcells	GPSM3	0.679	8.63E–23	5.98E–01	4.20E–42	0.515
B.Bcells	H3F3A	0.586	1.26E–06	7.04E–01	4.66E–76	0.772
B.Bcells	HLA-DMA	1.086	8.58E–54	6.11E–01	1.35E–30	0.600
B.Bcells	HLA-DPA1	0.602	1.74E–16	1.03E+00	7.98E–50	0.803
B.Bcells	HLA-DPB1	0.797	5.81E–31	9.67E–01	2.04E–33	1.059
B.Bcells	HLA-DQA1	0.880	5.41E–37	9.73E–01	5.18E–45	0.661
B.Bcells	HLA-DRA	0.580	5.76E–16	1.16E+00	4.34E–34	0.783
B.Bcells	HLA-DRB1	0.686	1.94E–22	1.17E+00	1.06E–48	0.905
B.Bcells	HOPX	1.829	2.48E–45	5.15E–01	3.43E–05	1.804
B.Bcells	IGHA1	–1.355	4.90E–48	–2.56E+00	7.40E–136	–2.004
B.Bcells	IGHA2	–1.541	4.79E–99	–2.61E+00	2.21E–114	–0.952
B.Bcells	IGJ	–1.186	3.38E–47	–1.77E+00	8.06E–84	–0.915
B.Bcells	ITGB2	1.489	9.36E–57	7.06E–01	3.79E–24	0.847
B.Bcells	LAPTM5	1.327	2.70E–77	8.69E–01	3.53E–46	1.557
B.Bcells	LCP1	1.729	2.92E–84	3.32E–01	5.59E–07	0.967
B.Bcells	LIMD2	1.040	1.95E–50	9.12E–01	1.30E–62	0.786
B.Bcells	LSP1	0.374	2.12E–07	6.18E–01	3.73E–62	0.502
B.Bcells	LST1	1.447	3.82E–25	3.84E–01	3.07E–03	0.703
B.Bcells	LTB	0.945	1.56E–39	5.70E–01	5.62E–14	1.258
B.Bcells	MT-ND3	0.437	1.64E–09	9.87E–01	6.68E–38	0.631
B.Bcells	MYL12A	0.262	1.13E–03	6.57E–01	2.57E–55	0.513
B.Bcells	PKM	0.751	7.21E–24	8.45E–01	1.18E–69	0.595
B.Bcells	PPIA	0.727	4.42E–17	7.26E–01	8.00E–72	0.781
B.Bcells	PPP1R18	1.280	7.03E–49	7.09E–01	5.00E–35	0.682
B.Bcells	PSMB9	0.578	2.60E–15	6.89E–01	6.34E–69	0.502
B.Bcells	PTPRC	1.464	7.12E–70	4.40E–01	9.28E–13	1.071
B.Bcells	PTPRCAP	0.753	8.87E–21	1.05E+00	1.61E–120	1.056
B.Bcells	RAC2	0.712	2.69E–24	7.58E–01	4.61E–74	0.552
B.Bcells	RPL17	–1.084	1.83E–41	–1.24E–01	6.59E–04	–0.663
B.Bcells	RPS24	0.267	7.32E–02	7.49E–01	5.36E–76	0.556
B.Bcells	SERF2	0.495	6.78E–03	5.69E–01	1.17E–67	0.752
B.Bcells	SOCS1	1.066	8.64E–34	5.95E–01	2.20E–19	0.518
B.Bcells	STMN1	0.845	9.34E–21	1.15E+00	2.85E–32	0.559
B.Bcells	TTC39C	1.991	1.01E–20	2.00E–01	2.17E–01	0.651
B.Bcells	UCP2	1.124	2.55E–55	6.00E–01	1.13E–27	0.688
B.Cycling	ACTB	1.210	5.44E–02	2.80E+00	4.48E–85	3.533
B.Cycling	ACTG1	1.344	2.46E–04	1.59E+00	2.71E–41	2.152
B.Cycling	ACTR3	1.650	1.29E–13	8.00E–01	3.56E–12	1.051
B.Cycling	ARHGDIB	1.737	1.49E–10	1.54E+00	7.59E–35	2.945
B.Cycling	ARPC1B	1.372	1.64E–09	1.05E+00	5.92E–17	1.678
B.Cycling	ARPC2	1.134	2.00E–03	1.47E+00	3.77E–46	1.514
B.Cycling	ARPC3	1.198	2.47E–05	1.13E+00	1.48E–26	1.208
B.Cycling	ARPC5	1.874	1.37E–16	7.33E–01	4.59E–09	1.374
B.Cycling	CD53	1.217	3.35E–09	1.30E+00	4.46E–26	1.383
B.Cycling	CORO1A	2.167	8.33E–21	1.63E+00	1.66E–31	3.301
B.Cycling	GAPDH	3.021	2.42E–04	1.73E+00	1.17E–52	4.052
B.Cycling	H2AFZ	0.760	5.45E–02	1.46E+00	3.54E–40	0.961
B.Cycling	HLA-DPA1	1.450	1.27E–11	1.31E+00	8.25E–10	1.891
B.Cycling	HLA-DRA	1.884	2.94E–17	1.66E+00	1.86E–09	2.805
B.Cycling	HMGB1	2.006	3.96E–07	1.71E+00	6.45E–51	2.517
B.Cycling	HMGB2	1.657	2.93E–12	1.13E+00	8.29E–17	1.265
B.Cycling	HMGN1	1.706	4.25E–09	1.11E+00	1.15E–24	1.579
B.Cycling	HMGN2	1.559	2.18E–07	1.80E+00	6.33E–57	1.922
B.Cycling	HNRNPA1	0.889	1.13E–02	1.35E+00	2.77E–37	1.422
B.Cycling	HNRNPA2B1	1.175	1.93E–05	1.28E+00	6.89E–32	1.187
B.Cycling	HNRNPK	1.101	8.09E–06	1.04E+00	1.77E–23	0.841
B.Cycling	LAPTM5	1.865	3.52E–20	8.75E–01	1.07E–08	2.088
B.Cycling	LAT2	2.014	5.93E–19	4.85E–01	9.69E–03	0.632
B.Cycling	LCP1	2.072	5.27E–22	–4.47E–02	7.54E–01	1.018
B.Cycling	LDHA	1.530	1.23E–09	9.28E–01	7.24E–14	1.346
B.Cycling	LDHB	1.097	7.52E–06	1.00E+00	8.69E–20	1.187

TABLE 13-continued

Inflamed vs Healthy Markers

B.Cycling	LIMD2	1.883	2.98E–20	7.23E–01	2.17E–07	1.574
B.Cycling	MS4A1	2.125	1.51E–22	5.90E–01	5.47E–03	0.516
B.Cycling	NAP1L1	1.046	4.82E–07	9.50E–01	4.50E–17	0.916
B.Cycling	NCF1	0.935	2.95E–06	1.04E+00	4.82E–20	0.622
B.Cycling	NPM1	0.917	8.69E–03	1.09E+00	3.34E–24	1.375
B.Cycling	PKM	1.263	1.73E–07	1.33E+00	1.14E–28	1.033
B.Cycling	RAC2	1.456	4.14E–12	1.06E+00	1.28E–18	1.554
B.Cycling	RAN	1.151	1.12E–05	1.10E+00	1.24E–24	0.943
B.Cycling	RPL39	0.407	6.43E–02	1.85E+00	1.29E–21	0.602
B.Cycling	STMN1	1.816	2.22E–15	7.47E–01	1.12E–07	1.165
B.Cycling	TUBA1B	1.809	5.39E–09	1.60E+00	3.95E–33	2.359
B.Cycling	TUBB	1.915	1.40E–13	1.43E+00	5.06E–31	2.022
B.FO	ACAP1	1.242	4.69E–20	3.91E–01	2.55E–06	0.810
B.FO	ACP5	1.487	1.63E–28	3.10E–01	5.22E–03	0.949
B.FO	ACTB	0.101	8.13E–01	1.25E+00	6.28E–44	0.799
B.FO	ACTG1	0.573	3.21E–03	8.80E–01	3.05E–32	0.844
B.FO	ALOX5AP	1.327	1.53E–20	8.10E–02	4.32E–01	1.142
B.FO	ARHGDIB	1.129	5.19E–13	4.51E–01	1.28E–09	1.511
B.FO	ARPC1B	0.705	1.42E–07	5.79E–01	1.76E–14	0.757
B.FO	BATF	2.222	1.48E–21	3.48E–01	1.15E–01	0.878
B.FO	BIRC3	1.205	3.46E–20	1.41E–01	1.32E–01	0.501
B.FO	CD48	1.132	3.70E–19	3.05E–01	2.67E–05	0.952
B.FO	CD52	0.743	2.15E–06	9.97E–01	5.23E–34	1.419
B.FO	CD53	1.245	6.33E–21	4.51E–01	1.57E–10	1.043
B.FO	CLEC2B	1.793	2.09E–21	3.04E–01	2.69E–02	1.020
B.FO	CORO1A	1.454	2.43E–22	7.04E–01	3.11E–20	1.896
B.FO	COTL1	1.048	4.20E–16	5.22E–01	8.07E–10	0.742
B.FO	DHRS9	3.753	1.38E–33	5.78E–01	2.16E–01	2.150
B.FO	EPSTI1	1.920	2.42E–19	1.41E–01	3.51E–01	0.503
B.FO	EVL	1.416	2.07E–26	1.64E–01	5.08E–02	1.268
B.FO	GBP1	2.259	2.65E–20	2.87E–01	1.59E–01	0.853
B.FO	GBP2	2.682	1.37E–30	5.04E–01	9.17E–03	1.837
B.FO	GBP4	3.236	3.95E–29	9.92E–02	7.16E–01	1.130
B.FO	GMFG	1.019	7.41E–16	3.64E–01	1.86E–06	1.069
B.FO	GYPC	1.437	8.07E–29	5.61E–01	1.60E–14	1.382
B.FO	HCLS1	1.059	2.60E–15	4.10E–01	1.73E–07	0.531
B.FO	HCST	1.403	3.21E–19	1.92E–01	8.82E–02	1.350
B.FO	HLA-B	0.225	5.45E–01	7.46E–01	9.81E–24	0.553
B.FO	HOPX	2.240	2.75E–28	4.97E–01	9.34E–03	2.321
B.FO	IGJ	–1.260	2.53E–23	1.53E–01	5.27E–01	–1.065
B.FO	IRF1	1.113	3.14E–16	4.47E–01	5.43E–06	0.766
B.FO	ITGB2	2.100	6.23E–40	1.20E–01	2.89E–01	1.190
B.FO	LAPTM5	1.462	1.98E–27	5.88E–01	7.58E–16	1.526
B.FO	LCP1	1.555	4.77E–26	2.13E–02	8.12E–01	0.755
B.FO	LIMD2	1.238	6.56E–22	4.73E–01	7.16E–11	0.796
B.FO	LSP1	1.126	2.19E–18	2.86E–01	7.86E–05	1.147
B.FO	LY6E	1.309	5.92E–21	–4.74E–02	6.41E–01	1.071
B.FO	PPP1R18	1.690	4.06E–29	1.40E–01	1.15E–01	0.801
B.FO	PTPRC	1.577	1.92E–30	2.07E–01	1.66E–02	1.058
B.FO	PTPRCAP	1.252	3.80E–17	7.36E–01	1.25E–22	1.585
B.FO	RAC2	1.128	1.74E–18	3.32E–01	2.36E–06	0.899
B.FO	RHOH	0.947	7.00E–14	4.86E–01	4.32E–10	0.558
B.FO	RPS4Y1	0.994	6.52E–12	7.54E–01	2.92E–10	0.866
B.FO	6-Sep	1.453	5.58E–25	2.92E–01	1.55E–03	0.543
B.FO	SOCS1	1.798	1.08E–25	–5.09E–02	6.99E–01	0.987
B.FO	VAMP5	1.550	7.55E–21	2.74E–01	4.35E–02	1.038
B.GC	ACTB	1.429	8.36E–02	1.66E+00	1.28E–20	2.884
B.GC	CD52	2.524	1.96E–13	1.05E+00	7.19E–10	3.356
B.GC	HLA-DQB1	2.254	2.57E–14	1.08E+00	6.51E–08	1.945
B.Plasma	DHRS9	2.692	8.88E–27	9.71E–01	2.14E–04	1.535
B.Plasma	IGHA1	–3.590	2.13E–23	–2.33E+00	3.21E–130	–3.007
B.Plasma	IGHA2	–3.629	1.96E–55	–2.81E+00	4.82E–125	–1.563
B.Plasma	IGJ	–4.003	1.81E–27	–1.59E+00	2.78E–94	–1.620
B.Plasma	MS4A1	2.416	2.90E–17	1.58E+00	2.93E–05	1.191
B.Plasma	RGS2	–1.140	4.07E–23	–2.48E–01	1.12E–04	–0.544
B.Plasma	RPL17	–1.494	1.00E–23	–1.48E–01	2.75E–03	–0.956
E.Absorptive	AC009501.4	–2.051	2.54E–62	5.49E–01	9.89E–08	–1.515
E.Absorptive	B2M	–1.377	5.95E–02	7.43E–01	1.29E–21	–1.703
E.Absorptive	BIRC3	1.039	2.28E–17	8.71E–01	3.54E–28	0.513
E.Absorptive	C2	2.730	2.21E–32	3.39E–01	5.88E–02	0.892
E.Absorptive	C4orf3	0.745	1.22E–07	7.64E–01	1.16E–38	0.515
E.Absorptive	CA2	–1.604	6.80E–18	–7.71E–01	3.08E–18	–0.504
E.Absorptive	CXCL1	3.150	1.07E–42	2.61E+00	2.15E–09	2.180
E.Absorptive	F3	2.139	1.95E–20	7.40E–01	1.71E–03	0.721
E.Absorptive	FSTL1	3.103	7.52E–19	1.01E+00	4.22E–03	1.251
E.Absorptive	GBP4	2.153	7.68E–18	7.64E–01	1.26E–05	0.564
E.Absorptive	GSN	0.648	5.56E–04	8.55E–01	3.38E–31	0.705
E.Absorptive	HLA-B	0.505	3.69E–01	9.39E–01	8.66E–41	1.084

TABLE 13-continued

Inflamed vs Healthy Markers

E.Absorptive	HLA-DRB1	1.843	7.53E–44	1.27E+00	3.16E–26	2.336
E.Absorptive	HLA-E	0.433	2.54E–02	6.42E–01	1.64E–28	0.564
E.Absorptive	HSPB1	–1.796	1.84E–30	–4.37E–01	1.69E–07	–0.732
E.Absorptive	IDO1	4.788	4.77E–33		1.00E+00	5.394
E.Absorptive	IFI6	1.134	2.63E–10	1.05E+00	9.73E–13	0.541
E.Absorptive	IFITM3	0.973	8.41E–13	1.35E+00	2.01E–33	1.180
E.Absorptive	IL2RG	1.161	3.70E–21	8.22E–01	1.34E–40	0.995
E.Absorptive	ITM2B	0.707	1.18E–03	9.07E–01	4.66E–44	0.935
E.Absorptive	LAPTM4A	0.723	4.42E–06	8.38E–01	1.24E–36	0.501
E.Absorptive	LGALS4	–0.690	2.11E–01	–7.02E–01	3.14E–20	–0.601
E.Absorptive	LPCAT1	2.997	4.17E–24	5.03E–01	4.52E–02	0.520
E.Absorptive	MMP7	4.751	1.86E–24		1.00E+00	5.394
E.Absorptive	MUC12	1.647	3.32E–17	1.41E+00	2.18E–100	0.726
E.Absorptive	PARP8	3.844	1.43E–27	–3.03E–01	5.12E–01	0.836
E.Absorptive	PDLIM7	1.800	1.73E–18	7.62E–01	9.29E–09	0.596
E.Absorptive	PFKFB3	2.431	9.07E–32	5.85E–01	1.06E–05	0.504
E.Absorptive	PLA2G16	1.381	1.15E–15	5.83E–01	9.23E–07	0.585
E.Absorptive	PLA2G2A	1.639	6.27E–32	1.55E+00	9.26E–36	0.508
E.Absorptive	PNRC1	0.757	9.17E–09	7.40E–01	3.96E–26	0.579
E.Absorptive	PSMB9	0.626	6.99E–06	8.54E–01	3.79E–46	0.607
E.Absorptive	PSME2	1.164	6.57E–08	8.15E–01	1.40E–45	1.088
E.Absorptive	RARRES3	1.558	3.64E–33	9.72E–01	9.80E–54	1.625
E.Absorptive	REG4	2.931	1.55E–43	1.65E+00	5.19E–05	1.418
E.Absorptive	RNASE1	1.637	6.05E–30	1.30E+00	1.50E–41	0.982
E.Absorptive	S100A11	0.839	5.39E–09	1.67E+00	3.16E–88	1.341
E.Absorptive	S100A6	1.276	3.38E–01	7.96E–01	2.13E–21	1.728
E.Absorptive	S100A9	3.985	1.12E–37	1.99E+00	9.81E–03	1.209
E.Absorptive	SEPPI	0.558	5.30E–05	1.09E+00	4.66E–33	0.759
E.Absorptive	SLC25A6	–1.779	6.80E–19	–4.44E–01	1.48E–12	–0.644
E.Absorptive	SLC6A14	5.158	8.49E–41		1.00E+00	5.394
E.Absorptive	SOCS1	1.130	2.55E–12	1.33E+00	1.08E–27	0.710
E.Absorptive	SOD3	1.634	7.87E–26	1.58E+00	2.74E–27	0.986
E.Absorptive	TFF1	1.636	6.62E–37	1.62E+00	3.71E–43	0.619
E.Absorptive	VAMP5	1.323	1.18E–22	7.36E–01	4.33E–15	0.969
E.Absorptive	VNN1	4.531	1.58E–23		1.00E+00	5.394
E.Absorptive	WARS	1.396	1.04E–14	9.54E–01	3.17E–13	0.538
E.Absorptive_All	AC009501.4	–1.792	1.15E–163	4.81E–01	1.04E–22	–1.362
E.Absorptive_All	AGR2	0.782	6.21E–23	1.04E+00	5.64E–84	0.507
E.Absorptive_All	ANXA5	0.954	2.34E–18	6.57E–01	4.45E–13	0.676
E.Absorptive_All	C2	2.754	1.09E–39	6.00E–01	4.15E–03	1.003
E.Absorptive_All	COX4I1	–0.853	3.27E–12	–5.60E–01	1.37E–65	–0.604
E.Absorptive_All	CXCL1	2.908	9.82E–81	2.04E+00	1.38E–10	1.577
E.Absorptive_All	DAPP1	3.328	2.96E–30	7.70E–01	5.62E–02	0.582
E.Absorptive_All	DDX5	0.523	3.14E–12	6.62E–01	6.50E–62	0.579
E.Absorptive_All	FABP1	–2.045	3.38E–53	–6.57E–01	4.44E–27	–0.617
E.Absorptive_All	FOS	–0.936	1.18E–35	1.75E–01	1.10E–03	–0.671
E.Absorptive_All	FSTL1	2.851	2.95E–25	9.20E–01	1.49E–03	0.968
E.Absorptive_All	FTH1	–0.974	6.31E–03	–4.70E–01	1.01E–22	–1.551
E.Absorptive_All	FTL	–0.747	3.28E–07	–7.28E–01	2.29E–67	–1.280
E.Absorptive_All	GLRA2	4.198	3.03E–23		1.00E+00	4.481
E.Absorptive_All	H3F3B	0.244	8.30E–03	4.44E–01	1.01E–34	0.505
E.Absorptive_All	HLA-DMA	1.347	1.29E–40	7.79E–01	1.67E–16	0.784
E.Absorptive_All	HLA-DMB	1.612	3.18E–22	3.70E–01	2.49E–02	0.680
E.Absorptive_All	HLA-DRB1	1.433	1.16E–88	1.14E+00	7.09E–40	1.590
E.Absorptive_All	IDO1	3.952	7.80E–22		1.00E+00	4.481
E.Absorptive_All	IFI16	2.247	8.22E–31	4.37E–01	1.58E–02	0.943
E.Absorptive_All	IFITM3	0.685	2.16E–19	1.08E+00	6.15E–57	0.795
E.Absorptive_All	IL2RG	1.007	9.58E–45	6.21E–01	2.87E–35	0.751
E.Absorptive_All	JUN	–1.110	8.43E–48	2.69E–03	9.54E–01	–0.593
E.Absorptive_All	KYNU	3.935	1.46E–21		1.00E+00	4.481
E.Absorptive_All	LYZ	1.481	4.03E–35	8.61E–01	9.01E–06	0.718
E.Absorptive_All	MMP7	4.430	1.64E–23		1.00E+00	4.481
E.Absorptive_All	MTRNR2L1	0.449	4.87E–11	1.43E+00	1.57E–43	0.538
E.Absorptive_All	MYL6	–0.955	7.44E–12	–3.37E–01	8.80E–26	–0.673
E.Absorptive_All	OLFM4	1.788	7.27E–98	1.05E+00	4.42E–22	0.655
E.Absorptive_All	PARP8	3.785	6.51E–41	1.48E–01	7.36E–01	1.034
E.Absorptive_All	PHGR1	–2.038	3.78E–17	–6.91E–01	4.99E–42	–0.784
E.Absorptive_All	PLA2G2A	2.131	4.09E–182	1.55E+00	5.54E–96	0.758
E.Absorptive_All	PPDPF	–0.839	3.41E–14	–2.78E–01	3.96E–17	–0.508
E.Absorptive_All	RARRES3	1.064	7.21E–50	6.87E–01	8.29E–39	1.037
E.Absorptive_All	RBPMS	3.743	7.60E–47	7.07E–01	1.04E–01	2.445
E.Absorptive_All	REG4	2.831	9.24E–112	1.58E+00	6.02E–09	1.812
E.Absorptive_All	RNASE1	1.207	2.86E–52	9.10E–01	3.07E–53	0.765
E.Absorptive_All	S100A11	1.169	6.07E–58	1.23E+00	6.71E–148	1.584
E.Absorptive_All	S100A6	0.331	2.90E–01	8.55E–01	1.16E–96	0.820
E.Absorptive_All	S100A9	4.103	5.97E–66	1.24E+00	8.10E–02	1.174
E.Absorptive_All	S100P	3.310	5.39E–308	1.75E+00	2.53E–77	0.906
E.Absorptive_All	SEPP1	0.543	5.00E–17	8.41E–01	1.28E–39	0.565

TABLE 13-continued

Inflamed vs Healthy Markers

E.Absorptive_All	SLC25A6	−1.053	1.01E−33	−3.60E−01	2.98E−24	−0.565
E.Absorptive_All	SLC6A14	4.946	3.95E−49		1.00E+00	4.481
E.Absorptive_All	SOCS1	1.315	1.57E−27	1.10E+00	3.29E−27	0.793
E.Absorptive_All	SOD3	1.638	8.80E−50	1.15E+00	1.53E−20	0.926
E.Absorptive_All	TFF1	1.851	1.10E−135	1.27E+00	1.20E−35	1.028
E.Absorptive_All	TIMP1	3.502	8.11E−199	1.28E+00	1.56E−09	3.673
E.Absorptive_All	TNIP3	4.300	2.15E−59	1.38E+00	3.48E−02	0.639
E.Absorptive_All	TRIM22	2.732	1.06E−24	8.20E−01	1.73E−03	0.823
E.Absorptive_All	VAMP5	1.000	1.29E−23	5.06E−01	6.45E−10	0.612
E.Absorptive_All	VNN1	3.903	9.55E−19		1.00E+00	4.481
E.Absorptive_All	XKR9	4.027	4.63E−21		1.00E+00	4.481
E.Absorptive_TA_1	COX4I1	−1.237	7.85E−14	−4.51E−01	1.06E−10	−0.813
E.Absorptive_TA_1	DUOX2	4.483	9.35E−22		1.00E+00	3.487
E.Absorptive_TA_1	DUOXA2	4.970	1.86E−32		1.00E+00	3.487
E.Absorptive_TA_1	LGALS3	−1.243	2.05E−15	−4.97E−01	1.55E−07	−0.764
E.Absorptive_TA_1	LGALS4	−1.865	1.50E−22	−6.63E−01	2.27E−13	−0.794
E.Absorptive_TA_1	MTRNR2L1	1.007	2.80E−13	1.46E+00	2.30E−12	1.006
E.Absorptive_TA_1	MUC12	1.924	1.08E−41	9.71E−01	2.25E−14	0.746
E.Absorptive_TA_1	PI3	2.873	3.95E−51	1.17E+00	8.61E−04	0.989
E.Absorptive_TA_1	REG4	3.493	3.77E−48	2.00E+00	3.91E−04	1.910
E.Absorptive_TA_1	RPL13A	−1.230	1.49E−06	−6.81E−01	1.08E−19	−1.944
E.Absorptive_TA_1	RPL15	−1.123	3.27E−12	−6.16E−01	1.90E−14	−1.623
E.Absorptive_TA_1	RPL8	−0.957	2.66E−06	−5.23E−01	8.97E−15	−0.952
E.Absorptive_TA_1	RPLP0	−1.399	4.40E−17	−4.28E−01	2.11E−08	−1.250
E.Absorptive_TA_1	RPS14	−1.078	2.20E−07	−6.92E−01	1.13E−20	−1.631
E.Absorptive_TA_1	RPS18	−1.506	2.37E−07	−6.14E−01	6.68E−15	−2.203
E.Absorptive_TA_1	RPS2	−1.112	1.30E−06	−7.95E−01	2.76E−20	−1.830
E.Absorptive_TA_1	RPS5	−1.200	1.11E−16	−3.71E−01	1.91E−06	−1.125
E.Absorptive_TA_1	S100A11	0.801	2.56E−11	7.99E−01	9.69E−18	0.902
E.Absorptive_TA_1	S100P	3.499	7.00E−64	5.73E−01	5.27E−02	0.608
E.Absorptive_TA_1	SAA1	4.759	1.88E−19		1.00E+00	3.487
E.Absorptive_TA_2	AC009501.4	−2.035	1.89E−46	4.32E−01	8.41E−06	−1.587
E.Absorptive_TA_2	ARPC1B	0.803	8.00E−06	6.70E−01	9.84E−23	0.861
E.Absorptive_TA_2	ATP6V1G1	0.696	1.44E−04	7.10E−01	1.93E−30	0.590
E.Absorptive_TA_2	CD44	1.225	3.74E−14	8.89E−01	2.59E−18	0.827
E.Absorptive_TA_2	CXCL1	2.030	4.68E−21	1.74E+00	7.62E−09	0.740
E.Absorptive_TA_2	FAM3B	−4.763	3.39E−26		1.00E+00	5.362
E.Absorptive_TA_2	FOS	−2.217	1.09E−33	3.52E−01	1.33E−03	−1.065
E.Absorptive_TA_2	GPX2	1.975	1.93E−06	1.18E+00	4.04E−59	0.988
E.Absorptive_TA_2	IFITM3	0.713	3.27E−05	1.14E+00	1.16E−33	0.780
E.Absorptive_TA_2	JUN	−2.140	1.07E−30	2.13E−01	2.99E−02	−0.715
E.Absorptive_TA_2	KRT19	1.926	6.67E−05	1.04E+00	1.44E−24	2.057
E.Absorptive_TA_2	LGALS4	−2.052	2.94E−03	−8.31E−01	7.58E−21	−1.057
E.Absorptive_TA_2	MUC12	2.943	6.71E−55	1.60E+00	2.73E−82	1.962
E.Absorptive_TA_2	OLFM4	2.263	2.18E−47	1.43E+00	8.82E−21	0.912
E.Absorptive_TA_2	PARP8	4.359	6.47E−27		1.00E+00	5.362
E.Absorptive_TA_2	PDIA3	1.138	2.14E−07	9.74E−01	1.53E−58	0.682
E.Absorptive_TA_2	PI3	2.532	4.68E−55	2.03E+00	3.86E−22	1.026
E.Absorptive_TA_2	PITX2	−5.183	2.15E−36		1.00E+00	5.362
E.Absorptive_TA_2	PLA2G2A	2.672	1.34E−35	2.35E+00	9.57E−124	1.526
E.Absorptive_TA_2	PRAC1	4.172	1.17E−107	6.60E−01	1.16E−14	0.845
E.Absorptive_TA_2	PSMB9	0.727	2.84E−06	8.15E−01	9.01E−28	0.702
E.Absorptive_TA_2	PSME2	0.656	5.51E−02	6.36E−01	2.68E−24	0.539
E.Absorptive_TA_2	REG4	2.978	5.55E−59	1.41E+00	1.65E−06	1.499
E.Absorptive_TA_2	RNASE1	1.197	5.71E−13	8.73E−01	1.38E−22	0.518
E.Absorptive_TA_2	RP11-708H21.4	−5.510	1.52E−35		1.00E+00	5.362
E.Absorptive_TA_2	RPS20	−2.005	5.54E−05	6.04E−01	1.49E−17	−1.030
E.Absorptive_TA_2	S100A10	0.724	4.05E−01	7.44E−01	1.05E−21	0.965
E.Absorptive_TA_2	S100A11	1.708	2.98E−07	1.34E+00	2.00E−79	2.043
E.Absorptive_TA_2	S100A6	0.806	6.47E−01	9.97E−01	1.50E−24	1.526
E.Absorptive_TA_2	S100A9	3.719	7.49E−29	1.11E+00	1.42E−01	0.636
E.Absorptive_TA_2	S100P	4.775	7.32E−142	1.82E+00	9.71E−41	2.118
E.Absorptive_TA_2	7-Sep	0.806	1.11E−07	7.46E−01	4.33E−22	0.521
E.Absorptive_TA_2	SH3BGRL3	0.384	2.41E−01	7.49E−01	1.17E−24	0.694
E.Absorptive_TA_2	SOD3	1.752	2.49E−26	1.22E+00	5.87E−19	1.117
E.Absorptive_TA_2	SSR4	1.419	4.08E−05	6.51E−01	2.25E−21	1.212
E.Absorptive_TA_2	ST3GAL4	2.321	1.54E−21	7.09E−01	1.95E−04	0.503
E.Absorptive_TA_2	ST6GALNAC6	2.484	1.09E−44	7.02E−01	1.02E−13	0.740
E.Best4_Enterocytes	AC009501.4	−2.044	3.27E−22	4.88E−01	1.47E−02	−1.532
E.Best4_Enterocytes	AQP8	−2.602	1.40E−28	1.56E−01	7.08E−01	−0.517
E.Best4_Enterocytes	ARF4	1.190	3.64E−05	8.83E−01	1.07E−19	0.584
E.Best4_Enterocytes	EIF4G2	1.075	2.23E−04	9.59E−01	5.21E−27	0.515
E.Best4_Enterocytes	ITM2B	1.023	8.35E−03	1.05E+00	2.50E−21	1.406
E.Best4_Enterocytes	LAPTM4A	0.907	4.12E−03	1.03E+00	9.39E−21	0.701
E.Best4_Enterocytes	MT-ND4L	1.168	1.29E−04	1.06E+00	3.28E−29	0.614
E.Best4_Enterocytes	MUC12	1.802	3.33E−09	1.07E+00	2.31E−19	0.784
E.Best4_Enterocytes	RPL37	0.400	3.34E−01	1.03E+00	3.93E−20	0.714
E.Best4_Enterocytes	RPL38	0.517	2.06E−01	9.36E−01	3.81E−20	0.648

TABLE 13-continued

Inflamed vs Healthy Markers

E.Best4_Enterocytes	RPL39	0.270	3.66E–01	2.26E+00	6.86E–40	0.567
E.Best4_Enterocytes	S100A11	1.141	3.66E–04	1.32E+00	1.10E–30	1.492
E.Cycling_TA	AK1	2.364	2.05E–47	5.53E–01	1.75E–09	0.894
E.Cycling_TA	ANXA5	0.741	1.64E–07	8.29E–01	2.42E–27	0.569
E.Cycling_TA	ARPC1B	0.754	4.22E–05	1.10E+00	2.61E–63	0.987
E.Cycling_TA	C2	2.248	1.79E–22	1.01E+00	4.50E–09	0.707
E.Cycling_TA	CAPG	0.852	1.98E–06	8.04E–01	1.75E–39	0.507
E.Cycling_TA	CLDN2	4.506	2.72E–21		1.00E+00	5.347
E.Cycling_TA	DDX5	0.446	4.03E–02	8.98E–01	1.59E–41	0.588
E.Cycling_TA	DUOXA2	4.748	3.48E–46	1.70E+00	1.72E–01	0.584
E.Cycling_TA	ENO1	1.107	8.45E–03	9.17E–01	1.33E–59	0.925
E.Cycling_TA	FAM3B	–4.685	2.85E–25		1.00E+00	5.347
E.Cycling_TA	FN1	3.408	5.62E–29	1.26E+00	9.56E–03	1.190
E.Cycling_TA	H3F3B	1.033	1.94E–02	7.37E–01	1.81E–26	1.500
E.Cycling_TA	HLA-DMA	1.344	6.68E–20	1.22E+00	2.89E–27	0.881
E.Cycling_TA	HLA-DRB1	1.673	5.80E–31	2.18E+00	1.38E–35	2.587
E.Cycling_TA	HSPA5	1.222	7.03E–10	9.93E–01	1.89E–56	0.944
E.Cycling_TA	IFI16	1.535	4.03E–16	8.25E–01	5.72E–11	0.564
E.Cycling_TA	IFITM3	0.709	9.80E–04	1.29E+00	1.05E–52	0.800
E.Cycling_TA	JUN	–1.938	2.62E–20	6.40E–02	4.41E–01	–0.685
E.Cycling_TA	LDHA	0.582	4.22E–02	9.94E–01	8.79E–58	0.557
E.Cycling_TA	LYZ	1.419	4.50E–19	1.08E+00	2.71E–07	0.824
E.Cycling_TA	MMP7	4.756	2.07E–20		1.00E+00	5.347
E.Cycling_TA	MTRNR2L1	1.059	7.81E–16	1.00E+00	4.48E–09	1.035
E.Cycling_TA	MUC12	2.558	1.09E–34	1.34E+00	2.06E–78	1.307
E.Cycling_TA	PDIA3	1.005	2.85E–04	1.12E+00	2.93E–88	0.712
E.Cycling_TA	PI3	1.750	2.09E–26	2.36E+00	1.06E–25	0.573
E.Cycling_TA	PITX1	3.389	2.83E–33	5.86E–01	3.64E–02	1.746
E.Cycling_TA	PITX2	–5.266	3.04E–38		1.00E+00	5.347
E.Cycling_TA	PLA2G2A	2.181	6.66E–23	2.00E+00	3.70E–108	1.037
E.Cycling_TA	PRAC1	4.338	1.08E–106	5.88E–01	1.59E–13	0.933
E.Cycling_TA	PSMB9	0.574	7.69E–04	1.11E+00	1.52E–66	0.671
E.Cycling_TA	PSME2	0.840	3.36E–02	1.01E+00	3.67E–64	0.783
E.Cycling_TA	REG4	3.108	3.27E–91	2.18E+00	1.61E–22	2.029
E.Cycling_TA	RPL36AL	0.535	2.03E–01	7.16E–01	1.81E–43	0.691
E.Cycling_TA	RPL38	–1.396	1.21E–03	6.04E–01	5.50E–24	–0.518
E.Cycling_TA	S100A10	0.542	3.09E–01	6.87E–01	7.21E–20	0.728
E.Cycling_TA	S100A11	1.278	1.93E–05	1.48E+00	9.57E–108	1.704
E.Cycling_TA	S100P	4.483	2.51E–135	1.53E+00	3.04E–29	1.934
E.Cycling_TA	SAA1	4.886	3.06E–38		1.00E+00	5.347
E.Cycling_TA	SH3BGRL3	0.466	2.04E–01	9.51E–01	4.79E–42	0.896
E.Cycling_TA	SPCS1	0.997	1.14E–03	7.51E–01	2.22E–49	0.702
E.Cycling_TA	ST6GALNAC6	2.373	5.30E–36	7.72E–01	1.53E–11	0.641
E.Cycling_TA	TESC	3.977	5.68E–31	7.30E–01	1.78E–01	1.524
E.Cycling_TA	UBL5	0.763	4.90E–02	7.22E–01	7.05E–46	0.562
E.Enterocyte_Immature_1	AC009501.4	–1.578	1.07E–27	4.98E–01	4.99E–05	–1.207
E.Enterocyte_Immature_1	MUC1	2.225	1.32E–28	1.25E+00	9.20E–14	0.989
E.Enterocyte_Immature_1	MUC4	2.580	1.36E–27	1.01E+00	7.66E–10	0.648
E.Enterocyte_Immature_1	OAZ1	–0.919	2.43E–06	–5.61E–01	4.55E–15	–0.526
E.Enterocyte_Immature_1	PLA2G2A	3.060	8.53E–55	1.01E+00	2.00E–04	1.432
E.Enterocyte_Immature_1	RNASE1	1.506	1.12E–19	7.19E–01	2.15E–06	0.652
E.Enterocyte_Immature_1	S100P	3.636	1.24E–50	1.18E+00	3.28E–04	0.858
E.Enterocyte_Immature_1	TNIP3	4.533	1.08E–18		1.00E+00	3.737
E.Enterocyte_Immature_1	XIST	1.241	2.78E–11	9.86E–01	6.99E–12	0.558
E.Enterocyte_Immature_2	AC009501.4	–2.768	2.25E–73	3.42E–01	6.64E–03	–1.914
E.Enterocyte_Immature_2	AGR2	1.354	2.45E–08	1.63E+00	3.94E–52	1.375
E.Enterocyte_Immature_2	AQP8	–2.453	1.34E–53	–1.12E+00	4.78E–09	–0.542
E.Enterocyte_Immature_2	BHLHE40	2.162	3.21E–25	7.35E–01	3.35E–08	0.747
E.Enterocyte_Immature_2	CCL20	2.820	5.35E–24	2.45E+00	5.30E–09	0.855
E.Enterocyte_Immature_2	CEACAM5	1.784	6.07E–09	1.20E+00	3.93E–42	1.233
E.Enterocyte_Immature_2	CEACAM6	1.929	1.16E–34	1.13E+00	1.89E–36	0.560
E.Enterocyte_Immature_2	CLIC3	2.244	5.14E–20	8.02E–01	3.27E–05	0.515
E.Enterocyte_Immature_2	CRIP1	1.028	3.37E–11	7.47E–01	1.57E–25	0.637
E.Enterocyte_Immature_2	CTSE	3.988	1.76E–39	9.98E–01	2.51E–02	0.948
E.Enterocyte_Immature_2	CXCL1	3.232	4.63E–31	2.99E+00	2.20E–08	1.874
E.Enterocyte_Immature_2	CXCL2	2.355	1.36E–17	1.83E+00	1.06E–07	0.796
E.Enterocyte_Immature_2	DDX5	0.541	5.23E–03	7.54E–01	1.97E–23	0.608
E.Enterocyte_Immature_2	FAM3C	1.790	9.09E–23	7.90E–01	1.03E–14	0.504
E.Enterocyte_Immature_2	FOSB	–2.318	3.62E–41	8.57E–02	3.99E–01	–0.563
E.Enterocyte_Immature_2	FTL	–1.369	4.53E–02	–9.90E–01	5.23E–26	–1.925
E.Enterocyte_Immature_2	GPX2	1.336	1.26E–13	1.58E+00	2.45E–62	0.700
E.Enterocyte_Immature_2	HSPA5	0.720	3.48E–05	1.16E+00	4.47E–47	0.566
E.Enterocyte_Immature_2	HSPB1	–1.098	2.00E–04	–8.02E–01	3.51E–22	–0.552
E.Enterocyte_Immature_2	IL2RG	1.424	3.34E–22	6.95E–01	2.30E–18	1.183
E.Enterocyte_Immature_2	MDK	1.022	1.38E–10	6.62E–01	6.49E–12	0.506
E.Enterocyte_Immature_2	MUC12	2.103	1.06E–18	1.75E+00	1.24E–108	1.048
E.Enterocyte_Immature_2	PDIA3	0.832	2.28E–05	8.17E–01	3.32E–34	0.527
E.Enterocyte_Immature_2	PITX2	–5.108	9.63E–37		1.00E+00	4.699

TABLE 13-continued

Inflamed vs Healthy Markers

E.Enterocyte_Immature_2	PLA2G2A	3.223	1.25E–74	2.16E+00	1.22E–52	2.024
E.Enterocyte_Immature_2	RARRES3	1.373	2.76E–20	8.93E–01	1.94E–24	1.463
E.Enterocyte_Immature_2	RNASE1	1.490	3.23E–18	9.83E–01	8.18E–21	0.722
E.Enterocyte_Immature_2	S100A11	2.296	1.40E–34	1.73E+00	4.50E–84	3.042
E.Enterocyte_Immature_2	S100A6	0.487	8.95E–01	1.22E+00	1.13E–33	1.347
E.Enterocyte_Immature_2	S100A9	4.778	1.09E–35		1.00E+00	4.699
E.Enterocyte_Immature_2	S100P	4.403	5.49E–119	2.48E+00	1.80E–93	2.215
E.Enterocyte_Immature_2	SAA1	4.632	2.47E–25		1.00E+00	4.699
E.Enterocyte_Immature_2	SDCBP	1.046	2.94E–11	8.86E–01	2.61E–28	0.730
E.Enterocyte_Immature_2	SEC24D	3.545	1.92E–21	7.11E–01	1.14E–01	0.740
E.Enterocyte_Immature_2	SEPP1	1.501	5.03E–16	1.06E+00	6.71E–25	1.821
E.Enterocyte_Immature_2	SERPINB5	4.888	2.54E–29		1.00E+00	4.699
E.Enterocyte_Immature_2	SLC6A14	4.678	1.75E–25		1.00E+00	4.699
E.Enterocyte_Immature_2	TFF1	2.726	2.86E–65	1.43E+00	2.79E–19	1.847
E.Enterocyte_Immature_2	TIMP2	1.921	1.69E–15	6.59E–01	1.42E–05	0.648
E.Enterocyte_Immature_2	TNIP3	4.989	2.93E–32		1.00E+00	4.699
E.Enterocyte_Immature_2	TPM4	1.104	8.57E–11	6.95E–01	6.54E–26	0.528
E.Enterocyte_Immature_2	TRAM1	1.156	5.21E–12	7.44E–01	2.20E–18	0.621
E.Enterocyte_Progenitor	AC009501.4	–1.790	4.78E–28	8.23E–01	1.42E–07	–1.363
E.Enterocyte_Progenitor	AGR2	0.874	2.18E–07	1.07E+00	7.14E–15	0.618
E.Enterocyte_Progenitor	CCL20	3.364	7.51E–25	9.45E–01	5.44E–02	0.971
E.Enterocyte_Progenitor	CEACAM5	1.304	1.77E–16	1.11E+00	4.55E–19	0.797
E.Enterocyte_Progenitor	CEACAM6	2.165	4.16E–21	1.25E+00	2.50E–09	0.725
E.Enterocyte_Progenitor	CXCL1	3.601	2.78E–26	1.55E+00	2.06E–02	2.451
E.Enterocyte_Progenitor	CXCL3	2.597	3.47E–20	1.69E+00	2.00E–06	0.832
E.Enterocyte_Progenitor	DUOXA2	5.301	6.59E–34		1.00E+00	4.362
E.Enterocyte_Progenitor	GPX2	1.489	2.06E–20	1.17E+00	7.68E–23	0.648
E.Enterocyte_Progenitor	HSPB1	–1.810	3.57E–27	–3.83E–01	2.31E–03	–0.614
E.Enterocyte_Progenitor	LCN2	2.265	4.40E–38	2.19E+00	1.65E–28	0.771
E.Enterocyte_Progenitor	OLFM4	2.962	6.59E–34	1.43E+00	2.90E–05	1.256
E.Enterocyte_Progenitor	PI3	2.248	6.99E–37	2.35E+00	3.39E–25	0.698
E.Enterocyte_Progenitor	PLA2G2A	2.744	4.26E–57	1.65E+00	8.27E–20	1.295
E.Enterocyte_Progenitor	S100A11	1.487	1.34E–20	1.16E+00	5.79E–25	1.808
E.Enterocyte_Progenitor	S100A6	1.420	2.81E–01	1.21E+00	5.11E–27	2.188
E.Enterocyte_Progenitor	S100A9	4.821	1.22E–24		1.00E+00	4.362
E.Enterocyte_Progenitor	S100P	4.217	7.74E–100	1.40E+00	3.88E–11	1.481
E.Enterocyte_Progenitor	TFF1	2.396	4.72E–26	1.24E+00	2.37E–04	1.400
E.Enterocyte_Progenitor	TNIP3	4.724	2.35E–19		1.00E+00	4.362
E.Enterocyte_Progenitor	TPT1	0.631	1.65E–03	7.81E–01	1.21E–19	0.944
E.Enterocytes	AC009501.4	–2.349	9.38E–52	5.09E–01	3.37E–05	–1.707
E.Enterocytes	BHLHE40	2.112	1.35E–30	7.65E–01	1.16E–10	0.777
E.Enterocytes	C4orf3	1.121	3.18E–11	9.20E–01	7.30E–34	0.869
E.Enterocytes	CA2	–2.970	9.81E–18	–1.13E+00	4.28E–27	–0.602
E.Enterocytes	CARD16	0.989	5.33E–08	1.40E+00	2.00E–33	0.754
E.Enterocytes	CASP1	1.981	1.44E–22	1.42E+00	1.62E–24	1.256
E.Enterocytes	CCNJL	–4.668	5.35E–22		1.00E+00	5.613
E.Enterocytes	CD55	1.595	2.02E–21	1.36E+00	4.01E–34	0.776
E.Enterocytes	CTSE	3.644	7.81E–41	1.38E+00	1.03E–04	0.623
E.Enterocytes	CXCL1	3.416	1.52E–39	2.76E+00	2.35E–07	2.315
E.Enterocytes	CXCL3	2.170	4.29E–24	2.21E+00	5.65E–16	0.668
E.Enterocytes	FSTL1	4.180	4.28E–21		1.00E+00	5.613
E.Enterocytes	FTH1	0.338	8.97E–01	–1.26E+00	5.68E–33	–0.744
E.Enterocytes	GLDN	4.849	1.07E–29		1.00E+00	5.613
E.Enterocytes	GLUL	1.393	2.71E–11	1.29E+00	2.02E–15	0.668
E.Enterocytes	GPX2	1.242	1.22E–11	2.19E+00	2.23E–47	0.744
E.Enterocytes	GPX4	–2.068	3.20E–22	–4.83E–01	1.02E–11	–0.516
E.Enterocytes	GUCA2A	–4.568	4.77E–31	–8.72E–01	2.27E–11	–0.540
E.Enterocytes	HLA-B	1.277	3.56E–01	8.45E–01	5.24E–23	2.037
E.Enterocytes	HLA-F	1.058	2.46E–10	7.24E–01	4.55E–27	0.529
E.Enterocytes	IDO1	4.493	2.75E–27		1.00E+00	5.613
E.Enterocytes	IFITM3	1.886	4.92E–26	1.91E+00	2.31E–23	2.733
E.Enterocytes	IL2RG	0.819	4.99E–07	8.66E–01	1.06E–32	0.645
E.Enterocytes	ITM2B	0.372	1.66E–01	9.06E–01	1.02E–27	0.602
E.Enterocytes	KDELR3	3.122	1.27E–19	7.14E–01	4.43E–02	0.587
E.Enterocytes	LAPTM4A	0.767	2.50E–05	8.99E–01	1.91E–24	0.575
E.Enterocytes	LPCAT1	3.289	9.48E–23	4.78E–01	1.42E–01	0.543
E.Enterocytes	MARCKSL1	1.542	2.40E–17	7.01E–01	1.60E–16	0.785
E.Enterocytes	MMP7	4.672	5.17E–23		1.00E+00	5.613
E.Enterocytes	MUC1	1.629	4.62E–20	1.45E+00	4.47E–35	0.630
E.Enterocytes	OLFM4	2.237	6.26E–23	1.76E+00	1.51E–08	0.670
E.Enterocytes	PFKFB3	3.265	3.75E–34	9.27E–01	2.44E–04	1.121
E.Enterocytes	PITX2	–5.485	2.67E–47		1.00E+00	5.613
E.Enterocytes	PKM	0.850	3.61E–06	1.44E+00	6.67E–61	0.716
E.Enterocytes	PLA2G16	1.790	2.78E–18	7.22E–01	2.02E–06	0.863
E.Enterocytes	PLA2G2A	2.920	9.64E–57	2.21E+00	4.22E–24	1.774
E.Enterocytes	PNRC1	0.761	1.47E–06	8.21E–01	1.00E–18	0.645
E.Enterocytes	PSMB9	0.428	1.26E–02	1.05E+00	4.20E–44	0.502
E.Enterocytes	PSME2	1.196	8.23E–06	1.13E+00	3.69E–54	1.201

TABLE 13-continued

Inflamed vs Healthy Markers

E.Enterocytes	RARRES3	2.176	1.34E–22	1.02E+00	2.51E–48	2.320
E.Enterocytes	REG4	3.497	2.26E–36	1.99E+00	3.33E–03	2.049
E.Enterocytes	RNASE1	1.914	3.26E–29	1.36E+00	3.41E–27	1.372
E.Enterocytes	S100A11	2.028	4.04E–28	2.69E+00	7.68E–72	3.482
E.Enterocytes	S100A9	4.819	1.77E–36		1.00E+00	5.613
E.Enterocytes	S100P	2.774	8.64E–45	1.83E+00	2.45E–21	0.527
E.Enterocytes	SERPINB5	4.782	2.34E–28		1.00E+00	5.613
E.Enterocytes	SLC6A14	4.958	2.33E–32		1.00E+00	5.613
E.Enterocytes	SOCS1	1.172	1.49E–10	1.45E+00	2.99E–26	0.654
E.Enterocytes	SRI	–1.855	1.09E–03	–7.90E–01	8.80E–24	–0.511
E.Enterocytes	TC2N	2.673	1.04E–24	6.58E–01	1.36E–03	0.608
E.Enterocytes	TFF1	1.694	2.24E–24	1.78E+00	6.57E–38	0.631
E.Enterocytes	TNIP3	4.597	1.38E–38	1.96E+00	4.96E–02	0.752
E.Enterocytes	UBE2L6	1.501	2.38E–17	6.19E–01	8.51E–09	0.885
E.Enterocytes	VAMP5	1.397	6.09E–19	7.76E–01	2.78E–12	1.132
E.Enterocytes	WARS	1.943	5.03E–16	1.11E+00	4.93E–08	0.904
E.Epithelial	AC009501.4	–1.443	7.79E–132	4.72E–01	6.10E–31	–1.149
E.Epithelial	ANXA1	1.532	1.71E–21	9.34E–01	5.59E–05	2.273
E.Epithelial	C2	2.419	4.00E–35	4.07E–01	2.16E–02	0.718
E.Epithelial	CLDN2	4.210	6.55E–22		1.00E+00	3.712
E.Epithelial	CLIC3	1.511	2.81E–16	7.55E–01	5.91E–06	0.730
E.Epithelial	CLU	1.765	3.90E–24	4.83E–01	2.92E–02	0.713
E.Epithelial	CXCL1	2.124	3.72E–61	1.59E+00	4.85E–12	0.799
E.Epithelial	CXCL14	–0.977	1.47E–43	2.74E–01	1.18E–02	–0.638
E.Epithelial	DAPP1	3.360	3.08E–22	6.57E–01	3.29E–01	0.689
E.Epithelial	DDX5	0.586	1.04E–15	5.38E–01	2.57E–53	0.735
E.Epithelial	DUSP1	–0.762	4.30E–29	1.82E–01	1.58E–04	–0.600
E.Epithelial	EMB	2.867	8.44E–25	4.77E–01	2.03E–01	1.071
E.Epithelial	FN1	2.696	7.40E–24	1.01E+00	1.27E–02	0.755
E.Epithelial	FOS	–0.854	5.67E–35	–3.32E–02	4.67E–01	–0.748
E.Epithelial	FTL	–0.865	1.12E–11	–6.64E–01	1.34E–65	–1.441
E.Epithelial	FYB	1.577	3.28E–24	3.85E–01	9.34E–03	1.069
E.Epithelial	GNB2L1	–0.865	6.70E–21	–3.72E–01	1.89E–29	–1.038
E.Epithelial	HLA-DMA	1.393	9.54E–48	6.45E–01	1.16E–13	0.980
E.Epithelial	HLA-DMB	1.558	1.95E–21	3.37E–01	3.23E–02	0.699
E.Epithelial	HLA-DRB5	0.896	2.04E–19	7.32E–01	5.36E–10	0.744
E.Epithelial	HLA-E	0.299	1.23E–05	4.98E–01	1.09E–47	0.503
E.Epithelial	HOXD13	4.124	7.08E–25		1.00E+00	3.712
E.Epithelial	IFI16	1.281	9.80E–16	5.37E–01	5.23E–06	0.583
E.Epithelial	IFITM2	0.683	9.63E–14	4.51E–01	5.34E–09	0.863
E.Epithelial	IL2RG	1.125	7.11E–55	5.06E–01	3.53E–20	1.076
E.Epithelial	JUN	–1.096	7.03E–55	–1.23E–01	2.44E–03	–0.544
E.Epithelial	LYZ	1.686	3.73E–65	7.01E–01	2.11E–05	1.159
E.Epithelial	MMP7	4.672	5.73E–32		1.00E+00	3.712
E.Epithelial	MTRNR2L1	0.769	2.37E–35	1.50E+00	1.88E–65	0.583
E.Epithelial	MYL6	–0.723	1.96E–08	–2.21E–01	7.35E–14	–0.543
E.Epithelial	NPSR1	4.209	1.31E–20		1.00E+00	3.712
E.Epithelial	PARP8	3.281	5.72E–27	5.60E–01	2.18E–01	1.215
E.Epithelial	PDIA3	0.781	9.84E–26	7.38E–01	9.60E–107	0.577
E.Epithelial	PITX1	3.327	1.93E–29	5.18E–01	2.50E–01	1.404
E.Epithelial	PLA2G16	1.312	6.03E–16	5.71E–01	3.33E–05	0.818
E.Epithelial	RARRES3	0.983	5.05E–46	5.61E–01	1.35E–26	1.172
E.Epithelial	RBPMS	3.215	8.44E–25	8.90E–01	8.58E–02	1.970
E.Epithelial	RPL10A	–0.494	4.20E–10	–2.63E–01	3.96E–12	–0.638
E.Epithelial	RPL11	–0.604	4.93E–07	–3.64E–01	4.47E–29	–0.840
E.Epithelial	RPL12	–0.703	4.84E–12	–3.45E–01	3.32E–22	–0.949
E.Epithelial	RPL15	–0.607	3.55E–11	–4.52E–01	6.87E–36	–0.808
E.Epithelial	RPL3	–0.432	2.77E–05	–3.97E–01	1.04E–27	–0.599
E.Epithelial	RPL8	–0.453	1.38E–04	–4.33E–01	2.01E–42	–0.754
E.Epithelial	RPLP0	–0.670	5.02E–14	–3.92E–01	3.93E–27	–0.893
E.Epithelial	RPS14	–0.714	5.62E–09	–5.30E–01	4.82E–55	–1.072
E.Epithelial	RPS3	–0.562	8.06E–07	–5.03E–01	6.89E–46	–0.920
E.Epithelial	RPS4X	–0.747	3.99E–15	–3.57E–01	4.14E–22	–0.793
E.Epithelial	RPS5	–0.778	1.04E–18	–4.38E–01	2.13E–34	–1.056
E.Epithelial	RPS6	–0.345	1.94E–03	–4.07E–01	4.67E–25	–0.516
E.Epithelial	RPS7	–0.553	1.08E–10	–2.31E–01	3.16E–11	–0.722
E.Epithelial	RPS8	–0.421	1.64E–06	–2.92E–01	1.81E–14	–0.608
E.Epithelial	RPS9	–0.499	6.83E–07	–3.42E–01	6.59E–25	–0.724
E.Epithelial	S100A11	1.027	3.60E–50	1.14E+00	5.42E–174	1.438
E.Epithelial	S100A6	0.316	2.20E–01	9.80E–01	7.47E–166	0.766
E.Epithelial	S100A9	3.465	6.87E–51	1.36E+00	1.54E–02	0.852
E.Epithelial	SEPP1	0.517	9.21E–18	6.80E–01	1.65E–25	0.513
E.Epithelial	SLC25A6	–0.922	1.36E–28	–3.28E–01	2.06E–25	–0.505
E.Epithelial	SLC6A14	4.840	3.60E–45		1.00E+00	3.712
E.Epithelial	SOCS1	1.303	5.89E–25	9.77E–01	4.12E–19	1.015
E.Epithelial	SOD3	1.247	7.61E–45	6.69E–01	1.58E–17	0.526
E.Epithelial	TESC	3.086	1.80E–29	–1.68E–01	6.55E–01	0.938
E.Epithelial	TGFBI	2.541	1.53E–24	5.92E–01	4.34E–02	1.252

TABLE 13-continued

Inflamed vs Healthy Markers

E.Epithelial	TGM2	3.983	1.26E−26		1.00E+00	3.712
E.Epithelial	TIMP1	2.832	3.53E−214	7.38E−01	1.84E−09	2.805
E.Epithelial	TNIP3	4.624	1.56E−50		1.00E+00	3.712
E.Goblet	CD55	1.848	2.06E−17	5.48E−01	4.68E−04	0.782
E.Goblet	REG4	2.119	7.02E−31	1.68E+00	2.41E−14	0.585
E.Immature_Enterocytes	AC009501.4	−1.996	2.17E−109	4.73E−01	9.38E−10	−1.467
E.Immature_Enterocytes	ACTB	0.736	5.40E−03	4.95E−01	2.53E−18	1.195
E.Immature_Enterocytes	AGR2	0.813	2.93E−16	1.11E+00	2.45E−51	0.652
E.Immature_Enterocytes	ATP5G2	−1.021	3.18E−20	−1.40E−01	9.24E−03	−0.522
E.Immature_Enterocytes	BHLHE40	1.813	1.08E−28	6.05E−01	8.32E−08	0.533
E.Immature_Enterocytes	C2	3.396	1.06E−23	6.41E−01	1.22E−01	1.513
E.Immature_Enterocytes	CCL20	2.626	2.55E−53	1.72E+00	4.25E−13	0.694
E.Immature_Enterocytes	CD55	1.431	4.60E−29	7.57E−01	8.67E−18	0.528
E.Immature_Enterocytes	COX4I1	−0.986	1.64E−10	−6.32E−01	5.86E−41	−0.656
E.Immature_Enterocytes	CTSE	3.705	4.13E−51	7.71E−01	2.08E−02	0.720
E.Immature_Enterocytes	CXCL1	3.293	1.44E−60	1.96E+00	6.03E−07	2.170
E.Immature_Enterocytes	CXCL2	2.244	3.20E−26	1.52E+00	6.15E−09	0.717
E.Immature_Enterocytes	CXCL3	1.917	8.57E−32	2.03E+00	9.47E−24	0.675
E.Immature_Enterocytes	DDX5	0.668	1.49E−11	5.71E−01	2.49E−26	0.688
E.Immature_Enterocytes	FABP1	−3.053	1.37E−11	−4.59E−01	3.65E−10	−0.930
E.Immature_Enterocytes	FSTL1	3.298	1.82E−20	9.38E−01	2.20E−02	1.375
E.Immature_Enterocytes	FTL	−0.984	2.24E−07	−8.67E−01	1.10E−47	−1.585
E.Immature_Enterocytes	GLRA2	4.429	1.50E−22		1.00E+00	3.780
E.Immature_Enterocytes	GPX2	1.284	7.15E−38	1.34E+00	1.93E−78	0.727
E.Immature_Enterocytes	GSN	0.622	2.20E−11	5.12E−01	6.60E−17	0.566
E.Immature_Enterocytes	H3F3B	0.379	1.83E−03	4.65E−01	1.29E−20	0.648
E.Immature_Enterocytes	HLA-DMA	1.146	1.05E−14	7.23E−01	2.28E−07	0.629
E.Immature_Enterocytes	HLA-DRB1	1.115	5.71E−32	8.99E−01	2.54E−16	1.133
E.Immature_Enterocytes	IFITM3	0.996	1.88E−17	1.21E+00	1.10E−24	1.235
E.Immature_Enterocytes	IL2RG	1.050	2.54E−29	4.06E−01	1.21E−11	0.680
E.Immature_Enterocytes	LCN2	1.652	5.00E−55	2.28E+00	2.32E−81	0.630
E.Immature_Enterocytes	MUC12	1.575	2.63E−52	1.49E+00	5.82E−173	0.507
E.Immature_Enterocytes	MYL6	−1.070	8.96E−08	−3.39E−01	2.58E−14	−0.809
E.Immature_Enterocytes	PARP8	4.286	2.54E−27		1.00E+00	3.780
E.Immature_Enterocytes	PITX2	−5.336	1.15E−51		1.00E+00	3.780
E.Immature_Enterocytes	PLA2G2A	2.792	1.36E−159	1.74E+00	1.05E−55	1.666
E.Immature_Enterocytes	PPDPF	−0.764	4.22E−07	−4.13E−01	7.60E−19	−0.573
E.Immature_Enterocytes	RARRES3	1.072	9.26E−31	5.27E−01	3.33E−18	0.946
E.Immature_Enterocytes	REG4	2.421	2.29E−41	1.33E+00	3.34E−05	0.904
E.Immature_Enterocytes	RNASE1	1.291	2.61E−34	8.99E−01	1.66E−28	0.679
E.Immature_Enterocytes	S100A11	1.519	2.59E−54	1.36E+00	1.34E−88	2.079
E.Immature_Enterocytes	S100A6	2.704	1.21E−03	9.85E−01	3.00E−65	2.484
E.Immature_Enterocytes	S100A9	5.071	3.74E−55		1.00E+00	3.780
E.Immature_Enterocytes	S100P	3.659	2.13E−223	2.01E+00	8.60E−74	1.180
E.Immature_Enterocytes	SDCBP	0.829	1.54E−15	6.27E−01	4.94E−22	0.519
E.Immature_Enterocytes	SEC24D	3.280	1.34E−28	5.32E−01	6.92E−02	0.541
E.Immature_Enterocytes	SEPP1	1.092	5.01E−32	7.78E−01	7.85E−29	1.165
E.Immature_Enterocytes	SLC25A6	−1.100	2.75E−22	−4.08E−01	2.29E−16	−0.552
E.Immature_Enterocytes	SLC6A14	4.944	1.67E−36		1.00E+00	3.780
E.Immature_Enterocytes	SOCS1	1.505	5.40E−20	1.04E+00	2.25E−15	0.930
E.Immature_Enterocytes	SPINK1	0.967	9.15E−18	1.72E+00	8.72E−61	0.613
E.Immature_Enterocytes	TFF1	2.048	8.47E−97	1.33E+00	4.98E−33	1.056
E.Immature_Enterocytes	TGM2	3.379	1.71E−20	1.33E+00	3.61E−03	0.737
E.Immature_Enterocytes	TNIP3	5.326	4.69E−59		1.00E+00	3.780
E.Immature_Goblet	AC009501.4	−1.337	4.88E−18	5.82E−01	3.69E−05	−1.044
E.Immature_Goblet	CCL20	2.890	3.18E−19	8.86E−01	5.94E−02	0.727
E.Immature_Goblet	COX4I1	−1.191	5.15E−05	−7.55E−01	6.18E−24	−0.820
E.Immature_Goblet	RPL10	−1.902	2.44E−04	−7.44E−01	1.13E−17	−2.877
E.Immature_Goblet	RPL8	−1.005	8.44E−03	−6.59E−01	2.58E−19	−1.040
E.Immature_Goblet	S100P	3.344	8.37E−84	1.23E+00	1.13E−19	0.534
E.Immature_Goblet	TFF1	2.786	6.36E−57	1.44E+00	6.23E−09	1.843
E.Immature_Goblet	XIST	1.805	3.50E−20	6.50E−01	1.68E−05	0.796
E.Secretory	CD55	1.774	1.22E−18	5.78E−01	5.94E−05	0.720
E.Secretory	MT-ND3	0.612	2.87E−04	1.74E+00	1.68E−42	0.840
E.Secretory_All	AC009501.4	−1.407	1.77E−55	2.10E−01	3.91E−03	−1.175
E.Secretory_All	ANXA5	0.814	6.68E−15	3.89E−01	4.64E−08	0.500
E.Secretory_All	C2	2.862	7.54E−34	5.68E−01	4.29E−03	0.984
E.Secretory_All	C2CD4A	4.621	3.44E−22		1.00E+00	3.977
E.Secretory_All	COX4I1	−1.041	3.46E−12	−6.80E−01	3.70E−51	−0.782
E.Secretory_All	DDX5	0.746	3.77E−13	5.55E−01	2.80E−25	0.726
E.Secretory_All	F3	2.004	6.47E−27	5.77E−01	1.18E−03	0.622
E.Secretory_All	FN1	3.749	4.17E−30	1.04E+00	1.26E−01	1.293
E.Secretory_All	GNB2L1	−0.763	2.24E−08	−4.37E−01	4.28E−18	−0.718
E.Secretory_All	GSN	0.687	4.27E−12	5.83E−01	9.40E−19	0.760
E.Secretory_All	HLA-E	0.552	2.99E−08	5.37E−01	8.98E−28	0.710
E.Secretory_All	HSPB1	−0.997	2.07E−21	−1.16E−01	1.00E−01	−0.515
E.Secretory_All	IGFALS	4.692	1.58E−22		1.00E+00	3.977
E.Secretory_All	LGALS4	−0.832	9.78E−07	−6.12E−01	7.75E−26	−0.554

TABLE 13-continued

Inflamed vs Healthy Markers

E.Secretory_All	LYZ	2.134	6.69E–71	5.62E–01	1.37E–03	1.474
E.Secretory_All	MTRNR2L1	0.697	1.03E–13	1.06E+00	5.67E–15	0.708
E.Secretory_All	MUC5AC	4.738	1.60E–25		1.00E+00	3.977
E.Secretory_All	MYL6	–0.771	2.97E–05	–3.64E–01	9.90E–17	–0.611
E.Secretory_All	RARRES3	0.880	8.46E–18	3.05E–01	1.87E–05	0.671
E.Secretory_All	RPL10	–0.754	6.30E–05	–5.97E–01	4.67E–25	–1.350
E.Secretory_All	RPL11	–0.775	1.13E–05	–4.09E–01	2.73E–16	–1.037
E.Secretory_All	RPL12	–0.637	3.49E–05	–4.50E–01	4.19E–17	–0.864
E.Secretory_All	RPL13A	–0.451	2.29E–02	–5.80E–01	8.75E–27	–0.905
E.Secretory_All	RPL15	–0.448	1.20E–03	–5.43E–01	3.56E–21	–0.803
E.Secretory_All	RPL8	–0.363	3.38E–02	–6.33E–01	4.82E–40	–0.616
E.Secretory_All	RPLP0	–0.392	3.24E–03	–5.07E–01	4.81E–21	–0.541
E.Secretory_All	RPS14	–0.703	4.32E–05	–5.44E–01	1.02E–24	–1.105
E.Secretory_All	RPS2	–0.292	6.78E–02	–8.30E–01	1.92E–36	–0.895
E.Secretory_All	RPS3	–0.460	6.04E–03	–6.15E–01	1.01E–29	–0.814
E.Secretory_All	RPS5	–0.666	3.53E–07	–5.84E–01	4.59E–27	–0.790
E.Secretory_All	RPS6	–0.440	1.61E–02	–5.67E–01	1.45E–21	–0.859
E.Secretory_All	S100A11	0.648	2.98E–10	6.82E–01	8.40E–38	0.632
E.Secretory_All	TESC	3.081	1.10E–26	–3.44E–01	2.63E–01	0.640
E.Secretory_All	TGFBI	2.094	8.71E–26	4.21E–01	8.92E–03	0.906
E.Secretory_All	TIMP1	2.353	1.54E–111	2.76E–01	1.43E–02	2.162
E.Secretory_All	TRIM22	2.716	6.77E–21	4.84E–01	4.41E–02	0.720
E.Secretory_TA	AC009501.4	–1.922	8.21E–33	3.93E–01	1.28E–03	–1.493
E.Secretory_TA	AGR2	0.853	1.63E–01	1.34E+00	6.39E–32	0.743
E.Secretory_TA	ATP6V1G1	0.927	1.17E–04	6.61E–01	1.05E–21	0.720
E.Secretory_TA	CLDN2	4.820	2.51E–21		1.00E+00	5.000
E.Secretory_TA	FN1	4.014	5.26E–30	1.24E+00	6.58E–02	1.790
E.Secretory_TA	FRZB	1.444	1.41E–15	7.15E–01	2.96E–06	0.564
E.Secretory_TA	HLA-F	1.278	9.14E–13	8.25E–01	1.00E–22	0.711
E.Secretory_TA	HSPA5	0.707	3.67E–04	9.37E–01	6.96E–31	0.504
E.Secretory_TA	ID3	–2.462	3.54E–33	1.86E–02	8.68E–01	–0.521
E.Secretory_TA	IFITM3	0.474	3.08E–02	1.19E+00	5.35E–29	0.552
E.Secretory_TA	MUC12	1.620	1.67E–15	1.00E+00	1.50E–27	0.560
E.Secretory_TA	PDIA3	1.223	6.40E–06	8.66E–01	1.63E–36	0.820
E.Secretory_TA	PI3	1.933	5.42E–20	1.40E+00	7.05E–07	0.511
E.Secretory_TA	PITX2	–4.655	3.26E–22		1.00E+00	5.000
E.Secretory_TA	PRAC1	3.889	7.68E–69	8.65E–01	8.21E–21	0.641
E.Secretory_TA	PSMB9	0.578	1.62E–03	1.09E+00	3.57E–40	0.664
E.Secretory_TA	REG4	2.058	5.48E–35	2.08E+00	8.85E–28	0.795
E.Secretory_TA	S100A11	0.914	2.80E–03	9.52E–01	9.56E–31	1.044
E.Secretory_TA	S100P	3.744	1.30E–76	1.55E+00	1.46E–27	1.083
E.Secretory_TA	SAA1	4.764	3.13E–27		1.00E+00	5.000
E.Secretory_TA	ST6GALNAC6	2.139	6.48E–23	6.58E–01	3.40E–08	0.504
E.Secretory_TA	SUB1	0.866	1.14E–04	8.38E–01	1.60E–30	0.578
E.Secretory_TA	TESC	4.021	2.87E–26	9.33E–01	7.33E–02	1.638
E.Stem	PLA2G2A	2.205	3.62E–15	1.30E+00	8.28E–11	0.780
E.Stem	PRAC1	4.659	1.44E–42	8.96E–01	4.25E–10	1.215
E.Stem	WFDC2	1.916	8.85E–11	1.27E+00	4.00E–15	0.610
F.Crypt	MME	4.670	1.98E–19		1.00E+00	1.880
F.Crypt	MT-ND2	0.554	5.48E–03	7.23E–01	6.74E–18	1.118
F.Crypt	MTRNR2L1	1.470	7.43E–23	1.35E+00	9.35E–11	1.524
F.Crypt	NEAT1	0.816	8.97E–11	6.22E–01	2.99E–14	0.697
F.Crypt	TAGLN	1.972	9.97E–40	7.73E–01	9.39E–06	0.919
F.Crypt_hiFos	GSN	–2.426	2.22E–11	–1.15E+00	1.94E–14	–0.619
F.Crypt_hiFos	TAGLN	2.893	1.13E–27	7.76E–01	2.01E–02	1.916
F.Crypt_loFos_1	TAGLN	2.131	3.20E–18	8.60E–01	3.21E–03	1.061
F.Crypt_loFos_2	APOE	–2.835	4.08E–17	–1.43E+00	8.91E–15	–0.785
F.Crypt_loFos_2	MTRNR2L1	2.610	1.48E–28	1.02E+00	6.59E–03	2.694
F.Endothelial	AC005540.3	3.774	3.20E–22	5.85E–01	4.07E–01	0.660
F.Endothelial	ANXA2	0.809	2.90E–09	1.02E+00	5.78E–45	0.721
F.Endothelial	CD9	1.131	3.61E–20	3.90E–01	2.00E–05	1.049
F.Endothelial	GAPDH	0.640	1.38E–03	5.31E–01	1.38E–17	0.754
F.Endothelial	HLA-A	–1.590	1.36E–06	–6.64E–01	1.04E–24	–1.462
F.Endothelial	HLA-C	–0.617	9.10E–02	–5.77E–01	5.04E–24	–0.617
F.Endothelial	LGALS1	0.527	1.88E–05	8.46E–01	4.01E–19	1.028
F.Endothelial	MTRNR2L1	2.205	8.01E–57	–6.75E–02	7.67E–01	1.668
F.Endothelial	S100A6	0.691	5.92E–06	1.01E+00	2.42E–27	1.430
F.Endothelial	TAGLN	1.624	4.97E–20	9.22E–01	1.52E–03	0.651
F.Endothelial	TIMP1	0.703	4.10E–08	6.73E–01	7.05E–17	0.694
F.Endothelial	VIM	0.938	3.36E–08	7.75E–01	2.34E–29	1.462
F.Fibroblast	AREG	2.762	2.41E–20	4.30E–01	2.17E–01	0.528
F.Fibroblast	C12orf75	1.837	5.90E–28	3.48E–01	1.96E–02	0.659
F.Fibroblast	EMP3	0.505	1.25E–09	4.92E–01	9.97E–34	0.590
F.Fibroblast	GLIPR1	1.473	3.84E–31	2.25E–01	9.47E–03	0.866
F.Fibroblast	IL13RA2	5.211	6.14E–32		1.00E+00	2.254
F.Fibroblast	INHBA	4.213	2.59E–21		1.00E+00	2.254
F.Fibroblast	MME	4.715	1.69E–35		1.00E+00	2.254
F.Fibroblast	MTRNR2L1	1.638	4.80E–70	8.33E–01	2.73E–10	1.487

TABLE 13-continued

Inflamed vs Healthy Markers						
F.Fibroblast	PRRX1	4.491	2.38E–24		1.00E+00	2.254
F.Fibroblast	PRSS23	1.544	1.03E–52	6.89E–01	9.84E–13	0.783
F.Fibroblast	PTMA	0.290	8.33E–02	5.14E–01	5.87E–33	0.617
F.Fibroblast	RPL7	–0.783	2.22E–06	–3.72E–01	4.41E–17	–0.992
F.Fibroblast	RPS26	–0.737	2.77E–14	–3.74E–01	1.63E–16	–0.707
F.Fibroblast	S100A6	0.310	7.37E–02	6.45E–01	2.95E–31	0.722
F.Fibroblast	SGK1	1.600	2.79E–22	8.71E–01	2.31E–09	0.688
F.Fibroblast	STC1	4.459	5.39E–24		1.00E+00	2.254
F.Fibroblast	TIMP1	0.803	1.52E–10	1.07E+00	1.73E–122	0.604
F.Glia	ANXA1	2.251	1.06E–07	2.05E+00	2.20E–25	4.008
F.Glia	S100A3	4.450	4.92E–21	–3.87E–01	4.85E–01	0.677
F.Pcap_Venules	ANXA2	0.635	1.29E–02	1.18E+00	6.99E–23	0.685
F.Pcap_Venules	COL4A2	2.336	7.99E–27	5.62E–01	2.29E–04	0.910
F.Pcap_Venules	FKBP1A	1.402	3.44E–04	7.98E–01	1.52E–18	0.977
F.Pcap_Venules	PRKCDBP	1.778	5.49E–19	8.81E–01	2.11E–10	1.276
F.Pcap_Venules	PRSS23	1.992	4.28E–22	1.13E+00	1.25E–12	1.271
F.Pcap_Venules	VAMP5	2.074	1.37E–21	6.46E–01	4.93E–04	1.770
F.Stromal	DEFA5	4.171	5.18E–27		1.00E+00	2.053
F.Stromal	GLIPR1	1.206	3.78E–21	1.32E–01	1.41E–01	0.620
F.Stromal	IL13RA2	4.847	5.21E–26		1.00E+00	2.053
F.Stromal	LINC00152	0.880	1.35E–22	4.20E–01	1.13E–10	0.511
F.Stromal	MME	4.368	7.34E–28		1.00E+00	2.053
F.Stromal	MTRNR2L1	1.652	1.46E–93	5.61E–01	2.24E–06	1.346
F.Stromal	PRRX1	4.419	1.14E–22		1.00E+00	2.053
F.Stromal	RGCC	0.835	2.42E–22	2.70E–01	1.42E–02	1.006
F.Stromal	RPL7	–0.662	2.11E–06	–3.05E–01	3.33E–15	–0.852
F.Stromal	RPS26	–0.666	7.83E–15	–3.25E–01	1.12E–16	–0.646
F.Stromal	S100A10	0.447	2.43E–09	4.83E–01	9.92E–23	0.558
F.Stromal	S100A6	0.162	1.84E–01	5.76E–01	2.03E–30	0.503
F.Stromal	TMSB10	0.385	2.10E–02	4.72E–01	3.46E–30	0.736
F.Villus	COL3A1	1.221	2.23E–11	5.24E–01	5.11E–12	0.746
F.Villus	DCN	1.537	3.42E–30	3.62E–01	1.30E–03	1.307
F.Villus	IGFBP7	1.049	1.07E–03	9.90E–01	4.40E–19	1.542
F.Villus	PLAC9	1.552	8.20E–31	2.20E–01	2.27E–03	0.669
F.Villus	TIMP1	1.228	3.53E–08	1.21E+00	1.69E–49	1.394
F.Villus_1	DCN	2.175	1.34E–21	5.02E–01	6.38E–03	2.265
F.Villus_1	LUM	2.080	7.39E–23	5.76E–01	3.15E–02	2.117
F.Villus_1	TIMP1	1.842	1.31E–06	1.49E+00	1.35E–30	2.426
F.Villus_2	PLAC9	1.583	1.57E–19	2.01E–01	4.07E–02	0.794
F.Villus_2	TIMP1	0.864	1.72E–03	1.01E+00	2.78E–20	0.965
I.Immune	AC009501.4	–0.856	2.31E–50	5.93E–02	1.52E–01	–0.784
I.Immune	IGHA2	–0.760	7.42E–37	–9.80E–01	3.00E–21	–0.646
I.Lymphoid	AC009501.4	–0.789	3.67E–43	3.15E–02	4.45E–01	–0.773
I.Lymphoid	ANXA1	–0.548	3.52E–20	–1.52E–01	1.05E–02	–0.526
I.Lymphoid	DHRS9	1.968	3.85E–20	–6.42E–02	7.68E–01	0.711
I.Lymphoid	IGHA2	–0.653	8.92E–28	–7.76E–01	5.33E–13	–0.522
M.CD69pos_Mast	SAMSN1	1.332	4.44E–18	3.55E–01	2.81E–06	1.064
M.CD69pos_Mast	SRGN	1.688	7.65E–12	5.22E–01	1.72E–09	2.121
M.Macrophages	FTL	–1.951	3.23E–03	–6.58E–01	6.94E–21	–2.086
M.Mast	PPAP2A	2.425	1.61E–23	1.70E–01	4.90E–01	1.631
M.Mast	SAMSN1	1.258	1.50E–17	3.46E–01	9.27E–07	0.886
M.Mast	SRGN	1.668	2.53E–12	5.90E–01	3.29E–13	2.145
M.Monocytes	AC009501.4	–0.751	1.25E–16	2.40E–01	3.36E–05	–0.601
M.Monocytes	CD300E	4.435	1.27E–19		1.00E+00	2.268
M.Monocytes	CD74	–0.857	1.69E–02	–6.80E–01	5.05E–25	–0.651
M.Monocytes	CST3	–0.938	4.63E–06	1.04E+00	6.47E–92	–0.611
M.Monocytes	RGS1	–0.963	9.92E–27	1.23E–01	1.00E–01	–0.519
M.Myeloid	CD300E	4.420	1.39E–19		1.00E+00	2.065
M.Myeloid	IL2RG	0.761	5.19E–14	4.04E–01	6.77E–08	0.550
M.Myeloid	JUNB	–0.815	2.96E–18	–1.46E–01	9.95E–03	–0.708
M.Myeloid	SH3BGRL3	0.359	2.28E–04	4.97E–01	3.22E–29	0.522
M.Myeloid	TMEM176B	0.775	8.35E–22	1.47E–01	1.92E–02	0.518
M.Neutrophils	CST3	–1.508	6.90E–03	–1.84E+00	4.29E–28	–1.016
M.Neutrophils	TIMP1	0.622	6.08E–02	1.91E+00	6.49E–24	1.077
T.Activated_CD4_hiFos	RPL39	0.601	2.66E–06	1.20E+00	1.09E–18	0.570
T.Activated_CD4_loFos	ANXA1	–2.040	5.80E–37	–4.49E–01	1.65E–06	–1.270
T.Activated_CD4_loFos	RPL39	0.499	1.23E–04	1.29E+00	9.00E–22	0.557
T.Activated_CD4_loFos	RPS29	0.391	9.55E–02	7.71E–01	1.98E–20	0.680
T.CD4	AC009501.4	–0.674	2.50E–27	1.01E–01	3.23E–02	–0.590
T.CD4	ACP5	1.065	7.77E–22	6.83E–02	5.52E–01	0.628
T.CD4	ANXA1	–1.551	6.16E–138	–4.15E–01	4.74E–14	–0.969
T.CD4	CCL5	–1.068	1.87E–64	5.50E–02	4.40E–01	–0.675
T.CD4	CXCL13	4.921	3.71E–40		1.00E+00	1.584
T.CD4	MT-ND3	0.741	2.99E–30	6.72E–01	1.16E–16	0.679
T.CD4	NPDC1	2.292	9.11E–30	–3.40E–01	1.27E–01	0.730
T.CD4	RPL10	–0.862	3.17E–03	–3.97E–01	7.90E–40	–1.413
T.CD4	RPL13A	–0.805	3.03E–03	–2.81E–01	2.44E–21	–1.161
T.CD4	RPL3	–0.487	3.75E–02	–3.65E–01	1.02E–31	–0.779

TABLE 13-continued

Inflamed vs Healthy Markers

T.CD4	RPS18	−0.525	3.46E−02	−3.14E−01	1.77E−22	−0.857
T.CD4	RPS2	−0.381	1.44E−01	−3.47E−01	9.61E−25	−0.701
T.CD4	RPS3	−0.379	4.81E−02	−3.89E−01	1.29E−38	−0.531
T.CD4	RPS6	−0.737	2.86E−03	−3.12E−01	1.45E−22	−1.117
T.CD4	SRGN	0.451	3.54E−09	3.10E−01	8.66E−18	0.604
T.CD4	VIM	−0.782	2.19E−38	−2.27E−01	3.69E−06	−0.853
T.CD8	ANXA1	−0.806	1.03E−25	−3.22E−01	2.67E−06	−0.760
T.CD8	CD2	0.761	8.07E−20	3.65E−01	3.50E−19	0.632
T.CD8	CD63	−0.780	2.66E−21	−3.56E−01	4.41E−11	−0.689
T.CD8	FOS	−0.623	2.75E−15	−3.31E−01	1.24E−06	−0.559
T.CD8	GADD45G	1.698	2.47E−22	1.85E−01	2.17E−01	0.548
T.CD8	HLA-B	0.858	1.33E−03	4.19E−01	1.45E−22	1.265
T.CD8	RPL3	−0.622	5.58E−02	−4.10E−01	8.03E−22	−1.003
T.CD8	RPL8	−0.736	7.33E−05	−3.74E−01	2.23E−23	−0.824
T.CD8	RPS29	0.341	4.24E−03	4.98E−01	7.90E−24	0.524
T.CD8	TNFRSF4	1.540	7.08E−20	4.29E−01	2.87E−02	0.655
T.CD8	ZFP36	−0.737	4.37E−20	−2.73E−01	7.01E−07	−0.535
T.CD8_IELs	KLRB1	1.674	1.58E−25	1.11E+00	1.72E−14	1.381
T.CD8_LP	ANXA1	−1.174	2.14E−24	−4.29E−01	1.37E−06	−1.040
T.CD8_LP	CD27	0.900	8.38E−15	4.65E−01	6.62E−10	0.522
T.CD8_LP	CST7	0.910	7.31E−14	2.98E−01	3.74E−08	0.519
T.CD8_LP	RPL39	0.594	1.71E−07	9.88E−01	4.26E−14	0.553
T.Cycling_T	CXCR6	2.805	1.15E−19	7.05E−01	4.74E−03	1.903
T.Memory_CD4	ANXA1	−1.660	1.40E−40	−4.97E−01	2.42E−04	−1.223
T.Memory_CD4	CCL5	−1.316	1.96E−21	−2.16E−01	2.97E−01	−1.076
T.Memory_CD4	TOX2	3.301	9.76E−21	4.04E−01	3.30E−01	0.543
T.Tcells	AC009501.4	−0.910	4.89E−56	4.51E−02	2.76E−01	−0.815
T.Tcells	ANXA1	−0.849	1.27E−49	−1.73E−01	6.37E−04	−0.615
T.Tcells	CTSH	1.589	1.59E−25	−6.19E−02	6.77E−01	0.605
T.Tcells	CXCL13	4.630	3.60E−29		1.00E+00	1.874
T.Tcells	NPDC1	2.424	2.51E−27	−2.81E−01	3.16E−01	0.897
T.Tcells	SRGN	0.583	1.62E−16	3.28E−01	8.70E−22	0.664
T.Tcells	TMSB4X	−1.614	6.61E−03	−3.91E−01	8.77E−32	−2.065
T.Tcells	VIM	−0.618	2.92E−27	−7.84E−02	6.91E−02	−0.669
T.Tregs	CD7	1.258	3.50E−22	6.20E−01	4.06E−14	1.382
T.Tregs	LINC00152	1.269	6.98E−23	3.66E−01	1.55E−06	0.749
T.Tregs	MIR4435-1HG	1.248	1.64E−21	3.03E−01	7.06E−05	0.533

	ident	pvalH	n	ref_n	mu	ref_mu	total	ref_total
	B.Bcells	1.04E−38	483	1399	2.242	2.300	0.045	0.136
	B.Bcells	8.87E−74	498	432	1.766	2.020	0.148	0.154
	B.Bcells	5.35E−52	450	439	2.304	1.853	0.141	0.100
	B.Bcells	4.21E−189	1205	1893	4.576	3.181	0.174	0.104
	B.Bcells	8.84E−89	815	780	2.462	2.103	0.215	0.160
	B.Bcells	1.73E−67	412	261	2.558	2.798	0.134	0.100
	B.Bcells	1.01E−110	1105	1696	3.373	2.914	0.154	0.172
	B.Bcells	1.50E−111	928	1091	3.250	2.626	0.175	0.134
	B.Bcells	6.18E−144	1210	1891	3.572	2.654	0.192	0.159
	B.Bcells	4.50E−104	802	713	2.586	2.009	0.182	0.109
	B.Bcells	5.45E−109	1197	1847	3.031	2.347	0.109	0.105
	B.Bcells	1.18E−46	174	44	1.913	1.716	0.163	0.036
	B.Bcells	1.38E−64	757	743	2.158	1.906	0.152	0.126
	B.Bcells	8.67E−80	750	806	2.343	1.813	0.120	0.089
	B.Bcells	4.24E−91	854	1210	3.282	3.224	0.225	0.306
	B.Bcells	1.35E−130	820	1150	4.566	4.059	0.211	0.209
	B.Bcells	2.09E−120	933	1229	3.044	2.562	0.294	0.277
	B.Bcells	3.30E−125	1225	1949	4.009	2.968	0.121	0.093
	B.Bcells	7.49E−158	971	1157	3.959	3.249	0.250	0.182
	B.Bcells	2.57E−82	640	451	3.255	3.056	0.199	0.122
	B.Bcells	7.18E−87	277	27	2.057	1.822	0.302	0.025
	B.Bcells	3.70E−21	48	0	0.632	−17.176	0.031	0.000
	B.Bcells	7.85E−72	470	383	2.264	2.448	0.113	0.105
	B.Bcells	6.61E−145	1275	2048	4.351	3.203	0.117	0.085
	B.Bcells	3.60E−38	154	39	1.755	1.769	0.148	0.038
	B.Bcells	2.82E−41	155	68	1.830	0.739	0.079	0.016
	B.Bcells	7.73E−62	708	864	2.165	2.088	0.173	0.200
	B.Bcells	8.58E−80	1248	2005	3.488	2.912	0.109	0.118
	B.Bcells	3.28E−81	865	854	2.952	2.811	0.260	0.233
	B.Bcells	2.71E−63	992	1484	4.370	4.045	0.204	0.244
	B.Bcells	2.64E−61	843	1074	4.756	4.445	0.214	0.220
	B.Bcells	7.95E−79	779	908	4.032	3.601	0.276	0.239
	B.Bcells	3.96E−47	957	1404	5.906	5.712	0.213	0.273
	B.Bcells	4.69E−68	918	1220	5.136	4.581	0.230	0.208
	B.Bcells	8.27E−48	204	77	2.496	2.746	0.119	0.054
	B.Bcells	2.07E−180	992	2293	10.016	10.713	0.167	0.624
	B.Bcells	8.01E−210	645	2002	7.927	9.053	0.111	0.750
	B.Bcells	1.21E−127	911	2160	8.371	9.095	0.157	0.616

TABLE 13-continued

Inflamed vs Healthy Markers							
B.Bcells	9.10E–78	374	195	2.116	1.882	0.213	0.095
B.Bcells	4.00E–120	727	651	3.945	3.519	0.295	0.197
B.Bcells	2.59E–88	458	209	2.385	2.686	0.262	0.147
B.Bcells	9.96E–110	762	795	3.149	2.853	0.295	0.251
B.Bcells	1.12E–66	945	1525	2.304	1.948	0.149	0.188
B.Bcells	6.26E–26	156	73	1.943	2.469	0.087	0.059
B.Bcells	1.39E–50	631	748	4.703	4.629	0.216	0.244
B.Bcells	1.38E–44	838	1094	3.810	3.127	0.073	0.059
B.Bcells	2.52E–56	1010	1516	2.836	2.441	0.092	0.105
B.Bcells	2.40E–90	820	864	2.757	1.961	0.151	0.092
B.Bcells	8.51E–86	1095	1476	2.904	2.239	0.119	0.101
B.Bcells	1.01E–80	413	262	1.918	1.807	0.199	0.117
B.Bcells	3.65E–81	936	1235	2.460	1.948	0.163	0.151
B.Bcells	1.34E–79	484	297	2.028	2.371	0.138	0.107
B.Bcells	4.97E–138	1100	1723	3.484	2.776	0.236	0.226
B.Bcells	3.65E–95	910	1223	2.569	2.128	0.209	0.207
B.Bcells	9.44E–43	892	1968	1.978	2.456	0.060	0.183
B.Bcells	2.50E–75	1284	2234	3.998	3.235	0.115	0.118
B.Bcells	6.56E–68	1309	2259	4.110	3.482	0.110	0.123
B.Bcells	3.32E–50	380	272	2.055	1.696	0.163	0.091
B.Bcells	4.71E–50	352	269	3.503	2.736	0.235	0.106
B.Bcells	5.59E–20	85	20	1.440	2.189	0.086	0.034
B.Bcells	7.87E–80	688	594	2.676	2.613	0.241	0.199
B.Cycling	1.73E–84	247	174	7.126	5.318	0.092	0.018
B.Cycling	5.54E–43	240	144	5.178	4.016	0.073	0.020
B.Cycling	3.85E–23	209	76	2.861	2.359	0.112	0.029
B.Cycling	1.45E–42	231	133	3.844	2.892	0.070	0.021
B.Cycling	8.02E–24	212	91	3.597	3.114	0.076	0.023
B.Cycling	5.71E–47	240	151	4.273	3.328	0.093	0.030
B.Cycling	2.73E–29	229	120	3.523	2.612	0.064	0.018
B.Cycling	4.99E–23	206	61	2.958	2.422	0.088	0.018
B.Cycling	1.52E–32	190	93	3.093	2.225	0.132	0.035
B.Cycling	2.41E–49	222	99	4.402	3.454	0.135	0.031
B.Cycling	2.67E–54	249	171	5.563	4.394	0.067	0.020
B.Cycling	9.31E–40	240	162	4.498	3.578	0.140	0.050
B.Cycling	7.15E–19	206	93	3.988	3.518	0.063	0.021
B.Cycling	4.55E–24	217	86	5.384	4.656	0.071	0.017
B.Cycling	3.18E–55	244	143	4.953	3.918	0.136	0.039
B.Cycling	2.29E–26	221	94	4.563	4.045	0.293	0.087
B.Cycling	4.80E–31	235	119	3.988	3.437	0.131	0.045
B.Cycling	1.85E–61	236	128	4.838	3.643	0.207	0.049
B.Cycling	1.80E–37	238	153	4.078	3.108	0.068	0.022
B.Cycling	1.11E–34	227	117	3.716	2.806	0.081	0.022
B.Cycling	1.06E–26	216	102	2.854	1.895	0.069	0.017
B.Cycling	3.25E–26	173	53	3.612	3.180	0.109	0.025
B.Cycling	2.36E–19	140	24	2.164	1.371	0.228	0.023
B.Cycling	6.13E–21	154	31	2.328	2.730	0.136	0.036
B.Cycling	6.63E–21	220	91	3.354	2.544	0.064	0.015
B.Cycling	4.43E–23	220	115	3.195	2.347	0.073	0.021
B.Cycling	5.09E–25	188	61	2.981	2.794	0.134	0.038
B.Cycling	3.95E–23	161	31	3.630	2.981	0.363	0.045
B.Cycling	1.51E–21	187	80	2.718	2.124	0.076	0.021
B.Cycling	1.01E–23	173	85	2.356	1.536	0.148	0.041
B.Cycling	1.37E–24	238	154	4.104	3.464	0.070	0.029
B.Cycling	1.88E–33	213	91	3.527	2.469	0.090	0.018
B.Cycling	5.24E–28	201	90	2.794	2.002	0.093	0.024
B.Cycling	1.04E–27	224	114	3.694	2.991	0.110	0.034
B.Cycling	2.82E–21	187	96	4.783	3.306	0.068	0.013
B.Cycling	1.72E–20	218	84	3.978	3.890	0.237	0.086
B.Cycling	2.42E–39	238	124	4.983	4.198	0.137	0.041
B.Cycling	9.78E–42	230	99	4.397	3.556	0.175	0.042
B.FO	8.53E–24	157	191	2.338	2.889	0.082	0.146
B.FO	4.61E–29	185	172	2.828	2.996	0.103	0.108
B.FO	1.07E–42	346	886	6.547	5.472	0.077	0.093
B.FO	5.91E–33	320	636	4.777	3.888	0.067	0.071
B.FO	1.32E–19	135	153	2.756	3.301	0.060	0.099
B.FO	4.79E–20	308	663	3.749	3.828	0.071	0.162
B.FO	1.67E–19	256	441	3.575	3.342	0.077	0.113
B.FO	5.19E–21	64	22	2.335	2.708	0.086	0.038
B.FO	1.30E–19	185	216	3.051	3.392	0.120	0.178
B.FO	6.21E–22	216	330	2.583	3.130	0.086	0.191
B.FO	1.07E–37	298	736	4.974	4.587	0.122	0.231
B.FO	9.69E–29	269	464	3.294	3.481	0.140	0.274
B.FO	2.17E–21	86	46	2.090	2.916	0.068	0.064
B.FO	1.09E–39	305	593	4.035	3.817	0.113	0.189
B.FO	2.77E–23	222	293	3.507	3.312	0.104	0.120
B.FO	9.81E–33	71	3	2.270	2.417	0.112	0.005
B.FO	1.79E–18	76	28	1.912	2.337	0.106	0.052

TABLE 13-continued

Inflamed vs Healthy Markers							
B.FO	4.13E–26	174	198	2.430	3.137	0.057	0.106
B.FO	1.15E–19	63	17	2.007	2.685	0.081	0.035
B.FO	6.68E–31	81	15	2.190	2.182	0.062	0.011
B.FO	5.23E–28	65	6	1.842	2.346	0.148	0.019
B.FO	8.78E–20	199	311	2.591	2.886	0.058	0.112
B.FO	1.78E–40	209	240	2.609	2.695	0.101	0.124
B.FO	3.07E–20	158	202	2.279	2.676	0.104	0.175
B.FO	8.54E–19	109	105	2.143	2.803	0.031	0.047
B.FO	1.04E–22	347	882	5.567	5.194	0.053	0.104
B.FO	1.31E–28	81	34	2.751	2.799	0.066	0.029
B.FO	2.61E–22	135	655	8.300	7.716	0.080	0.258
B.FO	1.06E–19	165	171	2.806	2.748	0.078	0.078
B.FO	5.92E–39	140	70	2.395	2.901	0.121	0.086
B.FO	2.11E–40	278	466	4.067	3.725	0.161	0.213
B.FO	6.19E–25	139	115	2.181	2.949	0.097	0.137
B.FO	4.78E–30	249	388	3.235	3.400	0.145	0.254
B.FO	1.00E–20	251	426	2.947	3.109	0.083	0.157
B.FO	6.31E–20	149	153	2.368	3.076	0.047	0.079
B.FO	1.65E–28	139	97	1.987	2.737	0.099	0.116
B.FO	1.57E–30	166	157	2.351	2.981	0.072	0.105
B.FO	6.28E–37	301	615	4.006	3.826	0.125	0.226
B.FO	2.83E–22	249	406	2.957	3.220	0.098	0.192
B.FO	2.31E–21	205	336	3.024	3.304	0.142	0.283
B.FO	1.36E–19	131	137	3.426	2.895	0.069	0.050
B.FO	4.87E–26	157	137	2.445	2.712	0.124	0.131
B.FO	1.32E–24	107	60	2.219	2.971	0.061	0.058
B.FO	1.17E–20	109	72	1.997	2.474	0.043	0.040
B.GC	3.38E–20	184	94	7.326	6.520	0.079	0.023
B.GC	1.04E–20	176	62	4.966	4.158	0.107	0.021
B.GC	1.14E–19	168	48	4.267	3.147	0.187	0.025
B.Plasma	1.27E–28	72	11	1.428	–0.956	0.061	0.002
B.Plasma	2.63E–150	513	1325	10.681	11.221	0.162	0.606
B.Plasma	5.56E–177	443	1319	8.371	9.410	0.118	0.720
B.Plasma	1.78E–118	509	1326	8.796	9.476	0.144	0.601
B.Plasma	5.02E–20	47	10	3.860	0.076	0.161	0.002
B.Plasma	2.94E–25	349	1113	2.132	2.616	0.056	0.252
B.Plasma	1.44E–24	430	1235	1.500	1.718	0.025	0.083
E.Absorptive	3.63E–67	96	1244	3.047	2.477	0.017	0.146
E.Absorptive	2.65E–21	368	1671	7.505	7.222	0.048	0.179
E.Absorptive	1.21E–42	190	387	1.659	1.214	0.063	0.094
E.Absorptive	5.55E–32	88	17	–0.143	0.976	0.035	0.015
E.Absorptive	1.59E–43	258	628	1.227	0.982	0.034	0.071
E.Absorptive	2.53E–33	305	1551	3.289	4.431	0.035	0.393
E.Absorptive	3.05E–49	98	14	4.137	1.495	0.224	0.005
E.Absorptive	1.67E–21	65	25	0.004	0.987	0.017	0.013
E.Absorptive	1.41E–19	39	4	0.106	0.014	0.024	0.002
E.Absorptive	6.06E–21	53	21	0.786	0.777	0.060	0.023
E.Absorptive	1.28E–32	339	1314	3.011	2.752	0.057	0.184
E.Absorptive	9.74E–40	368	1639	5.426	4.978	0.048	0.156
E.Absorptive	5.58E–67	294	498	2.895	1.921	0.029	0.025
E.Absorptive	1.89E–28	336	1328	2.345	2.218	0.035	0.127
E.Absorptive	3.06E–35	251	1384	2.155	3.528	0.019	0.264
E.Absorptive	4.77E–33	54	0	2.628	–16.350	0.305	0.000
E.Absorptive	1.89E–20	74	87	2.443	1.702	0.089	0.062
E.Absorptive	2.35E–43	219	378	2.533	1.516	0.027	0.023
E.Absorptive	9.93E–59	265	638	1.643	1.188	0.053	0.093
E.Absorptive	4.23E–45	344	1349	2.750	2.245	0.034	0.093
E.Absorptive	5.24E–40	291	857	1.725	1.341	0.034	0.077
E.Absorptive	1.68E–19	367	1664	5.041	5.531	0.048	0.303
E.Absorptive	7.19E–24	60	7	–0.129	0.206	0.061	0.009
E.Absorptive	1.86E–24	54	0	4.033	–16.350	0.787	0.000
E.Absorptive	2.07E–114	348	1120	3.784	2.433	0.184	0.233
E.Absorptive	1.59E–26	53	2	–0.482	2.042	0.038	0.008
E.Absorptive	1.33E–24	69	44	0.194	0.781	0.030	0.029
E.Absorptive	8.20E–35	95	29	0.344	0.063	0.098	0.025
E.Absorptive	6.88E–20	85	89	0.778	0.921	0.042	0.049
E.Absorptive	1.36E–64	245	306	3.534	1.581	0.107	0.035
E.Absorptive	3.60E–32	198	380	0.437	0.549	0.017	0.035
E.Absorptive	2.80E–49	281	838	1.844	1.287	0.044	0.089
E.Absorptive	1.14E–50	346	1269	2.922	2.023	0.059	0.117
E.Absorptive	1.05E–83	298	675	2.781	2.124	0.100	0.144
E.Absorptive	7.50E–46	100	21	3.802	0.828	0.058	0.002
E.Absorptive	2.22E–68	249	318	2.422	1.037	0.071	0.035
E.Absorptive	3.20E–94	259	597	3.764	1.869	0.067	0.042
E.Absorptive	1.62E–20	371	1672	7.159	6.231	0.106	0.252
E.Absorptive	6.48E–38	78	3	2.437	0.683	0.116	0.001
E.Absorptive	2.00E–35	298	1066	4.479	3.742	0.111	0.238
E.Absorptive	1.02E–28	283	1390	2.314	2.850	0.018	0.131

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Absorptive	8.49E–41	89	0	1.292	16.350	0.525	0.000
E.Absorptive	3.41E–37	90	123	1.233	0.242	0.030	0.021
E.Absorptive	3.92E–50	164	116	2.724	1.038	0.080	0.018
E.Absorptive	6.82E–77	282	511	3.886	2.445	0.134	0.089
E.Absorptive	6.35E–35	148	205	1.012	0.544	0.029	0.029
E.Absorptive	1.58E–23	40	0	0.468	−16.350	0.127	0.000
E.Absorptive	3.03E–25	94	68	1.088	0.087	0.045	0.016
E.Absorptive_All	5.06E–183	499	1770	3.543	2.771	0.096	0.200
E.Absorptive_All	1.07E–103	1420	1658	4.318	3.137	0.192	0.099
E.Absorptive_All	1.07E–28	369	140	1.080	1.047	0.042	0.016
E.Absorptive_All	2.98E–40	196	11	0.329	0.516	0.083	0.005
E.Absorptive_All	8.56E–75	1546	2357	4.293	4.737	0.122	0.254
E.Absorptive_All	2.66E–88	344	23	3.817	1.783	0.413	0.007
E.Absorptive_All	6.90E–30	119	3	0.444	−0.040	0.170	0.003
E.Absorptive_All	3.80E–71	1056	1138	2.072	1.589	0.084	0.065
E.Absorptive_All	3.95E–77	1522	2444	7.166	7.331	0.214	0.385
E.Absorptive_All	9.02E–37	856	1500	2.216	2.345	0.032	0.062
E.Absorptive_All	2.50E–26	105	5	0.881	0.092	0.090	0.002
E.Absorptive_All	3.01E–23	1735	2489	7.437	7.860	0.150	0.289
E.Absorptive_All	1.08E–71	1624	2409	4.913	5.477	0.066	0.146
E.Absorptive_All	3.03E–23	91	0	0.408	−17.539	0.638	0.000
E.Absorptive_All	4.82E–35	1419	1960	3.283	2.913	0.073	0.078
E.Absorptive_All	3.80E–54	431	141	1.562	1.256	0.089	0.024
E.Absorptive_All	3.16E–22	160	36	0.933	1.601	0.042	0.015
E.Absorptive_All	3.42E–125	920	460	3.002	1.778	0.087	0.019
E.Absorptive_All	7.80E–22	69	0	2.368	−17.539	0.257	0.000
E.Absorptive_All	6.50E–31	177	17	0.337	1.431	0.037	0.007
E.Absorptive_All	3.04E–73	773	591	2.612	1.755	0.084	0.036
E.Absorptive_All	7.60E–77	730	452	1.506	1.165	0.108	0.053
E.Absorptive_All	1.54E–46	843	1549	1.949	2.368	0.041	0.100
E.Absorptive_All	1.46E–21	76	0	0.542	−17.539	0.169	0.000
E.Absorptive_All	3.29E–38	325	84	2.983	1.893	0.082	0.010
E.Absorptive_All	1.64E–23	93	0	3.614	−17.539	0.846	0.000
E.Absorptive_All	1.12E–51	620	634	5.729	4.769	0.196	0.103
E.Absorptive_All	7.61E–35	1588	2402	4.612	4.908	0.127	0.236
E.Absorptive_All	1.04E–116	729	219	3.864	2.852	0.385	0.057
E.Absorptive_All	1.04E–39	159	2	0.058	1.779	0.118	0.005
E.Absorptive_All	3.45E–56	1691	2487	7.162	7.586	0.193	0.381
E.Absorptive_All	2.14E–274	1177	517	4.189	2.265	0.436	0.050
E.Absorptive_All	1.39E–28	1505	2317	4.054	4.443	0.135	0.272
E.Absorptive_All	1.83E–85	739	442	2.499	2.072	0.170	0.076
E.Absorptive_All	3.67E–46	155	3	2.961	1.219	0.259	0.002
E.Absorptive_All	1.17E–117	432	39	4.135	1.191	0.214	0.003
E.Absorptive_All	3.25E–102	833	482	2.349	1.403	0.161	0.048
E.Absorptive_All	2.68E–202	1159	957	3.596	2.147	0.197	0.060
E.Absorptive_All	1.74E–95	1745	2469	6.831	5.829	0.275	0.194
E.Absorptive_All	2.81E–65	259	3	2.452	1.956	0.265	0.002
E.Absorptive_All	0.00E+00	1060	152	3.259	1.072	0.406	0.013
E.Absorptive_All	1.13E–53	983	971	4.085	3.343	0.238	0.140
E.Absorptive_All	5.91E–55	1159	1974	2.878	3.300	0.078	0.177
E.Absorptive_All	3.95E–49	216	0	1.169	−17.539	0.707	0.000
E.Absorptive_All	9.70E–52	255	89	1.308	0.390	0.076	0.014
E.Absorptive_All	2.95E–67	465	106	2.102	1.260	0.117	0.015
E.Absorptive_All	6.51E–168	910	319	3.398	2.057	0.183	0.025
E.Absorptive_All	3.72E–205	683	37	2.154	0.887	0.059	0.001
E.Absorptive_All	4.74E–59	213	2	2.231	0.680	0.657	0.002
E.Absorptive_All	1.02E–25	109	6	0.210	0.649	0.066	0.005
E.Absorptive_All	8.34E–31	325	165	0.971	0.712	0.056	0.024
E.Absorptive_All	9.55E–19	63	0	0.619	−17.539	0.153	0.000
E.Absorptive_All	4.63E–21	82	0	−0.334	−17.539	0.382	0.000
E.Absorptive_TA_1	6.59E–22	287	1127	4.349	4.683	0.038	0.188
E.Absorptive_TA_1	9.35E–22	32	0	2.997	−16.123	0.159	0.000
E.Absorptive_TA_1	1.86E–32	48	0	4.117	−16.123	0.280	0.000
E.Absorptive_TA_1	2.17E–20	282	1113	4.277	4.599	0.032	0.156
E.Absorptive_TA_1	3.94E–33	305	1175	4.861	5.329	0.041	0.218
E.Absorptive_TA_1	5.38E–23	124	181	6.262	5.640	0.098	0.093
E.Absorptive_TA_1	4.01E–53	158	124	3.474	2.132	0.107	0.033
E.Absorptive_TA_1	2.90E–52	113	28	4.725	2.681	0.184	0.011
E.Absorptive_TA_1	1.29E–49	89	10	5.391	2.272	0.137	0.002
E.Absorptive_TA_1	1.17E–23	345	1190	5.632	6.131	0.028	0.139
E.Absorptive_TA_1	5.40E–24	288	1114	4.851	5.283	0.024	0.127
E.Absorptive_TA_1	1.45E–18	324	1160	4.973	5.378	0.034	0.159
E.Absorptive_TA_1	7.17E–23	284	1135	4.886	5.183	0.038	0.186
E.Absorptive_TA_1	1.97E–25	326	1166	5.373	5.832	0.030	0.146
E.Absorptive_TA_1	1.05E–19	353	1201	6.053	6.492	0.036	0.167
E.Absorptive_TA_1	2.64E–24	342	1178	5.895	6.451	0.032	0.162
E.Absorptive_TA_1	1.39E–20	248	1066	4.626	4.803	0.030	0.147
E.Absorptive_TA_1	2.31E–26	200	420	4.010	2.805	0.061	0.056

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Absorptive_TA_1	2.27E−63	118	16	3.177	2.420	0.090	0.007
E.Absorptive_TA_1	1.88E−19	28	0	4.104	−16.123	0.206	0.000
E.Absorptive_TA_2	1.67E−49	108	978	2.753	2.209	0.016	0.099
E.Absorptive_TA_2	5.72E−26	244	762	1.317	1.042	0.018	0.046
E.Absorptive_TA_2	2.03E−32	230	709	1.100	0.888	0.020	0.052
E.Absorptive_TA_2	1.04E−29	125	136	0.487	0.004	0.017	0.014
E.Absorptive_TA_2	3.17E−27	80	33	3.099	1.067	0.101	0.010
E.Absorptive_TA_2	3.39E−26	0	196	15.775	1.382	0.000	0.414
E.Absorptive_TA_2	9.60E−35	179	1000	1.859	2.173	0.006	0.045
E.Absorptive_TA_2	9.89E−63	285	1071	3.715	2.380	0.129	0.192
E.Absorptive_TA_2	3.17E−36	236	723	2.088	1.210	0.021	0.035
E.Absorptive_TA_2	1.48E−30	174	955	1.427	1.858	0.007	0.054
E.Absorptive_TA_2	6.59E−27	286	1098	4.565	3.788	0.069	0.155
E.Absorptive_TA_2	1.08E−21	284	1168	5.498	6.173	0.051	0.335
E.Absorptive_TA_2	8.69E−134	260	393	2.514	0.418	0.092	0.033
E.Absorptive_TA_2	4.16E−65	203	174	3.529	2.182	0.143	0.048
E.Absorptive_TA_2	6.47E−27	52	0	−0.858	−15.775	0.028	0.000
E.Absorptive_TA_2	4.48E−63	258	869	2.012	1.269	0.042	0.084
E.Absorptive_TA_2	4.35E−74	181	98	4.252	1.520	0.207	0.017
E.Absorptive_TA_2	2.15E−36	0	223	−15.775	0.428	0.000	0.383
E.Absorptive_TA_2	5.99E−156	275	640	4.217	1.691	0.176	0.071
E.Absorptive_TA_2	3.72E−119	263	173	2.341	1.663	0.191	0.079
E.Absorptive_TA_2	2.16E−31	194	453	1.214	0.782	0.022	0.037
E.Absorptive_TA_2	5.48E−24	278	1099	2.848	2.347	0.047	0.130
E.Absorptive_TA_2	1.17E−62	133	38	2.935	0.315	0.044	0.002
E.Absorptive_TA_2	8.97E−33	217	469	1.352	0.707	0.033	0.046
E.Absorptive_TA_2	1.52E−35	0	128	−15.775	0.241	0.000	0.480
E.Absorptive_TA_2	4.75E−20	277	1164	3.804	3.300	0.032	0.096
E.Absorptive_TA_2	8.98E−21	287	1160	4.829	4.037	0.064	0.149
E.Absorptive_TA_2	9.43E−84	282	1031	3.086	1.900	0.045	0.073
E.Absorptive_TA_2	1.75E−23	288	1168	6.355	5.263	0.063	0.120
E.Absorptive_TA_2	3.59E−28	67	3	1.502	1.961	0.049	0.003
E.Absorptive_TA_2	3.81E−179	264	91	2.802	0.469	0.146	0.010
E.Absorptive_TA_2	4.03E−27	162	295	0.156	0.557	0.014	0.033
E.Absorptive_TA_2	7.64E−24	276	1102	3.102	2.616	0.024	0.068
E.Absorptive_TA_2	2.21E−42	157	126	0.848	0.179	0.021	0.010
E.Absorptive_TA_2	5.98E−24	280	1075	2.697	2.218	0.031	0.085
E.Absorptive_TA_2	1.80E−23	79	19	−0.213	−0.276	0.035	0.008
E.Absorptive_TA_2	1.86E−55	168	76	0.440	0.306	0.071	0.029
E.Best4_Enterocytes	2.05E−22	25	560	2.688	2.214	0.004	0.061
E.Best4_Enterocytes	1.82E−27	26	382	3.039	4.311	0.004	0.148
E.Best4_Enterocytes	2.45E−22	96	270	1.260	0.959	0.018	0.041
E.Best4_Enterocytes	7.78E−29	101	353	1.532	1.073	0.026	0.065
E.Best4_Enterocytes	9.26E−22	115	620	2.667	2.338	0.012	0.050
E.Best4_Enterocytes	1.81E−21	105	447	1.823	1.591	0.014	0.049
E.Best4_Enterocytes	3.05E−31	107	429	2.315	1.465	0.039	0.088
E.Best4_Enterocytes	6.68E−26	110	369	2.730	2.114	0.045	0.099
E.Best4_Enterocytes	2.87E−19	114	679	4.122	3.100	0.021	0.063
E.Best4_Enterocytes	1.99E−19	114	667	3.374	2.549	0.019	0.064
E.Best4_Enterocytes	7.59E−39	99	459	4.832	2.087	0.035	0.024
E.Best4_Enterocytes	2.80E−32	111	503	3.229	2.037	0.021	0.042
E.Cycling_TA	5.07E−54	192	73	−0.165	−0.156	0.064	0.024
E.Cycling_TA	3.68E−32	229	414	0.233	0.023	0.016	0.025
E.Cycling_TA	1.26E−65	295	772	1.373	0.610	0.023	0.036
E.Cycling_TA	7.50E−29	99	20	−0.848	−0.545	0.023	0.006
E.Cycling_TA	3.57E−43	290	712	0.945	0.435	0.038	0.066
E.Cycling_TA	2.72E−21	43	0	0.046	−16.039	0.400	0.000
E.Cycling_TA	3.31E−41	300	884	1.345	0.986	0.019	0.043
E.Cycling_TA	2.46E−45	95	1	1.899	−0.996	0.129	0.000
E.Cycling_TA	8.52E−60	335	1115	3.118	2.367	0.070	0.138
E.Cycling_TA	2.85E−25	0	196	−16.039	1.191	0.000	0.437
E.Cycling_TA	2.76E−29	86	4	0.594	−0.174	0.046	0.001
E.Cycling_TA	1.58E−26	331	1124	3.177	2.784	0.020	0.051
E.Cycling_TA	3.05E−44	185	168	0.709	−0.238	0.027	0.013
E.Cycling_TA	1.83E−63	216	187	2.645	0.621	0.020	0.004
E.Cycling_TA	2.09E−63	300	721	1.352	0.729	0.034	0.053
E.Cycling_TA	2.00E−24	109	52	−0.617	0.124	0.014	0.012
E.Cycling_TA	8.80E−54	313	920	1.986	0.980	0.026	0.038
E.Cycling_TA	2.28E−19	261	1008	1.140	1.931	0.009	0.062
E.Cycling_TA	2.25E−57	317	1010	2.274	1.402	0.041	0.072
E.Cycling_TA	9.20E−24	150	106	1.316	0.861	0.015	0.008
E.Cycling_TA	2.07E−20	59	0	1.276	−16.039	0.363	0.000
E.Cycling_TA	2.71E−22	171	276	3.852	3.351	0.032	0.037
E.Cycling_TA	8.20E−110	312	552	1.899	0.016	0.077	0.037
E.Cycling_TA	1.01E−89	317	963	1.906	1.041	0.047	0.078
E.Cycling_TA	3.95E−49	166	87	3.890	0.168	0.152	0.006
E.Cycling_TA	4.80E−33	77	6	−0.386	−0.939	0.027	0.001
E.Cycling_TA	3.04E−38	0	215	−16.039	0.091	0.000	0.312

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Cycling_TA	8.54E−128	327	766	3.655	1.479	0.155	0.080
E.Cycling_TA	4.47E−117	317	204	2.128	1.458	0.193	0.078
E.Cycling_TA	1.15E−67	284	737	1.509	0.823	0.037	0.059
E.Cycling_TA	8.16E−64	332	1109	3.154	2.406	0.065	0.130
E.Cycling_TA	1.65E−110	218	71	3.325	−0.106	0.088	0.003
E.Cycling_TA	1.40E−42	330	1123	3.010	2.584	0.036	0.091
E.Cycling_TA	3.72E−25	326	1148	3.522	3.094	0.052	0.137
E.Cycling_TA	4.98E−19	338	1144	4.344	3.572	0.057	0.113
E.Cycling_TA	2.88E−110	330	1020	2.905	1.523	0.049	0.058
E.Cycling_TA	3.37E−161	300	75	1.995	−0.225	0.102	0.005
E.Cycling_TA	3.06E−38	88	0	1.949	−16.039	0.160	0.000
E.Cycling_TA	3.67E−41	329	1104	3.205	2.516	0.031	0.064
E.Cycling_TA	2.07E−50	322	1015	1.589	1.204	0.039	0.094
E.Cycling_TA	1.10E−44	175	44	−0.361	−0.773	0.046	0.009
E.Cycling_TA	3.35E−30	70	2	0.257	−1.101	0.074	0.001
E.Cycling_TA	1.82E−45	327	1094	2.266	1.793	0.044	0.107
E.Enterocyte_Immature_1	3.94E−30	71	674	3.489	2.577	0.018	0.091
E.Enterocyte_Immature_1	1.62E−39	76	50	3.467	1.480	0.127	0.021
E.Enterocyte_Immature_1	1.14E−34	59	29	2.781	1.184	0.113	0.018
E.Enterocyte_Immature_1	6.80E−19	194	876	3.054	3.556	0.017	0.111
E.Enterocyte_Immature_1	1.66E−56	104	36	3.813	1.624	0.065	0.005
E.Enterocyte_Immature_1	1.71E−23	99	143	3.221	2.143	0.053	0.036
E.Enterocyte_Immature_1	3.70E−52	80	13	3.021	1.017	0.060	0.002
E.Enterocyte_Immature_1	1.08E−18	24	0	3.099	−15.690	0.276	0.000
E.Enterocyte_Immature_1	1.45E−20	65	94	3.071	1.521	0.090	0.044
E.Enterocyte_Immature_2	1.28E−73	65	980	3.494	2.688	0.015	0.133
E.Enterocyte_Immature_2	1.33E−57	237	900	3.860	1.992	0.043	0.045
E.Enterocyte_Immature_2	9.38E−60	112	983	3.543	4.692	0.018	0.354
E.Enterocyte_Immature_2	1.01E−30	79	40	0.025	0.252	0.027	0.016
E.Enterocyte_Immature_2	2.72E−30	60	11	3.704	1.756	0.171	0.008
E.Enterocyte_Immature_2	3.06E−48	246	967	3.873	2.885	0.115	0.228
E.Enterocyte_Immature_2	5.41E−68	189	301	1.953	0.832	0.140	0.102
E.Enterocyte_Immature_2	1.07E−22	57	24	1.056	0.286	0.074	0.018
E.Enterocyte_Immature_2	5.95E−34	173	431	1.181	0.348	0.032	0.045
E.Enterocyte_Immature_2	2.38E−39	78	4	0.534	−0.290	0.088	0.003
E.Enterocyte_Immature_2	1.08E−36	64	9	3.656	0.681	0.116	0.002
E.Enterocyte_Immature_2	1.07E−22	52	15	1.809	0.622	0.050	0.006
E.Enterocyte_Immature_2	5.04E−24	199	756	1.317	0.913	0.012	0.035
E.Enterocyte_Immature_2	1.14E−34	120	99	0.559	0.331	0.038	0.027
E.Enterocyte_Immature_2	4.30E−40	88	736	0.584	1.254	0.005	0.069
E.Enterocyte_Immature_2	9.39E−26	249	1141	5.004	5.844	0.014	0.113
E.Enterocyte_Immature_2	6.11E−73	196	528	3.327	1.076	0.088	0.050
E.Enterocyte_Immature_2	1.54E−49	166	470	1.710	0.659	0.025	0.034
E.Enterocyte_Immature_2	4.27E−24	230	1103	2.452	3.667	0.022	0.243
E.Enterocyte_Immature_2	1.05E−37	169	330	0.959	0.556	0.024	0.035
E.Enterocyte_Immature_2	6.48E−20	144	288	1.805	1.058	0.044	0.052
E.Enterocyte_Immature_2	4.08E−124	239	796	3.756	1.942	0.168	0.159
E.Enterocyte_Immature_2	6.48E−37	199	703	1.494	0.811	0.024	0.052
E.Enterocyte_Immature_2	9.63E−37	0	266	−15.642	0.429	0.000	0.428
E.Enterocyte_Immature_2	6.71E−124	213	202	3.893	1.041	0.130	0.017
E.Enterocyte_Immature_2	8.08E−42	141	237	1.227	0.480	0.021	0.021
E.Enterocyte_Immature_2	3.46E−36	166	294	1.462	0.586	0.029	0.028
E.Enterocyte_Immature_2	2.39E−115	216	455	3.102	0.909	0.039	0.018
E.Enterocyte_Immature_2	1.71E−32	253	1145	7.420	6.162	0.101	0.190
E.Enterocyte_Immature_2	1.09E−35	60	0	2.563	−15.642	0.112	0.000
E.Enterocyte_Immature_2	7.40E−209	229	130	3.547	0.233	0.202	0.012
E.Enterocyte_Immature_2	2.47E−25	43	0	0.839	−15.642	0.034	0.000
E.Enterocyte_Immature_2	9.10E−37	152	319	0.941	0.464	0.021	0.031
E.Enterocyte_Immature_2	6.64E−21	47	2	−0.567	−0.713	0.036	0.001
E.Enterocyte_Immature_2	4.54E−38	225	691	3.275	2.417	0.053	0.089
E.Enterocyte_Immature_2	2.54E−29	55	0	−0.463	−15.642	0.043	0.000
E.Enterocyte_Immature_2	1.75E−25	53	0	0.218	−15.642	0.229	0.000
E.Enterocyte_Immature_2	1.94E−81	191	166	2.581	0.688	0.048	0.011
E.Enterocyte_Immature_2	1.39E−18	50	30	0.011	−0.183	0.022	0.012
E.Enterocyte_Immature_2	2.93E−32	54	0	1.504	−15.642	0.221	0.000
E.Enterocyte_Immature_2	6.20E−34	184	486	1.050	0.498	0.031	0.056
E.Enterocyte_Immature_2	1.12E−27	114	164	0.468	0.336	0.019	0.026
E.Enterocyte_Progenitor	6.40E−33	43	730	4.134	2.797	0.016	0.109
E.Enterocyte_Progenitor	1.04E−19	154	718	4.526	3.249	0.040	0.078
E.Enterocyte_Progenitor	1.54E−24	36	8	3.640	3.171	0.109	0.017
E.Enterocyte_Progenitor	9.54E−33	125	399	3.877	2.457	0.074	0.088
E.Enterocyte_Progenitor	9.52E−28	51	45	3.397	1.546	0.113	0.028
E.Enterocyte_Progenitor	2.55E−26	36	6	4.054	2.459	0.076	0.004
E.Enterocyte_Progenitor	5.02E−24	38	20	3.835	1.636	0.091	0.010
E.Enterocyte_Progenitor	6.59E−34	37	0	3.588	−15.791	0.160	0.000
E.Enterocyte_Progenitor	2.31E−40	126	372	3.980	2.527	0.083	0.089
E.Enterocyte_Progenitor	4.70E−28	88	985	3.157	3.622	0.014	0.219
E.Enterocyte_Progenitor	1.65E−63	101	124	5.392	2.337	0.175	0.026

TABLE 13-continued

Inflamed vs Healthy Markers

E.Enterocyte_Progenitor	1.61E–36	58	25	3.823	2.042	0.063	0.008
E.Enterocyte_Progenitor	4.98E–59	96	108	5.484	2.505	0.251	0.036
E.Enterocyte_Progenitor	8.16E–74	122	118	4.703	2.794	0.123	0.032
E.Enterocyte_Progenitor	1.20E–42	125	359	4.224	2.418	0.047	0.039
E.Enterocyte_Progenitor	3.89E–26	205	1181	7.046	5.789	0.067	0.161
E.Enterocyte_Progenitor	1.22E–24	27	0	3.071	–15.791	0.059	0.000
E.Enterocyte_Progenitor	6.78E–108	128	33	3.785	1.938	0.141	0.010
E.Enterocyte_Progenitor	7.32E–28	56	40	3.942	1.617	0.030	0.004
E.Enterocyte_Progenitor	2.35E–19	21	0	2.816	–15.791	0.224	0.000
E.Enterocyte_Progenitor	9.85E–21	162	974	4.744	3.701	0.022	0.064
E.Enterocytes	3.29E–54	71	684	3.154	2.661	0.014	0.097
E.Enterocytes	1.87E–38	112	57	0.696	0.222	0.053	0.019
E.Enterocytes	3.02E–42	175	293	1.501	0.733	0.030	0.029
E.Enterocytes	6.23E–42	218	834	3.330	4.681	0.032	0.317
E.Enterocytes	1.14E–38	97	99	1.409	0.445	0.024	0.012
E.Enterocytes	3.73E–44	100	43	1.540	0.413	0.045	0.009
E.Enterocytes	5.35E–22	0	94	15.546	0.155	0.000	0.226
E.Enterocytes	1.50E–52	127	109	2.084	0.480	0.093	0.026
E.Enterocytes	6.97E–43	97	7	1.678	–0.684	0.234	0.003
E.Enterocytes	3.97E–44	87	9	4.272	1.896	0.211	0.004
E.Enterocytes	3.20E–37	92	32	3.499	1.773	0.173	0.018
E.Enterocytes	4.28E–21	36	0	0.182	–15.546	0.021	0.000
E.Enterocytes	8.51E–32	248	841	8.636	9.465	0.060	0.359
E.Enterocytes	1.07E–29	65	0	0.184	–15.546	0.301	0.000
E.Enterocytes	4.72E–24	88	51	1.237	0.074	0.021	0.006
E.Enterocytes	4.32E–56	126	118	3.658	0.425	0.078	0.008
E.Enterocytes	3.48E–31	178	762	1.690	2.598	0.018	0.147
E.Enterocytes	1.36E–39	209	841	6.294	6.837	0.080	0.466
E.Enterocytes	4.28E–22	248	839	5.747	5.340	0.044	0.111
E.Enterocytes	1.24E–34	192	391	1.815	1.378	0.071	0.107
E.Enterocytes	2.75E–27	49	0	2.465	–15.546	0.268	0.000
E.Enterocytes	1.91E–46	136	88	2.979	1.572	0.022	0.005
E.Enterocytes	5.18E–37	194	479	1.779	1.105	0.047	0.073
E.Enterocytes	5.39E–27	229	729	2.790	2.162	0.024	0.049
E.Enterocytes	1.93E–19	51	4	–0.021	–0.302	0.043	0.003
E.Enterocytes	3.42E–27	186	410	1.667	1.006	0.022	0.030
E.Enterocytes	4.00E–22	53	4	–0.068	0.548	0.061	0.007
E.Enterocytes	4.33E–31	192	303	1.701	1.062	0.038	0.039
E.Enterocytes	5.17E–23	50	0	4.122	–15.546	0.762	0.000
E.Enterocytes	3.74E–52	131	100	2.405	0.805	0.115	0.029
E.Enterocytes	8.63E–29	91	26	2.903	0.208	0.055	0.002
E.Enterocytes	6.89E–36	77	9	0.446	–0.229	0.082	0.006
E.Enterocytes	2.67E–47	0	244	–15.546	0.626	0.000	0.468
E.Enterocytes	3.02E–64	171	320	2.578	0.513	0.039	0.018
E.Enterocytes	3.85E–22	73	44	0.926	0.707	0.042	0.022
E.Enterocytes	1.04E–77	165	60	3.837	0.490	0.099	0.004
E.Enterocytes	1.03E–22	125	204	0.722	0.347	0.013	0.016
E.Enterocytes	3.27E–44	189	499	2.170	1.288	0.040	0.058
E.Enterocytes	3.47E–57	233	675	3.182	1.867	0.054	0.063
E.Enterocytes	7.65E–68	235	528	3.016	2.234	0.096	0.125
E.Enterocytes	4.84E–37	73	7	4.233	1.021	0.059	0.001
E.Enterocytes	2.15E–53	173	165	2.644	1.062	0.061	0.019
E.Enterocytes	9.71E–97	148	94	4.066	0.314	0.051	0.002
E.Enterocytes	1.77E–36	68	0	2.542	–15.546	0.102	0.000
E.Enterocytes	4.50E–63	139	41	3.038	0.623	0.104	0.006
E.Enterocytes	2.34E–28	58	0	0.669	–15.546	0.088	0.000
E.Enterocytes	2.33E–32	72	0	1.442	–15.546	0.466	0.000
E.Enterocytes	4.92E–34	76	86	1.177	0.259	0.027	0.016
E.Enterocytes	5.42E–25	241	837	4.131	4.960	0.057	0.350
E.Enterocytes	7.96E–26	77	13	0.155	1.455	0.041	0.017
E.Enterocytes	3.08E–59	203	332	4.155	2.209	0.138	0.059
E.Enterocytes	3.29E–38	75	1	2.458	0.451	0.473	0.002
E.Enterocytes	1.62E–23	103	83	0.758	0.933	0.025	0.022
E.Enterocytes	1.71E–28	125	147	1.130	0.424	0.025	0.018
E.Enterocytes	1.80E–21	63	24	1.327	0.022	0.037	0.006
E.Epithelial	2.13E–159	839	1715	3.231	2.717	0.119	0.170
E.Epithelial	6.16E–24	198	35	3.025	2.847	0.024	0.004
E.Epithelial	4.46E–35	338	14	0.143	0.148	0.115	0.005
E.Epithelial	6.55E–22	98	0	0.913	–17.770	0.806	0.000
E.Epithelial	1.02E–19	199	26	0.696	0.389	0.079	0.008
E.Epithelial	4.64E–24	247	26	0.592	0.061	0.034	0.002
E.Epithelial	3.31E–70	497	46	3.316	1.590	0.418	0.012
E.Epithelial	1.08E–43	424	747	1.433	1.137	0.009	0.012
E.Epithelial	2.34E–21	165	1	0.116	–0.004	0.175	0.001
E.Epithelial	5.29E–66	1547	1170	1.943	1.519	0.088	0.050
E.Epithelial	4.84E–31	893	1001	1.392	1.587	0.028	0.036
E.Epithelial	4.88E–24	231	4	–0.302	1.057	0.061	0.003
E.Epithelial	4.23E–24	226	5	1.148	–0.241	0.131	0.001

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Epithelial	6.77E–34	1353	1568	2.315	2.483	0.045	0.059
E.Epithelial	2.80E–74	2283	2393	4.849	5.360	0.080	0.119
E.Epithelial	1.44E–24	227	38	1.658	2.925	0.060	0.024
E.Epithelial	2.14E–47	1986	2179	4.030	4.341	0.119	0.162
E.Epithelial	1.92E–58	692	142	1.358	1.060	0.093	0.016
E.Epithelial	2.37E–21	308	33	0.569	1.572	0.047	0.010
E.Epithelial	9.94E–27	448	147	1.699	1.108	0.054	0.012
E.Epithelial	1.41E–50	1618	1351	2.237	2.072	0.100	0.074
E.Epithelial	7.08E–25	178	0	–0.162	–17.770	0.545	0.000
E.Epithelial	3.12E–19	323	39	0.084	0.665	0.039	0.007
E.Epithelial	3.67E–20	524	197	1.037	1.273	0.024	0.010
E.Epithelial	5.76E–72	933	330	1.322	1.311	0.091	0.032
E.Epithelial	1.40E–55	1348	1663	2.104	2.505	0.063	0.102
E.Epithelial	9.47E–68	633	107	2.974	2.402	0.126	0.014
E.Epithelial	5.73E–32	176	0	2.875	–17.770	0.906	0.000
E.Epithelial	1.50E–97	1019	596	5.516	4.447	0.322	0.090
E.Epithelial	9.97E–20	2291	2385	4.475	4.737	0.168	0.210
E.Epithelial	1.31E–20	92	0	0.319	–17.770	0.568	0.000
E.Epithelial	3.64E–26	192	2	–0.274	–0.967	0.089	0.001
E.Epithelial	3.45E–129	1589	1154	2.248	1.581	0.184	0.084
E.Epithelial	1.41E–28	187	2	0.115	0.095	0.082	0.001
E.Epithelial	1.13E–18	216	38	0.980	1.343	0.073	0.017
E.Epithelial	1.65E–69	968	397	2.219	2.053	0.143	0.052
E.Epithelial	2.51E–24	211	2	2.524	–0.295	0.237	0.000
E.Epithelial	1.18E–19	1912	2023	4.445	4.668	0.129	0.159
E.Epithelial	2.04E–33	2270	2357	4.877	5.154	0.120	0.151
E.Epithelial	1.75E–31	2145	2278	4.760	5.076	0.129	0.171
E.Epithelial	3.26E–44	2081	2208	4.699	5.094	0.102	0.142
E.Epithelial	2.18E–30	2207	2280	5.026	5.375	0.107	0.141
E.Epithelial	2.42E–44	2268	2338	4.878	5.215	0.143	0.187
E.Epithelial	2.59E–38	2017	2167	4.476	4.837	0.140	0.193
E.Epithelial	4.00E–61	2269	2369	5.373	5.725	0.131	0.175
E.Epithelial	6.38E–50	2242	2331	5.044	5.451	0.124	0.170
E.Epithelial	2.02E–34	2100	2252	4.871	5.236	0.104	0.144
E.Epithelial	3.82E–50	1949	2130	4.329	4.688	0.124	0.174
E.Epithelial	5.00E–26	2265	2315	5.477	5.857	0.124	0.165
E.Epithelial	2.41E–19	1964	2089	4.239	4.440	0.119	0.146
E.Epithelial	1.81E–18	2057	2143	4.702	4.946	0.131	0.161
E.Epithelial	3.79E–29	2145	2242	4.599	4.880	0.137	0.174
E.Epithelial	1.29E–220	1772	1196	3.351	1.969	0.220	0.057
E.Epithelial	1.21E–164	2476	2461	6.627	5.634	0.380	0.190
E.Epithelial	6.89E–51	347	5	2.014	0.112	0.205	0.001
E.Epithelial	2.19E–40	1204	795	3.740	3.222	0.253	0.117
E.Epithelial	5.15E–51	1773	2001	3.174	3.549	0.133	0.194
E.Epithelial	3.60E–45	258	0	0.980	–17.770	0.778	0.000
E.Epithelial	3.58E–41	369	69	0.908	0.298	0.062	0.008
E.Epithelial	2.30E–59	800	206	1.653	0.915	0.134	0.021
E.Epithelial	2.32E–28	192	4	1.092	2.658	0.174	0.011
E.Epithelial	2.57E–24	208	7	0.762	0.119	0.067	0.001
E.Epithelial	1.26E–26	126	0	1.453	–17.770	0.302	0.000
E.Epithelial	1.97E–220	1135	105	2.030	1.996	0.071	0.006
E.Epithelial	1.56E–50	251	0	1.818	–17.770	0.505	0.000
E.Goblet	4.89E–19	65	49	1.932	1.652	0.043	0.027
E.Goblet	2.40E–42	109	106	4.608	2.874	0.104	0.031
E.Immature_Enterocytes	4.47E–116	179	1782	3.674	2.807	0.040	0.220
E.Immature_Enterocytes	5.85E–19	701	2422	5.364	4.770	0.063	0.144
E.Immature_Enterocytes	1.42E–64	531	1451	3.921	2.608	0.077	0.084
E.Immature_Enterocytes	1.25E–20	372	1685	2.473	2.669	0.028	0.144
E.Immature_Enterocytes	8.76E–34	114	62	1.042	0.714	0.073	0.031
E.Immature_Enterocytes	4.07E–23	48	3	0.678	0.057	0.032	0.001
E.Immature_Enterocytes	1.94E–63	141	36	3.999	2.544	0.338	0.032
E.Immature_Enterocytes	6.15E–44	175	153	2.143	1.137	0.129	0.056
E.Immature_Enterocytes	1.33E–48	613	2356	4.225	4.702	0.056	0.298
E.Immature_Enterocytes	5.39E–51	113	7	1.397	0.790	0.187	0.008
E.Immature_Enterocytes	1.17E–64	128	16	3.901	2.106	0.216	0.008
E.Immature_Enterocytes	1.97E–32	82	25	2.359	0.891	0.085	0.009
E.Immature_Enterocytes	1.53E–52	127	60	3.504	1.417	0.185	0.021
E.Immature_Enterocytes	4.29E–35	416	1093	2.099	1.521	0.039	0.069
E.Immature_Enterocytes	3.48E–19	698	2507	7.664	7.791	0.131	0.514
E.Immature_Enterocytes	1.55E–20	39	3	1.593	0.918	0.064	0.003
E.Immature_Enterocytes	3.01E–52	653	2426	4.807	5.516	0.027	0.166
E.Immature_Enterocytes	1.50E–22	43	0	0.817	–17.136	0.587	0.000
E.Immature_Enterocytes	5.26E–113	394	708	3.566	1.849	0.155	0.085
E.Immature_Enterocytes	1.32E–25	461	1230	2.604	2.094	0.060	0.112
E.Immature_Enterocytes	1.18E–21	568	1904	3.283	2.760	0.034	0.079
E.Immature_Enterocytes	1.59E–19	112	113	1.528	1.469	0.025	0.024
E.Immature_Enterocytes	2.24E–45	331	525	2.780	1.677	0.030	0.022
E.Immature_Enterocytes	2.90E–39	205	280	2.516	1.519	0.024	0.016

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Immature_Enterocytes	3.79E–38	315	511	1.538	1.289	0.056	0.077
E.Immature_Enterocytes	5.49E–133	306	311	4.871	1.766	0.281	0.033
E.Immature_Enterocytes	1.03E–221	578	1299	4.124	2.429	0.307	0.213
E.Immature_Enterocytes	1.55E–19	657	2439	4.816	5.070	0.068	0.299
E.Immature_Enterocytes	2.54E–27	47	0	0.482	–17.136	0.070	0.000
E.Immature_Enterocytes	1.15E–51	0	335	–17.136	1.332	0.000	0.625
E.Immature_Enterocytes	9.59E–212	439	262	4.152	1.922	0.235	0.030
E.Immature_Enterocytes	2.37E–23	623	2345	4.161	4.603	0.068	0.350
E.Immature_Enterocytes	4.96E–46	316	506	2.507	1.988	0.090	0.100
E.Immature_Enterocytes	7.12E–44	110	35	3.715	0.764	0.051	0.002
E.Immature_Enterocytes	9.35E–60	312	458	2.565	1.514	0.086	0.061
E.Immature_Enterocytes	1.71E–139	418	656	3.543	1.786	0.086	0.040
E.Immature_Enterocytes	3.42E–66	716	2486	7.092	6.015	0.162	0.267
E.Immature_Enterocytes	3.74E–55	95	0	2.752	–17.136	0.125	0.000
E.Immature_Enterocytes	1.68E–293	437	130	3.542	0.830	0.295	0.013
E.Immature_Enterocytes	9.40E–35	257	450	1.832	1.332	0.054	0.067
E.Immature_Enterocytes	3.60E–28	69	5	0.391	0.133	0.094	0.006
E.Immature_Enterocytes	8.23E–58	533	1225	4.159	3.311	0.155	0.198
E.Immature_Enterocytes	8.08E–36	411	1843	2.260	2.811	0.023	0.152
E.Immature_Enterocytes	1.67E–36	76	0	1.232	–17.136	0.475	0.000
E.Immature_Enterocytes	1.42E–32	93	73	1.567	0.190	0.040	0.012
E.Immature_Enterocytes	1.80E–75	242	378	3.974	1.646	0.168	0.052
E.Immature_Enterocytes	1.67E–126	382	317	3.326	1.579	0.116	0.029
E.Immature_Enterocytes	2.92E–21	37	3	2.374	0.303	0.214	0.004
E.Immature_Enterocytes	4.69E–59	99	0	2.355	–17.136	0.465	0.000
E.Immature_Goblet	1.08E–20	52	536	2.942	2.472	0.009	0.069
E.Immature_Goblet	6.12E–19	40	7	2.868	2.057	0.077	0.008
E.Immature_Goblet	2.18E–26	224	1027	3.912	4.587	0.024	0.173
E.Immature_Goblet	1.47E–19	239	1063	6.042	6.699	0.020	0.144
E.Immature_Goblet	9.16E–20	235	1046	4.949	5.517	0.025	0.162
E.Immature_Goblet	2.65E–100	191	95	3.178	1.753	0.135	0.025
E.Immature_Goblet	5.94E–63	136	60	4.142	1.956	0.083	0.008
E.Immature_Goblet	3.89E–23	76	56	2.986	2.331	0.099	0.046
E.Secretory	4.32E–21	71	55	1.881	1.575	0.046	0.029
E.Secretory	4.04E–44	217	768	6.071	3.721	0.082	0.057
E.Secretory_All	5.43E–56	186	1439	2.490	2.417	0.020	0.150
E.Secretory_All	2.17E–20	257	376	0.761	1.187	0.025	0.049
E.Secretory_All	1.95E–34	92	12	0.381	0.262	0.053	0.006
E.Secretory_All	3.44E–22	44	0	0.224	–17.009	0.715	0.000
E.Secretory_All	2.15E–60	617	2286	4.044	4.617	0.051	0.284
E.Secretory_All	1.29E–35	447	968	2.042	1.769	0.041	0.074
E.Secretory_All	4.55E–28	96	38	1.493	1.517	0.064	0.026
E.Secretory_All	1.86E–29	66	2	1.578	–0.049	0.076	0.001
E.Secretory_All	7.64E–24	581	2105	4.109	4.548	0.046	0.226
E.Secretory_All	3.99E–28	566	1507	4.011	4.091	0.119	0.335
E.Secretory_All	2.66E–33	527	1389	2.622	2.603	0.058	0.151
E.Secretory_All	6.46E–21	304	1213	1.453	2.328	0.016	0.119
E.Secretory_All	1.58E–22	45	0	0.572	–17.009	0.882	0.000
E.Secretory_All	6.42E–30	660	2383	5.048	5.494	0.070	0.344
E.Secretory_All	8.95E–72	256	122	3.104	2.914	0.078	0.032
E.Secretory_All	5.50E–26	262	526	5.573	4.918	0.104	0.133
E.Secretory_All	1.60E–25	43	0	2.332	–17.009	0.780	0.000
E.Secretory_All	1.71E–19	665	2372	4.094	4.443	0.048	0.220
E.Secretory_All	9.73E–21	239	355	1.705	2.202	0.043	0.090
E.Secretory_All	2.04E–27	668	2378	5.856	6.413	0.042	0.219
E.Secretory_All	1.86E–19	657	2349	4.978	5.365	0.047	0.221
E.Secretory_All	8.54E–20	634	2261	5.035	5.410	0.055	0.254
E.Secretory_All	8.90E–27	679	2377	5.780	6.265	0.049	0.240
E.Secretory_All	2.24E–22	614	2156	4.810	5.301	0.042	0.207
E.Secretory_All	8.45E–40	658	2291	4.915	5.454	0.052	0.262
E.Secretory_All	7.52E–22	594	2062	4.443	4.892	0.050	0.236
E.Secretory_All	3.10E–27	654	2331	5.584	5.985	0.053	0.251
E.Secretory_All	5.76E–36	656	2277	5.725	6.412	0.045	0.249
E.Secretory_All	3.35E–30	654	2294	5.129	5.662	0.048	0.243
E.Secretory_All	1.46E–31	574	2063	4.392	4.898	0.048	0.243
E.Secretory_All	9.71E–22	671	2351	5.513	6.014	0.047	0.234
E.Secretory_All	3.28E–45	513	1284	2.627	2.022	0.055	0.090
E.Secretory_All	7.95E–26	59	7	1.212	3.224	0.101	0.049
E.Secretory_All	3.78E–26	84	31	0.817	1.254	0.037	0.018
E.Secretory_All	2.16E–111	367	190	1.991	2.936	0.029	0.029
E.Secretory_All	1.06E–20	53	8	0.507	0.705	0.043	0.007
E.Secretory_TA	6.93E–34	67	762	2.016	1.736	0.006	0.060
E.Secretory_TA	3.58E–31	205	948	5.003	3.805	0.070	0.141
E.Secretory_TA	7.63E–24	182	659	1.193	0.989	0.017	0.052
E.Secretory_TA	2.51E–21	31	0	0.852	–15.563	0.481	0.000
E.Secretory_TA	1.39E–29	55	2	1.518	–0.493	0.059	0.001
E.Secretory_TA	2.58E–19	93	112	–0.123	0.144	0.011	0.017
E.Secretory_TA	1.04E–32	131	214	0.668	0.288	0.024	0.030

TABLE 13-continued

Inflamed vs Healthy Markers							
E.Secretory_TA	1.78E−32	157	470	1.308	0.614	0.018	0.033
E.Secretory_TA	5.29E−32	123	829	1.015	1.932	0.007	0.084
E.Secretory_TA	7.34E−29	178	699	1.975	1.026	0.015	0.030
E.Secretory_TA	3.49E−40	170	385	1.717	0.423	0.040	0.037
E.Secretory_TA	9.81E−40	189	702	1.694	1.029	0.026	0.060
E.Secretory_TA	2.86E−24	85	50	2.785	0.438	0.044	0.005
E.Secretory_TA	3.26E−22	0	145	−15.563	0.302	0.000	0.258
E.Secretory_TA	1.65E−86	190	174	2.626	1.649	0.167	0.078
E.Secretory_TA	4.15E−41	151	465	1.456	0.576	0.020	0.033
E.Secretory_TA	1.04E−59	137	164	3.663	0.951	0.068	0.012
E.Secretory_TA	1.60E−31	196	820	2.335	1.556	0.020	0.050
E.Secretory_TA	6.08E−101	174	85	2.445	0.603	0.088	0.012
E.Secretory_TA	3.13E−27	48	0	1.467	−15.563	0.092	0.000
E.Secretory_TA	1.96E−28	95	45	−0.018	−0.222	0.030	0.012
E.Secretory_TA	1.35E−32	175	597	1.434	0.739	0.021	0.045
E.Secretory_TA	7.74E−26	44	2	1.126	−1.075	0.093	0.001
E.Stem	2.50E−23	74	148	3.162	1.471	0.031	0.019
E.Stem	8.44E−50	85	70	2.597	1.657	0.088	0.038
E.Stem	2.94E−23	74	179	2.280	0.755	0.037	0.031
F.Crypt	1.98E−19	20	0	1.954	−16.921	0.283	0.000
F.Crypt	1.56E−18	327	2176	5.041	4.216	0.024	0.089
F.Crypt	7.18E−31	97	192	5.654	4.084	0.057	0.038
F.Crypt	2.16E−22	233	1232	3.855	2.862	0.051	0.134
F.Crypt	9.05E−43	113	147	3.698	2.610	0.070	0.043
F.Crypt_hiFos	3.60E−23	75	694	3.780	4.902	0.016	0.331
F.Crypt_hiFos	1.05E−27	47	35	3.524	2.199	0.034	0.010
F.Crypt_loFos_1	4.61E−19	43	66	3.554	2.123	0.030	0.017
F.Crypt_loFos_2	3.84E−29	110	615	6.214	7.384	0.041	0.519
F.Crypt_loFos_2	5.18E−29	62	33	6.053	4.850	0.052	0.012
F.Endothelial	2.78E−21	47	1	0.968	0.308	0.086	0.001
F.Endothelial	2.27E−51	376	555	4.040	2.994	0.103	0.074
F.Endothelial	4.73E−23	305	316	3.545	3.217	0.062	0.052
F.Endothelial	8.95E−19	454	831	4.686	4.120	0.060	0.074
F.Endothelial	1.15E−28	472	972	5.206	5.921	0.064	0.218
F.Endothelial	1.54E−23	484	968	5.303	5.938	0.073	0.225
F.Endothelial	4.82E−22	382	648	4.926	4.096	0.106	0.101
F.Endothelial	1.53E−55	219	74	4.257	4.980	0.052	0.029
F.Endothelial	1.16E−30	434	739	4.965	3.807	0.042	0.032
F.Endothelial	3.80E−21	103	46	5.034	4.605	0.152	0.050
F.Endothelial	2.17E−22	400	640	4.404	3.357	0.129	0.100
F.Endothelial	7.96E−35	457	805	4.862	4.155	0.135	0.146
F.Fibroblast	1.32E−19	49	7	2.706	2.526	0.273	0.034
F.Fibroblast	5.35E−28	117	45	2.743	2.323	0.093	0.027
F.Fibroblast	1.48E−40	717	1585	3.721	3.260	0.162	0.260
F.Fibroblast	1.94E−31	168	113	2.089	2.273	0.099	0.076
F.Fibroblast	6.14E−32	69	0	3.069	−17.109	0.919	0.000
F.Fibroblast	2.59E−21	38	0	1.956	−17.109	0.315	0.000
F.Fibroblast	1.69E−35	66	0	1.718	−17.109	0.440	0.000
F.Fibroblast	2.36E−77	364	256	4.988	4.375	0.110	0.051
F.Fibroblast	2.38E−24	45	0	1.883	−17.109	0.439	0.000
F.Fibroblast	1.77E−62	295	201	3.026	2.214	0.157	0.061
F.Fibroblast	1.98E−32	910	2319	5.271	4.805	0.085	0.157
F.Fibroblast	6.46E−21	888	2397	4.993	5.369	0.069	0.243
F.Fibroblast	4.59E−28	657	1933	3.324	3.809	0.044	0.180
F.Fibroblast	8.74E−31	920	2340	5.419	4.709	0.093	0.144
F.Fibroblast	6.10E−29	105	55	2.990	2.114	0.148	0.042
F.Fibroblast	5.39E−24	43	0	2.835	−17.109	0.727	0.000
F.Fibroblast	6.38E−130	891	2100	5.637	4.077	0.308	0.246
F.Glia	2.11E−30	47	207	6.097	4.677	0.063	0.104
F.Glia	4.60E−20	24	2	2.928	3.996	0.311	0.054
F.Pcap_Venules	3.97E−23	168	163	4.186	3.081	0.060	0.027
F.Pcap_Venules	1.22E−28	125	31	2.471	1.782	0.205	0.032
F.Pcap_Venules	2.80E−20	195	215	4.447	3.783	0.141	0.098
F.Pcap_Venules	1.07E−26	135	61	2.764	1.834	0.106	0.025
F.Pcap_Venules	5.94E−32	151	66	3.759	2.793	0.208	0.047
F.Pcap_Venules	3.83E−23	111	31	3.011	2.740	0.085	0.020
F.Stromal	5.18E−27	60	0	2.677	−17.437	0.068	0.000
F.Stromal	1.53E−20	175	95	2.093	2.476	0.097	0.068
F.Stromal	5.21E−26	75	0	2.969	−17.437	0.926	0.000
F.Stromal	1.56E−30	335	261	2.621	2.292	0.150	0.093
F.Stromal	7.34E−28	67	0	1.704	−17.437	0.448	0.000
F.Stromal	5.18E−97	583	269	4.755	4.581	0.136	0.056
F.Stromal	1.14E−22	58	0	1.822	−17.437	0.503	0.000
F.Stromal	1.47E−22	358	309	4.532	4.779	0.137	0.140
F.Stromal	4.36E−19	1344	2379	4.908	5.246	0.094	0.211
F.Stromal	9.19E−29	1033	1928	3.279	3.731	0.063	0.161
F.Stromal	2.30E−29	1041	1451	3.919	3.291	0.113	0.102
F.Stromal	1.22E−29	1354	2268	5.288	4.642	0.119	0.128

TABLE 13-continued

Inflamed vs Healthy Markers							
F.Stromal	3.48E−30	1409	2367	5.497	4.938	0.126	0.143
F.Villus	8.61E−21	277	953	4.656	4.105	0.131	0.308
F.Villus	2.80E−31	230	508	4.183	3.868	0.077	0.137
F.Villus	2.35E−20	297	1189	6.482	5.598	0.114	0.247
F.Villus	1.13E−31	163	250	3.229	2.957	0.172	0.218
F.Villus	7.92E−55	288	1065	6.131	4.367	0.210	0.229
F.Villus__1	3.92E−22	102	210	4.101	3.592	0.042	0.061
F.Villus__1	9.12E−23	79	104	4.507	3.997	0.035	0.033
F.Villus__1	1.62E−34	116	440	6.109	4.030	0.130	0.117
F.Villus__2	2.22E−19	96	133	3.314	3.091	0.141	0.167
F.Villus__2	2.38E−21	172	625	6.146	4.565	0.151	0.183
I.Immune	1.55E−49	895	1415	3.606	3.541	0.155	0.235
I.Immune	4.26E−55	672	1082	7.127	7.775	0.201	0.507
I.Lymphoid	4.76E−42	891	1383	3.525	3.493	0.146	0.222
I.Lymphoid	1.56E−20	720	1058	4.300	4.512	0.141	0.241
I.Lymphoid	4.29E−19	119	15	1.892	2.304	0.121	0.020
I.Lymphoid	6.05E−38	703	1057	7.564	7.959	0.239	0.473
M.CD69pos__Mast	8.40E−22	189	255	4.288	4.007	0.221	0.246
M.CD69pos__Mast	8.92E−19	248	482	5.527	5.053	0.134	0.187
M.Macrophages	1.08E−21	405	1020	9.202	9.664	0.150	0.519
M.Mast	1.61E−22	70	16	3.561	3.432	0.083	0.017
M.Mast	9.61E−22	215	308	4.302	4.051	0.227	0.273
M.Mast	6.93E−23	276	538	5.537	5.010	0.145	0.196
M.Monocytes	2.42E−19	366	1237	3.727	3.459	0.082	0.230
M.Monocytes	1.27E−19	33	0	2.730	−16.729	0.829	0.000
M.Monocytes	3.80E−25	699	1775	7.238	7.798	0.145	0.543
M.Monocytes	4.59E−95	658	1743	5.981	6.943	0.106	0.549
M.Monocytes	3.47E−26	315	1208	3.733	3.629	0.066	0.235
M.Myeloid	1.39E−19	33	0	2.730	−17.202	0.831	0.000
M.Myeloid	2.35E−19	216	286	2.492	1.889	0.074	0.065
M.Myeloid	1.18E−18	708	2093	4.784	4.902	0.089	0.286
M.Myeloid	5.11E−31	816	1919	4.614	4.019	0.138	0.215
M.Myeloid	6.53E−22	538	967	4.008	3.606	0.136	0.185
M.Neutrophils	1.55E−28	139	101	5.153	6.964	0.039	0.100
M.Neutrophils	1.43E−23	130	78	6.818	4.463	0.238	0.028
T.Activated__CD4__hiFos	1.99E−22	186	396	5.084	4.054	0.072	0.075
T.Activated__CD4__loFos	9.55E−41	190	980	4.647	4.983	0.059	0.383
T.Activated__CD4__loFos	6.89E−24	175	459	5.409	4.321	0.081	0.099
T.Activated__CD4__loFos	5.79E−20	290	953	5.257	4.669	0.067	0.146
T.CD4	3.46E−27	609	1150	3.759	3.661	0.127	0.224
T.CD4	7.92E−21	259	116	2.939	3.015	0.134	0.063
T.CD4	8.80E−149	626	1712	4.589	4.983	0.122	0.437
T.CD4	2.96E−63	530	1299	5.073	5.153	0.137	0.354
T.CD4	3.71E−40	114	0	4.953	−17.403	0.824	0.000
T.CD4	5.26E−44	928	616	4.815	4.116	0.140	0.057
T.CD4	4.06E−29	141	15	2.266	3.009	0.098	0.017
T.CD4	1.69E−40	2004	2492	6.946	7.310	0.175	0.280
T.CD4	3.62E−22	2001	2488	6.447	6.696	0.171	0.252
T.CD4	1.73E−31	1995	2475	6.126	6.468	0.177	0.278
T.CD4	2.34E−22	1998	2479	6.362	6.628	0.162	0.241
T.CD4	4.29E−24	2003	2482	6.476	6.819	0.170	0.267
T.CD4	2.99E−38	1980	2449	5.861	6.212	0.173	0.273
T.CD4	2.10E−23	1994	2483	6.313	6.585	0.175	0.264
T.CD4	2.54E−24	1706	1943	4.685	4.416	0.284	0.268
T.CD4	7.99E−42	842	1536	3.807	4.013	0.098	0.206
T.CD8	2.23E−29	367	1396	3.958	4.457	0.067	0.359
T.CD8	3.71E−36	743	1473	4.015	3.854	0.232	0.411
T.CD8	1.19E−29	538	1501	3.494	3.896	0.040	0.146
T.CD8	2.16E−19	526	1484	4.204	4.593	0.065	0.242
T.CD8	1.42E−21	103	42	2.723	2.616	0.140	0.053
T.CD8	1.04E−23	975	2294	6.012	5.688	0.138	0.259
T.CD8	1.57E−21	973	2371	5.696	6.100	0.084	0.272
T.CD8	1.08E−25	936	2301	4.784	5.147	0.071	0.225
T.CD8	1.68E−24	891	1994	4.868	4.412	0.121	0.198
T.CD8	7.49E−20	97	54	2.923	2.770	0.098	0.049
T.CD8	2.30E−24	577	1701	3.863	4.309	0.084	0.338
T.CD8__IELs	3.52E−37	107	163	4.332	3.519	0.139	0.121
T.CD8__LP	2.38E−28	234	831	4.205	4.712	0.058	0.291
T.CD8__LP	4.36E−22	213	272	3.785	3.279	0.226	0.203
T.CD8__LP	1.85E−19	369	644	4.183	3.900	0.269	0.386
T.CD8__LP	4.74E−19	222	336	5.037	4.217	0.081	0.070
T.Cycling__T	2.46E−20	62	14	2.621	2.705	0.098	0.024
T.Memory__CD4	2.79E−42	92	565	4.414	4.883	0.031	0.260
T.Memory__CD4	1.37E−20	63	382	5.277	5.550	0.031	0.224
T.Memory__CD4	7.19E−20	46	3	3.185	2.559	0.426	0.018
T.Tcells	5.36E−55	812	1376	3.860	3.792	0.162	0.261
T.Tcells	6.96E−51	876	1412	4.448	4.659	0.170	0.318
T.Tcells	1.93E−24	197	39	2.531	2.768	0.122	0.029

TABLE 13-continued

Inflamed vs Healthy Markers							
T.Tcells	3.60E–29	96	0	4.859	–17.752	0.889	0.000
T.Tcells	2.08E–26	137	10	2.331	2.875	0.093	0.010
T.Tcells	1.80E–35	2108	1886	4.624	4.310	0.319	0.230
T.Tcells	3.25E–32	2495	2521	7.967	8.342	0.220	0.289
T.Tcells	7.65E–27	1195	1589	3.861	3.944	0.129	0.182
T.Tregs	1.68E–33	327	277	4.124	3.647	0.212	0.129
T.Tregs	8.45E–27	264	166	3.660	3.334	0.273	0.137
T.Tregs	7.35E–24	245	145	3.525	3.280	0.306	0.153

TABLE 14

Inflamed vs Non-Inflamed Markers							
ident	gene	coefD	pvalD	coefC	pvalC	mastfc	pvalH
B.Bcells	ACTG1	0.270	5.04E–02	7.92E–01	7..87E–37	0.683	1.86E–36
B.Bcells	ALOX5AP	1.113	2.65E–23	4.41E–01	5.15E–06	1.206	1.03E–26
B.Bcells	ARHGDIB	0.388	2.70E–04	6.71E–01	2.39E–31	0.794	4.64E–33
B.Bcells	ARPC1B	0.579	3.83E–10	7.39E–01	5.22E–31	0.862	2.35E–38
B.Bcells	ARPC5	0.667	7.21E–13	5.39E–01	4.36E–19	0.581	3.26E–29
B.Bcells	CD52	0.369	3.12E–05	7.63E–01	2.40E–21	0.733	4.94E–24
B.Bcells	CD53	0.583	1.33E–10	8.15E–01	2.47E–42	0.665	4.66E–50
B.Bcells	CFL1	0.234	1.10E–01	7.65E–01	1.27E–41	0.640	6.06E–41
B.Bcells	CORO1A	0.567	8.48E–10	7.67E–01	4.11E–26	0.952	3.68E–33
B.Bcells	COTL1	0.656	9.48E–13	6.51E–01	1.10E–15	0.881	9.67E–26
B.Bcells	DHRS9	2.253	1.67E–38	6.91E–01	2.03E–04	0.667	2.75E–40
B.Bcells	EVL	0.637	7.66E–11	5.01E–01	8.00E–15	0.598	5.05E–23
B.Bcells	GAPDH	0.703	6.02E–05	7.07E–01	2.86E–40	1.072	1.53E–42
B.Bcells	HLA-DMA	0.623	3.76E–12	5.61E–01	3.07E–18	0.742	1.13E–27
B.Bcells	HLA-DPA1	0.341	3.29E–04	7.53E–01	2.61E–17	0.886	4.45E–19
B.Bcells	HLA-DPB1	0.518	4.22E–09	7.06E–01	3.94E–12	1.223	1.12E–18
B.Bcells	HLA-DQA1	0.464	1.19E–07	7.19E–01	3.46E–17	0.918	3.04E–22
B.Bcells	HLA-DRB1	0.411	6.00E–06	9.67E–01	2.71E–20	1.120	1.13E–23
B.Bcells	IGHA1	–0.818	2.00E–13	–1.76E+00	1.66E–33	–1.536	4.75E–44
B.Bcells	IGHA2	–1.021	2.10E–29	–4.84E–01	1.07E–03	–0.548	1.41E–30
B.Bcells	IGJ	–0.595	2.67E–09	–1.53E+00	6.12E–33	–0.735	1.89E–39
B.Bcells	IRF8	1.119	1.27E–25	4.66E–01	2.46E–09	0.595	3.17E–32
B.Bcells	ITGB2	0.919	5.59E–16	5.53E–01	8.84E–11	0.819	4.23E–24
B.Bcells	JUN	–0.878	2.18E–18	–4.02E–01	1.80E–10	–0.519	3.57E–26
B.Bcells	LAPTM5	0.556	2.49E–10	7.54E–01	1.55E–24	0.900	4.07E–32
B.Bcells	LCP1	0.940	1.74E–19	3.73E–01	3.02E–07	0.635	3.99E–24
B.Bcells	LMO2	2.231	1.51E–26	1.92E–01	2.88E–01	0.531	1.16E–25
B.Bcells	UCP2	0.650	4.07E–13	5.08E–01	3.28E–15	0.592	1.24E–25
B.Cycling	ACTB	0.439	6.44E–01	1.99E+00	1.93E–21	2.038	2.09E–20
B.Cycling	HMGB1	1.804	5.95E–04	1.28E+00	4.98E–17	2.065	1.46E–18
B.Cycling	HMGN2	1.138	8.01E–03	1.45E+00	3.95E–21	1.203	1.40E–21
B.FO	PFN1	0.359	1.82E–01	9.87E–01	1.32E–24	1.005	7.00E–24
B.Plasma	IGHA1	–0.203	3.71E–01	–1.88E+00	3.28E–37	–1.279	3.53E–36
B.Plasma	IGJ	–0.360	1.15E–01	–1.55E+00	2.98E–43	–0.787	1.49E–42
E.Absorptive	CXCL1	1.378	3.33E–12	1.76E+00	1.91E–09	0.526	4.37E–19
E.Absorptive	GSN	0.716	1.02E–03	8.13E–01	3.03E–25	0.533	1.80E–26
E.Absorptive	HLA-DRB1	1.345	4.90E–18	9.64E–01	3.85E–11	2.221	1.76E–26
E.Absorptive	RARRES3	0.801	1.82E–07	6.14E–01	1.42E–22	0.858	2.16E–27
E.Absorptive	REG4	1.946	1.69E–19	4.60E–01	2.56E–01	0.505	1.02E–18
E.Absorptive	S100A11	0.628	1.59E–04	9.39E–01	3.68E–22	0.966	3.62E–24
E.Absorptive_All	CXCL1	1.593	8.90E–30	1.30E+00	1.79E–09	0.579	1.76E–36
E.Absorptive_All	FOSB	–1.301	4.06E–32	–6.54E–02	3.47E–01	–0.603	3.89E–31
E.Absorptive_All	HLA-DRB1	0.979	3.64E–28	8.31E–01	7.00E–14	1.658	3.38E–39
E.Absorptive_All	RBPMS	2.383	1.48E–22	2.24E–01	3.62E–01	0.951	1.21E–21
E.Absorptive_All	S100A11	0.495	6.82E–08	6.73E–01	1.37E–27	0.763	9.01E–33
E.Absorptive_All	S100A7	4.547	7.36E–19		1.00E+00	3.200	7.36E–19
E.Absorptive_All	S100A9	1.871	1.30E–27	1.27E+00	3.26E–06	0.910	3.54E–31
E.Absorptive_All	SOCS1	1.163	9.71E–15	7.36E–01	9.29E–09	0.521	6.59E–21
E.Absorptive_All	TIMP1	1.310	5.00E–36	4.23E–01	2.36E–04	1.458	9.17E–38
E.Absorptive_TA_2	FOS	–1.880	5.78E–18	–3.44E–01	4.50E–03	–1.292	1.12E–18
E.Absorptive_TA_2	MUC12	2.134	1.50E–19	8.02E–01	1.48E–17	0.648	2.77E–34
E.Absorptive_TA_2	PRAC1	4.156	3.34E–65	–3.64E–01	3.07E–05	0.675	1.21E–67
E.Absorptive_TA_2	RP11-708H21.4	–4.967	1.18E–22		1.00E+00	3.217	1.18E–22
E.Cycling_TA	MUC12	1.573	1.73E–09	6.38E–01	2.92E–13	0.606	3.64E–20
E.Cycling_TA	PRAC1	4.651	9.03E–79	–8.12E–01	1.67E–18	1.017	3.97E–94
E.Enterocyte_Immature_2	MUC12	1.674	7.19E–09	1.16E+00	1.13E–36	0.584	9.65E–43
E.Enterocyte_Immature_2	S100A11	1.180	9.06E–07	9.33E–01	3.01E–20	1.632	2.03E–24
E.Enterocytes	C4orf3	0.792	6.34E–05	7.19E–01	6.37E–18	0.632	2.34E–20
E.Enterocytes	PSME2	1.231	3.38E–05	7.97E–01	1.37E–19	1.177	2.92E–22
E.Enterocytes	RARRES3	0.990	1.09E–03	6.33E–01	5.35E–18	0.954	2.83E–19

TABLE 14-continued

Inflamed vs Non-Inflamed Markers

E.Enterocytes	S100A11	1.304	2.80E−10	1.59E+00	2.99E−21	2.035	8.12E−29
E.Epithelial	CXCL1	1.347	4.30E−21	1.45E+00	5.43E−13	0.681	2.57E−31
E.Epithelial	FOSB	−1.273	1.00E−27	−1.49E−01	1.64E−02	−0.573	7.74E−28
E.Epithelial	MMP7	4.654	5.46E−27		1.00E+00	2.888	5.46E−27
E.Epithelial	RBPMS	2.173	1.61E−19	1.78E−01	3.76E−01	0.988	1.25E−18
E.Epithelial	S100A11	0.488	1.28E−05	6.56E−01	1.03E−29	0.760	1.07E−32
E.Epithelial	S100A9	1.738	5.54E−20	8.89E−01	1.70E−03	0.843	4.67E−21
E.Epithelial	SOCS1	1.325	2.37E−16	6.41E−01	1.01E−06	0.713	1.60E−20
E.Epithelial	TIMP1	1.536	4.81E−41	3.71E−01	4.52E−04	1.705	1.73E−42
E.Immature__Enterocytes	CXCL1	2.078	2.05E−28	1.48E+00	2.50E−06	1.034	4.41E−32
E.Immature__Enterocytes	HLA-DRB1	0.924	1.72E−17	6.09E−01	1.44E−05	1.336	1.52E−20
E.Immature__Enterocytes	PPP1R14A	−2.410	1.12E−20	−6.04E−01	6.20E−02	−0.741	2.31E−20
E.Immature__Enterocytes	S100A11	0.547	9.26E−07	5.89E−01	1.07E−15	0.771	6.43E−20
E.Immature__Enterocytes	S100A6	2.392	1.87E−02	5.95E−01	6.29E−19	1.944	4.46E−19
E.Immature__Enterocytes	S100A9	1.532	3.65E−15	1.52E+00	1.20E−07	0.650	2.99E−20
E.Secretory__All	TIMP1	1.089	1.83E−23	2.08E−01	4.67E−02	1.093	3.21E−23
E.Secretory__TA	PRAC1	4.571	2.02E−60	−5.40E−01	8.66E−07	0.941	2.32E−64
E.Stem	PRAC1	3.706	7.35E−23	−3.74E−01	2.63E−03	0.554	9.92E−24
F.Fibroblast	TIMP1	0.593	1.59E−04	8.03E−01	8.36E−35	0.649	1.04E−36
M.Monocytes	RGS1	−1.005	1.10E−18	−2.29E−01	1.01E−02	−0.504	4.50E−19
T.CD4	TPT1	−0.473	4.86E−03	−3.97E−01	1.05E−18	−0.529	2.23E−19

ident	n	ref__n	mu	ref__mu	total	ref__total
B.Bcells	1088	784	4.568	3.684	0.356	0.139
B.Bcells	363	113	2.490	2.404	0.267	0.078
B.Bcells	996	698	3.365	2.788	0.324	0.152
B.Bcells	830	483	3.223	2.507	0.308	0.109
B.Bcells	727	376	2.578	2.122	0.318	0.120
B.Bcells	738	489	4.554	4.249	0.454	0.243
B.Bcells	843	509	3.015	2.089	0.511	0.163
B.Bcells	1103	803	4.002	3.139	0.275	0.110
B.Bcells	878	553	3.954	3.425	0.459	0.200
B.Bcells	579	280	3.274	2.800	0.266	0.093
B.Bcells	251	22	2.056	1.627	0.644	0.042
B.Bcells	428	204	2.247	2.074	0.314	0.133
B.Bcells	1148	820	4.349	3.461	0.279	0.108
B.Bcells	777	433	2.966	2.496	0.330	0.133
B.Bcells	892	609	4.349	3.839	0.213	0.102
B.Bcells	756	458	4.753	4.354	0.218	0.100
B.Bcells	699	423	4.029	3.483	0.258	0.107
B.Bcells	824	526	5.128	4.513	0.238	0.099
B.Bcells	898	801	10.040	10.530	0.437	0.547
B.Bcells	586	660	7.980	8.085	0.447	0.541
B.Bcells	834	733	8.424	9.119	0.408	0.580
B.Bcells	427	131	2.748	2.460	0.564	0.142
B.Bcells	331	116	2.119	1.727	0.261	0.070
B.Bcells	773	714	3.640	4.069	0.271	0.337
B.Bcells	656	374	3.965	3.333	0.461	0.170
B.Bcells	416	150	2.374	2.251	0.418	0.138
B.Bcells	171	14	1.940	2.195	0.640	0.063
B.Bcells	627	319	2.674	2.286	0.385	0.150
B.Cycling	247	66	7.126	5.999	0.141	0.017
B.Cycling	244	56	4.953	4.301	0.270	0.040
B.Cycling	236	54	4.838	3.868	0.374	0.044
B.FO	331	301	5.213	4.171	0.123	0.054
B.Plasma	513	439	10.681	11.096	0.449	0.513
B.Plasma	509	441	8.796	9.454	0.403	0.551
E.Absorptive	98	41	4.137	2.399	0.299	0.037
E.Absorptive	339	478	3.011	2.206	0.150	0.121
E.Absorptive	294	279	2.895	1.786	0.022	0.010
E.Absorptive	298	365	2.781	2.203	0.173	0.142
E.Absorptive	100	25	3.802	2.852	0.194	0.025
E.Absorptive	259	294	3.764	2.592	0.098	0.049
E.Absorptive__All	231	62	3.762	2.713	0.414	0.054
E.Absorptive__All	266	494	1.325	1.467	0.038	0.078
E.Absorptive__All	620	396	3.145	1.983	0.048	0.014
E.Absorptive__All	103	10	3.442	2.027	0.438	0.016
E.Absorptive__All	774	714	3.645	3.004	0.201	0.119
E.Absorptive__All	58	0	2.227	−16.655	0.974	0.000
E.Absorptive__All	170	32	2.499	0.471	0.090	0.004
E.Absorptive__All	163	59	1.370	0.337	0.098	0.017
E.Absorptive__All	438	201	2.289	2.938	0.049	0.035
E.Absorptive__TA__2	179	306	1.859	2.794	0.012	0.041
E.Absorptive__TA__2	260	226	2.514	1.359	0.226	0.088
E.Absorptive__TA__2	263	144	2.341	2.749	0.310	0.225
E.Absorptive__TA__2	0	62	−14.615	−0.994	0.000	0.621
E.Cycling__TA	312	271	1.899	0.879	0.102	0.044

TABLE 14-continued

Inflamed vs Non-Inflamed Markers						
E.Cycling_TA	317	144	2.128	3.093	0.180	0.160
E.Enterocyte_Immature_2	239	274	3.756	2.470	0.346	0.163
E.Enterocyte_Immature_2	216	244	3.102	2.071	0.049	0.027
E.Enterocytes	175	142	1.501	0.868	0.050	0.026
E.Enterocytes	233	256	3.182	2.363	0.088	0.055
E.Enterocytes	235	270	3.016	2.530	0.176	0.144
E.Enterocytes	148	73	4.066	2.916	0.076	0.017
E.Epithelial	219	75	3.487	1.606	0.419	0.039
E.Epithelial	341	513	1.365	1.481	0.063	0.103
E.Epithelial	83	0	3.198	−16.298	0.976	0.000
E.Epithelial	101	13	0.301	1.545	0.078	0.024
E.Epithelial	770	683	3.325	2.826	0.198	0.124
E.Epithelial	140	32	1.890	−0.213	0.054	0.003
E.Epithelial	161	50	1.120	0.474	0.107	0.021
E.Epithelial	491	234	2.033	2.160	0.049	0.025
E.Immature_Enterocytes	128	30	3.901	2.461	0.218	0.019
E.Immature_Enterocytes	331	289	2.780	1.885	0.024	0.011
E.Immature_Enterocytes	8	123	1.439	2.462	0.003	0.108
E.Immature_Enterocytes	418	507	3.543	3.087	0.110	0.097
E.Immature_Enterocytes	716	1046	7.092	6.491	0.312	0.301
E.Immature_Enterocytes	95	34	2.752	0.286	0.064	0.004
E.Secretory_All	367	273	1.991	2.174	0.037	0.031
E.Secretory_TA	190	128	2.626	3.132	0.215	0.206
E.Stem	85	123	2.597	3.008	0.152	0.293
F.Fibroblast	891	857	5.637	4.449	0.515	0.218
M.Monocytes	315	434	3.733	3.747	0.206	0.286
T.CD4	1003	1101	5.109	5.533	0.222	0.327

TABLE 15

Non-inflamed vs Healthy Markers							
ident	gene	coefD	pvalD	coefC	pvalC	mastfc	pvalH
B.Bcells	AC009501.4	−0.916	1.55E−31	−0.107	6.46E−02	−0.937	4.15E−31
B.Bcells	ATP5E	0.717	3.01E−10	0.379	1.33E−21	0.759	3.93E−29
B.Bcells	IGHA2	−0.527	3.04E−09	−2.008	1.75E−72	−0.743	9.22E−79
B.Bcells	KLF6	0.650	7.92E−16	0.382	2.87E−13	0.510	2.17E−26
B.Bcells	MT-ND3	0.607	7.92E−14	1.195	1.36E−44	0.881	1.81E−55
B.Bcells	PTPRC	1.051	4.91E−27	0.155	2.46E−02	0.623	5.35E−27
B.Bcells	RPL37	0.554	6.90E−04	0.717	1.27E−55	0.737	7.91E−57
B.Bcells	RPL37A	0.455	1.21E−02	0.588	2.93E−41	0.620	2.14E−41
B.Bcells	RPL39	0.601	1.10E−12	1.357	4.74E−68	0.777	1.04E−77
B.Bcells	RPS21	0.504	6.05E−05	0.538	3.12E−33	0.581	1.52E−35
B.Bcells	RPS29	0.650	2.45E−04	0.760	2.70E−44	1.063	5.70E−46
B.Bcells	TPT1	0.749	1.23E−03	0.468	5.06E−34	0.893	4.18E−35
B.FO	RPL39	0.886	1.90E−10	1.068	6.35E−19	0.825	1.11E−26
B.Plasma	IGHA2	−2.624	3.65E−18	−1.896	5.43E−59	−1.489	4.45E−74
E.Absorptive	AC009501.4	−1.463	4.21E−49	−0.120	8.47E−02	−1.284	1.77E−48
E.Absorptive	HLA-B	0.270	4.72E−01	0.595	1.05E−24	0.590	1.06E−23
E.Absorptive	MTRNR2L1	0.895	1.84E−19	1.658	4.14E−33	1.112	1.32E−49
E.Absorptive	RARRES3	0.747	3.06E−14	0.347	1.38E−09	0.581	3.19E−21
E.Absorptive	RPL39	0.677	2.87E−09	1.244	1.17E−39	0.626	4.26E−46
E.Absorptive_All	AC009501.4	−1.264	7.06E−103	0.123	1.28E−03	−1.066	1.07E−103
E.Absorptive_All	FTL	−0.526	2.31E−04	−0.455	1.65E−33	−0.900	2.86E−35
E.Absorptive_All	HLA-B	0.362	6.39E−04	0.449	2.48E−34	0.703	1.12E−35
E.Absorptive_All	MTRNR2L1	0.785	2.86E−38	1.951	2.10E−98	0.999	2.59E−133
E.Absorptive_All	RARRES3	0.675	2.18E−23	0.231	5.64E−06	0.516	9.20E−27
E.Absorptive_All	REG4	1.752	3.37E−33	1.859	3.20E−11	0.815	1.39E−41
E.Absorptive_All	S100A11	0.548	2.71E−17	0.545	1.55E−33	0.619	6.88E−48
E.Absorptive_All	TIMP1	2.067	1.81E−50	0.866	5.73E−05	2.216	1.04E−52
E.Absorptive_TA_1	MTRNR2L1	1.146	8.46E−19	1.516	7.17E−15	1.172	6.75E−31
E.Absorptive_TA_2	AC009501.4	−1.739	2.56E−40	0.117	1.47E−01	−1.461	1.50E−39
E.Absorptive_TA_2	DDX5	0.525	1.79E−03	0.636	2.15E−21	0.544	1.98E−22
E.Absorptive_TA_2	IFITM3	0.720	2.42E−06	0.852	1.52E−22	0.710	2.80E−26
E.Absorptive_TA_2	LDHA	1.028	1.02E−05	0.611	1.09E−24	0.761	8.33E−28
E.Absorptive_TA_2	MTRNR2L1	0.757	4.60E−09	1.727	1.02E−21	0.900	4.28E−28
E.Absorptive_TA_2	PDIA3	1.141	4.53E−09	0.697	4.79E−36	0.613	2.59E−42
E.Absorptive_TA_2	S100A11	0.607	6.77E−03	0.723	4.50E−28	0.621	1.60E−28
E.Best4_Enterocytes	RPL39	0.631	7.34E−04	1.861	4.91E−48	0.792	3.01E−49
E.Cycling_TA	FN1	2.929	2.97E−19	1.569	1.55E−03	0.880	2.26E−20
E.Cycling_TA	HLA-DMA	1.190	3.46E−16	0.628	1.63E−08	0.619	4.26E−22
E.Cycling_TA	HLA-DRB1	1.763	2.23E−35	1.262	1.08E−13	2.259	3.56E−46
E.Cycling_TA	LDHA	0.909	1.46E−03	0.590	1.40E−22	0.699	1.10E−23
E.Cycling_TA	MTRNR2L1	0.929	7.85E−13	1.225	8.88E−13	0.969	5.82E−23

TABLE 15-continued

Non-inflamed vs Healthy Markers							
E.Cycling_TA	PITX1	3.030	3.58E−24	0.562	4.71E−02	1.405	6.40E−24
E.Cycling_TA	REG4	1.963	4.32E−33	1.134	1.47E−06	0.648	6.04E−37
E.Cycling_TA	RPL38	−1.583	6.37E−05	0.661	5.53E−29	−0.562	2.63E−31
E.Cycling_TA	S100A11	0.845	1.29E−03	0.879	8.92E−41	0.946	8.50E−42
E.Cycling_TA	S100P	2.892	1.31E−66	1.107	1.75E−15	0.576	5.05E−79
E.Enterocyte_Immature_1	MTRNR2L1	0.847	1.93E−11	1.959	6.13E−27	0.960	1.38E−35
E.Enterocyte_Immature_1	MUC1	2.061	6.50E−29	1.062	3.51E−11	0.817	2.72E−37
E.Enterocyte_Immature_1	PLA2G2A	2.363	1.20E−33	1.177	1.84E−05	0.916	1.90E−36
E.Enterocyte_Immature_2	AC009501.4	−1.893	1.08E−44	−0.057	4.96E−01	−1.574	1.52E−43
E.Enterocyte_Immature_2	CYBA	0.963	4.30E−04	0.635	2.64E−22	1.235	6.61E−24
E.Enterocyte_Immature_2	MTRNR2L1	0.546	2.06E−05	2.221	7.06E−35	0.745	1.27E−37
E.Enterocyte_Immature_2	S100A11	1.196	1.16E−15	0.792	5.29E−21	1.325	7.45E−34
E.Enterocyte_Immature_2	S100P	3.046	4.72E−88	1.572	1.22E−42	0.691	2.49E−127
E.Enterocyte_Progenitor	AC009501.4	−0.854	1.06E−13	0.590	4.97E−12	−0.577	4.42E−23
E.Enterocyte_Progenitor	AGR2	1.071	3.71E−15	1.141	4.91E−29	0.796	2.57E−41
E.Enterocyte_Progenitor	MTRNR2L1	0.728	8.62E−09	1.572	1.45E−16	0.795	9.74E−23
E.Enterocyte_Progenitor	PLA2G2A	2.281	3.64E−63	1.180	1.13E−13	0.796	8.26E−74
E.Enterocyte_Progenitor	REG4	2.664	1.23E−24	3.575	1.27E−11	1.488	1.76E−33
E.Enterocyte_Progenitor	S100A11	0.971	2.84E−15	0.673	1.71E−13	1.012	4.59E−26
E.Enterocyte_Progenitor	S100P	3.348	4.03E−89	0.786	1.07E−04	0.666	5.56E−91
E.Enterocyte_Progenitor	TFF1	1.890	5.74E−23	1.734	2.85E−08	1.005	1.47E−28
E.Enterocyte_Progenitor	TPT1	0.621	2.36E−04	0.665	1.18E−25	0.881	1.81E−27
E.Enterocytes	AC009501.4	−1.866	1.23E−40	−0.142	1.36E−01	−1.561	6.81E−40
E.Enterocytes	MDK	1.676	1.04E−12	0.471	5.07E−12	0.802	4.25E−22
E.Enterocytes	MTRNR2L1	0.692	2.57E−07	2.089	4.41E−29	0.927	1.07E−33
E.Enterocytes	MUC1	1.587	4.06E−23	1.250	4.29E−27	0.567	2.98E−47
E.Enterocytes	PLA2G2A	1.809	2.99E−24	1.895	3.53E−16	0.692	1.41E−37
E.Epithelial	AC009501.4	−1.108	9.77E−81	0.257	1.42E−11	−0.935	2.86E−89
E.Epithelial	CXCL14	−0.921	9.13E−40	0.230	3.49E−02	−0.614	1.64E−39
E.Epithelial	FTL	−0.513	1.00E−04	−0.458	4.59E−33	−0.910	3.60E−35
E.Epithelial	HLA-B	0.396	3.47E−04	0.443	1.30E−37	0.774	3.49E−39
E.Epithelial	MT-ATP6	−1.097	1.66E−23	−0.006	8.87E−01	−0.895	2.08E−22
E.Epithelial	MT-ND2	−1.167	2.79E−21	0.202	8.79E−08	−0.994	2.03E−26
E.Epithelial	MTRNR2L1	0.850	9.20E−44	1.674	4.88E−82	0.679	1.89E−122
E.Epithelial	RARRES3	0.620	4.04E−18	0.207	1.23E−04	0.628	2.79E−20
E.Epithelial	S100A11	0.530	3.23E−15	0.618	1.52E−51	0.661	9.39E−64
E.Epithelial	S100A6	0.301	2.31E−01	0.496	2.40E−45	0.516	2.09E−44
E.Epithelial	TIMP1	1.540	5.11E−48	0.459	3.01E−04	1.551	1.36E−49
E.Goblet	MT-ND3	0.498	7.33E−03	1.601	2.46E−32	0.739	1.01E−32
E.Immature_Enterocytes	AC009501.4	−1.260	3.04E−65	0.211	4.27E−05	−1.018	1.51E−67
E.Immature_Enterocytes	AGR2	0.728	3.16E−18	0.972	2.62E−53	0.555	1.76E−68
E.Immature_Enterocytes	CYBA	0.445	1.33E−06	0.395	3.12E−19	0.603	2.98E−23
E.Immature_Enterocytes	FTL	−0.752	1.21E−05	−0.465	1.90E−20	−1.181	1.56E−23
E.Immature_Enterocytes	IFITM3	0.915	9.50E−20	0.506	1.85E−06	0.883	1.26E−23
E.Immature_Enterocytes	LCN2	1.886	9.90E−101	1.402	1.25E−41	0.625	5.65E−139
E.Immature_Enterocytes	MTRNR2L1	0.695	7.45E−20	2.021	2.85E−66	0.874	5.30E−83
E.Immature_Enterocytes	PLA2G2A	1.989	4.36E−103	1.457	6.45E−42	0.857	1.30E−141
E.Immature_Enterocytes	REG4	1.956	1.41E−28	2.398	1.61E−13	0.746	2.99E−39
E.Immature_Enterocytes	S100A11	0.955	5.32E−30	0.750	6.89E−33	1.131	7.95E−60
E.Immature_Enterocytes	S100P	2.923	5.34E−176	1.278	3.65E−33	0.536	1.05E−205
E.Immature_Enterocytes	SPINK1	1.222	9.55E−40	1.004	8.36E−30	0.632	1.90E−66
E.Immature_Enterocytes	TPT1	0.539	2.35E−05	0.508	2.12E−42	0.772	4.75E−45
E.Immature_Goblet	AGR2	2.345	6.20E−08	0.764	2.47E−16	1.709	1.12E−21
E.lmmature_Goblet	TPT1	0.754	3.86E−02	0.643	2.05E−24	0.990	3.11E−24
E.Secretory	LCN2	1.855	5.39E−27	1.240	2.36E−07	0.531	1.16E−31
E.Secretory	MT-ND3	0.805	5.85E−10	1.765	4.64E−66	1.050	4.66E−73
E.Secretory_All	AC009501.4	−1.150	1.41E−54	0.201	2.88E−04	−0.968	3.84E−56
E.Secretory_All	FN1	3.218	2.44E−21	0.954	1.61E−01	0.852	1.10E−20
E.Secretory_All	HLA-B	0.401	8.51E−03	0.538	1.96E−33	0.786	9.36E−34
E.Secretory_All	LYZ	1.528	1.69E−40	0.007	9.67E−01	0.735	2.83E−39
E.Secretory_All	MTRNR2L1	1.057	1.86E−42	1.178	3.07E−26	1.126	1.31E−65
E.Secretory_All	TIMP1	1.285	2.27E−36	0.124	2.82E−01	1.065	2.01E−35
E.Secretory_TA	AC009501.4	−1.585	8.94E−31	0.115	2.12E−01	−1.330	5.97E−30
E.Secretory_TA	ITLN1	1.063	3.14E−05	1.247	4.03E−28	0.509	9.65E−31
E.Secretory_TA	MTRNR2L1	0.865	2.67E−10	1.319	2.47E−13	0.940	4.99E−21
E.Secretory_TA	SELK	0.530	8.31E−03	0.654	2.11E−28	0.531	9.05E−29
E.Secretory_TA	TMEM258	0.859	7.78E−03	0.616	1.36E−32	0.505	5.93E−33
E.Stem	FN1	2.880	3.19E−21	1.215	2.72E−03	0.920	4.28E−22
E.Stem	MT-ND3	0.794	1.31E−01	2.049	1.10E−54	1.199	6.90E−54
E.Stem	RPL38	0.661	4.33E−01	0.802	1.62E−26	0.721	1.61E−25
E.Stem	RPL39	0.477	2.20E−01	2.093	3.68E−66	0.708	3.76E−65
E.Stem	TPT1	1.665	1.60E−01	0.783	2.20E−24	2.134	1.06E−23
F.Crypt	CAV1	1.146	6.66E−21	0.425	1.19E−03	0.542	4.16E−22
F.Crypt	COX4I1	−0.620	5.73E−08	−0.433	1.89E−23	−0.556	9.59E−29
F.Crypt	FOS	0.221	1.37E−02	0.779	1.66E−33	0.510	1.21E−33
F.Crypt	HLA-A	−0.858	3.01E−08	−0.421	4.76E−21	−0.885	1.22E−26
F.Crypt	IFI27	−0.822	7.61E−24	−0.465	2.33E−09	−0.509	1.74E−30
F.Crypt	MTRNR2L1	1.954	5.69E−89	1.365	1.03E−19	2.153	1.69E−105

TABLE 15-continued

Non-inflamed vs Healthy Markers							
F.Crypt	TAGLN	1.641	6.57E−49	0.424	3.73E−03	0.610	1.82E−49
F.Crypt	ZFP36	0.444	6.98E−08	0.650	5.22E−28	0.708	3.52E−33
F.Crypt__loFos__1	COL1A1	1.239	2.41E−07	0.734	4.28E−25	0.705	9.06E−30
F.Crypt__loFos__1	PRSS23	1.334	2.62E−19	0.656	2.20E−07	0.605	4.41E−24
F.Crypt__loFos__1	TAGLN	1.894	1.12E−27	0.488	3.84E−02	0.784	1.80E−27
F.Crypt__loFos__2	MTRNR2L1	2.286	6.13E−29	1.325	1.91E−04	2.508	8.21E−31
F.Endothelial	MTRNR2L1	2.323	2.17E−63	0.404	7.42E−02	2.056	9.32E−63
F.Fibroblast	C12orf75	1.496	7.49E−23	0.580	4.57E−05	0.520	2.30E−25
F.Fibroblast	HLA-A	−0.834	1.16E−10	−0.397	4.80E−28	−0.798	6.37E−36
F.Fibroblast	MT-ND3	0.636	7.87E−21	0.470	2.89E−08	0.618	1.93E−26
F.Fibroblast	MTRNR2L1	1.675	2.60E−106	1.221	4.14E−25	1.696	3.88E−128
F.Fibroblast	PRSS23	1.294	2.72E−50	0.711	8.47E−16	0.612	4.42E−63
F.Fibroblast	RPL12	−0.736	1.89E−05	−0.282	3.85E−18	−0.905	4.50E−21
F.Fibroblast	RPL6	−0.596	4.05E−05	−0.302	1.03E−20	−0.723	2.68E−23
F.Fibroblast	ZFP36	0.398	4.12E−10	0.492	1.11E−22	0.574	4.56E−30
F.Stromal	COX4I1	−0.598	3.29E−14	−0.321	1.36E−22	−0.543	5.37E−34
F.Stromal	HLA-A	−0.702	1.63E−08	−0.431	3.40E−37	−0.748	6.50E−43
F.Stromal	MT-ND3	0.674	9.33E−26	0.462	7.66E−09	0.646	7.06E−32
F.Stromal	MTRNR2L1	1.682	8.15E−123	1.017	4.07E−20	1.568	1.14E−139
F.Stromal	RPL12	−0.826	1.12E−09	−0.241	3.27E−15	−0.957	2.87E−22
F.Stromal	RPL6	−0.475	9.80E−05	−0.296	5.70E−23	−0.646	3.61E−25
F.Villus	COL3A1	1.208	3.13E−18	0.428	5.03E−13	0.713	1.60E−28
F.Villus	DCN	1.226	4.58E−34	0.195	3.52E−02	0.911	7.65E−34
F.Villus	LUM	1.197	5.30E−33	0.434	2.30E−04	0.865	9.06E−35
F.Villus	MTRNR2L1	1.779	6.24E−54	0.986	2.13E−08	1.789	1.87E−59
F.Villus	PRSS23	2.155	5.51E−22	0.943	9.10E−04	1.436	2.75E−23
F.Villus__1	LUM	1.625	2.01E−27	0.865	9.13E−05	1.631	1.31E−29
F.Villus__1	MTRNR2L1	2.150	5.43E−37	1.250	8.12E−06	2.357	4.13E−40
I.Immune	AC009501.4	−0.932	5.84E−59	0.028	5.05E−01	−0.861	9.53E−58
I.Immune	MT-ND3	0.681	6.43E−30	0.847	8.29E−29	0.764	1.08E−55
I.Lymphoid	AC009501.4	−0.948	1.16E−60	−0.149	4.55E−04	−0.988	5.14E−62
I.Lymphoid	MT-ND3	0.758	2.23E−37	0.926	2.61E−36	0.923	1.48E−70
I.Lymphoid	RPL37	0.524	5.45E−11	0.503	1.44E−51	0.502	1.25E−59
I.Lymphoid	RPL37A	0.491	2.75E−09	0.453	4.13E−45	0.530	1.54E−51
I.Lymphoid	RPL39	0.827	8.12E−45	1.128	4.65E−71	0.655	1.50E−112
I.Lymphoid	RPS29	0.637	9.51E−12	0.707	1.10E−75	0.781	2.12E−84
M.CD69pos__Mast	RPL39	1.796	1.16E−28	0.968	1.14E−06	1.658	1.17E−32
M.Macrophages	TPT1	0.714	8.54E−03	0.737	8.30E−33	0.974	3.94E−33
M.Mast	RPL39	1.513	5.56E−24	0.951	2.55E−07	1.346	1.21E−28
M.Monocytes	AC009501.4	−1.060	6.57E−29	0.372	1.03E−08	−0.841	7.05E−35
M.Monocytes	MT-ND3	0.733	6.64E−13	0.813	1.66E−14	0.856	9.86E−25
M.Monocytes	TPT1	0.556	2.12E−02	0.816	1.23E−66	0.828	1.88E−66
M.Myeloid	AC009501.4	−0.944	2.00E−33	0.305	2.68E−07	−0.760	5.44E−38
M.Myeloid	MT-ND3	0.917	2.08E−27	0.800	5.64E−18	0.988	1.77E−42
M.Myeloid	RPL39	0.610	2.75E−13	1.381	1.80E−68	0.718	1.01E−78
M.Myeloid	RPS29	0.600	7.49E−09	0.445	2.32E−17	0.811	1.40E−23
M.Myeloid	TPT1	0.346	1.47E−02	0.601	5.47E−52	0.526	5.33E−52
T.Activated__CD4__hiFos	KLRB1	1.024	1.50E−15	0.959	5.25E−20	0.684	9.27E−33
T.Activated__CD4__hiFos	RPL39	0.774	2.49E−09	1.083	1.30E−16	0.673	2.62E−23
T.Activated__CD4__loFos	ANXA1	−1.580	2.54E−20	−0.564	1.84E−10	−1.148	4.46E−28
T.Activated__CD4__loFos	RPL39	0.795	1.80E−09	1.129	1.06E−18	0.758	1.66E−25
T.Activated__CD4__loFos	RPS29	0.887	1.46E−03	0.801	2.45E−22	1.237	1.91E−23
T.CD4	AC009501.4	−0.753	4.11E−29	−0.129	1.39E−02	−0.760	2.82E−29
T.CD4	ANXA1	−0.895	1.22E−42	−0.535	1.27E−24	−0.730	3.47E−64
T.CD4	CCL5	−0.778	3.45E−32	−0.105	1.46E−01	−0.556	1.79E−31
T.CD4	MT-ND3	1.088	2.62E−57	0.642	6.53E−15	0.984	3.40E−69
T.CD4	RPL3	−0.728	2.37E−03	−0.318	1.54E−21	−1.038	1.83E−22
T.CD4	RPL37A	0.475	2.69E−07	0.411	7.65E−33	0.501	2.07E−37
T.CD4	RPL39	0.923	5.13E−44	1.004	2.72E−51	0.705	4.65E−92
T.CD4	RPS29	0.711	1.15E−10	0.647	6.11E−58	0.900	1.17E−65
T.CD8	AC009501.4	−1.089	1.99E−36	−0.001	9.93E−01	−0.985	3.16E−35
T.CD8	KLRB1	1.135	1.12E−34	1.051	7.19E−31	0.531	1.81E−62
T.CD8	RPL23	0.767	1.27E−16	0.346	2.23E−13	0.538	2.80E−27
T.CD8	RPL37	0.627	8.81E−08	0.482	7.49E−26	0.634	6.07E−31
T.CD8	RPL37A	0.826	4.47E−12	0.319	2.98E−12	0.847	1.05E−21
T.CD8	RPL38	0.718	1.08E−13	0.414	1.41E−19	0.667	1.65E−30
T.CD8	RPL39	1.033	5.50E−34	1.030	9.55E−35	0.907	1.25E−65
T.CD8	RPS29	0.843	3.90E−09	0.789	8.10E−50	1.202	4.48E−56
T.CD8__IELs	KLRB1	1.786	3.21E−35	0.713	2.82E−08	1.362	1.01E−40
T.CD8__IELs	RPL39	1.082	1.71E−15	1.055	1.63E−15	0.933	2.86E−28
T.CD8__IELs	RPS29	0.856	1.86E−04	0.878	1.09E−24	1.294	1.31E−26
T.CD8__LP	RPL39	0.992	8.30E−15	0.870	1.58E−10	0.842	1.06E−22
T.Memory__CD4	ANXA1	−1.046	1.67E−16	−0.708	7.68E−09	−0.987	9.99E−23
T.Memory__CD4	RPL39	1.077	5.94E−17	1.031	1.19E−16	0.931	7.91E−31
T.Memory__CD4	RPS29	0.892	7.88E−05	0.830	1.78E−24	1.253	9.46E−27
T.Tcells	AC009501.4	−1.080	1.57E−72	−0.199	7.92E−06	−1.052	1.65E−75
T.Tcells	MT-ND3	0.937	1.37E−53	0.698	2.96E−21	0.877	9.43E−72
T.Tcells	RPL37	0.552	7.33E−12	0.504	1.21E−56	0.510	1.55E−65

TABLE 15-continued

Non-inflamed vs Healthy Markers

T.Tcells	RPL37A	0.695	1.59E−17	0.424	2.05E−41	0.689	6.00E−56
T.Tcells	RPL38	0.691	8.14E−25	0.410	3.13E−37	0.533	5.34E−59
T.Tcells	RPL39	0.917	7.15E−53	1.091	1.16E−73	0.692	3.64E−123
T.Tcells	RPS16	0.532	6.76E−06	0.345	1.27E−33	0.549	7.74E−37
T.Tcells	RPS23	0.460	7.92E−04	0.307	4.37E−24	0.604	2.01E−25
T.Tcells	RPS29	0.688	3.71E−12	0.717	7.00E−89	0.868	5.80E−98
T.Tcells	TMSB4X	−0.761	2.25E−01	−0.421	6.54E−35	−1.006	4.87E−34
T.Tregs	RPL39	1.289	3.69E−18	0.954	7.35E−09	1.110	2.23E−24

ident	n	ref_n	mu	ref_mu	total	ref_total
B.Bcells	315	1399	1.732	2.300	0.021	0.136
B.Bcells	818	1847	2.717	2.347	0.060	0.105
B.Bcells	660	2002	8.085	9.053	0.126	0.750
B.Bcells	587	1098	2.563	2.360	0.089	0.144
B.Bcells	579	1094	4.387	3.127	0.075	0.059
B.Bcells	255	297	2.180	2.371	0.081	0.107
B.Bcells	885	2227	3.902	3.143	0.099	0.147
B.Bcells	893	2284	3.925	3.297	0.087	0.144
B.Bcells	670	1378	4.908	3.627	0.154	0.131
B.Bcells	845	2058	3.313	2.862	0.092	0.164
B.Bcells	895	2273	4.561	3.910	0.104	0.168
B.Bcells	910	2320	4.586	3.872	0.085	0.133
B.FO	262	482	5.527	4.678	0.117	0.120
B.Plasma	429	1319	8.601	9.410	0.134	0.720
E.Absorptive	232	1244	2.454	2.477	0.027	0.146
E.Absorptive	582	1639	5.319	4.978	0.070	0.156
E.Absorptive	294	473	5.538	4.723	0.135	0.124
E.Absorptive	365	675	2.203	2.124	0.082	0.144
E.Absorptive	388	741	3.887	1.713	0.069	0.029
E.Absorptive_All	1006	1770	3.283	2.771	0.162	0.200
E.Absorptive_All	2353	2409	5.065	5.477	0.107	0.146
E.Absorptive_All	2292	2228	4.721	4.370	0.148	0.113
E.Absorptive_All	1078	634	5.863	4.769	0.375	0.103
E.Absorptive_All	817	442	2.047	2.072	0.137	0.076
E.Absorptive_All	248	39	5.078	1.191	0.236	0.003
E.Absorptive_All	1368	957	2.892	2.147	0.143	0.060
E.Absorptive_All	372	37	2.660	0.887	0.045	0.001
E.Absorptive_TA_1	157	181	6.221	5.640	0.120	0.093
E.Absorptive_TA_2	164	978	2.742	2.209	0.024	0.099
E.Absorptive_TA_2	283	778	1.155	1.041	0.015	0.039
E.Absorptive_TA_2	290	723	1.776	1.210	0.021	0.035
E.Absorptive_TA_2	337	1020	2.353	1.774	0.046	0.093
E.Absorptive_TA_2	153	277	4.987	3.981	0.058	0.052
E.Absorptive_TA_2	315	869	2.000	1.269	0.051	0.084
E.Absorptive_TA_2	337	1031	2.441	1.900	0.035	0.073
E.Best4_Enterocytes	211	459	4.588	2.087	0.064	0.024
E.Cycling_TA	60	4	0.716	−0.174	0.035	0.001
E.Cycling_TA	175	168	−0.050	−0.238	0.015	0.013
E.Cycling_TA	225	187	1.706	0.621	0.011	0.004
E.Cycling_TA	329	1010	2.055	1.402	0.037	0.072
E.Cycling_TA	165	276	4.088	3.351	0.036	0.037
E.Cycling_TA	58	6	0.112	−0.939	0.029	0.001
E.Cycling_TA	127	71	3.274	−0.106	0.050	0.003
E.Cycling_TA	332	1148	3.594	3.094	0.056	0.137
E.Cycling_TA	335	1020	2.945	1.523	0.051	0.058
E.Cycling_TA	237	75	1.477	−0.225	0.056	0.005
E.Enterocyte_Immature_1	174	298	6.433	5.302	0.152	0.119
E.Enterocyte_Immature_1	96	50	3.275	1.480	0.141	0.021
E.Enterocyte_Immature_1	94	36	3.492	1.624	0.047	0.005
E.Enterocyte_Immature_2	157	980	3.004	2.688	0.027	0.133
E.Enterocyte_Immature_2	327	1036	3.316	2.784	0.036	0.079
E.Enterocyte_Immature_2	152	337	5.575	4.159	0.083	0.069
E.Enterocyte_Immature_2	244	455	2.071	0.909	0.021	0.018
E.Enterocyte_Immature_2	254	130	2.673	0.233	0.122	0.012
E.Enterocyte_Progenitor	168	730	3.904	2.797	0.054	0.109
E.Enterocyte_Progenitor	339	718	5.063	3.249	0.129	0.078
E.Enterocyte_Progenitor	149	247	6.112	5.395	0.111	0.112
E.Enterocyte_Progenitor	222	118	4.377	2.794	0.179	0.032
E.Enterocyte_Progenitor	60	12	6.281	1.470	0.176	0.001
E.Enterocyte_Progenitor	229	359	3.665	2.418	0.059	0.039
E.Enterocyte_Progenitor	197	33	3.042	1.938	0.130	0.010
E.Enterocyte_Progenitor	86	40	4.833	1.617	0.085	0.004
E.Enterocyte_Progenitor	348	974	4.387	3.701	0.037	0.064
E.Enterocytes	127	684	2.550	2.661	0.017	0.097
E.Enterocytes	304	670	2.972	2.497	0.139	0.221
E.Enterocytes	157	272	5.572	4.456	0.087	0.070
E.Enterocytes	129	100	2.732	0.805	0.142	0.029

TABLE 15-continued

Non-inflamed vs Healthy Markers						
E.Enterocytes	106	60	3.870	0.490	0.065	0.004
E.Epithelial	1040	1715	3.458	2.717	0.172	0.170
E.Epithelial	418	747	2.000	1.137	0.013	0.012
E.Epithelial	2313	2393	4.946	5.360	0.086	0.119
E.Epithelial	2303	2268	4.649	4.295	0.122	0.094
E.Epithelial	2165	2368	6.556	6.541	0.252	0.273
E.Epithelial	2214	2400	6.759	6.517	0.261	0.239
E.Epithelial	1065	596	5.621	4.447	0.362	0.090
E.Epithelial	739	397	1.841	2.053	0.084	0.052
E.Epithelial	1509	1196	3.018	1.969	0.149	0.057
E.Epithelial	2474	2461	6.133	5.634	0.269	0.190
E.Epithelial	569	105	2.584	1.996	0.052	0.006
E.Goblet	211	527	5.902	3.597	0.084	0.042
E.Immature__Enterocytes	459	1782	3.507	2.807	0.092	0.220
E.Immature__Enterocytes	817	1451	4.347	2.608	0.158	0.084
E.Immature__Enterocytes	852	1726	3.348	2.928	0.078	0.119
E.Immature__Enterocytes	1037	2426	5.064	5.516	0.052	0.166
E.Immature__Enterocytes	299	280	1.936	1.519	0.023	0.016
E.Immature__Enterocytes	529	311	3.748	1.766	0.223	0.033
E.Immature__Enterocytes	475	660	6.100	4.939	0.248	0.154
E.Immature__Enterocytes	500	262	3.949	1.922	0.233	0.030
E.Immature__Enterocytes	113	35	5.628	0.764	0.196	0.002
E.Immature__Enterocytes	530	656	3.071	1.786	0.079	0.040
E.Immature__Enterocytes	518	130	2.782	0.830	0.207	0.013
E.Immature__Enterocytes	422	378	3.014	1.646	0.150	0.052
E.Immature__Enterocytes	1002	2180	4.413	3.797	0.089	0.126
E.Immature__Goblet	344	969	6.360	5.245	0.206	0.268
E.lmmature__Goblet	338	981	4.883	4.192	0.048	0.087
E.Secretory	120	55	3.684	1.893	0.066	0.009
E.Secretory	398	768	6.215	3.721	0.166	0.057
E.Secretory__All	354	1439	2.920	2.417	0.052	0.150
E.Secretory__All	64	2	0.437	–0.049	0.033	0.001
E.Secretory__All	1088	2284	4.746	4.429	0.084	0.141
E.Secretory__All	268	122	1.816	2.914	0.033	0.032
E.Secretory__All	513	526	5.467	4.918	0.189	0.133
E.Secretory__All	314	190	2.285	2.936	0.030	0.029
E.Secretory__TA	126	762	1.989	1.736	0.012	0.060
E.Secretory__TA	301	818	4.563	3.164	0.153	0.158
E.Secretory__TA	154	259	4.454	3.805	0.043	0.046
E.Secretory__TA	278	720	1.320	1.046	0.026	0.057
E.Secretory__TA	303	877	1.944	1.608	0.044	0.102
E.Stem	63	6	1.178	–0.485	0.050	0.002
E.Stem	237	575	6.088	3.493	0.105	0.042
E.Stem	239	604	3.797	3.107	0.052	0.081
E.Stem	233	549	5.235	2.766	0.103	0.044
E.Stem	240	613	4.911	3.971	0.037	0.050
F.Crypt	162	148	3.001	2.403	0.101	0.061
F.Crypt	739	2049	3.273	3.686	0.049	0.180
F.Crypt	689	1621	5.550	4.853	0.183	0.266
F.Crypt	833	2285	4.229	4.750	0.059	0.231
F.Crypt	429	1470	3.041	3.819	0.027	0.157
F.Crypt	359	192	5.360	4.084	0.171	0.038
F.Crypt	238	147	3.168	2.610	0.102	0.043
F.Crypt	630	1331	4.625	4.035	0.163	0.228
F.Crypt__loFos__1	284	814	4.116	3.384	0.183	0.316
F.Crypt__loFos__1	129	147	2.980	1.974	0.106	0.060
F.Crypt__loFos__1	101	66	2.784	2.123	0.042	0.017
F.Crypt__loFos__2	88	33	6.193	4.850	0.081	0.012
F.Endothelial	226	74	4.910	4.980	0.085	0.029
F.Fibroblast	174	45	3.194	2.323	0.190	0.027
F.Fibroblast	1700	2351	4.642	5.131	0.129	0.249
F.Fibroblast	812	637	4.188	3.642	0.098	0.053
F.Fibroblast	723	256	5.408	4.375	0.293	0.051
F.Fibroblast	488	201	3.293	2.214	0.313	0.061
F.Fibroblast	1778	2426	4.932	5.216	0.137	0.227
F.Fibroblast	1750	2392	4.780	5.109	0.145	0.248
F.Fibroblast	1162	1237	4.547	4.098	0.237	0.185
F.Stromal	1791	1990	3.355	3.683	0.109	0.152
F.Stromal	2171	2366	4.816	5.330	0.167	0.261
F.Stromal	1025	630	4.241	3.673	0.128	0.053
F.Stromal	949	269	5.304	4.581	0.323	0.056
F.Stromal	2195	2397	4.831	5.095	0.150	0.197
F.Stromal	2183	2360	4.695	5.023	0.162	0.219
F.Villus	569	953	4.500	4.105	0.242	0.308
F.Villus	436	508	4.004	3.868	0.129	0.137
F.Villus	372	386	4.842	4.352	0.164	0.121
F.Villus	277	145	5.429	4.722	0.139	0.044
F.Villus	79	18	3.522	2.186	0.099	0.009

TABLE 15-continued

Non-inflamed vs Healthy Markers						
F.Villus__1	181	104	5.000	3.997	0.114	0.033
F.Villus__1	157	50	5.170	4.481	0.076	0.015
I.Immune	848	1415	3.516	3.541	0.138	0.235
I.Immune	1244	798	4.731	3.743	0.152	0.049
I.Lymphoid	800	1383	3.317	3.493	0.114	0.222
I.Lymphoid	1323	823	4.803	3.751	0.172	0.052
I.Lymphoid	2199	1983	4.285	3.752	0.239	0.149
I.Lymphoid	2218	2021	4.192	3.728	0.200	0.132
I.Lymphoid	1537	987	5.084	3.996	0.316	0.096
I.Lymphoid	2314	2141	5.089	4.344	0.286	0.158
M.CD69pos_Mast	145	96	5.003	4.035	0.059	0.020
M.Macrophages	354	936	5.437	4.616	0.069	0.103
M.Mast	160	115	4.935	3.926	0.062	0.022
M.Monocytes	273	1237	3.685	3.459	0.059	0.230
M.Monocytes	387	696	4.540	3.756	0.060	0.063
M.Monocytes	601	1679	5.546	4.538	0.109	0.151
M.Myeloid	321	1396	3.664	3.488	0.065	0.250
M.Myeloid	518	765	4.488	3.794	0.078	0.071
M.Myeloid	566	1047	4.766	3.594	0.142	0.117
M.Myeloid	785	1787	4.171	3.829	0.080	0.144
M.Myeloid	864	2173	5.316	4.525	0.120	0.175
T.Activated_CD4_hiFos	199	381	4.555	3.648	0.208	0.212
T.Activated_CD4_hiFos	210	396	5.055	4.054	0.079	0.075
T.Activated_CD4_loFos	220	980	4.314	4.983	0.054	0.383
T.Activated_CD4_loFos	201	459	5.305	4.321	0.086	0.099
T.Activated_CD4_loFos	298	953	5.264	4.669	0.069	0.146
T.CD4	453	1150	3.452	3.661	0.076	0.224
T.CD4	739	1712	4.319	4.983	0.119	0.437
T.CD4	514	1299	4.767	5.153	0.107	0.354
T.CD4	851	616	4.812	4.116	0.128	0.057
T.CD4	1562	2475	6.156	6.468	0.141	0.278
T.CD4	1408	1953	4.371	4.008	0.152	0.164
T.CD4	1009	918	5.245	4.426	0.232	0.120
T.CD4	1489	2118	5.240	4.704	0.198	0.195
T.CD8	213	1267	3.751	3.703	0.047	0.268
T.CD8	305	415	4.826	3.743	0.299	0.192
T.CD8	596	1318	3.743	3.374	0.101	0.174
T.CD8	689	1817	4.275	3.801	0.099	0.188
T.CD8	698	1775	4.113	3.818	0.078	0.162
T.CD8	622	1457	3.891	3.495	0.104	0.185
T.CD8	487	819	4.945	4.075	0.132	0.121
T.CD8	730	1994	5.173	4.412	0.123	0.198
T.CD8_IELs	148	163	4.141	3.519	0.169	0.121
T.CD8_IELs	191	399	4.975	4.012	0.072	0.077
T.CD8_IELs	274	907	5.291	4.350	0.069	0.118
T.CD8_LP	195	336	4.890	4.217	0.064	0.070
T.Memory_CD4	117	565	3.972	4.883	0.029	0.260
T.Memory_CD4	239	365	5.688	4.809	0.121	0.101
T.Memory_CD4	334	810	5.759	4.996	0.100	0.143
T.Tcells	652	1376	3.553	3.792	0.105	0.261
T.Tcells	1213	730	4.762	4.006	0.157	0.056
T.Tcells	1981	1945	4.445	3.975	0.228	0.161
T.Tcells	2000	1915	4.298	3.911	0.193	0.141
T.Tcells	1791	1560	3.983	3.609	0.229	0.154
T.Tcells	1410	940	5.156	4.167	0.290	0.097
T.Tcells	2149	2267	5.070	4.717	0.219	0.180
T.Tcells	2178	2344	5.307	5.022	0.209	0.185
T.Tcells	2106	2150	5.215	4.563	0.259	0.168
T.Tcells	2256	2521	7.939	8.342	0.195	0.289
T.Tregs	183	157	4.882	4.028	0.064	0.030

Example 18—STAR Methods

Computational Analyses

Processing FASTQ reads into gene-expression matrices. Cell Ranger v2.0 was used to demultiplex the FASTQ reads, align them to the hg19 human transcriptome, and extract their "cell" and "UMI" barcodes. The output of this pipeline is a digital gene-expression (DGE) matrix for each sample, which records the number of UMIs for each gene that are associated with each cell barcode. DGE matrices were filtered to remove low quality cells, defined as cells in which fewer than 250 unique genes were detected. This cutoff was determined empirically: higher cutoffs led to disproportionate filtering of mast and T cells, whereas lower cutoffs did not affect the cell type distribution, but did reduce overall data quality. To account for differences in sequencing depth across cells, UMI counts were normalized by the total number of UMIs per cell and converted to transcripts-per-10,000 (henceforth "TPM").

Cell clustering overview. To cluster single cells into distinct cell subsets, Applicants followed the general procedure outlined in with additional modifications. This workflow includes the following steps: partitioning cells into epithelial, stromal, and immune compartments; and clustering the cells within each compartment, which entails the selection of "variable" genes, batch correction, dimension-

ality reduction (PCA), and graph clustering. Each step of this workflow is explained in detail below.

Partitioning cells into epithelial, stromal, and immune compartments. Cells were partitioned into epithelial, stromal, and immune compartments based on the expression of known marker genes. First, Applicants clustered the cells within each sample by their gene-expression profiles (with the clustering procedure below). The clusters were scored for the following gene signatures: epithelial cells (EPCAM, KRT8, KRT18), stromal cells (COL1A1, COL1A2, COL6A1, COL6A2, VWF, PLVAP, CDH5, S100B), and immune cells (CD52, CD2, CD3D, CD3G, CD3E, CD79A, CD79B, CD14, CD16, CD68, CD83, CSF1R, FCER1G). Signature scores were calculated as the mean $\log_2$(TPM) across all genes in the signature. Each cluster was assigned to the compartment of its maximal score and all cluster assignments were manually inspected to ensure the accurate segregation of cells. Finally, the cells within each compartment were assembled into three DGE matrices, comprising all epithelial cells, all stromal cells, and all immune cells.

Variable gene selection. Applicants identified sets of variable genes, defined as genes with high variance of expression relative to their mean expression. To prevent "batch" differences between samples from unduly impacting these gene sets, Applicants performed variable gene selection separately for each sample, then merged the results to form a consensus variable gene list. To identify variable genes within a sample, Applicants first calculated the mean (μ) and the coefficient of variation (CV) of expression of each gene. Genes were then grouped into 20 equal-frequency bins (ventiles) according to their mean expression levels. LOESS regression was used to fit the relationship, log(CV)~log(s), and the 1,500 genes with the highest residuals were evenly sampled across these expression bins. After this procedure was performed for each sample, genes were ranked according to the number of samples from which they were recovered. A consensus set of 1,500 variable genes was then formed by selecting the genes with the greatest recovery rates across all samples and ties were broken by random sampling. This consensus gene set was then pruned through the removal of all ribosomal, mitochondrial, immunoglobulin, and HLA genes, which were found to induce unwanted batch effects in downstream clustering steps.

Batch correction. Applicants observed substantial variability between cells that had been obtained from different human subjects, which likely reflects a combination of technical and biological differences. In some cases, these "batch effects" led to cells clustering by patient or disease phenotype, rather than by cell type or cell state. To eliminate these batch differences, Applicants ran ComBat with default parameters on the $\log_2$(TPM) expression matrix, allowing cells to be clustered by cell type or cell state. Importantly, these batch-corrected data were only used for the PCA and all steps relying on PCA (e.g. clustering, diffusion map, t-SNE visualization); all other analyses (e.g. differential expression analysis) were based on the original expression data.

Dimensionality reduction, graph clustering, and t-SNE visualization. Cells were clustered at two stages of the analysis: first, to initially partition the cells within each sample into epithelial, stromal, and immune compartments (single sample clustering), and second, to cluster cells from multiple samples into distinct subsets (multi sample clustering). For single-sample clustering, Applicants first ran PCA on the variable genes of the entire $\log_2$(TPM) expression matrix. The Infomap graph clustering algorithm was then applied to the k-nearest neighbor (k-NN) graph defined using PCs 1 to 20 and k=50 nearest neighbors. These parameters were designed to "over-cluster" the cells, ensuring that cells from distinct compartments were not grouped together. In contrast, for multi-sample clustering, Applicants ran PCA on the variable genes of the batch-corrected expression matrix. Applicants then applied Phenograph to the k-NN graph defined using PCs 1 to 20 and a varying k, which was selected through close inspection of the data: k=750 for epithelial cells, k=500 for stromal cells, and k=500 for immune cells. Although most clusters were stable over a range of k, some rare epithelial cell subsets, such as tuft cells and M cells, were not well represented because they had been merged with larger clusters, requiring a higher granularity (k=750) and merged the clusters for the tuft cells, enteroendocrine cells, M cells, and BEST4$^+$ enterocytes with the original clusters. In addition, Applicants partitioned the immune cells into myeloid, B cell, and T cell compartments, and repeated the clustering using the k-NN graph defined with PCs 1 to 15 and k=50 for myeloid cells, k=100 for B cells, and k=100 for T cells. Finally, the Barnes-Hut t-Distributed Stochastic Neighbor Embedding (t-SNE) algorithm was run on the PCs with perplexity=20 and for 10,000 iterations to produce a two-dimensional embedding of the data for visualization (FIG. **1**B).

Differential expression analysis. Differential expression (DE) tests were performed using MAST, which fits a hurdle model to the expression of each gene, consisting of logistic regression for the zero process (i.e. whether the gene is expressed) and linear regression for the continuous process (i.e. the expression level). To reduce the size of the inference problem, separate models were fit for all levels of the cell tree, comparing cells within the given group to all other cells (e.g. ISCs vs. non-ISCs). The regression model includes terms to capture the effects of the cell subset and the disease state on gene expression, while controlling for cell complexity (i.e. the number of genes detected per cell).

Specifically, Applicants used the regression formula, Y_i~X+D+N, where Y_i is the standardized $\log_2$(TPM) expression vector for gene i across all cells, X is a binary variable reflecting cell subset membership (e.g. ISCs vs. non-ISCs), D is the disease state associated with each cell, and N is the number of genes detected in each cell. Overall, Applicants fit three types of DE models, which varied by the encoded disease states: (1) to identify cell subset markers and DE genes in UC patients relative to healthy controls, Applicants used three disease states: Healthy, UC non-inflamed, and UC inflamed; (2) to identify DE genes between non-inflamed and inflamed patient samples, Applicants used two disease states: UC non-inflamed and UC inflamed; and (3) to identify genes that are specific to cell subsets in healthy subjects and UC patients, Applicants used two disease states: Healthy and UC. Additionally, a few heuristics were used to increase the speed of the tests: Applicants required all tested genes to be expressed by at least 1% of cells and to have a minimum fold change of 1.2 within the group of interest, and cells were evenly downsampled across groups so that a maximum of 2,500 cells were tested for each cell subset. In all cases, the discrete and continuous coefficients of the model were retrieved and p-values were calculated using the likelihood ratio test in MAST. Q-values were separately estimated for each cell subset comparison using the Benjamini-Hochberg correction. Unless otherwise indicated, all reported DE coefficients and q-values correspond to the discrete component of the model (i.e. the logistic regression).

Estimation of the droplet contamination rate and filtering of putative ambient RNA contaminants. Droplets encapsu-

late single cells with small portions of the extracellular environment, leading to low but persistent levels of contamination by ambient RNA [REF-Macosko]. To correct for this, Applicants explicitly modeled droplet contamination. First, Applicants partitioned individual cells into the following groups: epithelial cells, fibroblasts, endothelial cells, myeloid cells, B cells, and T cells. Applicants reasoned that each group should uniquely express a subset of genes that are not found in other cells; for example, B cells uniquely express IGHA1 and T cells uniquely express CD3D. Therefore, the off-target expression of such genes in the incorrect group (e.g. IGHA1 expression in T cells) should reflect contamination rather than intrinsic gene expression. Moreover, Applicants hypothesized that the levels of such off-target gene expression could serve as an accurate indicator of contamination rates in the entire dataset. To test this hypothesis, Applicants compared the mean expression levels of genes within each group (i.e. "within-group" expression) to their mean expression levels in all other cells (i.e. "non-group" expression), which Applicants used as a proxy for the composition of extracellular RNA (e.g. B cells vs. non-B cells, FIG. **39**, see "Normalization and scaling of expression levels for contamination filtering" below for details). As expected, known markers for cell groups were enriched at the edges of the point distribution, where the difference between "within-group" and "non-group" expression was greatest. For example, known B cell markers were enriched on the left edge of the point distribution (e.g. IGHA1 and IGJ, FIG. **39**), while markers for other cell types were enriched on the right edge, likely reflecting droplet contamination (e.g. CD3D and TPSAB1, FIG. **39**). Furthermore, Applicants noticed two other patterns that yielded insights into droplet contamination: first, genes with sufficiently high "non-group" expression always had positive "within-group" expression, and second, there was a strong linear relationship between "within-group" and "non-group" expression levels, particularly for the potential contaminants on the right edge of the point distribution (FIG. **39**). Taken together, these observations suggest that contamination uniformly affects all genes and that overall levels of contamination for each gene are proportional to its representation in the extracellular RNA pool.

Therefore, to estimate the contamination rate for each cell group, Applicants fit a robust linear model to the genes on the right edge of the point distribution, whose expression is likely driven by contamination. Surprisingly, the fitted models were nearly identical across groups (slope=1.33±0.07, intercept=−7.22±0.33) and Applicants constructed a consensus model using the mean slope and mean intercept. This model corresponds to a contamination rate between 0.5% and 5% of the total RNA pool in each sample. Applicants used this model to identify potential contaminants in all cell subsets by conservatively flagging genes with residuals <5 (i.e. 32-fold increase over the estimated contamination rate) and genes in each cell subset whose expression did not exceed 1% of its total expression across all cells. This approach filtered out nearly all known contamination throughout the full dataset.

Normalization and scaling of expression levels for contamination filtering. To estimate the contamination rate, Applicants compared the within-group and non-group expression levels of each gene (see above, FIG. **39**).

To estimate the droplet contamination rate, Applicants compared for each gene its within-group and non-group expression levels (e.g. B cells vs. non-B cells, FIG. **39**). However, because the composition of extracellular RNA varies across samples, contamination can have different effects within each sample. For example, cells derived from EPI samples have high levels of contaminating MUC2, while cells from LP samples have high levels of contaminating IGHA1. To account for these differences across samples, Applicants used a weighted mean to compute the non-group expression levels for each gene, where the weights were chosen to match the sample distribution of the target cell group.

Gene specificity. For each expressed gene, Applicants tested whether that gene was specific to any cell subset (e.g. T_{regs}) or any node of the cell hierarchy (e.g. $CD4^+$ T cells). Applicants defined a gene as specific to a cell group, if it was significantly and positively DE in all pairwise comparisons to non-overlapping cell subsets and its mean expression level within the group was at least 2-fold higher than its mean expression in all other cell subsets. Additionally, Applicants searched for cases where a gene gained, lost, or changed its cell specificity between health and disease. As such cases may reflect differences in statistical power between the two cohorts, rather than changes in gene specificity, Applicants required that another cell subset have significantly higher expression of the gene in the appropriate group of cells (i.e. healthy subjects or UC patients, depending on the hypothesis being tested).

Using receptor-ligand pairs to infer cell-cell interactions. To identify cell-cell interactions, Applicants used the FANTOM5 database of literature supported receptor-ligand interactions. These receptors and ligands were mapped onto the lists of cell subset markers and DE genes within healthy, UC non-inflamed, and UC inflamed cells. To focus on genes that were enriched within a cell subset, Applicants considered a gene to be expressed within a cell only if its adjusted p-value was less than 0.05 and its discrete coefficient was greater than 1. In addition, to examine changes in cell-cell interactions with disease state, Applicants mapped the DE genes onto this network, removing edges that were not affected by DE, or adding edges in which both genes were DE.

For DE genes, receptors and ligands require that at least one gene within the interaction is differentially expressed. Because many genes showed relatively small changes in gene expression, Applicants required that all DE genes also be found as cell subset markers in either the healthy cells or cells isolated from the corresponding health state. In this way, Applicants constructed a network of cell-cell interactions, where each node is a cell type, each edge is a receptor-ligand interaction that is expressed.

Various modifications and variations of the described methods, pharmaceutical compositions, and kits of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific embodiments, it will be understood that it is capable of further modifications and that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention that are obvious to those skilled in the art are intended to be within the scope of the invention. This application is intended to cover any variations, uses, or adaptations of the invention following, in general, the principles of the invention and including such departures from the present disclosure come within known customary practice within the art to which the invention pertains and may be applied to the essential features herein before set forth.

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Arg Pro Pro Arg Ala Lys Pro Ala Pro Arg Arg Arg Ala Ala Gln Pro
    130                 135                 140

Ser Asp Ala Ser Pro Ala Ala Gln Val Asp Leu Arg Thr Leu Gly Tyr
145                 150                 155                 160

Ser Gln Gln Gln Gln Glu Lys Ile Lys Pro Lys Val Arg Ser Thr Val
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Ala Gln His His Glu Ala Leu Val Gly His Gly Phe Thr His Ala His
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Leu Leu Thr Val Ala Gly Glu Leu Arg Gly Pro Pro Leu Gln Leu Asp
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Pro Ala Leu Ile Lys Arg Thr Asn Arg Arg Ile Pro Glu Arg Thr Ser
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His Arg Val Ala Asp His Ala Gln Val Val Arg Val Leu Gly Phe Phe
65                  70                  75                  80

Gln Cys His Ser His Pro Ala Gln Ala Phe Asp Asp Ala Met Thr Gln
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Phe Gly Met Ser Arg His Gly Leu Leu Gln Leu Phe Arg Arg Val Gly
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Val Thr Glu Leu Glu Ala Arg Ser Gly Thr Leu Pro Pro Ala Ser Gln
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Ala Asp Ser Leu Glu Arg Asp Leu Asp Ala Pro Ser Pro Met His Glu
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Gly Asp Gln Thr Arg Ala Ser
            180
```

What is claimed is:

1. A method for treating a subject suffering from inflammatory bowel disease (IBD) comprising the steps of:

determining the presence of colitis-associated inflammatory fibroblasts (CAIFs) by:

a. obtaining a biological sample from the subject,

b. detecting MMP3, MMP10, PLAU, IL11, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, TNFRSF11B, CHI3L1, WNT2 gene expression, or any combination thereof in the biological sample, and

c. administering to the subject determined to have CAIFs, a treatment comprising modulating the activity of one or more gastrointestinal tract cell types,

wherein the one or more gastrointestinal tract cell types is chosen from the group consisting of: plasma B cells, class switching B cells, follicular B cells, microvascular cells, post-capillary venules, vitamin metabolizing, endothelial pericytes, enterocytes, tuft cells, goblet 2, absorptive TA 1, secretory TA, absorptive TA 2, cycling TA, goblet 1, stem cells, enteroendocrine, glial cells, inflammatory fibroblasts, fibroblast pericytes, myofibroblasts, villus fibroblasts, crypt fibroblasts (hiFos), crypt fibroblasts (loFos), T cells, macrophages, dendritic cells, mast cells, cycling monocytes, tolerogenic DCs, neutrophils, activated CD4 cells loFos, activated CD4 cells hiFos, CD8 IELs, CD8 LP cells, T regs, memory T cells, NK cells and cycling CD8 cells.

2. The method of claim **1**, wherein the gene expression is detected by single-cell RNA-seq.

3. The method of claim **1**, wherein the treatment induces intestinal stem cells to differentiate into absorptive transit amplifying (TA) 1 cells, absorptive TA 2 cells or class switching B cells.

4. The method of claim **3**, wherein the treatment comprises a CRISPR-Cas system that targets WNT2, CHI3L1, or TREM1.

5. The method of claim **3**, wherein the treatment comprises a CRISPR-Cas system that targets a fibrinolytic enzyme comprising MMP3, MMP10, and PLAU.

6. The method of claim **3**, wherein the treatment comprises a CRISPR-Cas system that targets a fibrinolytic enzyme chosen from MMP3, MMP10, or PLAU.

7. The method of claim **3**, wherein the CRISPR-Cas system targets an immune signaling molecule comprising IL11, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, and TNFRSF11B.

8. The method of claim **3**, wherein the CRISPR-Cas system targets an immune signaling molecule chosen from IL11, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, or TNFRSF11B.

9. The method of claim **1**, wherein the treatment comprises a CRISPR-Cas system that targets a signaling molecule of the JAK-STAT signaling pathway.

10. The method of claim **9**, wherein the signaling molecule is STAT3.

11. The method of claim **3**, wherein the treatment comprises an RNAi that targets WNT2, CHI3L1, or TREM1.

12. The method of claim **3**, wherein the treatment comprises an RNAi that targets a fibrinolytic enzyme comprising MMP3, MMP10, or PLAU.

13. The method of claim **3**, wherein the treatment comprises an RNAi that targets a fibrinolytic enzyme chosen from MMP3, MMP10, or PLAU.

14. The method of claim **3**, wherein the treatment comprises an RNAi that targets an immune signaling molecule comprising IL11, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, or TNFRSF11B.

15. The method of claim **3**, wherein the treatment comprises an RNAi that targets an immune signaling molecule chosen from IL11, IL1R1, IL13RA2, CXCL6, CCL11, TNFSF11, or TNFRSF11B.

16. The method of claim **1**, wherein the treatment comprises an RNAi that targets a signaling molecule of the JAK-STAT signaling pathway.

17. The method of claim **16**, wherein the signaling molecule is STAT3.

18. The method of claim **1**, wherein the treatment targets a receptor-ligand interaction in the gut.

19. The method of claim **18**, wherein the treatment comprises a CRISPR-Cas system that targets CCR7 and one or more of CCL19 and CCL21, TNFB and LTBR, LGR5 and RSPO3, IL15 and IL15RA, FGF23 and FGFR1, CCL8 and CCR1, CXCL2 and XCR1, XCL2 and XCR1 or CHI3L1 and IL13RA2.

20. The method of claim **18**, wherein the treatment comprises an RNAi that targets CCR7 and one or more of CCL19 and CCL21, TNFB and LTBR, LGR5 and RSPO3, IL15 and IL15RA, FGF23 and FGFR1, CCL8 and CCR1, CXCL2 and XCR1, XCL2 and XCR1 or CHI3L1 and IL13RA2.

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