ISSUED US/EP PATENTS RELATING TO ANTIBODY GLYCOSYLATION

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
1A	**1986-03-07**	**US4925796 A** **06/837,604** **METHOD FOR ENHANCING GLYCOPROTEIN STABILITY** ***FAMILY MEMBERS*** **US5272066A EXPIRED [see TAB 1B]** **NO OTHER FAMILY MEMBERS**	**MASSACHUSETTS INSTITUTE OF TECHNOLOGY** (Cambridge, MA) **LAPSED 1994-05-15** **Issue Date: 1990-05-15** **Filing Date: 1986-03-07*** **(*: pre-GATT filing)** **Earliest Effective Filing Date: 1986-03-07** **Priority Date: 1986-03-07**	**Bergh; Michel L. E. (Somerville, MA)** **Hubbard; S. Catherine (Somerville, MA)** **Rasmussen; James (Ithaca, NY)**	1. **A method for modifying a glycoprotein** including at least one asparagine linked oligosaccharide chain comprising: attaching a galactose residue to an N-acetylglucosamine residue which is linked to an asparagine through an N-glycosidic bond to form a Gal→GlcNAc→Asn (protein) sequence as part of a glycoprotein. 2. The method of claim 1 further comprising first cleaving asparagine-linked oligosaccharide chains of the glycoprotein to remove all sugars other than core n-acetylglucosamine residues bound to the glycoprotein. 7. The method of claim 2 wherein the oligosaccharide chain is cleaved by digestion with an exoglycosidase. 8. The method of claim 7 wherein the exoglycosidase is selected from the group consisting of sialidase, α-mannosidase, β-mannosidase, α-galactosidase, β-galactosidase, α-fucosidase, β-hexosaminidase, and combinations thereof. 21. The method of claim 1 wherein the galactose residue is attached to the N-acetylglucosamine residue by a galactosyltransferase. 22. The method of claim 21 wherein the galactosyltransferase is selected from the group consisting of UDP-Gal: GlcNAc-R β1→4 galactosyltransferase and UDP-Gal:GlcNAc-R β1→3 galactosyltransferase.	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 1994-05-15 ***METHODOLOGY*** *IN VITRO* PROTEIN GLYCOSYLATION *In vitro* glycosylation of proteins where all carbohydrate "exterior to the two innermost GlcNAc residues" has been removed with an exoglycosidase. Modification of glycoproteins to extend *in vivo* circulatory lifetime and to target protein for recognition by sugar-specific cell surface receptors.
1B	**1986-03-07**	**US5272066 A** **07/785,913** **SYNTHETIC METHOD FOR**	**MASSACHUSETTS INSTITUTE OF TECHNOLOGY** (Cambridge, MA) **LAPSED 1998-03-03**	**Bergh; Michel L. E. (Somerville, MA)** **Hubbard; S. Catherine (Somerville, MA)** **Rasmussen; James**	1. A method for modifying proteins comprising: the step wherein when the protein contains carbohydrate, removing all carbohydrate exterior to the two innermost GlcNAc residues from the protein to be modified prior to derivatizing the amino acids, reacting the free amino groups of one or more lysines or the amino terminal amino acid or the thiol groups of one or more free cysteines on the protein with a glycoside or thioglycoside represented by the formula S-X, wherein S is a first saccharide or disaccharide selected from the	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 1998-03-03 ***METHODOLOGY***

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		ENHANCING GLYCOPROTEIN STABILITY ***FAMILY MEMBERS*** **SEE ABOVE**	**Issue Date: 1993-12-21** **Filing Date: 1991-11-04*** **(*: pre-GATT filing)** **Earliest Effective Filing Date: 1986-03-07** **Priority Date: 1986-03-07**	**(Ithaca, NY)**	group consisting of N-acetylglucosamine, N-acetyllactosamine and galactose and X is an aglycone, and enzymatically attaching to S one or more additional saccharides selected from the group consisting of galactose, fucose, and sialic acid. 5. The method of claim 1, wherein the first saccharide is GlcNAc, and wherein said enzymatic attachment comprises: attaching a galactose residue to the N-acetylglucosamine to form a Gal-GlcNAc→ sequence; and attaching a sialic acid residue to the galactose to form a Sa-Gal-GlcNAc→ sequence. 6. The method of claim 1, wherein the first saccharide is galactose, and wherein said enzymatic attachment comprises: attaching a sialic acid residue to the galactose to form a Sa-Gal sequence.	*IN VITRO* PROTEIN GLYCOSYLATION Modifying glycosylation of proteins by reacting protein with a glycoside or thio-glycoside and enzymatically attaching one or more saccharide(s). Modification of glycoproteins to extend *in vivo* circulatory lifetime and to target protein for recognition by sugar-specific cell surface receptors.
2	**1988-12-21**	**US5047335 A** **07/288,618** **PROCESS FOR CONTROLLING INTRACELLULAR GLYCOSYLATION OF PROTEINS**	**UNIVERSITY OF CALIFORNIA** (Oakland, CA) **EXPIRED 2008-12-21** **Issue Date: 1991-09-10** **Filing Date: 1988-12-21***	**Paulson; James (Sherman Oaks, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Weinstein; Jasminder (Culver City, CA)**	1. A process for altering the glycosylation of a protein produced by a eukaryotic cell, said process comprising the steps of: introducing into said eukaryotic cell at least one gene which is capable of expressing at least one enzyme which is selected from the group consisting of glycosyltransferase, fucosyltransferases, galactosyltransferases, β-acetylgalactosaminyltransferases, N-acetylglycosaminyltransferases and sulfotransferases; and expressing a sufficient amount of at least one of said enzymes in said eukaryotic cell to thereby alter the glycosylation of said protein in said eukaryotic cell.	**"PAULSON I" FAMILY** ***STATUS*** • EXPIRED 2008-12-21 ***METHODOLOGY*** *IN VIVO* PROTEIN GLYCOSYLATION Altering glycosylation of proteins produced in a mammalian cell line (e.g. CHO cells) by co-

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		FAMILY MEMBERS **NONE**	**(*: pre-GATT filing)** **Earliest Effective Filing Date: 1988-12-21** **Priority Date: 1988-12-21**		2. A process according to claim 1 wherein said cell is selected from the group consisting of Chinese hamster ovary cells, mouse L cells, mouse A9 cells, baby hamster kidney cells, C127 cells and PC8 cells. 9. A process for altering the glycosylation of a protein produced by a cell wherein attachment of the carbohydrate moiety to said protein during glycosylation is dependent upon at least one naturally occurring enzyme present in said cell, said process comprising the steps of: introducing into said cell at least one gene which is capable of expressing at least one supplemental enzyme selected from the group consisting of sialyltransferase, fucosyltransferase, galactosyltransferase, N-acetylgalactosaminyltransferase, N-acetylglucosaminyltransferase and sulfotransferase; and expressing a sufficient amount of at least one of said supplemental enzymes in said cell to produce a cell having both naturally occurring and supplemental enzymes wherein the presence of said supplemental enzyme alters the glycosylation of said protein. 10. A process according to claim 9, wherein said cell is selected from the group consisting of Chinese hamster ovary cells, mouse L cells, mouse A9 cells, baby hamster kidney cells, C127 cells and PC8 cells. 11. A process according to claim 10 wherein said cell is a Chinese Hamster ovary cell and said enzyme is β-galactoside α 2,6-sialyltransferase.	expression of an enzyme which alters glycosylation, for example, • glycosyltransferase, • fucosyltransferases, • galactosyltransferases, • β-acetyl galactosaminyltransferases, • N-acetylglycosaminyltransferases and • sulfotransferases Appears to be first prior art patent document disclosing a method of altering protein glycosylation in a eukaryotic cell
3	**1989-08-23**	**EP414171 B1** **PROCESS FOR THE ENZYMATIC SYNTHESIS OF COMPONENTS OF GALACTOSYLATED GLYCOPROTEINS.** ***FAMILY MEMBERS*** **NONE**	**HOECHST AG** (Frankfurt, DE) **EXPIRED 2010-08-18** **Issue Date: 1994-11-23** **Filing Date: 1990-08-18** **Priority Date: 1989-08-23**	**THIEM JOACHIM [DE]** **WIEMANN; TORSTEN [DE]**	1. A process for the enzymatic preparation of compounds of the formula I or II:	***STATUS*** • EXPIRED 2010-08-18 • NO OPPOSITION FILED ***METHODOLOGY*** *IN* VITRO PROTEIN GLYCOSYLATION *In vitro* methods of producting glycoproteins having oligosaccharides of formula I or II

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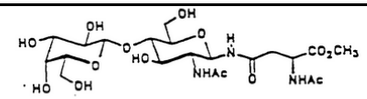
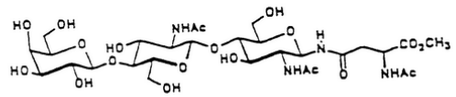
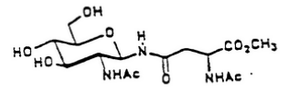
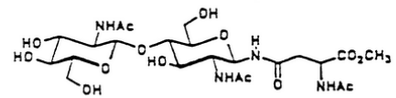
					 I  II which comprises incubating the compound of the formula III or the compound of the formula IV  III  IV with galactosyltransferase in the presence of a galactosyl donor. 2. The process as claimed in claim 1, wherein UDP-Gal is used as galactosyl donor. 3. The process as claimed in claim 1 or 2, wherein UDP-Gal is synthesized from UDP-Glc with catalysis by UDP-galactose 4-epimerase. 4. The process as claimed in one or more of claims 1 to 3, wherein the reaction is carried out in a buffered solution. 5. The process as claimed in one or more of claims 1 to 4, wherein the reaction is carried out at 32 to 37°C.	
4A	**1989-10-24**	**US5032519 A** **07/426,577** **METHOD FOR PRODUCING SECRETABLE GLYCOSYL-**	**THE REGENTS OF THE UNIV. OF CALIFORNIA** (Oakland, CA) **AMGEN**	**Paulson; James C. (Sherman Oaks, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Colley; Karen J. (Los Angeles, CA)**	1. A method for producing a soluble glycosyltransferase which is secreted by a cell having Golgi apparatus as part of the secretory pathway of said cell, wherein the naturally occurring glycosyltransferase includes a membrane anchor and a retention signal located in an NH2 - terminal region not required for catalytic activity, said method comprising the steps of: introducing into said cell at least one gene which is capable of expressing a soluble and secretable glycosyltransferase wherein said anchor domain and a sufficient portion of said NH2 -	**"PAULSON II" FAMILY** ***STATUS*** • EXPIRED 2011-07-16

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		TRANSFERASES AND OTHER GOLGI PROCESSING ENZYMES ***FAMILY MEMBERS*** **AT161044T** **AU199066480A** **AU646233B** **CA2065839C** **DE69031805T2** **DK497878T3** **EP497878B1** **EXPIRED 2010-10-24** **[see TAB 4D]** **ES2112254T3** **GR3026217T3** **JP03121342B2** **JP5504678A** **US5541083** **EXPIRED 2013-07-30** **[see TAB 4B]** **US5776772** **EXPIRED 2009-10-24** **[see TAB 4C]** **WO1991006635A1**	(Thousand Oaks, CA) **EXPIRED 2011-07-16** **Issue Date:** **1991-07-16** **Filing Date:** **1989-10-24*** **(*: pre-GATT filing)** **Earliest Effective Filing Date:** **1989-10-24**	**Adler; Beverly (Newbury Park, CA)** **Browne; Jeffrey K. (Camarillo, CA)**	terminal region is replaced with a cleavable signal sequence so that said glycosyltransferase lacks said membrane anchor and said retention signal; expressing said soluble and secretable glycosyltransferase in said cell wherein said cell secretes said soluble enzyme via said secretory pathway which includes said Golgi apparatus; and recovering the soluble glycosyltransferase secreted by said cell. 2. A method for producing a secretable glycosyltransferase according to claim 1 wherein said glycosyltransferase is selected from the group consisting of N-acetylglucosaminyltransferases, N-acetylgalactosaminyltransferases, sialyltransferases, fucosyltransferases, galactosyltransferases, mannosyltransferases, sulfotransferases, accetyltransferases and mannosidases. 3. A method for producing secretable glycosyltransferase according to claim 2 wherein said glycosyltransferase is a sialyltransferase. 4. A method for producing a secretable glycosyltransferase according to claim 3 wherein said sialyltransferase is β-galactoside α2,6-sialyltransferase. 17. A composition of matter comprising cells which have Golgi apparatus as part of the secretory pathway of said cell and wherein said cells include at least one recombinant gene which encodes a soluble and secretable glycosyltransferase in which the anchor domain and a sufficient portion of the NH2 -terminal region of said glycosyltransferase is replaced with a cleavable signal sequence so that said glycosyltransferase lacks the membrane anchor and the retention signal, whereby said glycosyltransferase is secreted by the cell via said Golgi apparatus and said secretory pathway. 22. A vector for use in expressing a soluble sialyltransferase in a host cell, said vector comprising DNA having a nucleotide sequence which codes for a sialyltransferase which lacks the membrane anchor and retention signal of said sialyltransferase.	***METHODOLOGY*** EXPRESSION OF A SOLUBLE AND SECRETABLE GLYCOSYL-TRANSFERASE IN A MAMMALIAN CELL LINE
4B	**1989-10-24**	**US5541083 A** **08/209,604** **METHOD FOR PRODUCING SECRETABLE GLYCOSYL-TRANSFERASES AND OTHER GOLGI**	**THE REGENTS OF THE UNIV. OF CALIFORNIA** (Oakland, CA) **EXPIRED 2013-07-30** **Issue Date:** **1996-07-30**	**Paulson; James C. (Sherman Oaks, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Colley; Karen J. (Los Angeles, CA)** **Adler; Beverly (Newbury Park, CA)**	1. In a method for enzymatically synthesizing an oligosaccharide product, said method comprising the steps of reacting a starting oligosaccharide with a nucleoside phosphate sugar in the presence of a glycosyltransferase selected from the group consisting of N-acetylgulcosaminyltransferases, N-acetylgalactosaminyltransferases, sialyltransferases, fucosyltransferases, galactosyltransferases, mannosyltransferases, sulfotransferases, and accelytransferases under conditions in which the glycosyltransferase catalyzes the transfer of a monosaccharide from the nucleoside phosphate sugar to the starting oligosaccharide to produce the oligosaccharide product, said glycosyltransferase comprising a membrane anchor and a golgi retention signal located in an NH.sub.2 -terminal region not required for the glycosyltransferase catalytic activity, the improvement comprising using a secretable glycosyltransferase in said	**"PAULSON II" FAMILY** ***STATUS*** • EXPIRED 2013-07-30 ***METHODOLOGY***

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		PROCESSING ENZYMES ***FAMILY MEMBERS*** **SEE ABOVE**	**Filing Date: 1994-03-10*** **(*: pre-GATT filing)** **Earliest Effective Filing Date: 1989-10-24**	**Browne; Jeffrey K. (Camarillo, CA)** **Weinstein; Jasminder (Westlake Village, CA)**	method which is produced by secretion from a cell having Golgi apparatus as part of the secretory pathway of said cell, said secretable glycosyltransferase being produced by a method comprising the steps of: introducing into said cell having Golgi apparatus a gene encoding a secretable glycosyltransferase wherein said anchor domain and said golgi retention signal are replaced with a cleavable signal sequence so that said secretable glycosyltransferase is secretable via the secretory pathway of said cell which includes the Golgi apparatus; expressing said secretable glycosyltransferase in said cell wherein said cell secretes said secretable glycosyltransferase via said secretory pathway which includes said Golgi apparatus; and recovering the secretable glycosyltransferase secreted by said cell. 2. An improved method for enzymatically synthesizing an oligosaccharide product according to claim 1 wherein said secretable glycosyltransferase is a sialyltransferase. 3. An improved method for enzymatically synthesizing an oligosaccharide product according to claim 2 wherein said sialyltransferase is β-galactoside α2,6sialyltransferase.	EXPRESSION OF A SOLUBLE AND SECRETABLE GLYCOSYL-TRANSFERASE IN A MAMMALIAN CELL LINE
4C	**1989-10-24**	**US5776772 A** **08/593,865** **METHOD FOR PRODUCING SECRETABLE GLYCOSYL-TRANSFERASES AND OTHER GOLGI PROCESSING ENZYMES**	**THE REGENTS OF THE UNIV. OF CALIFORNIA** (Oakland, CA) **EXPIRED 2009-10-24** **Issue Date: 1998-07-07** **Filing Date: 1996-01-30** **Earliest Effective**	**Paulson; James C. (Sherman Oaks, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Colley; Karen J. (Los Angeles, CA)** **Adler; Beverly (Newbury Park, CA)** **Browne; Jeffrey K. (Camarillo, CA)**	1. An expression cassette comprising a promoter operably linked to a DNA sequence, said DNA sequence encoding a secretable glycosyltransferase which lacks the membrane anchor and golgi retention signal. 2. An expression cassette according to claim 1 wherein the DNA sequence is a cDNA sequence. 3. An expression cassette according to claim 1 wherein the DNA sequence encodes a glycosyltransferase which consists of a catalytic domain and less than ten stem region amino acid residues. 4. An expression cassette according to claim 1 further comprising a DNA sequence encoding a cleavable signal sequence in operable linkage to said DNA sequence encoding said secretable glycosyltransferase.	**"PAULSON II" FAMILY** ***STATUS*** • EXPIRED 2009-10-24 ***METHODOLOGY*** EXPRESSION OF A SOLUBLE AND SECRETABLE GLYCOSYL-TRANSFERASE IN A MAMMALIAN CELL LINE

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		FAMILY MEMBERS **SEE ABOVE**	**Filing Date: 1989-10-24**	**Weinstein; Jasminder (Westlake Village, CA)**	5. An expression cassette according to claim 4 wherein said DNA sequence encoding the cleavable signal sequence encodes a human γ-interferon signal sequence.	
4D	**1989-10-24**	**EP497878B1** **METHOD FOR PRODUCING SECRETABLE GLYCOSYL-TRANSFERASES** ***FAMILY MEMBERS*** **SEE ABOVE**	**THE REGENTS OF THE UNIV. OF CALIFORNIA** (Oakland, CA) **AMGEN** (Thousand Oaks, CA) **EXPIRED 2010-10-24** **Issue Date: 1997-12-10** **Filing Date: 1990-10-24** **Priority Date: 1989-10-24**	**Paulson; James C. (Sherman Oaks, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Colley; Karen J. (Los Angeles, CA)** **Adler; Beverly (Newbury Park, CA)** **Browne; Jeffrey K. (Camarillo, CA)**	1. A method for producing a soluble Golgi processing enzyme which is secreted by a cell, wherein the naturally occurring enzyme includes a retention signal and a membrane anchor, said method comprising the steps of: introducing into said cell at least one gene which is capable of expressing a soluble and secretable enzyme which lacks said retention signal and anchor domain; expressing said soluble and secretable enzyme is said cell wherein said cell secretes said soluble enzyme; and recovering the soluble enzyme secreted by said cell. 2. A method for producing an enzyme according to claim 1 wherein said enzyme is a glycosyltransferase. 3. A method for producing a secretable enzymeaccording to claim 2 wherein said glycosyltransferase is selected from the group consisting of Nacetylglucosaminyltransferases, N-acetylgatactosaminyltransferases, sialyltransferases, fucosyltransferases, galactosyltransferases, mannosyltransferases, sulfoltransferases, accetyltransierases and mannosidases.	**"PAULSON II" FAMILY** ***STATUS*** • EXPIRED 2010-10-24 • NO OPPOSITION FILED ***METHODOLOGY*** EXPRESSION OF A SOLUBLE AND SECRETABLE GLYCOSYL-TRANSFERASE IN A MAMMALIAN CELL LINE

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					4. A method for producing secretable glycosyltransferase according to claim 3 wherein said glycosyltransferase is a sialyltransferase. 5. A method for producing a secretable glycosyltransferase according to claim 4 wherein said sialyltransferase is β-galactoside a2,6- sialyltransferase. 6. A method for producing a secretable glycosyltransferase according to claim 2 wherein the cell into which said gene is introduced is selected from the group consisting of Chinese hamster ovary cells, mouse L cells, mouse A9 cells, baby hamster kidney cells, C127 cells, PC8 cells and insect cells. 13. In a method for producing glycosyltransferase wherein said glycosyltransferase is produced within a cell and remains within said cell, said glycosyltransferase including a membrane anchor and a retention signal which causes said glycosyltransferase to be retained within said cell and an enzymatic domain which provides said glycosyltransferase with enzymatic activity, the improvement comprising: introducing at least one gene into said cell which is capable of a glycosyltransferase which does not have said membrane anchor and retention signal whereby a soluble glycosyltransferase is produced which is secreted by the cell; expressing said soluble glycosyltransferase in said cell in a sufficient amount which is secreted by said cell; and recovering the soluble glycosyltransferase secreted by said cell. 18. A composition of matter comprising a soluble glycosyltransferase made by a method comprising the steps of: introducing into a cell at least one gene which is capable of expressing a soluble glycosyltransferase which is secreted by said cell; expressing said soluble glycosyltransferase in said cell in a sufficient amount wherein said cell secretes said soluble glycosyltransferase; and recovering the soluble glycosyltransferase secreted by said cell. 21. A composition of matter comprising cells which have been genetically altered to produce a soluble glycosyltransferase which is secreted by the cell. 29. A method of enzymatically synthesizing an oligosaccharide product comprising: reacting a starting oligosaccharide with a sugar nucleotide and a homogeneous, soluble glycosyltransferase under conditions in which the glycosyltransferase catalyzes the transfer of a monosaccharide from the sugar nucleotide to the starting oligosaccharide to produce the oligosaccharide product. 38. An expression cassette comprising a promoter operably linked to a DNA sequence encoding a secretable, soluble glycosyltransferase. 47. A method for producing a sialylated oligosaccharide comprising: reacting an starting oligosaccharide with CMP-NeuAc and a homogeneous, soluble sialyltransferase under conditions	

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					in which the sialyltransferase catalyzes the transfer of a sialic acid from the CMP-NeuAc to the starting oligosaccharide to produce a sialylated oligosaccharide. 48. A composition comprising a homogeneous soluble sialyltransferase in substantially pure form which lacks a functional retention signal and a signal anchor domain.	
5	**1990-03-16**	**EP456986 B1** **HEAT RESISTANT BETA-GALACTOSYL-TRANSFERASE, ITS PRODUCTION PROCESS AND ITS USE** ***FAMILY MEMBERS*** **AT131869T** **AU199172958A** **AU633707B** **CA2038352A1** **CA2038352C** **DE69115556D1** **DE69115556T2** **DK456986T3** **JP02970932B2** **US5153128A** **EXPIRED** **US5234828A** **EXPIRED**	**SUNTORY LTD** (Osaka, Japan) **LAPSED 2010-04-30** **Issue Date:** **1991-11-21** **Filing Date:** **1991-03-14** **Priority Date:** **1990-03-16**	**Nakayama Toru** **[JP]** **Kodama Yukiko** **[JP]** **Amano Norihide** **[JP]** **Nakao Masahiro** **[JP]** **Shibano Yuji** **[JP]** **Amachi Teruo** **[JP]**	1. A novel β-galactosyltransferase having the following physicochemical properties: (1) Action Transfer reaction: Forms 1 mole of a β-D-galactopyranoside Gal-Y and 1 mole of X from 1 mole of another β-D-galactopyranoside Gal-X and 1 mole of a galactosyl group receptor, Y wherein X and Y are both compounds other than water and are each a saccharide or aglycon. Hydrolysis: Forms 1 mole of X and 1 mole of galactose by hydrolyzing 1 mole of the β-D-galactopyranoside Gal-X. (2) Substrate specificity Hydrolyzes lactose and p-nitrophenyl-β-D-galactopyranoside but does not hydrolyze p-nitrophenyl-α-D-galactopyranoside. (3) Optimal pH 5.0-8.0 (4) pH Stability Stable at pH 5-8 (both inclusive) when treated at 55°C for 15 minutes. (5) Heat stability Retains at least 80% of its initial activity even after incubated at 60°C for 1 hour in 0.01 M phosphate buffer (pH 7.2) or at least 80% of its initial activity even after incubated at 65°C for 24 hours in the same buffer containing at least 1 M of lactose. 6. A process for the production of an oligosaccharide or a saccharide-modified glycoside represented by the following formula (I): Gal-(Gal)n-X (I) wherein Gal means a galactosyl group, X denotes a saccharide or glycoside and n stands for an integer of 0-4, which comprises using the novel β-galactosyltransferase according to claim 1.	***STATUS*** • LAPSED 2010-04-30 • NO OPPOSITION FILED ***METHODOLOGY*** *IN VITRO* PROTEIN GLYCOSYLATION USING A HEAT RESISTANT BETA-GALACTOSYL-TRANSFERASE, ITS PRODUCTION PROCESS AND ITS USE

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		US5861289A **EXPIRED**				
7A	**1992-03-09**	**US5858751** **08/446,875** **COMPOSITIONS AND METHODS FOR PRODUCING SIALYL-TRANSFERASES** ***FAMILY MEMBERS*** **AT228565T** **AU199337919A** **AU668714B** **BG62492B1, BG99100A** **CA2131703C, CA2167521C** **CZ199402204A3** **DE69332520T2** **DK632831T3** **EP632831B1** **EXPIRED 2012-03-09** **[see TAB 7C]** **ES2191011T3** **FI119692B, FI199404136A** **FI944136A0** **HU199402586D0** **HU219260B, HU69933T** **JP2007020587A** **JP7505771A, JP9501317A** **NO314666B1** **NZ251096A** **SK199401088A3** **US5962294** **GRANTED**	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** (Oakland, CA) **EXPIRED 2012-03-09** **Issue Date:** **1999-01-12** **Filing Date:** **1995-07-12** **Earliest Effective Filing Date:** **1992-03-09** **Priority Date:** **1992-03-09**	**Paulson; James C.** **(Del Mar, CA)** **Wen; Xiaohong** **(San Diego, CA)** **Livingston; Brian (San Diego, CA)** **Burlingame; Alma** **(Sausalito, CA)** **Medzihradszky; Katalin** **(San Francisco, CA)** **Kelm; Sorge** **(Uiel, DE)** **Gillespie; William** **(Santa Monica, CA)**	1. A sialyltransferase which consists of an amino terminal cytoplasmic domain, an amino transmembrane domain, a stem region domain and a catalytic domain, said sialyltransferase having the amino acid sequence as shown in SEQ. ID. NO. 8. 2. A sialyltransferase according to claim 1 wherein said amino terminal cytoplasmic domain is deleted. 3. A sialyltransferase according to claim 2 wherein said amino transmembrane domain is deleted. 4. A sialyltransferase according to claim 3 wherein said stem region domain is deleted. 5. A sialyltransferase which consists of an amino terminal cytoplasmic domain, an amino transmembrane domain, a stem region domain and a catalytic domain, said sialyltransferase having the amino acid sequence as shown in SEQ. ID. NO. 14. 6. A sialyltransferase according to claim 5 wherein said amino terminal cytoplasmic domain is deleted. 7. A sialyltransferase according to claim 6 wherein said amino transmembrane domain is deleted. 8. A sialyltransferase according to claim 7 wherein said stem region domain is deleted.	**"PAULSON III" FAMILY** ***STATUS*** • EXPIRED 2012-03-09 ***METHODOLOGY*** MAMMALIAN SIALYLTRANSFERASE(S) USEFUL IN THE ADDITION OF SIALIC ACIDS ON CARBOHYDRATE(S) Claims drawn to an enzyme with synthetic alpha 2, 3 - 0 sialyltransferase not alpha 2,6 sialyltransferase activity Specification: Objects of this invention have been accomplished by a method comprising: identifying and cloning genes which code for mammalian sialyltransferases (defined hereinafter) including, but not limited to porcine Ga1β1,3GalNAc α2,3 sialyltransferase and rat Ga1 β1,3(4)G1cNAc α2,3 sialyl-transferase (other than rat Gal β 1,4 Glc NAc α2,6 sialyltransferase); incorporating that gene into a recombinant DNA vector; transforming a suitable host with the vector including that gene; expressing the mammalian sialyltransferase genes in such a host; and

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		EXPIRES 2016-10-05 [see TAB 7B] **WO1993018157A1** **WO1995004816A**				recovering the mammalian sialyltransferase that is produced. . ..
7B	**1992-03-09**	**US5962294** **08/102,385** **COMPOSITIONS AND METHODS FOR PRODUCING SIALYL-TRANSFERASES** ***FAMILY MEMBERS*** **SEE ABOVE**	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** (Oakland, CA) **AMGEN** (Thousand Oaks, CA) **EXPIRES 2016-10-05** **Issue Date: 1999-10-05** **Filing Date: 1993-08-04*** **(*: pre-GATT filing)** **Earliest Effective Filing Date: 1992-03-09** **Priority Date: 1992-03-09**	**Paulson; James C. (Del Mar, CA)** **Wen; Xiaohong (San Diego, CA)** **Livingston; Brian (San Diego, CA)** **Burlingame; Alma (Sausalito, CA)** **Medzihradszky; Katalin (San Francisco, CA)** **Kelm; Sorge (Uiel, DE)** **Gillespie; William (Santa Monica, CA)**	1. A synthetic enzyme which exhibits sialyltransferase activity, said enzyme comprising a catalytic domain, said catalytic domain comprising a conserved region having amino acid SEQ. ID. NO: 28 and wherein the amino acid sequence of said conserved region is not SEQ. ID NO: 14, SEQ. ID NO:15 or SEQ. ID. NO: 16. 2. A synthetic enzyme according to claim 1 which further comprises a stem region. 3. A synthetic enzyme according to claim 2 which further comprises an amino terminal cytoplasmic domain. 4. A synthetic enzyme according to claim 3 which further comprises an amino terminal transmembrane domain.	***STATUS*** • GRANTED – EXPIRES 2016-10-05 • ALL MAINTENANCE FEES PAID ***METHODOLOGY*** MAMMALIAN SIALYLTRANSFERASE(S) USEFUL IN THE ADDITION OF SIALIC ACIDS ON CARBOHYDRATE(S) Claims drawn to an enzyme with synthetic alpha 2, 3 - 0 sialyltransferase not alpha 2,6 sialyltransferase activity

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
7C	**1992-03-09**	**EP632831B1** **COMPOSITIONS AND METHODS FOR THE IDENTIFICATION AND SYNTHESIS OF SIALYL-TRANSFERASES** ***FAMILY MEMBERS*** **SEE ABOVE**	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA** (Oakland, CA) **EXPIRED 2013-03-09** **Issue Date: 2002-11-27** **Filing Date: 1993-03-09** **Priority Date: 1992-03-09**	**Paulson; James C. (Del Mar, CA)** **Wen; Xiaohong (San Diego, CA)** **Livingston; Brian (San Diego, CA)** **Burlingame; Alma (Sausalito, CA)** **Medzihradszky; Katalin (San Francisco, CA)** **Kelm; Sorge (Uiel, DE)** **Gillespie; William (Santa Monica, CA)**	1. A DNA molecule encoding a recombinant polypeptide enzyme which exhibits sialyltransferase enzymatic activity, said polypeptide enzyme comprising a catalytic domain wherein said catalytic domain comprises a conserved region of homology comprising an amino acid sequence selected from the group consisting of: and variants thereof wherein said variants have at least 70% sequence idendity with said recombinant polypeptide enzyme. 2. The DNA molecule according to claim 1 encoding a sialyltransferase having the amino acid sequence set forth in Fig. 14. 3. The DNA molecule according to claim 1, wherein said recombinant polypeptide enzyme comprises a transmembrane domain. 4. The DNA molecule according to claim 3, wherein said recombinant polypeptide enzyme comprises a cytoplasmic domain. 5. The DNA molecule according to claim 1, wherein said recombinant polypeptide enzyme is essentially free of substances found in an in vivo physiological milieu, and comprises the amino acid sequences set forth in Fig. 14. 6. A recombinant expression vector comprising the DNA molecule according to any of claims 1 to 5. 7. A composition comprising a cell transformed with the recombinant expression vector according to claim 6.	***STATUS*** • EXPIRED 2013-03-09 • NO OPPOSITION FILED ***METHODOLOGY*** DNA ISOLATES ENCODING SIALYL TRANSFERASE PROVIDING EXPRESSION SYSTEMS FOR RECOMBINANT PRODUCTION OF ENZYME IN A MAMMALIAN CELL LINE Claims drawn to an enzyme with synthetic alpha 2, 3 - O sialyltransferase not alpha 2,6 sialyltransferase activity
8	**1992-11-27**	**US5641668 A** **08/446,777**	**CIBA GEIGY CORP** (Tarrytown, NY) **LAPSED 2001-06-24**	**Berger; Eric G. (Schofflisdorf, CH)**	1. A protein having glycosyltransferase activity comprising identical or different catalytically active domains of glycosyltransferases. 2. A protein according to claim 1 which is a hybrid protein.	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2001-06-24

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		PROTEINS HAVING GLYCOSYL-TRANSFERASE ACTIVITY ***FAMILY MEMBERS*** **AU199456242A** **AU682837B** **CA2148929A1** **EP788548A1** **WITHDRAWN 1999-06-01** **FI199502574A0** **FI199502574A** **FI952574A0** **JP8503373A** **MX9307465A** **NO199502039A** **NO199502039D0** **NZ258525A** **WO1994012646A1**	**Issue Date:** **1997-06-24** **Filing Date:** **1995-05-26*** **(*: pre-GATT filing)** **Earliest Effective Filing Date:** **1992-11-27 (EP)** **Priority Date:** **1993-11-15**	**Watzele; Manfred** **(Weilheim, DE)** **Iwanow; Svetoslav** **(Sofia, BG)**	3. A protein according to claim 2 comprising a membrane-bound or soluble glycosyltransferase linked to a soluble glycosyltransferase. 4. A protein according to claim 2 comprising a suitable linker consisting of genetically encoded amino acids. 5. A protein according to claim 2 selected from the group consisting of the protein having the amino acid sequence depicted in SEQ ID NO. 6 and the protein having the amino acid sequence depicted in SEQ ID NO. 8. 6. A method for preparing a protein according to claim 2 comprising culturing a suitable transformed yeast strain under conditions which allow the expression of said protein. 7. A DNA molecule coding for a protein according to claim 2. 8. A hybrid vector comprising a DNA molecule according to claim 7. 9. A transformed yeast strain comprising a hybrid vector according to claim 8.	***METHODOLOGY*** PROTEINS WITH GLYCOSYL-TRANSFERASE ACTIVITY USEFUL FOR SYNTHESIS OR MODIFICATION OF GLYCOPROTEINS, GLYCO-LIPID(S) AND OLIGOSACCHARIDES IN YEAST
9A	**1993-05-17**	**US5928915** **08/871,074** **CHO CELL SIALIDASE BY RECOMBINANT DNA TECHNOLOGY** ***FAMILY MEMBERS*** **AT175239T, AT474925T** **AU199468349A** **AU199878419A**	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRED 2013-05-17** **Issue Date:** **1999-07-27** **Filing Date:**	**Warner; Thomas G.** **(San Carlos, CA)** **Sliwkowski; Mary B.** **(San Carlos, CA)**	1. An isolated DNA comprising a nucleotide sequence that encodes the amino acid sequence of SEQ. ID NO. 26. 2. An expression vector comprising a nucleotide sequence that encodes the amino acid sequence of SEQ. ID NO. 26. 3. A host cell transformed with an isolated DNA that encodes the amino acid sequence of SEQ. ID NO. 26. 4. A process comprising transforming a host cell with an expression vector capable, in the host cell transformed with the vector, of expressing a polypeptide having the amino acid sequence of SEQ. ID NO. 26.	**"WARNER I" FAMILY** ***STATUS*** • EXPIRED 2013-05-17 ***METHODOLOGY*** PROTEINS WITH SIALIDASE ACTIVITY

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		AU200116688A AU771747B2 CA2160458A1 DE69415669T2 DE69435304D1 DK700443T3, DK866130T3 EP700443B1 EXPIRED 2014-05-17 [see TAB 9D] EP0866130 B1 EXPIRED 2014-05-17 [see TAB 9E] ES2128562T3, ES2346941T3 GR3029781T3, JP8510133A, NZ266714A, PT866130E US6562588 EXPIRED 2013-05-17 [see TAB 9B] US6916916B2 EXPIRED 2013-06-26 [see TAB 9C] WO1994026908A1	**1997-06-09 Earliest Effective Filing Date: 1993-05-17 Priority Date: 1993-05-17**		5. The process of claim 4 that further comprises the steps of culturing the transformed host cell, and recovering the polypeptide from the host cell culture.	
9B	**1993-05-17**	**US6562588 08/871,076 US20020076791 SIALIDASE AND RECOMBINANT CELL LINES *FAMILY MEMBERS* SEE ABOVE**	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRED 2013-05-17 Issue Date: 2003-05-13 Publication Date: 2002-06-20 Filing Date: 1997-06-09**	**Warner; Thomas G. (San Carlos, CA) Sliwkowski; Mary B. (San Carlos, CA)**	1. A process for the production of a glycoprotein, comprising expressing a nucleic acid encoding the glycoprotein in a Chinese Hamster Ovary cell line, wherein a constitutive sialidase gene of the Chinese Hamster Ovary cell line is not functionally expressed. 2. A recombinant Chinese Hamster Ovary cell line comprising: a nucleic acid sequence encoding a sialidase normally expressed constitutively in the recombinant Chinese Hamster Ovary cell line; wherein the nucleic acid sequence encoding the sialidase is not functionally expressed in the cell; and an exogenous nucleic acid sequence encoding a glycoprotein. 3. A recombinant eukaryotic cell line wherein a constitutive sialidase gene of the cell line is not functionally expressed and wherein the cell line is Chinese Hamster Ovary cell line.	**"WARNER I" FAMILY** ***STATUS*** • EXPIRED 2013-05-17 ***METHODOLOGY*** RECOMBINANT CHO CELL LINE DEFECTIVE FOR SIALIDASE EXPRESSION

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
			Earliest Effective Filing Date: 1993-05-17 **Priority Date: 1993-05-17**			
9C	**1993-05-17**	**US6916916 B2** **10/324,302** **US20030148493** **SIALIDASE AND RECOMBINANT CELL LINES** ***FAMILY MEMBERS*** **SEE ABOVE**	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRED 2013-06-26** **Issue Date: 2005-07-12** **PTA: 40 days** **Publication Date: 2003-08-07** **Filing Date: 2002-12-19** **Earliest Effective Filing Date: 1993-05-17**	**Warner; Thomas G. (San Carlos, CA)** **Sliwkowski; Mary B. (San Carlos, CA)**	1. A nucleic acid sequence encoding a sialidase, obtained by a process comprising: (a) preparing an oligonucleotide probe encoding a peptide having a sequence of SEQ. ID NO. 11; (b) hybridizing the probe with a nucleic acid in a Chinese Hamster Ovary cell line DNA library to form hybrids; (c) isolating hybrids, thereby obtaining the said nucleic acid sequence encoding a sialidase. 2. A nucleic acid sequence according to claim 1 wherein the sialidase is obtainable from a cell culture fluid of a Chinese Hamster cell line.	**"WARNER I" FAMILY** ***STATUS*** • EXPIRED 2013-06-26 ***METHODOLOGY*** NUCLEIC ACID ENCODING SIALIDASE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
			Priority Date: 1993-05-17			
9D	**1993-05-17**	**EP700443 B1** **SIALIDASE-DEFICIENT CELLS** ***FAMILY MEMBERS*** **SEE ABOVE**	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRED 2014-05-17** **Publication Date: 1998-12-30** **Filing Date: 1994-05-17** **Priority Date: 1993-05-17**	**Warner; Thomas G. (San Carlos, CA)** **Sliwkowski; Mary B. (San Carlos, CA)**	1. A cell wherein the function of a constitutive sialidase gene normally expressed in the cell is disrupted so that the sialidase is not functionally expressed. 2. The cell of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene by any of mutation, addition and deletion of a nucleotide. 3. The cell of claim 1 wherein the sialidase gene is not functionally expressed because of deletion of the gene. 4. The cell of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene by homologous recombination. 5. The cell of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene function by regulation of transcription using antisense RNA. 6. The cell of any of the preceding claims which is a Chinese hamster ovary derived cell line. 7. A process for the production of a glycoprotein, comprising expressing nucleic acid encoding a glycoprotein in a host cell wherein the function of a constitutive sialidase gene normally expressed in the cell is disrupted so that the sialidase is not functionally expressed. 8. The process according to claim 7 wherein the sialidase gene is not functionally expressed because of disruption of the gene by any of mutation, addition and deletion of a nucleotide. 9. The process according to claim 7 wherein the sialidase gene is not functionally expressed because of deletion of the gene.	**"WARNER I" FAMILY** ***STATUS*** • EXPIRED 2014-05-17 • NO OPPOSITION FILED ***METHODOLOGY*** RECOMBINANT CELL LINE DEFECTIVE FOR SIALIDASE EXPRESSION AND METHODS OF PRODUCING A GLYCOPROTEIN IN THE CELL LINE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					10. The process according to claim 7 wherein the sialidase gene is not functionally expressed because of disruption of the gene by homologous recombination. 11. The process according to claim 7 wherein the sialidase gene is not functionally expressed because of disruption of the gene function by regulation of transcription using antisense RNA. 12. The process according to any of claims 7 to 11 wherein the host cell is a Chinese hamster ovary derived cell line.	
9E	**1993-05-17**	**EP0866130 B1** **CHO CELL SIALIDASE BY RECOMBINANT DNA TECHNOLOGY** ***FAMILY MEMBERS*** **SEE ABOVE**	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRED 2014-05-17** **Publication Date: 2010-07-21** **Filing Date: 1994-05-17** **Priority Date: 1993-05-17**	**Warner; Thomas G. (San Carlos, CA)** **Sliwkowski; Mary B. (San Carlos, CA)**	1. An isolated nucleic acid sequence encoding a sialidase obtainable from cell culture fluid of a Chinese hamster cell line, which sequence is obtained by a process comprising: (a) preparing an oligonucleotide probe encoding the amino acid sequence CRVQAQSPNSGLDFQDN (SEQ. ID. NO. 13); (b) hybridizing the probe with nucleic acid in a mammalian DNA library to form hybrids; (c) isolating hybrids, thereby obtaining a said nucleic acid sequence encoding a sialidase. 6. A substantially homogeneous polypeptide which is a sialidase and has the amino acid sequence encoded by nucleic acid according to claim 1 or a variant thereof by way of insertion, deletion and/or substitution of one or more amino acids which variant is a sialidase and to which binds an antibody obtained using a peptide of amino acid sequence CRVQAQSPNSGLDFQDN (SEQ. ID. NO. 13). 7. Sialidase according to claim 6 having a molecular weight of about 43 kDa. 9. An oligonucleotide probe useful in obtaining a sialidase-encoding gene and having a sequence encoding the amino acid sequence CRVQAQSPNSGLDFQDN (SEQ. ID. NO. 13).	**"WARNER I" FAMILY** ***STATUS*** • EXPIRED 2014-05-17 • NO OPPOSITION FILED ***METHODOLOGY*** RECOMBINANT SIALIDASE NUCLEIC ACID AND PROTEIN

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
10	**1994-03-09**	**US6204431 B1** **08/925,834** **TRANSGENIC NON-HUMAN MAMMALS EXPRESSING HETEROLOGOUS GLYCOSYL-TRANSFERASE DNA SEQUENCES PRODUCE OLIGOSACCHARIDES AND GLYCOPROTEINS IN THEIR MILK** ***FAMILY MEMBERS*** **AR17515A1** **AU199516888A** **AU199516901A** **AU199517353A,** **AU199892203A** **AU692841B, AU694181B** **AU697523B, BG104236A** **BR199811733A** **CA2184686A1, CA2184687A1** **CA2184688A1, CA2302777A1** **CN1273602A, CO4930313A1** **EP1007651A1** **WITHDRAWN 2003-04-01** **EP749492A1** **WITHDRAWN 2003-03-05** **EP750671A1** **WITHDRAWN 2003-07-01** **EP750673A1** **WITHDRAWN 2003-03-19**	**ABBOTT LAB** (Abbott Park, IL) **LAPSED 2012-03-09** **PTA: 0 days** **Publication Date: 2001-03-20** **Filing Date: 1997-09-05** **Earliest Effective Filing Date: 1994-03-09** **Priority Date: 1994-03-09**	**Prieto; Pedro A. (West Worthington, OH)** **Kopchick; John J. (Athens, OH),** **Cummings; Richard (Edmond, OK),** **Pierce; James M. (Athens, GA),** **Smith; David F. (Athens, GA),** **Moremen; Kelley W. (Athens, GA)**	1. A non-human, transgenic mammal, wherein the genome of said mammal comprises at least one heterologous DNA sequence encoding an enzyme, wherein said enzyme is a glycosyltransferase operatively linked to a mammary gland-specific promoter, wherein expression of said at least one DNA sequence results in the production of oligosaccharides and glycoproteins in the milk of said mammal. 3. The non-human, transgenic mammal of claim 1, wherein said glycosyltransferase is selected from the group consisting of a fucosyltransferase, a galactosyltransferase, an acetylase, a glucoronyltransferase, a gluconylepimerase, a sialyltransferase, a mannosyltransferase, a sulfotransferase, a S-acetylgalactosaminyltransferase and a N-acetylglucosaminyltransferase. 4. The non-human, transgenic mammal of claims, wherein said oligosaccharides are selected from the group consisting of galactose .alpha.1-3galactose .beta.1-4 glucose, 2'fucosyllactose, 3'fucosyllactose, lacto-N-neo-tetraose, lacto-N-tetraose, lacto-N-fucopentaose, a sialylated derivative of lacto-N-fucopentaose, lacto-N-fucopentaose II, a sialylated derivative of lacto-N-fucopentaose II, lacto-N-fucopentaose III, a sialylated derivative of lacto-N-fucopentaose III, lacto-N-fucopentaose IV, a sialylated derivative of lacto-N-fucopentaose IV, lacto-N-fucopentaose V, a sialylated derivative of lacto-N-fucopentaose V, lacto-N-di-fucopentaose I, a sialylated derivative of lacto-N-di-fucopentaose, lacto-N-di-fucopentaose II, a sialylated derivative of lacto-N-di-fucopentaose II, lacto-N-hexaose, a fucosylated derivative of lacto-N-hexaose, sialyltetrasaccharide a, a fucosylated derivative of sialyltetrasaccharide a, sialyltetrasaccharide b, a fucosylated derivative of sialyltetrasaccharide b, sialyltetrasaccharide c and a fucosylated derivative of sialyltetrasaccharide c. 5. A method for producing a non-human, transgenic mammal whose somatic and germ cells contain at least one transgene, wherein expression of said at least one transgene results in the production of oligosaccharides and glycoproteins in the milk of said mammal, the method comprising the steps of: (a) preparing at least one transgene, said at least one transgene comprising in operable association 1) at least one expression regulatory sequence functional in mammary secretory cells, 2) a DNA sequence encoding a signal sequence functional in mammary secretory cells, and 3) a DNA sequence encoding an enzyme;	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2005-03-20 ***METHODOLOGY*** TRANSGENIC MAMMALS CONTAINING A TRANSGENE COMPRISING A PROMOTER FUNCTIONAL IN MAMMARY SECRETORY CELLS AND DNA ENCODING AN GLYCOSYL-TRANSFERASE FOR THE PRODUCTION OF GLYCOPROTEINS IN MILK

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		HU200004709A2, IL133992D0 JP2001520001A, JP9509847A, JP9509848A, JP9510094A KR2001023645A MX193700B, MX198456B MX199603890A, MX199603892A MX199603893A MX2000002266A MX2000PA002266A NO200001105A NO200001105D0 NZ279676A, NZ279686A NZ281041A, PL339132A1 SK200000304A3, SK200030420A3 TR200000500T2 **US5700671A EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2005-12-23** **US5750176A EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2006-05-12** **US5891698A EXPIRED DUE TO FAILURE TO PAY MAINTENANCE 2003-04-06** **US5892070A EXPIRED DUE TO FAILURE TO PAY MAINTENANCE 2003-04-06** **WO1995024488A1 WO1995024494A1 WO1995024495A1 WO1999011773A1** **ZA199807504A**			(b) introducing said at least one transgene into a non-human, mammalian embryo, and transferring the resulting embryo into a recipient female; (c) identifying at least one female offspring, where expression of said at least one transgene results in the production of at least one enzyme which then catalyzes the production of oligosaccharides and glycoproteins in the milk of said mammal, wherein said at least one enzyme is a glycosyltransferase. 9. A method of producing milk in a non-human, transgenic mammal, said method comprising the steps of: (a) preparing at least one transgene, said at least one transgene comprising is operable association 1) a promoter functional in mammary secretory cells, 2) a DNA sequence encoding an enzyme, wherein said enzyme is a glycosyltransferase and wherein expression of said at least one transgene results in production of oligosaccharides and glycoproteins in said milk of said mammal; (b) inserting said at least one transgene into said non-human, transgenic mammal; (c) milking said non-human, transgenic mammal in order to obtain said milk, wherein said milk comprises said oligosaccharides and glycoproteins. 13. A method for producing oligosaccharides and glycoproteins in the milk of a non-human transgenic mammal, the method comprising the steps of: (a) preparing at least one transgene, said at least one transgene comprising in operable association 1) at least one expression regulatory sequence functional in mammary secretory cells, 2) a DNA sequence encoding a signal sequence functional in mammary secretory cells, and 3) a DNA sequence encoding an enzyme, wherein said enzyme is a glycosyltransferase; (b) introducing said at least one transgene into a non-human, mammalian embryo, and transferring the resulting embryo into a recipient female; (c) identifying at least one female offspring, where expression of said at least one transgene results in the production of at least one enzyme which then catalyzes the production of said oligosaccharides and glycoproteins in the milk of said mammal, wherein said at least one enzyme is a glycosyltransferase; (d) milking said mammal; and (e)isolating said oligosaccharides and glycoproteins from said milk.	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
11A	**1994-12-30**	**US5834251** **08/366,800** **METHODS OF MODIFYING CARBOHYDRATE MOIETIES** ***FAMILY MEMBERS*** **AT321146T** **AU199643486A** **DE69635948D1** **DE69635948T2** **DE69635948T3** **DK799318T3** **DK799318T4** **EP1715057A3** **PENDING** **EP799318 B2** **EXPIRES 2016-01-02** **[see TAB 11B]** **ES2260768T3** **ES2260768T5** **PT799318E** **PT799318T** **WO1996021038A1**	**AB ENZYMES GMBH** (Darmstadt, Germany) **previously** **ALKO GROUP LTD** (Helsinki, FI) **EXPIRES 2015-11-10** **Publication Date:** **1998-11-10** **Filing Date:** **1994-12-30*** ***: pre-GATT filing** **Earliest Effective Filing Date:** **1994-12-30** **Priority Date:** **1994-12-30**	**Maras; Marleen (Gentbrugge, BE)** **Contreras; Roland (Merelbeke, BE)**	1. A process for producing a hybrid glycoprotein, said process comprising: (a) reacting a high mannose type glycoprotein that has been produced in filamentous fungi with GlcNAc Tr I in the presence of a UDP-GlcNAc sugar nucleotide; (b) reacting the glycoprotein product of step (a) with β-1,4 galactosyltransferase in the presence of a UDP-galactose sugar nucleotide; and (c) reacting the glycoprotein product of step (b) with a sialyltransferase in the presence of a CMP-sialic acid sugar nucleotide; wherein said filamentous fungus is a member of the group consisting of: Aspergillis and Trichoderma. 4. The process of claim 1, wherein said filamentous fungus is a Trichoderma. 6. The process of claim 1, wherein said filamentous fungus expresses recombinant GlcNAc Tr I and step (a) occurs intracellularly in said filamentous fungus. 7. The process of claim 1, wherein said filamentous fungus is Aspergillus niger. 8. The process of claim 1, wherein steps (a), (b) and (c) are performed in vitro. 9. The process of claim 8, wherein said glycoprotein is reacted with α-1,2 mannosidase between steps (a) and (b). 10. A process for producing a hybrid glycoprotein, said method comprising: (a) reacting a high mannose type glycoprotein expressed in yeast or a filamentous fungus with an α-1,2-mannosidase; (b) reacting the glycoprotein product of step (a) with GlcNAc Tr I in the presence of a UDP-GlcNAc sugar nucleotide; (c) reacting the glycoprotein product of step (b) with β-1,4 galactosyltransferase in the presence of a UDP-galactose sugar nucleotide; and (d) reacting the glycoprotein product of step (c) with a sialyltransferase in the presence of a CMP-sialic acid sugar nucleotide; wherein said yeast or said filamentous fungus is selected from the group consisting of: Aspergillus, Trichoderma, Pichia pastoris, Hansenula polymorpha, Kluyveromyces lactis, Saccharomyces cerevisiae and Yarrowia lipolytica.	***STATUS*** • GRANTED - EXPIRES 2015-11-10 • ALL MAINTENANCE FEES PAID ***METHODOLOGY*** Production of hybrid glycoprotein(s) using N-acetyl:glucosaminyl-transferase I, beta-1, 4-galactosyl transferase and a sialyl:transferase *in vitro* METHOD OF *IN VITRO* GLYCOSYLATION OF A HIGH MANNOSE TYPE GLYCOPROTEIN PRODUCED IN FILAMENTOUS FUNGI

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
11B	**1994-12-30**	**EP799318 B2** **METHODS OF MODIFYING CARBOHYDRATE MOIETIES** ***FAMILY MEMBERS*** **SEE ABOVE**	**AB ENZYMES GMBH** (Darmstadt, Germany) **EXPIRES 2016-01-02** **Publication Date: 2012-11-07** **Filing Date: 1996-01-02** **Priority Date: 1994-12-30**	**Maras; Marleen (Gentbrugge, BE)** **Contreras; Roland (Merelbeke, BE)**	1. A process for producing a hybrid glycoprotein, characterized in that said process comprises culturing a Trichoderma fungus so as to produce a high mannose type glycoprotein that is an acceptor substrate for GlcNAc Tr I, and reacting said high mannose type of glycoprotein with GlcNAc Tr I. 2. The process of claim 1, wherein said high mannose type glycoprotein is a protein that is homologous to said fungus. 3. The process of claim 1, wherein said high mannose type glycoprotein is a protein that is heterologous to said fungus. 5. The process of claim 1, wherein said high mannose type glycoprotein is reacted with GlcNAc Tr I intracellularly in said fungus. 6. The process of claim 1, wherein said high mannose type glycoprotein is reacted with α-1,2-mannosidase. 7. A process for producing a hybrid glycoprotein in a filamentous fungus, characterized in that said process comprises (a) reacting a high mannose type glycoprotein produced in a filamentous fungus with an α-1,2-mannosidase in vivo so as to produce a high mannose type glycoprotein that is an acceptor substrate for GlcNAc Tr I; and (b) reacting the glycoprotein of step (a) with GlcNAc Tr I. 8. The process of claim 7, wherein step (b) occurs intracellularly. 10. The process of claim 9, wherein said fungus is Trichoderma reesei or Aspergillus niger. 11. The process of claim 1 or claim 7, wherein said high mannose type glycoprotein is reacted with a UDP-GlcNAc. 12. The process of claim 1 or claim 7, further comprising reacting said hybrid glycoprotein with β-1,4-galactosyl transferase. 13. The process of claim 12, wherein said hybrid glycoprotein is reacted with a UDP-galactose. 14. The process of claim 13, further comprising reacting said hybrid glycoprotein with α-2,6-sialyltransferase.	***STATUS*** • GRANTED - EXPIRES 2016-01-02 • ALL MAINTENANCE FEES PAID OPPOSITION FILED 2006-12-18 Opponent: GLYCODE SAS 2006-12-20 Opponent: NOVOZYMES A/S 2006-12-22 Opponent: NOVARTIS AG 2006-12-18 Opponent: GLYCODE SAS 2006-12-20 Opponent: NOVOZYMES A/S 2012-11-07 MAINTAINED AS AMENDED ***METHODOLOGY*** METHOD OF *IN VIVO* GLYCOSYLATION OF A HIGH MANNOSE TYPE GLYCOPROTEIN IN FILAMENTOUS FUNGI Production of hybrid glycoprotein(s) using N-acetyl:glucosaminyl-transferase I, beta-1, 4-galactosyl transferase and a sialyl:transferase *in vitro*
12A	**1995-04-11**	**US5728554**	**NEOSE TECHNOLOGIES***	**DeFrees; Shawn (San Marcos, CA)**	1. A method for the formation of glycosidic linkages, comprising:	***STATUS***

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		08/419,669 **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** ***FAMILY MEMBERS*** **AT222294T** **AU199653873A** **AU199654453A** **CA2218120C** **CA2218246C** **DE69611442T2** **DE69623005T2** **DK820520T3** **EP820519 B1** **LAPSED in 2009** **[see TAB 12E]** **EP820520 B1** **LAPSED in 2009** **[see TAB 12F]** **ES2180757T3** **JP11503328A** **JP11503329A** **US5876980 A** **EXPIRED 2011-03-02** **[see TAB 12B]** **US5922577A** **EXPIRED 2007-07-13** **[see TAB 12C]** **US6030815A** **EXPIRED 2008-02-29** **[see TAB 12D]** **WO1996032491A1** **WO1996032492A1**	(Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **LAPSED 2010-03-17** **Publication Date: 1998-03-17** **Filing Date: 1995-04-11*** ***: pre-GATT filing** **Earliest Effective Filing Date: 1995-04-11** **Priority Date: 1995-04-11**	**Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	(a) providing a reaction medium comprising at least one glycosyl transferase, a donor substrate, an acceptor sugar and a divalent metal cation at a concentration of between about 2 mM and about 75 mM; and, after initiation of a glycosidic linkage-forming reaction, as a separate step (b) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 2 mM and about 75 mM, and wherein step (b) occurs without interruption of said glycosidic linkage-forming reaction. 2. A method in accordance with claim 1 wherein said divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++, Cu++ and combinations thereof. 5. A method in accordance with claim 1, wherein said glycosyl transferase is sialyl transferase. 6. A method in accordance with claim 1, wherein said glycosyl transferase is galactosyl transferase. 7. A method in accordance with claim 1, wherein said glycosyl transferase is a combination of sialyl transferase and galactosyl transferase. 8. A method in accordance with claim 1, wherein said glycosyl transferase is fucosyl transferase. 9. A method in accordance with claim 1, wherein said glycosyl transferase is N-acetyl glucosaminyl transferase. 22. A method for the preparation of NeuAc.alpha.(2 -->3)Gal.beta.(1.-->.4)(Fuc.alpha. 1.-->.3)GlcN(R').beta.(1.-->.3)Gal.beta.-OR, wherein R is selected from the group consisting of hydrogen, a saccharide, an oligosaccharide and an aglycon group having at least one carbon atom; and R' is selected from the group consisting of acetyl and allyloxycarbonyl; said method comprising: (a) galactosylating a compound of the formula GlcN(R').beta.(1.-->.3)Gal.beta.-OR with a galactosyltransferase in the presence of a UDP-galactose under conditions sufficient to form the compound: Gal.beta.(1.-->.4)GlcN(R').beta.(1.-->.3)Gal.beta.-OR; (b) sialylating said compound formed in (a) with a sialyltransferase in the presence of a CMP derivative of a sialic acid using a .alpha.(2,3)sialyltransferase under conditions wherein sialic acid	• EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2010-03-17 ***METHODOLOGY*** METHOD OF *IN VITRO* GLYCOSYLATION IN THE PRESENCE OF DIVALENT CATIONS Production of glycosylated cpds., e.g. antigen, diagnostic reagents by transfer of monosaccharide from donor substrate to acceptor in medium supplemented with divalent metal cation

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					is transferred to the non-reducing sugar to form the compound: NeuAc.alpha.(2.-->.3)Gal.beta.(1.-->.4)GlcN(R').beta.(1.-->.3)Gal .beta.-OR; and (c) fucosylating said compound formed in (b) to provide said NeuAc.alpha.(2.-->.3)Gal.beta.(1.-->.4)(Fuc.alpha. 1.-->.3)GlcN(R').beta.(1.-->.3)Gal.beta.-OR; wherein said galactosylating and sialylating steps are conducted in a reaction medium comprising of from about 2 mM to about 75 mM of a divalent metal cation and wherein said divalent metal cation is added to said medium during one or both of said galactosylating and sialylating steps to restore a portion of the divalent metal cation lost during the course of the reaction and thereby achieve or maintain the concentration of said divalent metal cation between about 2 mM and about 75 mM, and wherein the addition of divalent metal cation occurs without interruption of the galactosylating and sialylating steps.	
12B	**1995-04-11**	**US5876980 A** **08/419,659** **ENZYMATIC SYNTHESIS OF**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008)	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray**	1. A method for sialylating a galactose-containing acceptor, comprising: (a) providing a reaction medium comprising: (i) a sialyl transferase; (ii) a catalytic amount of a CMP-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor for said sialyltransferase having a galactosyl unit;	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2011-03-02

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		GLYCOSIDIC LINKAGES ***FAMILY MEMBERS*** **SEE ABOVE**	**LAPSED 2011-03-02** **Publication Date: 1999-03-02** **Filing Date: 1995-04-11*** ***: pre-GATT filing** **Earliest Effective Filing Date: 1995-04-11** **Priority Date: 1995-04-11**	**(Carlsbad, CA)**	(v) a CMP-sialic acid recycling system comprising at least 2 moles of phosphate donor per each mole of sialic acid, and catalytic amounts of a nucleoside triphosphate, cytidine monophosphate, a kinase capable of transferring phosphate from said phosphate donor to a nucleoside diphosphate, and a nucleoside monophosphate kinase capable of transferring the terminal phosphate from a nucleoside triphosphate to CMP; and (vi) a divalent metal cation at a concentration of between about 2 mM to about 75 mM; and as a separate step occurring after initiation of a reaction in said reaction medium; (b) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation of between about 2 mM and about 75 mM. 2. A method in accordance with claim 1 wherein said divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++ and combinations thereof. 3. A method in accordance with claim 1 wherein said sialyltransferase is α(2,3)sialyltransferase. 4. A method in accordance with claim 1 wherein said sialyltransferase is α(2,6)sialyltransferase. 5. A method in accordance with claim 1 wherein said sialyltransferase is α(2,3)sialyltransferase and said divalent metal cation is Mn++. 9. A method in accordance with claim 1, wherein said sialic acid is 5-N-acetylneuraminic acid, said acceptor is lactose, said nucleoside triphosphate is ATP, said phosphate donor is phosphoenolpyruvate, said kinase is pyruvate kinase, said nucleoside monophosphate kinase is myokinase, said divalent metal cation is Mn++ and said sialyltransferase is α(2,3)sialyltransferase. 11. A method in accordance with claim 1, wherein said reaction cycle is conducted in a buffered aqueous medium having a pH value of about 6 to about 8. 12. A method for the enzymatic formation of sialylα2→3βgalactoside, comprising: (a) combining the following components in a single vessel to form a reaction mixture: (i) a catalytic amount of an α(2,3)sialyltransferase; (ii) a catalytic amount of a CMP-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor for said α(2,3)sialyltransferase having a galactosyl unit; (v) a CMP-sialic acid recycling system comprising at least 2 moles of phosphate donor per each mole of sialic acid, and catalytic amounts of a nucleoside triphosphate, cytidine monophosphate, a kinase capable of transferring phosphate from said phosphate donor to a	***METHODOLOGY*** METHOD OF *IN VITRO* GALACTOSYLATION IN THE PRESENCE OF DIVALENT CATIONS Enzymatic preparation. of oligosaccharide, esp. sialyl lactose using sialyl transferase cycle supplemented with divalent metal ion co-factor to increase yield.

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					nucleoside diphosphate, and a nucleoside monophosphate kinase capable of transferring the terminal phosphate from a nucleoside triphosphate to CMP; and (vi) a reaction medium containing a divalent metal cation in an amount of from about 2 mM to about 75 mM and having a pH value of about 6 to about 8; and as separate steps occurring after initiation of a reaction in said medium (b) maintaining said reaction medium at a temperature of about 0° C. to about 45° C. and adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal ion of between about 2 mM and about 75 mM for a time period sufficient for said acceptor (iv) to be sialylated and form said sialylα2→3βgalactoside. 13. A method in accordance with claim 12, wherein said divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++ and combinations thereof. 19. A method in accordance with claim 12, wherein said sialic acid is 5-N-acetylneuraminic acid, said acceptor is lactose, said nucleoside triphosphate is ATP, said phosphate donor is phosphoenolpyruvate, said kinase is pyruvate kinase, said nucleoside monophosphate kinase is myokinase and said divalent metal cation is Mn++. 20. A method in accordance with claim 12, wherein said sialic acid is 5-N-acetylneuraminic acid, said acceptor is lactose, said nucleoside triphosphate is ATP, said phosphate donor is acetyl phosphate, said kinase is acetyl kinase, said nucleoside monophosphate kinase is myokinase and said divalent metal cation is Mn++.	
12C	**1995-04-11**	**US5922577A** http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO1&Sect2=HITOFF&d=PALL&p=1&u=%2Fnetahtml%2FPTO%2Fsrchnum.htm&r=1&f=G&l=50&s1=5876980.PN.&OS=PN/5876980	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **LAPSED 2007-07-13** **Publication Date: 1999-07-13** **Filing Date: 1996-04-10**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. A method for the transfer of a monosaccharide from a donor substrate to an acceptor substrate, the method comprising: (a) providing a reaction medium comprising at least one glycosyl transferase, a donor substrate, an acceptor sugar and a divalent metal cation at a concentration of between about 2 mM and about 75 mM; and, after initiation of a glycosidic linkage-forming reaction, as a separate step; (b) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (b) occurs without interruption of said glycosidic linkage-forming reaction.	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2007-07-13 ***METHODOLOGY*** METHOD OF *IN VITRO* GLYCOSYLATION IN THE PRESENCE OF DIVALENT CATIONS 'One-pot' enzymatic manufacture of oligosaccharides for use as antigens, diagnostic agents or therapeutics

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		&RS=PN/5876980**0** **8/628,545** **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** ***FAMILY MEMBERS*** **SEE ABOVE**	**Earliest Effective Filing Date: 1995-04-11** **Priority Date: 1995-04-11**		3. A method in accordance with claim 1, wherein said soluble divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++, Cu++ and combinations thereof. 6. A method in accordance with claim 1, wherein said glycosylransferase is galactosyl transferase. 7. A method in accordance with claim 1, wherein said glycosyltransferase is galactosyl transferase and said reaction medium further comprises sialyl transferase. 8. A method in accordance with claim 1, wherein said glycosyltransferase is fucosyl transferase. 9. A method in accordance with claim 1, wherein said glycosyltransferase is N-acetyl glucosaminyl transferase. 25. A method for the preparation of NeuAcα(2→3)Galβ(1→4)(Fucα 1→3)GlcN(R')β(1→3)Galβ–OR, wherein R is selected from the group consisting of hydrogen, a saccharide, an oligosaccharide and an aglycon group having at least one carbon atom; and R' is selected from the group consisting of acetyl and allyloxycarbonyl; said method comprising: (a) galactosylating a compound of the formula GlcN(R')β(1→3)Galβ–OR with a galactosyltransferase in the presence of a UDP-galactose under conditions sufficient to form the compound: Galβ(1→4)GlcN(R')β(1→3)Galβ–OR; (b) sialylating said compound formed in (a) with a sialyltransferase in the presence of a CMP derivative of a sialic acid using a α(2,3)sialyltransferase under conditions wherein sialic acid is transferred to the non-reducing sugar to form the compound: NeuAcα(2→3)Galβ(1→4)GlcN(R')β(1→3)Galβ–OR; and (c) fucosylating said compound formed in (b) to provide said NeuAcα(2→3)Galβ(1→4)(Fucα1→3)GlcN(R')β(1→3)Galβ–OR; wherein said galactosylating and sialylating steps are conducted in a reaction medium comprising of from about 1 mM to about 75 mM of a divalent metal cation and wherein said divalent metal cation is added to said medium during the course of said reaction and thereby achieve or maintain the concentration of said divalent metal cation between about 1 mM and about 75 mM, and wherein the addition of divalent metal cation occurs without interruption of the galactosylating and sialylating steps. 34. A method for the synthesis of CMP-NeuAc, the method comprising:	

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					(a) providing a reaction medium comprising CMP-NeuAc synthetase, sialic acid, CTP and a soluble divalent metal cation at a concentration of between about 2 mM and about 75 mM; and, after initiation of a glycosidic linkage-forming reaction, as a separate step; (b) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (b) occurs without interruption of said glycosidic linkage-forming reaction.	
12D	**1995-04-11**	**US6030815A** **08/628,543** **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** ***FAMILY MEMBERS*** **SEE ABOVE**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **LAPSED 2008-02-29** **Publication Date: 2000-02-29** **Filing Date: 1996-04-10** **Earliest Effective Filing Date: 1995-04-11** **Priority Date: 1995-04-11**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. A method for sialylating an acceptor sugar, comprising: (a) providing a reaction medium comprising: (i) a sialyl transferase; (ii) a catalytic amount of a CMP-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor sugar for said sialyltransferase; (v) CTP; and (vi) a soluble divalent metal cation; and (b) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (b) occurs without interruption of said sialylating reaction. 15. A method for the enzymatic formation of sialyl$\alpha 2 \rightarrow 3\beta$galactoside, comprising: (a) combining the following components in a single vessel to form a reaction mixture: (i) a catalytic amount of an $\alpha(2,3)$sialyltransferase; (ii) a catalytic amount of a CMP-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor for said $\alpha(2,3)$sialyltransferase having a galactosyl unit;	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2008-02-29 ***METHODOLOGY*** METHOD OF *IN VITRO* SIALYLATION IN THE PRESENCE OF DIVALENT CATIONS Sialylating an acceptor sugar using sialyl transferase cycle in which the reaction conditions are optimized, useful for producing sialyl galactosides which are useful in various diagnostic and therapeutic applications

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					(v) a CMP-sialic acid recycling system comprising at least 2 moles of phosphate donor per each mole of sialic acid, and catalytic amounts of a nucleoside triphosphate, cytidine monophosphate, a kinase capable of transferring phosphate from said phosphate donor to a nucleoside diphosphate, and a nucleoside monophosphate kinase capable of transferring the terminal phosphate from a nucleoside triphosphate to CMP; and (vi) a reaction medium containing a soluble divalent metal cation in an amount of from about 1 mM to about 75 mM and having a pH value of about 6 to 8; (b) maintaining said reaction mixture at a temperature of about 0° C. to about 45° C.; and (c) adding sufficient divalent metal cation to said reaction medium to restore a portion of said divalent cation lost during the course of the reaction to thereby achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (d) occurs without interruption of formation of said sialyl2α→3βgalactoside.	
12E	**1995-04-11**	**EP820519 B1** **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** ***FAMILY MEMBERS*** **SEE ABOVE**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **LAPSED in 2009** **Publication Date: 2001-01-03** **Filing Date: 1996-04-10** **Priority Date: 1995-04-11**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. A method for the transfer of a monosaccharide from a donor substrate to an acceptor substrate, comprising: (a) providing a reaction medium comprising at least one glycosyl transferase, a donor substrate, an acceptor substrate and a soluble divalent metal cation; and (b) supplementing the concentration of said soluble divalent metal cation to achieve a concentration in said reaction medium of between 1 mM and 75 mM for a period of time sufficient to substantially complete said synthesis. 3. A method in accordance with claim 1, wherein said soluble divalent metal cation is a member selected from the group consisting of Mn++, Mg++, ca++, Co++, Zn++, Cu++ and combinations thereof. 6. A method in accordance with claim 1, wherein said enzyme is galactosyl transferase. 7. A method in accordance with claim 1, wherein said enzyme is galactosyl transferase and said reaction medium further comprises sialyl transferase. 8. A method in accordance with claim 1, wherein said enzyme is fucosyl transferase. 9. A method in accordance with claim 1, wherein said enzyme is N-acetyl glucosaminyl transferase. 25. A method for the preparation of NeuAcα(2→3)Galβ(1→4)(Fucα 1→3)GlcN(R') β(1→3)Galβ-OR, wherein R is selected from the group consisting of hydrogen, a saccharide, an oligosaccharide and an aglycon group having at least one carbon atom; and R' is selected from the group consisting of acetyl and allyloxycarbonyl;	***STATUS*** • LAPSED BECAUSE OF NON-PAYMENT OF DUE FEES IN 2009 ***METHODOLOGY*** METHOD OF *IN VITRO* GLYCOSYLATION IN THE PRESENCE OF DIVALENT CATIONS Sialylating an acceptor sugar using sialyl transferase cycle in which the reaction conditions are optimized, useful for producing sialyl galactosides which are useful in various diagnostic and therapeutic applications

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					said method comprising: (a) galactosylating a compound of the formula GlcN(R')β(1→3)Galβ-OR with a galactosyltransferase in the presence of a UDP-galactose under conditions sufficient to form the compound: Galβ(1→4)GlcN(R')β(1→3)Galβ-OR; (b) sialylating said compound formed in (a) with a sialyltransferase in the presence of a CMP derivative of a sialic acid using a α(2,3) sialyltransferase under conditions wherein sialic acid is transferred to the non-reducing sugar to form the compound: NeuAcα(2→3) Galβ(1→4)GlcN(R')β(1→3)Galβ-OR; and (c) fucosylating said compound formed in (b) to provide said NeuAcα (2→3)Galβ(1→4)(Fucα 1→3)GlcN(R')β(1→3) Galβ-OR; wherein said galactosylating and sialylating steps are conducted in a reaction medium comprising a soluble divalent metal cation and said medium is supplemented with said soluble divalent metal cation to maintain the concentration of said divalent metal cation between 1 mM and 75 mM. 34. A method for the synthesis of CMP-NeuAc, comprising: (a) providing a reaction medium comprising CMP-NeuAc synthetase, sialic acid, CTP and a soluble divalent metal cation; and (b) supplementing the concentration of said soluble divalent metal cation to achieve a concentration in said reaction medium of between 1 mM and 75 mM for a period of time sufficient to complete said synthesis.	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
12F	**1995-04-11**	**EP820520 B1** **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** ***FAMILY MEMBERS*** **SEE ABOVE**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **LAPSED in 2009** **Publication Date: 2001-01-03** **Filing Date: 1996-04-10** **Priority Date: 1995-04-11**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. A method for sialylating an acceptor sugar, comprising: (a) providing a reaction medium comprising: (i) a sialyl transferase; (ii) a catalytic amount of a cytosine 5'-monophosphate-sialic acid sythetase; (iii) a sialic acid; (iv) an acceptor sugar for said sialyltransferase, wherein the sugar comprises a galactosyl residue; (v) cytosine 5'-triphosphate; and (vi) a soluble divalent metal cation; and (b) adding sufficient divalent metal cation to said reaction medium to achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (b) occurs during the formation of a glycosidic linkage. 6. A method in accordance with any one of the preceding claims wherein said soluble divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++ and combinations thereof. 7. A method in accordance with any one of the claims 1 to 5, wherein said sialyltransferase is α(2,3) sialyltransferase. 8. A method in accordance with claim 1 wherein said sialyltransferase is α(2,6)sialyltransferase. 9. A method in accordance with claim 1 wherein said sialyltransferase is α(2,3)sialyltransferase and said soluble divalent metal cation is Mn++. 10. A method in accordance with any one of the preceding claims wherein said sialic acid is 5-N-acetylneuraminic acid. 11. A method in accordance with claim 1 wherein said acceptor is lactose. 12. A method in accordance with claim 1 wherein said sialic acid is 5-N-acetylneuraminic acid and said acceptor is lactose. 15. A method in accordance with claim 1 wherein said reaction medium further comprises a buffer to maintain said reaction medium at a pH value of about 6 to about 8. 17. A method for the enzymatic formation of sialyl α2→3β galactodise, comprising: (a) combining the following components in a single vessel to form a reaction mixture:	***STATUS*** • LAPSED BECAUSE OF NON-PAYMENT OF DUE FEES IN 2009 ***METHODOLOGY*** METHOD OF *IN VITRO* SIALYLATION IN THE PRESENCE OF DIVALENT CATIONS Enzymatic preparation. of oligosaccharide, esp. sialyl lactose using sialyl transferase cycle supplemented with divalent metal ion co-factor to increase yield.

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					(i) a catalytic amount of an α(2,3) sialyltransferase; (ii) a catalytic amount of a cytosine 5'-monophosphate-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor for said α(2,3) sialyltransferase having a galactosyl unit; (v) a cytosine 5'-monophosphate-sialic acid recycling system comprising at least 2 moles of phosphate donor per each mole of sialic acid, and catalytic amounts of a nucleoside triphosphate, cytidine monophosphate, a kinase capable of transferring phosphate from said phosphate donor to a nucleoside diphosphate, and a nucleoside monophosphate kinase capable of transferring the terminal phosphate from a nucleoside trihosphate from a nucleoside triphosphate to cytosine 5'-monophosphate; and (vi) a reaction medium containing a soluble divalent metal cation in an amount of from about 1 mM to about 75 mM and having a pH value of about 6 to about 8; (b) maintaining said reaction mixture at a temperature of about 0°C to about 45°C; and (c) adding sufficient divalent metal cation to said reaction medium to achieve or maintain a concentration of said divalent metal cation in said reaction medium between bout 1 mM and about 75 mM, and wherein step (c) occurs during the formation of said sialyl α 2→3β galactoside.	
13A	**1995-05-12**	**US5962275** **08/952,197**	**HOECHST AKTIEN-GESELLSCHAFT** (Frankfurt, DE)	**DeFrees; Shawn (San Marcos, CA)**	1. A method for sialylating an acceptor sugar, comprising: (a) providing a reaction medium comprising: (i) a sialyl transferase;	***STATUS***

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		METHOD FOR THE ENZYMATIC GALACTOSYLATION OF MONOSACCHARIDES AND OLIGOSACCHARIDES ***FAMILY MEMBERS*** **AT206166T** **CA2220675A1** **DE19516952A1** **DE59607786D1** **DK827549T3** **EP827549 B1** **LAPSED in 2004-2005 [see TAB 13B]** **ES2164885T3** **JP11504817A** **MX199708737A** **PT827549E** **WO1996035801A1**	**LAPSED 2007-10-05** **Publication Date: 1999-10-05** **Filing Date: 1998-02-13** **Earliest Effective Filing Date: 1995-05-12 (DE)** **Priority Date: 1996-05-02**	**Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	(ii) a catalytic amount of a cytosine 5'-monophosphate-sialic acid sythetase; (iii) a sialic acid; (iv) an acceptor sugar for said sialyltransferase, wherein the sugar comprises a galactosyl residue; (v) cytosine 5'-triphosphate; and (vi) a soluble divalent metal cation; and (b) adding sufficient divalent metal cation to said reaction medium to achieve or maintain a concentration of said divalent metal cation in said reaction medium between about 1 mM and about 75 mM, and wherein step (b) occurs during the formation of a glycosidic linkage. 6. A method in accordance with any one of the preceding claims wherein said soluble divalent metal cation is a member selected from the group consisting of Mn++, Mg++, Ca++, Co++, Zn++ and combinations thereof. 7. A method in accordance with any one of the claims 1 to 5, wherein said sialyltransferase is α(2,3) sialyltransferase. 8. A method in accordance with claim 1 wherein said sialyltransferase is α(2,6)sialyltransferase. 9. A method in accordance with claim 1 wherein said sialyltransferase is α(2,3)sialyltransferase and said soluble divalent metal cation is Mn++. 10. A method in accordance with any one of the preceding claims wherein said sialic acid is 5-N-acetylneuraminic acid. 11. A method in accordance with claim 1 wherein said acceptor is lactose. 12. A method in accordance with claim 1 wherein said sialic acid is 5-N-acetylneuraminic acid and said acceptor is lactose. 15. A method in accordance with claim 1 wherein said reaction medium further comprises a buffer to maintain said reaction medium at a pH value of about 6 to about 8. 17. A method for the enzymatic formation of sialyl α2→3β galactodise, comprising: (a) combining the following components in a single vessel to form a reaction mixture: (i) a catalytic amount of an α(2,3) sialyltransferase; (ii) a catalytic amount of a cytosine 5'-monophosphate-sialic acid synthetase; (iii) a sialic acid; (iv) an acceptor for said α(2,3) sialyltransferase having a galactosyl unit; (v) a cytosine 5'-monophosphate-sialic acid recycling system comprising at least 2 moles of phosphate donor per each mole of sialic acid, and catalytic amounts of a nucleoside triphosphate, cytidine monophosphate, a kinase capable of transferring phosphate from said phosphate donor	• EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2007-10-05 ***METHODOLOGY*** METHOD OF *IN VITRO* SIALYLATION IN THE PRESENCE OF DIVALENT CATIONS Enzymatic preparation. of oligosaccharide, esp. sialyl lactose using sialyl transferase cycle supplemented with divalent metal ion co-factor to increase yield.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					to a nucleoside diphosphate, and a nucleoside monophosphate kinase capable of transferring the terminal phosphate from a nucleoside trihosphate from a nucleoside triphosphate to cytosine 5'-monophosphate; and (vi) a reaction medium containing a soluble divalent metal cation in an amount of from about 1 mM to about 75 mM and having a pH value of about 6 to about 8; (b) maintaining said reaction mixture at a temperature of about 0°C to about 45°C; and (c) adding sufficient divalent metal cation to said reaction medium to achieve or maintain a concentration of said divalent metal cation in said reaction medium between bout 1 mM and about 75 mM, and wherein step (c) occurs during the formation of said sialyl α 2→3β galactoside.	
13B	**1995-05-12**	**EP827549 B1** **METHOD FOR THE ENZYMATIC GALACTOSYLATION OF MONOSACCHARIDES AND OLIGOSACCHARIDES** ***FAMILY MEMBERS***	**HOECHST AKTIEN-GESELLSCHAFT** (Frankfurt, DE) **LAPSED in 2004-2005** **Publication Date: 2001-09-26** **Filing Date: 1996-05-02** **Earliest Effective**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. A process for enzymically galactosylating monosaccharides and oligosaccharides, with in-situ regeneration of the nucleotide sugar, in the presence of sucrose synthase, β-1-4-galactosyl transferase and uridine diphosphate-glucose 4'-epimerase, wherein a ketosugar or a ketosugar derivative is added to the reaction mixture as an activator of the uridine diphosphate-glucose 4'-epimerase. 2. The process as claimed in claim 1, wherein a deoxynucleoside diphosphate ketosugar is employed as the activator. 3. The process as claimed in claim 2, wherein deoxyuridine diphosphate-6-deoxy-D-xylohexulose is employed as the activator. 4. The process as claimed in claim 2, wherein deoxythymidine diphosphate-6-deoxy-D-xylohexulose is employed as the activator. 5. The process as claimed in claim 1, wherein a ketosugar is employed as the activator.	***STATUS*** • LAPSED DUE TO FAILURE TO PAY MAINTENANCE FEE 2004-2005 ***METHODOLOGY*** METHOD OF IN VITRO GALACTOSYLATION Enzymatic galactosylation of sugars with in situ regeneration of nucleotide sugar in presence of keto-sugar or deriv. to regenerate epimerase

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		SEE ABOVE	**Filing Date: 1995-05-12 (DE)** **Priority Date: 1996-05-02**		6. The process as claimed in claim 5, wherein 6-deoxyglucosone is employed as the activator. 7. The process as claimed in claim 5, wherein galactosone is employed as the activator. 8. The process as claimed in claim 5, wherein allosone is employed as the activator. 9. The process as claimed in claim 5, wherein glucosone is employed as the activator.	enzyme giving prods. used for synthesis of, e.g. sialylated sugars
14	**1995-05-18**	**EP826054 B1** **EXPRESSION OF GLYCOSYL-TRANSFERASE IN ASPERGILLUS** ***FAMILY MEMBERS*** **AT256747T** **CA2221271A1** **DE69631127D1** **DE69631127T2** **DK826054T3** **US20050164351A1** **ABANDONED** **2009-08-04**	**GENENCOR INT** (Palo Alto, CA) **EXPIRES 2016-05-16** **Publication Date: 2003-12-17** **Filing Date: 1996-05-16** **Priority Date: 1995-05-18**	**KADOMA Katherine (Palo Alto, CA)** **WARD Michael (Palo Alto, CA)**	1. A fusion DNA sequence encoding a fusion polypeptide comprising from the 5' end of said fusion DNA sequence: a) DNA encoding a signal peptide functional in Aspergillus; b) DNA encoding a secreted polypeptide or portion thereof normally secreted from Aspergillus; c) DNA encoding a cleavable linker polypeptide; d) DNA encoding a desired glycosyltransferase from which the transmembrane anchor coding sequence has been deleted wherein c) is optional. 2. A fusion DNA sequence of Claim 1 wherein the desired glycosyltransferase is selected from the group consisting of sialyltransferase, galactosyltransferase and fucosyltransferase. 9. An expression vector for transforming an Aspergillus host cell comprising DNA sequences encoding regulatory sequences functionally recognized by the Aspergillus host, including promoter and transcription and translation initiation sequences operably linked to the 5' end of the fusion DNA sequence of Claim 1 and transcription stop sequences and polyadenylation sequences operably linked to the 3' end of said fusion DNA sequence.	***STATUS*** • GRANTED - EXPIRES 2016-05-16 • NO OPPOSITION FILED 2004-09-20 • ALL MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** METHOD OF PRODUCING GLUCOSYL-TRANSFERASE IN ASPERGILLUS Recombinant glucosyltransferase enzyme production expressed as a fusion protein with an Aspergillus secreted polypeptide in Aspergillus, useful in the synthesis of complex carbohydrate(s)

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		WO1996036718A1			10. An Aspergillus containing an expression vector of Claim 9. 11. A fusion polypeptide comprising from the 5' end: a) an amino acid sequence which is a signal peptide functional in Aspergillus; b) an amino acid sequence which is a secreted polypeptide or portion thereof normally secreted from Aspergillus; c) an amino acid sequence which is a cleavable linker; d) an amino acid sequence which is a desired glycosyltransferase from which the transmembrane anchor region has been deleted wherein c) is optional. 18. A fusion polypeptide of Claim 11 wherein the signal peptide comprises the signal peptide of A. niger var. awamori glucoamylase, the secreted polypeptide or portion thereof comprises glucoamylase from A. niger var. awamori, and the desired glycosyltransferase is selected from the group consisting of sialyltransferase, galactosyltransferase and fucosyltransferase.	
14	**1995-06-06**	**US5705364** **08/469,348** **MAMMALIAN CELL CULTURE PROCESS** ***FAMILY MEMBERS*** AR11439A2 AR4940A1 AT302266T AT425245T AU199660952A AU717847B2 BG102101A BG63213B1 BR199609150A CA2220684C CN1166772C CN1186514A CZ199703909A3 CZ293719B6 DE69635076T3 DE69637867D1 DK1609853T3 DK832189T3	**GENENTECH/ ROCHE** (South San Francisco, CA) **EXPIRES 2015-06-06** **Publication Date: 1996-12-12** **Filing Date: 1996-06-06** **Earliest Effective Filing Date: 1995-06-06** **Priority Date: 1995-06-06**	**Etcheverry; Tina (Berkeley, CA)** **Ryll; Thomas (San Mateo, CA)**	1. **A process for controlling the amount of sialic acid present on an oligosaccharide side chain of a glycoprotein produced by culture in a mammalian host cell** which comprises: culturing the mammalian host cell in a production phase of the culture which is characterized by: i**) adding an alkanoic acid or a salt thereof to the culture** at a concentration of about 0.1 mM to about 20 mM; ii) maintaining the osmolality of the culture at about 250 to about 600 mOsm; and iii) maintaining the temperature of the culture at a temperature about between 30° C. and 35° C. 4. The process according to claim 1 **wherein the amount of sialic acid present on the oligosaccharide side chain of the glycoprotein is increased** and wherein; cell specific productivity of the cell culture is decreased by culturing the host cell at a concentration of the alkanoic acid or salt thereof of about 1 to about 6 mM and maintaining the osmolality at about 300-450 mOsm. 5. The process of claim 4 wherein the production phase is a batch or fed batch culture phase. 6. The process of claim 5 where the production phase is preceded by a transition phase during which the temperature is lowered to about between 30° C. and 35° C. before the production phase begins. 7. The process of claim 6 in which the host cell is a **CHO cell**.	***STATUS*** • EXPIRES 2015-06-06 • 4TH, 8TH AND 12TH YEAR MAINTENANCE FEES PAID ***METHODOLOGY*** CLAIMS DRAWN TO TO A METHOD OF CONTROLLING THE AMOUNT OF SIALIC ACID PRESENT ON AN OLIGOSACCHARIDE SIDE CHAIN OF A MAMMALIAN GLYCOPROTEIN EXPRESSED IN A CHO CELL BY ADDING SODIUM BUTYRATE TO THE CULTURE MEDIA.

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		DK832189T4 EA1215B1 EP1609853B1 EP832189B2 ES2248812T3 ES2248812T5 ES2324046T3 GEP20012519B HK1017903A1 HK1087151A1 HU199900920A2 HU199900920A3 HU226420B1 IL122398A IL122398D0 IS2614B IS4626A JP04348376B2 JP11507523A JP2007190024A MX199709452A NO199705674A NO199705674D0 NO322276B1 NZ310202A OA10753A PL185484B1 PL323737A1 PT1609853E RO120267B1 SI1609853T1 SI832189T1 SI832189T2 SK199701670A3 SK282658B6 TR199701543T1 TW426734B TW516962B WO1996039488A1 ZA199604776A			8. The process of claim 7 in which the host cell is a **dhfr- CHO cell**. 9. The process according to claim 8 wherein the alkanoic acid or salt thereof is **sodium butyrate**. 10. The process according to claim 9 wherein the glycoprotein produced is a **mammalian glycoprotein**. 11. The process according to claim 10 wherein the glycoprotein is a **tumor necrosis factor receptor-immunoglobulin chimera**. 12. The process of claim 11 in which the host cell is a cell transfected with a vector carrying the cDNA for a **soluble type 1 tumor necrosis factor receptor-immunoglobin G1 TNFR1-IgG1 chimera**.	

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15	**1996-03-27**	**US5856159 A** **08/622,753** **PRODUCTION OF GALACTOSYL-TRANSFERASE** ***FAMILY MEMBERS*** **WO1997035959A1**	**CYTEL CORP*** (San Diego, CA) (*acquired by Neose Technologies in 1999) **EXPIRED 2007-01-05** **Publication Date: 1999-01-05** **Filing Date: 1996-03-27** **Earliest Effective Filing Date: 1996-03-27** **Priority Date: 1996-03-27**	**Perez; Carl (San Diego, CA)**	1. A method for producing galactosyltransferase, comprising the steps of: (a) culturing a gene expression system comprising the NSO cell having the accession number ATCC No. CRL 12066 which is recombinantly modified with a polynucleotide encoding the galactosyltransferase or an enzymatically active portion thereof which catalyzes the reaction: UDP-D-galactose+N-acetylglucosamine→UDP+D-galactosyl-N-acetyl-D-glucosamine; and (b) harvesting the galactosyltransferase. 2. A recombinantly modified NSO cell having the accession no. ATCC No. CRL 12066.	***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2007-01-05 ***METHODOLOGY*** METHOD OF PRODUCING GALACTOSYL-TRANSFERASE IN NSO CELLS Recombinant production of galactosyltransferase in NSO cells useful in biosynthesis of glycoprotein and glycolipid sugar chains

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16	**1996-08-16**	**US6461863 B1** **09/242,435** **MODIFYING INSECT CELL GYLCOSYLATION PATHWAYS WITH BACULOVIRUS EXPRESSION VECTORS** ***FAMILY MEMBERS*** **WO1997035959A1**	**UNIV WYOMING** (Laramie, WY) **EXPIRES 2017-08-15** **Publication Date: 2002-10-08** **PTA: 0 days** **Filing Date: 1999-11-29** **Earliest Effective Filing Date: 1996-08-16** **Priority Date: 1997-08-15**	**Jarvis; Donald L. (Laramie, WY)**	1. A baculovirus expression vector comprising at least a first glycosylation enzyme transcriptional unit and a second glycosylation enzyme transcriptional unit, the first glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a galactosyltransferase under the control of a first baculovirus early promoter, and the second glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a sialyltransferase operatively positioned under the control of a second baculovirus early promoter. 2. The vector of claim 1, further comprising a third glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a third oligosaccharide processing enzyme operatively positioned under the control of a promoter. 9. The vector of claim 2, wherein said third oligosaccharide processing enzyme is an α-glucosidase, an α-mannosidase, an N-acetylglucosaminyltransferase, or a fucosyltransferase. 28. The vector of claim 1, further comprising at least one heterologous nucleic acid encoding a selected protein, said nucleic acid operatively positioned under the control of a promoter. 42. A population of baculovirus expression vehicles comprising a baculovirus expression vector characterized as comprising at least a first glycosylation enzyme transcriptional unit and a second glycosylation enzyme transcriptional unit, the first glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a galactosyltransferase under the control of a first baculovirus early promoter, and the second glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a sialyltransferase operatively positioned under the control of a second baculovirus early promoter. 43. An insect cell comprising a baculovirus expression vector characterized as comprising at least a first glycosylation enzyme transcriptional unit and a second glycosylation enzyme transcriptional unit, the first glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a galactosyltransferase under the control of a first baculovirus early promoter, and the second glycosylation enzyme transcriptional unit comprising a nucleic acid encoding a sialyltransferase operatively positioned under the control of a second baculovirus early promoter.	***STATUS*** • GRANTED - EXPIRES 2017-08-15 • ALL MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** MODIFICATION OF PROTEIN GLYCOSYLATION IN INSECT CELLS USING BACULOVIRUS EXPRESSION VECTORS Baculovirus expression vector comprising oligosaccharide processing enzyme (e.g. galactosyltransferase, sialyltransferase useful to modify insect cell glycosylation pathways, in e.g. insecticidal preparations

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17A	**1997-01-16**	**US6399336 B1** **09/007,741** **PRACTICAL IN VITRO SIALYLATION OF RECOMBINANT GLYCOPROTEINS** ***FAMILY MEMBERS*** **AT263841T** **AU199862427A** **AU736993B2** **CA2278178A1** **CA2278178C** **DE69823046D1** **DE69823046T2** **DK1015622T3** **EP1015622 B1** **LAPSED** **[see TAB 17B]** **EP1445326A2** **PENDING** **ES2218806T3** **IL130964A** **IL130964D0** **JP2001507215A** **JP2011024597A** **NZ336780A** **US20020119516A1** **ABANDONED 2006-02-10** **US20020160460A1** **ABANDONED 2006-03-14** **US20030124645A1** **ABANDONED 2006-10-27**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **EXPIRES 2018-01-15** **Publication Date:** **2002-10-08** **PTE: 0 days** **Issue Date:** **2002-06-04** **Filing Date:** **1998-01-15** **Earliest Effective Filing Date:** **1997-01-16** **Priority Date:** **1998-01-15**	**Paulson; James C.** **(Del Mar, CA)** **Bayer; Robert J.** **(San Diego, CA)** **Sjoberg; Eric** **(San Diego, CA)**	1. A large-scale method of sialylating a saccharide group on a recombinant glycoprotein, the method comprising contacting a saccharide group which comprises a galactose or N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety and a recombinant sialyltransferase in a reaction mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group wherein at least about 80% of the saccharide groups are sialylated, and wherein said recombinant sialyltransferase is present at 50 mU or less per mg of said recombinant glycoprotein. 5. The method of claim 1, wherein the sialyltransferase includes a sialyl motif which has an amino acid sequence that is at least about 40% identical to a sialyl motif from a sialyltransferase selected from the group consisting of ST3Gal I, ST6Gal I, and ST3Gal III. 21. The method of claim 1, wherein the sialyltransferase is produced by recombinant expression of a sialyltransferase in a host cell selected from the group consisting of an insect cell, a mammalian cell, and a fungal cell. 23. A large-scale method of sialylating a saccharide group on a recombinant glycoprotein, the method comprising contacting a saccharide group which comprises a galactose or an N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety and a bacterial sialyltransferase in a reaction mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group and wherein at least about 80% of the saccharide groups are sialylated, wherein said bacterial sialyltransferase is present at 50 mU or less per mg of said recombinant glycoprotein. 32. A large-scale method for in vitro sialylation of saccharide group s present on a glycoprotein, said method comprising contacting said saccharide groups with a sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group, wherein said sialyltransferase is present at a concentration about 50 mU per mg of glycoprotein or less, and wherein at least about 80% of the saccharide groups are sialylated. 36. The method of claim 32, wherein the sialyltransferase is a recombinant sialyltransferase. 57. A large-scale method for in vitro sialylation of terminal galactose residues present on a glycoprotein, said method comprising contacting said glycoprotein with a reaction mixture that	**"PAULSON IV" FAMILY** ***STATUS*** • GRANTED - EXPIRES 2018-01-15 • ALL MAINTENANCE FEES PAID ***METHODOLOGY*** *IN VITRO SIALYLATION* Large scale sialylation of recombinant glycoprotein by reaction with sialic acid donor in presence of recombinant or bacterial sialyltransferase at low concentration, used e.g. to optimise or adjust sialylation in proteins from transformed cells or transgenic animals

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		US7220555 B2 **(US20020142370A1)** **EXPIRES 2018-04-19** **[see TAB 17C]** **WO1998031826A1**			comprises a sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity, for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said terminal galactose residues, wherein at least about 80% of the terminal galactose residues present on the glycoprotein are sialylated, and wherein said sialyltransferase is present at a concentration about 50 mU per mg of glycoprotein or less. 59. A large-scale method for in vitro sialylation of terminal galactose residues present on a glycoprotein, said method comprising contacting said glycoprotein with a reaction mixture that comprises a sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity, for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said terminal galactose residues, wherein a greater percentage of terminal galactose residues are sialylated compared to an unaltered glycoprotein, wherein said greater percentage is equal to at least about 80%, and wherein said sialyltransferase is present at a concentration about 50 mU per mg of glycoprotein or less. 60. The method of claim 59, wherein at least 90% of the terminal galactose residues present on the glycoprotein are sialylated. 61. The method of claim 59, wherein the terminal galactose residues comprise one or more saccharides selected from the group consisting of Galβ1,4GlcNAc, Galβ1,4GalNAc, Galβ1, 3GalNAc, Galβ1, 3GlcNAc, Galβ1,3Ara, Galβ1,6GlcNAc, and Galβ1,4Glc. 62. The method of claim 61, wherein the terminal galactose residues comprise Galβ1,4GlcNAc or Galβ1,3GlcNAc. 63. The method of claim 62, wherein at least 80% of the terminal Galβ1,4GlcNAc residues present on the glycoprotein are sialylated. 64. The method of claim 62, wherein at least 80% of the terminal Galβ1,3 GlcNAc residues present on the glycoprotein are sialylated. 66. The method of claim 59, wherein the terminal galactose residues are present on an N-linked oligosaccharide.	
17B	**1997-01-16**	**EP1015622 B1** **PRACTICAL IN VITRO SIALYLATION OF RECOMBINANT GLYCOPROTEINS**	**NEOSE TECHNOLOGIES** (Horsham, PA) **LAPSED IN 2008** **Publication Date: 2004-04-07**	**Paulson; James C. (Del Mar, CA)** **Bayer; Robert J. (San Diego, CA)** **Sjoberg; Eric (San Diego, CA)**	1. The use of a sialyltransferase enzyme to achieve at least about 80% sialylation of the saccharide groups of a target glycoprotein in a large-scale in vitro sialylation method, said sialyltransferase enzyme being used at a concentration of 50 mU/mg glycoprotein or less, together with a sialic acid donor moiety. 2. A use as claimed in claim 1, wherein the sialyltransferase is used (a) at a concentration of between about 5-25 mU per mg of glycoprotein, or	**"PAULSON IV" FAMILY** ***STATUS*** • NO OPPOSITION FILED 2005-01-10

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		FAMILY MEMBERS **SEE ABOVE**	**Filing Date: 1998-01-15** **Earliest Effective Filing Date: 1997-01-16** **Priority Date: 1998-01-15**		(b) at a concentration of between about 10-50 mU/ml of reaction mixture and the glycoprotein is present in the reaction mixture at a concentration of at least about 2 mg/ml. 5. A use as claimed in claim 1, wherein the glycoprotein is a recombinant glycoprotein, the sialylation method comprising contacting a saccharide group which comprises a galactose or N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety and (a) a recombinant sialyltransferase, or (b) a bacteria! sialyltransferase, preferably a recombinant bacterial sialyltransferase, in a reaction mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group. 13. A use for in vitro sialylation of saccharide groups present on a glycoprotein, the method comprising contacting the saccharide groups with an ST3Gal III sialyltransferase, a sialic acid donor moiety, and other reactants required for sialyltransferase activity for a sufficient time and under conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group, wherein said ST3Gal III sialyltransferase is present at a concentration of less than about 50 mU per mg of glycoprotein, wherein the method further comprises contacting the saccharide groups with an ST6Gal I sialyltransferase. 14. A use as claimed in any of claims 1 to 12, or a method as claimed in claim 13, wherein the glycoprotein comprises a moiety derived from an immunoglobulin. 15. The use as claimed in claim 14, wherein the immunoglobulin is an IgG.	• LAPSED BECAUSE OF NON-PAYMENT OF DUE FEES in 2008 ***METHODOLOGY*** *IN VITRO SIALYLATION* Large scale sialylation of recombinant glycoprotein by reaction with sialic acid donor in presence of recombinant or bacterial sialyltransferase at low concentration, used e.g. to optimise or adjust sialylation in proteins from transformed cells or transgenic animals
17C	**1997-01-16**	**US7220555 B2** **10/081,455** **US20020142370A1** **PRACTICAL IN VITRO SIALYLATION OF RECOMBINANT GLYCOPROTEINS** ***FAMILY MEMBERS***	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **EXPIRES 2018-04-19** **Publication Date: 2007-05-22**	**Paulson; James C. (Del Mar, CA)** **Bayer; Robert J. (San Diego, CA)** **Sjoberg; Eric (San Diego, CA)**	1. A method of sialylating a saccharide group on a recombinant glycoprotein, the method comprising contacting a saccharide group which comprises a galactose or an N-acetylgalactosamine acceptor moiety on a recombinant glycoprotein with a sialic acid donor moiety and a Campylobacter jejuni α2,3-sialyltransferase in a reaction mixture which provides reactants required for sialyltransferase activity for a sufficient time and under appropriate conditions to transfer sialic acid from said sialic acid donor moiety to said saccharide group, wherein the concentration of sialyltransferase is at least 2 mUnit/mg of glycoprotein acceptor. 2. The method of claim 1, wherein the α2,3-sialyltransferase is recombinant.	**"PAULSON IV" FAMILY** ***STATUS*** • GRANTED - EXPIRES 2018-01-15 • ALL MAINTENANCE FEES PAID ***METHODOLOGY*** *IN VITRO SIALYLATION*

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		SEE ABOVE	**PTA: 94 days** **Filing Date: 2002-02-21** **Earliest Effective Filing Date: 1997-01-16** **Priority Date: 1998-01-15**		3. The method of claim 1, wherein the α2,3-sialyltransferase is isolated. 4. The method of claim 1, wherein the sialic acid donor moiety is CMP-sialic acid. 5. The method of claim 2, wherein the CMP-sialic acid is enzyrnatically generated in situ. 6. The method of claim 1, wherein the sialic acid is selected from the group consisting of NeuAc and NeuGe. 7. The method of claim 1, wherein the concentration of sialyltransferase is less than 50 mUnits/mg of glycoprotein acceptor. 8. The method of claim 1, wherein the glycoprotein concentrations are from 1-10 mg/ml. 9. The method of claim 1, wherein the reaction mixture further comprises one or more additional recombinant or isolated sialyltransferases other than a α2,3-sialyltransferase.	**Large scale sialylation of recombinant glycoprotein by reaction with sialic acid donor in presence of recombinant or bacterial sialyltransferase at low concentration, used e.g. to optimise or adjust sialylation in proteins from transformed cells or transgenic animals**
18	**1997-06-24**	**EP0994903 B1** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** ***FAMILY MEMBERS*** AT296315T AU199881634A AU757627B2 CA2293829A1 CA2293829C DE69830315T2 DK994903T3 ES2244066T3 JP2002506353A PT994903E	**GENENTECH/ ROCHE** (South San Francisco, CA) **LAPSED 2014-02-28** **Publication Date: 2000-04-26** **Filing Date: 1998-06-23** **Earliest Effective Filing Date: 1997-06-24**	**Raju, T Shantha (San Mateo, CA)**	1. A composition comprising glycoprotein wherein at least one glycoprotein is a glycoprotein having at least one CH2 domain and the composition is substantially free of the glycoprotein having at least one CH2 domain and having an N-linked G1, G0, or Glc oligosaccharide in its CH2 domain. 2. The composition of claim 1 comprising an antibody glycoprotein. 3. The composition of claim 2 wherein the antibody glycoprotein is a monoclonal antibody. 4. The composition of claim 3 wherein the monoclonal antibody is an IgG. 5. The composition of claim 4 wherein the IgG is human IgG1. 6. The composition of claim 5 wherein the monoclonal antibody is selected from the group consisting of an anti-CD20 specific monoclonal antibody, an anti-HER2 specific monoclonal antibody, and antiVEGF specific monoclonal antibody, and an anti-IgE specific monoclonal antibody. 7. The composition of claim 1 wherein the glycoprotein is an immunoadhesin.	**"RAJU I" FAMILY** ***STATUS*** • NO OPPOSITION FILED • LAPSED BECAUSE OF NON-PAYMENT OF DUE FEES ***METHODOLOGY*** METHOD OF *IN VITRO* GLYCOSYLATION OF A GLYCOPROTEIN HAVING AN IMMUNOGLOBULIN CH2 DOMAIN

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		WO1998058964A1			8. The composition of claim 7 wherein the immunoadhesin is a tumor necrosis factorimmunoglobulin G 1 chimera. 9. The composition of claim 1 wherein the glycoprotein is an antibody-immunoadhesin chimera. 10. A method of producing the composition of claim 1 comprising the steps of reacting in an aqueous buffered solution at a temperature of about 25-40^{0}C; a) a metal salt at a concentration of about 5 mM to about 25 mM; b) an activated galactose at a concentration of about 5 mM to about 50 mM; c) a galactosyltransferase at a concentration of about 1 mUnit/ml to about 100 mUnit/ml; d) a substrate glycoprotein; and recovering the glycoprotein. 11. The method of claim 10 wherein the metal salt is selected from the group consisting of Mn2++, Ca2++, and Ba2++. 12. The method of claim 11 wherein the activated galactose is uridine diphosphate-galactose (UDP-galactose). 13. The method of claim 12 wherein the galactosyl transferase is a mammalian p 1-4, galactosyl transferase. 14. The method of claim 13 wherein the reaction temperature is about 37" C, the metal salt is Mn2++ at a concentration of about 5 mM, the UDP-galactose concentration is about 5mM and the p 1-4 galactosyl transferase concentration is about I mUnit/ml. 15. The method of claim 14 wherein the glycoprotein is an antibody. 16. The method of claim 15 wherein the antibody is an IgG. 17. The method of claim 16 wherein the IgG is human IgG1. 18. The method of claim 17 wherein the monoclonal antibody is selected from the group consisting of an anti-CD20 specific monoclonal antibody, an anti-HER2 specific monoclonal antibody, and anti-VEGF specific monoclonal antibody, and an anti-IgE specific monoclonal antibody. 19. The method of claim 13 wherein the glycoprotein is an immunoadhesin. 20. The method of claim 19 wherein the immunoadhesin is a bispecific immunoadhesin.	

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					21. The method of claim 13 wherein the glycoprotein is an antibody-immunoadhesin chimera. 22. A method for the treatment of a disease state comprising administering to a mammal in need thereof a therapeutically effective dose of the composition of claim 1. 24. The method of claim 22 wherein the disease state is selected from the group consisting of inflammatory disorder, cancer, neurofibromatosis, peripheral neuropathologies, and cardiac hypertrophy.	
19	**1997-10-31**	**EP1028751 B1** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** ***FAMILY MEMBERS*** **AT419009T** **AU199910960A** **AU759779B2** **CA2307166A1** **DE69840412D1** **JP2001521909A** **WO1999022764A1**	**GENENTECH/ ROCHE** (South San Francisco, CA) **LAPSED 2014-02-28** **Publication Date: 2000-08-23** **Filing Date: 1998-10-16** **Earliest Effective Filing Date: 1997-10-31**	**Raju, T Shantha (San Mateo, CA)**	1. A composition comprising glycoprotein wherein at least one glycoprotein is a glycoprotein having at least one immunoglobulin heavy chain CH2 domain containing N-linked G-2 oligosaccharide and the amount of glycoprotein having an N-linked G1, G0, or G-1 oligosaccharide in the CH2 domain does not exceed 10% by weight. 2. The composition of claim 1 wherein the heavy chain CH2 domain contains N-linked G2 and G-2 oligosaccharide. 3. The composition of claim 1 or 2 wherein the N-linked G2 or G-2 oligosaccharide further comprises a bisecting N-acetylglucosamine. 4. The composition of any one of claims 1 to 3 wherein the glycoprotein is an antibody. 5. The composition of claim 4 wherein the glycoprotein is a monoclonal antibody. 6. The composition of claim 4 or 5 wherein the antibody is an IgG. 7. The composition of claim 6 wherein the IgG is human IgG1. 8. The composition of any one of claims 5 to 7 wherein the antibody is selected from the group consisting of an anti-CD20 specific monoclonal antibody, an anti-HER2 specific monoclonal antibody, an anti-VEGF specific monoclonal antibody, and an anti-IgE specific monoclonal antibody. 9. The composition of claim 8 wherein the monoclonal antibody is an anti-CD20 antibody. 10. The composition of any one of claims 1 to 3 wherein the glycoprotein is an immunoadhesin glycoprotein.	**"RAJU II" FAMILY** ***STATUS*** • **NO OPPOSITION FILED** 2009-10-01 • **LAPSED** BECAUSE OF NON-PAYMENT OF DUE FEES 2013-2014 ***METHODOLOGY*** METHOD OF *IN VITRO* GLYCOSYLATION OF A GLYCOPROTEIN HAVING AN IMMUNOGLOBULIN CH2 DOMAIN

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					11. The composition of any one of claims 1 to 3 wherein the glycoprotein is an antibody-immunoadhesin chimera. 12. The composition of claim 11 wherein the immunoadhesin glycoprotein is a tumor necrosis factor-immunoglobulin G1 chimera. 13. The composition of any preceding claim wherein the amount of said glycoprotein having an N-linked G2 oligosaccharide in the CH2 domain does not exceed 10% by weight. 14. A method of producing the composition of any preceding claim comprising the steps of reacting in an aqueous buffered solution at a temperature of 25-40°C; a) a β-galactosidase; b) an N-acetyl-β-D-glucosaminidase; c) a substrate glycoprotein; and recovering the glycoprotein. 15. The method of claim 14 wherein the β-galactosidase is from Diplococcus pneumoniae. 16. The method of claim 14 or claim 15 wherein the N-acetyl-β-D-glucosaminidase is from Diplococcus pneumoniae or jack bean. 17. The method of claim 15 or claim 16 wherein the reaction temperature is 37°C. 18. The composition of any one of claims 1 to 13 for use in a method of medical treatment. 19. A pharmaceutical composition comprising the composition of any one of claims 1 to 13 and a pharmaceutically acceptable carrier. 20. An article of manufacture, comprising: a container; a label on said container; and the composition of any one of claims 1 to 13 contained within said container. 21. The article of claim 20 wherein the label on the container indicates that the composition can be used for the treatment of cancer.	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
20	**1998-02-04**	**US6830908 B2** **10/218,381** **US20030013175A1** **GLYCOSYL-TRANSFERASE AND DNA ENCODING THE SAME** ***FAMILY MEMBERS*** **AT432990T** **AU199920755A** **CA2319754A1** **CA2319754C** **DE69940950D1** **EP1054062B1** **EXPIRES 2019-01-27** **JP04188561B2** **JP11221079A** **US6475761B1** **EXPIRES 2019-01-27** **WO1999040205A1** **WO1999040205A8**	**KYOWA HAKKO KOGYO CO., LTD** **EXPIRES 2020-08-02** **PTA: 0 days** **Publication Date: 2004-12-14** **Filing Date: 2002-08-15** **Earliest Effective Filing Date: 1998-02-04 (JP)** **Priority Date: 2000-08-02**	**Koizumi; Satoshi (Tokyo, JP)** **Endo; Tetsuo (Tokyo, JP)** **Tabata; Kazuhiko (Yamaguchi, JP)** **Ozaki; Akio (Tokyo, JP)**	1. A process for producing a galactose-containing carbohydrate, which comprises: selecting an enzyme source comprising a culture of a transformed host cell harboring a DNA that has 95% or more homology to the nucleotide sequence shown in SEQ ID NO: 2 and encodes a protein having beta. 1,4-galactosyltransferase activity; and admixing said enzyme source with an acceptor carbohydrate and uridine diphosphogalactose in an aqueous medium. 2. The process according to claim 1, wherein said galactose-containing carbohydrate is lacto-N-neotetraose. 3. The process according to claim 1, wherein said protein comprises the peptide sequence of SEQ ID NO:1. 4. The process according to claim 3, wherein said galactose-containing carbohydrate is lacto-N-neotetraose. 5. The process according to claim 1, wherein said galactose-containing carbohydrate is N-acetyllactosamine. 6. The process according to claim 1, wherein said galactose-containing carbohydrate is N-acetyllactosamine.	***STATUS*** • EXPIRES 2020-08-02 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** NEW RECOMBINANT HOST FOR EFFECTIVE PRODUCTION OF *HELICOBACTER PYLORI* B 1, 4-GALACTOSYLTRANSFERASE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
21A	**1998-04-03**	**US6649737** **09/373,902** **HUMAN GALACTOSYL-TRANFERASES** ***FAMILY MEMBERS*** **AU199932102A** **CA2325007A1** **EP1067893A2** **JP2002510478A** **US20030203396A1** **US5955282A** **WO1999051185A2** **WO1999051185A3**	**INCYTE GENOMICS** (Palo Alto, CA) **EXPIRED 2007-11-18** **PTA: days** **Publication Date: 2003-11-18** **Filing Date: 1999-08-12** **Earliest Effective Filing Date:** **Priority Date:**	**Hillman; Jennifer L. (Mountain View, CA)** **Guegler; Karl J. (Menlo Park, CA)** **Corley; Neil C. (Mountain View, CA)** **Shah; Purvi (Sunnyvale, CA)** **Patterson; Chandra (Mountain View, CA)**	1. A purified polypeptide comprising the amino acid sequence of SEQ ID NO:3. 2. A purified polypeptide having at least 90% amino acid sequence identity to the amino acid sequence of claim 1, and which retains galactosyltransferase activity. 3. A composition comprising the polypeptide of claim 1 in conjunction with a suitable carrier.	**"HILLMAN" FAMILY** ***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2007-11-18 ***METHODOLOGY*** NEW HUMAN GALACTOSYL-TRANSFERASE (HUGA) POLYPEPTIDE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
21B	**1998-04-03**	**US5955282 A** **09/055,097** **HUMAN GALACTOSYL-TRANFERASES** ***FAMILY MEMBERS*** **SEE ABOVE**	**INCYTE GENOMICS** (Palo Alto, CA) **EXPIRED 2007-09-21** **PTA: days** **Publication Date: 1999-09-21** **Filing Date: 1998-04-03** **Earliest Effective Filing Date: 1998-04-03** **Priority Date: 1998-04-03**	**Hillman; Jennifer L. (Mountain View, CA)** **Guegler; Karl J. (Menlo Park, CA)** **Corley; Neil C. (Mountain View, CA)** **Shah; Purvi (Sunnyvale, CA)** **Patterson; Chandra (Mountain View, CA)**	1. An isolated and purified polynucleotide encoding a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3. 2. An isolated and purified polynucleotide having a sequence which is fully complementary to the polynucleotide sequence of claim 1. 3. An isolated and purified polynucleotide consisting of polynucleotide sequence selected from the group consisting of SEQ ID NO:2 and SEQ ID NO:4. 4. An isolated and purified polynucleotide consisting of a sequence which is fully complementary to the polynucleotide of claim 3. 5. An expression vector containing the polynucleotide of claim 1. 6. A host cell containing the expression vector of claim 5. 7. A method for detecting a polynucleotide encoding the polypeptide comprising the amino acid sequence selected from the group consisting of SEQ ID NO:1 and SEQ ID NO:3 in a biological sample, the method comprising the steps of: (a) hybridizing the polynucleotide of claim 2 to at least one of the nucleic acids in the biological sample, thereby forming a hybridization complex; and (b) detecting the hybridization complex, wherein the presence of the hybridization complex correlates with the presence of the polynucleotide encoding the polypeptide in the biological sample. 8. The method of claim 7 wherein the nucleic acids of the biological sample are amplified by the polymerase chain reaction prior to the hybridizing step.	**"HILLMAN" FAMILY** ***STATUS*** • EXPIRED DUE TO FAILURE TO PAY MAINTENANCE FEE 2007-09-21 ***METHODOLOGY*** NUCLEIC ACID ENCODING NEW HUMAN GALACTOSYL-TRANSFERASE (HUGA) POLYPEPTIDE, USEFUL FOR TREATING OR PREVENTING AUTOIMMUNE, INFLAMMATORY OR DEVELOPMENTAL DISORDERS
22A	**1998-04-20**	**US7517670 B2** **10/633,697**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA)	**Umana; Pablo (Zurich, CH)**	1. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell, wherein said glycoengineering	**"UMANA I" FAMILY**

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		US20050079605A1 **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY** ***FAMILY MEMBERS*** **AT458007T** **AU199936578A** **AU2002339845B2** **CA2455365A1** **CA2455365C** **CA2838062A1** **CN1555411A** **DE69942021D1** **DK1071700T3** **DK2180007T3** **EP1071700 B1** **EXPIRES 2019-04-20** **[see TAB 22B]** **EP1423510 A4** **WITHDRAWN** **EP2180007 B1** **EXPIRES 2019-04-20** **[see TAB 22C]** **EP2180044A1** **PENDING** **EP2261229A2** **REFUSED 2013-11-27** **ES2340112T3** **ES2434961T3** **HU200700103A2** **HU200700103A3**	**EXPIRES 2019-04-20** **PTA: days** **Publication Date: 2009-04-14** **Filing Date: 2003-08-05** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**	**Jean-Mairet; Joel (Zurich, CH)** **Bailey, legal representative** **M. Sean (Santa Monica, CA)** **Bailey; James E (Zurich, CH)**	comprises genetically manipulating said host cell so that said host cell has a decreased level of activity of at least one glycoprotein-modifying glycosyltransferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered. 2. The method of claim 1, wherein said antibody has increased Fc-mediated cellular cytotoxicity. 3. The method of claim 1, wherein said antibody has increased Fc receptor binding affinity. 4. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase selected from the group consisting of: .beta.(1,4)-N-acetylglucosaminyltransferase III and .alpha.-mannosidase II; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered. 5. The method of claim 4, wherein said antibody has increased Fc-mediated cellular cytotoxicity. 6. The method of claim 4, wherein said antibody has increased Fc receptor binding affinity. 9. The method of claim 5 or 6, wherein said glycoengineering comprises introducing into said host cell at least one polynucleotide encoding an exogenous glycoprotein-modifying glycosyl transferase selected from the group consisting of .beta.(1,4)-N-acetylglucosaminyltransferase III and .alpha.-mannosidase II. 18. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to	***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** A METHOD FOR PRODUCING A RECOMBINANT ANTIBODY HAVING INCREASED FC MEDIATED CELLULAR CYTOTOXICITY OR INCREASED FC RECEPTOR BINDING AFFINITY

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		IL160170A **IL160170D0** **JP04334141B2** **JP2002512014A** **JP2005524379A** **JP2009100748A** **JP2009114201A** **JP2012210209A** **KR2004054669A** **KR2010018071A** **MX2004001072A** **MX2004PA001072A** **NO200400453A** **NO332457B1** **NZ531219A** **NZ571596A** **NZ581474A** **NZ592087A** **NZ603111A** **PL217751B1** **PL374178A1** **PT1071700E** **PT2180007E** **RU2004106559A** **RU2321630C2** **US20030175884A1** **ABANDONED** **US20040072290A1** **US20050074843A1** **ABANDONED** **US20050079605A1** **US20050272128A1** **US20080280322A9** **US20090304690A1** **PENDING** **US20110142825A1** **US20110293609A1** **PENDING** **US20110294984A1** **PENDING**			the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the predominant N-linked oligosaccharide in the Fc region of said antibody produced by said glycoengineered host cell is not a high-mannose structure. 22. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the Fc region containing N-linked oligosaccharides in said antibody further comprises an increased proportion of GlcNAc residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered. 25. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an JgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltransferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody produced by said glycoengineered host cell has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity as a result of said glycoengineering. 31. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has	

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		US20120122206A1 **US6602684 B1** **EXPIRES 2019-04-20** **[see TAB 22D]** **US7906329 B2** **EXPIRES 2019-04-20** **[see TAB 22E]** **US8021856 B2** **EXPIRES 2019-04-20** **[see TAB 22H]** **US8623644 B2** **EXPIRES 2019-04-20** **[see TAB 22G]** **US8629248 B2** **EXPIRES 2019-04-20** **[see TAB 22F]** **WO1999054342A1** **WO2003011878A2** **WO2003011878A3**			increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said recombinant antibody produced by said glycoengineered host cell exhibits at least an 80% increase in maximal ADCC activity compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered. 34. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell, wherein said glycoengineering comprises genetically manipulating said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein said recombinant antibody has an increased proportion of nonfucosylated oligosaccharides in the Fc region as a result of said glycoengineering compared to the corresponding antibody produced by the same host cell that has not been glycoengineered. 37. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the predominant N-linked oligosaccharide in the Fc region of the antibody produced by said glycoengineered host cell is nonfucosylated. 40. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are bisected. 43. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein the majority of the N-linked oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are nonfucosylated. 47. A method for producing a recombinant antibody having increased Fc mediated cellular cytotoxicity or increased Fc receptor binding affinity, comprising: (a) providing a mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region containing N-linked oligosaccharides; (b) glycoengineering said host cell so that said host cell has an altered level of activity of at least one glycoprotein-modifying glycosyltranferase; (c) culturing said glycoengineered host cell under conditions which permit the production of said recombinant antibody; and (d) isolating said recombinant antibody; wherein said recombinant antibody has increased Fc-mediated cellular cytotoxicity or increased Fc receptor binding affinity compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and wherein at least 45% of the oligosaccharides in the Fc region of said antibody produced by said glycoengineered host cell are complex structures. 50. The method of any one of claims 2, 3, 5, 6, 23, 24, 25, 31, 35, 36, 37, 40, 43, or 47, wherein said host cell is selected from the group consisting of an engineered CHO cell, an engineered BHK cell, an engineered NS0 cell, and an engineered SP2/0 cell. 52. The method of any one of claims 1, 4, 22, or 31, wherein said recombinant antibody is a chimeric antibody. 53. The method of any one of claims 1, 4, 22, or 31, wherein said recombinant antibody is a humanized antibody.	

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					54. The method of any one of claims 1, 4, 22, or 31, wherein said recombinant antibody is an antibody fragment that contains a Fc region. 55. The method of any one of claims 1, 4, 22, or 31, wherein said recombinant antibody is a fusion protein that includes an Fc region of an immunoglobulin. 58. The method of claim 57, wherein said antigen is differentially expressed by said cancer cell. 59. The method of any one of claims 1, 4, 22, or 31, wherein said antibody is a monoclonal antibody. 60. The method of any one of claims 1, 4, 22, or 31, wherein said IgG Fc region containing N-linked oligosaccharides comprises an entire IgG Fc region. 61. The method of any one of claims 1, 4, 22, or 31, wherein said IgG Fc region containing N-linked oligosaccharides comprises an IgG fragment.	
22B	**1998-04-20**	**EP1071700B1** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY** ***FAMILY MEMBERS*** **SEE ABOVE**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **EXPIRES 2019-04-20** **Publication Date: 2001-01-31** **Filing Date: 1999-04-20** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	1. A host cell engineered to express at least one nucleic acid encoding a **glycoprotein-modifying glycosyl transferase at a regulated level**. 11. A host cell engineered to express at least one nucleic acid molecule encoding a glycoprotein-modifying glycosyl transferase, wherein said host cell is capable of producing a protein having **enhanced Fc-mediated cellular cytotoxicity**. 32. **A method for producing a protein compound having enhanced Fc-mediated cellular cytotoxicity in a host cell,** comprising: (a) providing a host cell engineered to express a glycoproteinmodifying glycosyl transferase at a regulated level, chosen to improve glycosylation of a protein compound of interest, wherein said host cell expresses at least one nucleic acid encoding an antibody, an antibody fragment, or a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin; (b) culturing said host cell under conditions which permit the production of said protein compound having enhanced Fc-mediated dependent cellular cytotoxicity; and (c) isolating said protein compound **having enhanced Fc-mediated cellular cytotoxicity**.	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** HOST CELLS USED TO PRODUCE ANTIBODIES HAVING ENHANCED FC-MEDIATED CELLULAR CYTOTOXICITY

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
22C	**1998-04-20**	**EP2180007B1** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY** ***FAMILY MEMBERS*** **SEE ABOVE**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **EXPIRES 2019-04-20** **Publication Date: 2013-10-02** **Filing Date: 1999-04-20** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	**1. A mammalian host cell that expresses a recombinant antibody comprising an IgG Fc region** containing N-linked oligosaccharides, wherein said host cell has been genetically modified to regulate the increased expression of at least one enzyme selected from the group consisting **of β(1,4)-N-acetylglucosaminyltransferase III, β(1,4)-N-acetylglucosaminyltransferase V, and mannosidase II,** wherein said recombinant antibody has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues and has i**ncreased Fc-mediated cellular cytotoxicity** compared to the corresponding antibody produced by the same host cell that has not been genetically modified. 2. The host cell of claim 1, wherein said at least one enzyme is β(1,4)-N-acetylglucosaminyltransferase III. 3. The host cell of claim 1, wherein said at least one enzyme is mannosidase II. 4. The host cell of claim 1, wherein said at least one enzyme is β(1,4)-N-acetylglucosaminyltransferase III and mannosidase II. 5. The host cell of claim 4, wherein said β(1,4)-N-acetylglucosaminyltransferase III and mannosidase II are under the control of (a) constitutive promoter(s). 6. The host cell of claim 1, wherein said genetic modification comprises introducing into said host cell at least one polynucleotide encoding an enzyme selected from the group consisting of β(1,4)-N-acetylglucosaminyltransferase III, β(1,4)-N-acetylglucosaminyltransferase V, and mannosidase II. 7. The host cell of claim 1, wherein said host cell is selected from the group consisting of a glycosylation engineered CHO cell, a glycosylation engineered BHK cell, a glycosylation engineered NS0 cell, and a glycosylation engineered SP2/0 cell.	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** HOST CELLS USED TO PRODUCE ANTIBODIES HAVING INCREASED FC-MEDIATED CELLULAR TOXICITY

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					8. The host cell of claim 1, wherein said recombinant antibody is a chimeric antibody. 9. The host cell of claim 1, wherein said recombinant antibody is selected from the group consisting of a whole antibody and an antibody fragment or a fusion protein that include an Fc region of an immunoglobulin. 12. The host cell of claim 1, wherein said at least one enzyme is rat GnT III or human GnT V.	
22D	**1998-04-20**	**US6602684** **09/294,584** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY** ***FAMILY MEMBERS*** **SEE ABOVE**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **PTA: 0 DAYS** **EXPIRES 2019-04-20** **Publication Date: 2003-08-05** **Filing Date: 1999-04-20** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	1. **A method for producing a polypeptide having increased Fc-mediated cellular cytotoxicity in a host cell,** comprising: (a) culturing a host cell engineered to express at least one nucleic acid encoding .beta.(1,4)-N-acetylglucosaminyltransferase III (GnT III) under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes the Fc region of an immunoglobulin, wherein said GnT III is expressed in an amount sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell and wherein said polypeptide has increased Fc-mediated cellular cytotoxicity as a result of said modification; and (b) isolating said polypeptide having **increased Fc-mediated cellular cytotoxicity**. 2. The method of claim 1, wherein in step (a), said host cell comprises at least one nucleic acid encoding a whole antibody. 3. The method of claim 1, wherein in step (a), said host cell comprises at least one nucleic acid encoding an antibody fragment. 4. The method of claim 1, wherein in step (a), said host cell comprises at least one nucleic acid encoding a fusion protein comprising a glycosylated Fc region of an immunoglobulin. 5. The method of claim 1, wherein the expression level of glycosyl transferase GnT III produces an antibody molecule, antibody fragment, or a fusion protein that includes the Fc region of an immunoglobulin having increased Fc-mediated cellular cytotoxicity at a higher level than the Fc-mediated cellular cytotoxicity obtained from a different expression level of the same glycosyl transferase GnT III gene. 6. The method of claim 1, wherein said host cell further comprises a nucleic acid encoding a glycosidase. 7. The method of claim 1, wherein the expression level of glycosyl transferase GnTIII is sufficient to form bisected oligosaccharides in the Fc region of said polypeptide.	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** METHODS FOR PRODUCING GLYCOENGINEERED RECOMBINANT ANTIBODY HAVING INCREASED FC-MEDIATED CELLULAR CYTOTOXICITY OR INCREASED FC RECEPTOR BINDING AFFINITY

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					8. The method of claim 7, wherein the proportion of bisected oligosaccharides in the Fc region to total oligosaccharides in the Fc region is at least 45 percent. 9. The method of claim 7, wherein said bisected oligosaccharides are bisected, complex oligosaccharides. 10. A method for producing a polypeptide having increased Fc-mediated cellular cytotoxicity in a host cell, comprising: (a) culturing a host cell engineered to express at least one nucleic acid encoding .beta.(1,4)-N-acetylglucosaminyltransferase III (GnT III) under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a Fc region of an immunoglobulin and an antigen binding region, wherein said GnTIII is expressed in an amount sufficient to modify oligosaccharides in the Fc region of said polypeptide produced by said host cell, and wherein said polypeptide has increased Fc-mediated cellular cytotoxicity as a result of said modification; and (b) isolating said polypeptide having increased Fc-mediated cellular cytotoxicity; wherein said increased Fc-mediated cellular cytotoxicity is determined by an increase in antibody-dependent cellular cytotoxicity as measured in the following standard in vitro assay which uses viable target cells that are known to express a target antigen recognized by the antigen-binding region of said polypeptide, and uses as effector cells human peripheral blood mononuclear cells (PBMCs), said standard in vitro assay comprising the steps of: (i) labeling said target cells with the fluorescent dye Calcein AM as a marker for cell integrity; (ii) obtaining a first portion of said labeled target cells and dividing said first portion into multiple equal subportions of said labeled target cells; (iii) obtaining second and third portions of said labeled target cells having the same number of labeled target cells as said multiple equal subportions; (iv) mixing each said multiple equal subportion of said labeled target cells with a different concentration of polypeptide in a multi-well assay plate, each concentration being tested in triplicate and said different concentrations of polypeptide chosen to give different percentages of specific lysis; (v) mixing said second portion of said labeled target cells with a detergent that lyses said labeled target cells in said multi-well assay plate to provide a total lysis control portion; (vi) mixing said third portion of said labeled target cells with antibody-free culture medium in said multi-well assay plate to provide a spontaneous release control portion; (vii) incubating said multi-well assay plate containing said multiple equal subportions, total lysis control portion, and spontaneous release control portion for 1 hr; (viii) adding effector cells to each of said multiple equal subportions, total lysis control portion, and spontaneous release control portion in said multi-well assay plate to yield an effector cell: target cell ratio of 19:1 and mixing; (ix) incubating said multi-well assay plate in an incubator under 5% CO.sub.2 atmosphere at 37.degree. C. for 16 hrs; (x) discarding the cell free supernatant from each well of said multi-well assay plate; (xi) washing said labeled target cells in said multi-well assay plate with buffered saline solution; (xii) lysing said labeled	

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					target cells in nonionic detergent t-octylphenoxypolyethoxyethanol at a final concentration of 0.1% (v/v); (xiii) measuring the experimentally retained fluorescence (EF) of said target cells with a fluorometer; wherein the percentage of specific cell lysis for each polypeptide concentration is calculated according to the formula (SR-EF)/(SR-MR).times.100, where EF is average fluorescence measured for a given polypeptide concentration, MR is the average fluorescence measured for said total lysis control portion, and SR is the average fluorescence measured for said spontaneous release control portion, and wherein an increase in antibody-dependent cellular cytotoxicity is measured as either an increase in the maximum percentage of specific lysis observed within the polypeptide concentration range tested, and/or a reduction in the concentration of polypeptide required to achieve one half of the maximum percentage of specific lysis observed within the polypeptide concentration range tested.	
22E	**1998-04-20**	**US7906329 B2** **10/437,388** **US 20040072290 A1**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **PTA: 893 DAYS**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)**	1. **A glycoengineered Chinese Hamster Ovary cell** that expresses a recombinant antibody comprising an IgG Fc region or fragment thereof containing N-linked oligosaccharides, wherein said Chinese Hamster Ovary cell has been genetically manipulated to have altered activity of at least one glycoprotein-modifying glycosyltransferase, wherein said antibody has an altered pattern of glycosylation in the Fc region compared to the corresponding antibody	**"UMANA I" FAMILY** ***STATUS***

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY ***FAMILY MEMBERS*** **SEE ABOVE**	**(subject to TD filed 2009-08-13 with respect to US6602684)** **EXPIRES 2019-04-20** **Publication Date: 2011-03-15** **Filing Date: 2003-05-14** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**	**Bailey; James E (deceased) (Zurich, CH)**	produced by the same Chinese Hamster Ovary cell that has not been glycoengineered, and wherein said antibody has **increased Fc-mediated cellular cytotoxicity** as a result of said altered glycosylation. 2. **A glycoengineered Chinese Hamster Ovary cell** that expresses a recombinant antibody comprising an IgG Fc region or fragment thereof containing N-linked oligosaccharides, wherein said Chinese Hamster Ovary cell has been genetically manipulated to have altered activity of at least one glycoprotein-modifying glycosyltransferase, wherein said antibody has an altered pattern of glycosylation in the Fc region compared to the corresponding antibody produced by the same Chinese Hamster Ovary cell that has not been glycoengineered, and wherein said antibody has **increased Fc receptor binding affinity** as a result of said altered glycosylation. 10. **A glycoengineered Chinese Hamster Ovary cell** that produces a recombinant antibody comprising an Fc region containing N-linked oligosaccharides, wherein said Chinese Hamster Ovary cell has been genetically manipulated to have altered activity of at least one glycoprotein-modifying glycosyltransferase, wherein said antibody has an increased proportion of GlcNAc residues in the Fc region relative to the proportion of fucose residues compared to the proportion of GlcNAc to fucose residues in the Fc region of a corresponding antibody produced by the same Chinese Hamster Ovary cell that has not been glycoengineered, and wherein said antibody has **increased Fc-mediated cellular cytotoxicity** as a result of said genetic manipulation. 32. **A glycoengineered Chinese Hamster Ovary cell** according to claim 1 or claim 2, wherein said Chinese Hamster Ovary cell is produced by a process comprising: (a) providing a Chinese Hamster Ovary cell comprising at least one nucleic acid encoding a recombinant antibody; and (b) genetically manipulating said Chinese Hamster Ovary cell to alter the activity in said cell of at least one glycoprotein-modifying glycosyltransferase. 33. **A glycoengineered Chinese Hamster Ovary cell** according to claim 32, wherein said genetic manipulation is achieved by introducing into said cell at least one gene encoding an exogenous glycoprotein-modifying glycosyltransferase.	• EXPIRES 2019-04-20 ***METHODOLOGY*** A GLYCOENGINEERED CHINESE HAMSTER OVARY CELL THAT EXPRESSES ANTIBODIES HAVING INCREASED FC-MEDIATED CELLULAR CYTOTOXICITY OR INCREASED FC RECEPTOR BINDING AFFINITY
22F	**1998-04-20**	**US8629248 B2** **12/790,716** **US 20110142825 A1** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **PTA: 0 DAYS** **EXPIRES 2019-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	1. **A recombinant antibody having a Fc region** with variant glycoforms obtained from a Chinese Hamster Ovary host cell that has altered glycosyltransferase expression, wherein said antibody has at least **about 33% increased maximal ADCC activity** compared to the corresponding antibody lacking the variant glycoforms produced by a CHO cell that does not have altered glycosyltransferase expression. 3. The recombinant antibody of claim 1, wherein said antibody is an antibody fragment that contains the Fc region.	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY ***FAMILY MEMBERS*** **SEE ABOVE**	**Publication Date: 2014-01-14** **Filing Date: 2010-05-28** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**		4. The recombinant antibody of claim 1, wherein said variant glycoforms comprise an increase in the proportion of GlcNAc residues. 5. The recombinant antibody of claim 1, wherein said variant glycoforms comprise a decrease in the proportion of fucose residues. 6. The recombinant antibody of claim 1, wherein said variant glycoforms comprise an increase in the proportion of GlcNAc residues relative to the proportion of fucose residues. 7. The recombinant antibody of claim 1, wherein said variant glycoforms comprise bisected N-linked oligosaccharides. 8. The recombinant antibody of claim 7, wherein said bisected N-linked oligosaccharides are selected from the group consisting of bisected, complex and bisected, hybrid. 10. The recombinant antibody of claim 1, wherein said antibody selectively binds to a cancer antigen. 11. The recombinant antibody of claim 10, wherein said antibody is a selected from the group consisting of: an anti-CD20 antibody, an anti-human neuroblastoma antibody, an anti-human renal cell carcinoma antibody, an anti-HER2 antibody, an anti-human colon, lung, and breast carcinoma antibody, an anti-human 17-1A antigen antibody, a humanized anti-human colorectal tumor antibody, an anti-human melanoma antibody, and an anti-human squamous-cell carcinoma antibody. 13. The recombinant antibody of claim 7, wherein the majority of N-linked oligosaccharides are bisected. 14. The recombinant antibody of claim 1, wherein the majority of N-linked oligosaccharides are nonfucosylated. 15. The recombinant antibody of claim 1, wherein the majority of N-linked oligosaccharides are bisected, nonfucosylated.	RECOMBINANT ANTIBODY HAVING ABOUT 33% INCREASED MAXIMAL ADCC ACTIVITY
22G	**1998-04-20**	**US8623644 B2** **12/790,715** **US 20120122206 A1** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **PTA: 214 DAYS** **(subject to TD filed 2013-06-13 with respect to US7906329)** **EXPIRES 2019-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	1. **A glycoengineered mammalian host cell that expresses a recombinant antibody comprising an Fc region or fragment thereof containing N-linked oligosaccharides**, wherein said host cell has been genetically manipulated to have altered activity of **at least one glycoprotein-modifying glycosyltransferase**, wherein said antibody has an altered pattern of glycosylation in the Fc region compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and **wherein said antibody has increased Fc-mediated cellular cytotoxicity** as a result of said altered glycosylation.	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** GLYCOENGINEERED MAMMALIAN HOST CELL FOR PRODUCING RECOMBINANT ANTIBODIES HAVING

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		FAMILY MEMBERS **SEE ABOVE**	**Publication Date: 2014-01-07** **Filing Date: 2010-05-28** **Earliest Effective Filing Date: 1998-04-20** **Priority Date: 1999-04-20**		2. **A glycoengineered mammalian host cell that expresses a recombinant antibody comprising an Fc region or fragment thereof containing N-linked oligosaccharides**, wherein said host cell has been genetically manipulated to have altered activity of at least one glycoprotein-modifying glycosyltransferase, wherein said antibody has an altered pattern of glycosylation in the Fc region compared to the corresponding antibody produced by the same host cell that has not been glycoengineered, and **wherein said antibody has increased Fc receptor binding affinity** as a result of said altered glycosylation. 5. A glycoengineered host cell according to claim 1, wherein said antibody is a chimeric antibody. 6. A glycoengineered host cell according to claim 1, wherein said antibody is a humanized antibody. 7. A glycoengineered host cell according to claim 1, wherein said antibody is an antibody fragment that **contains a Fc region**. 8. A glycoengineered host cell according to claim 1, wherein said antibody is a fusion protein that includes **a Fc region of an immunoglobulin**. 9. A glycoengineered host cell according to claim 1, **wherein the predominant N-linked oligosaccharide in the Fc region is not a high-mannose structure**. 15. A glycoengineered host cell according to claim 1, wherein said host cell is selected from the group consisting of an **engineered CHO cell**, and engineered BHK cell, an engineered NS0 cell, and an engineered SP2/0 cell. 16. A glycoengineered host cell according to claim 15, wherein said host cell is an **engineered CHO cell**. 17. A glycoengineered host cell according to claim 1, wherein said host cell has been **genetically manipulated to have altered expression of at least one glycoprotein-modifying glycosyl transferase**. 18. A glycoengineered host cell according to claim 17, wherein said at least one glycoprotein-modifying glycosyltransferase is selected from the group consisting of: β(1,4)-N-acetylglucosaminyltransferase III, β(1,4)N-acetylglucosaminyltransferase V, **β(1,4)-galactosyltransferase**, a-mannosidase II, and core α-1,6-fucosyltransferase. 37. A glycoengineered host cell according to claim 1, wherein said host cell is produced by a process comprising:	INCREASED FC-MEDIATED CELLULAR CYTOTOXICITY OR INCREASED FC RECEPTOR BINDING AFFINITY

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					(a) **providing a host cell comprising at least one nucleic acid encoding a recombinant antibody**; and (b) genetically manipulating said host cell to alter the activity in said host cell of **at least one glycoprotein-modifying glycosyltransferase.** 38. A glycoengineered host cell according to claim 37, wherein said genetic manipulation is achieved by **introducing into said host cell at least one gene encoding an exogenous glycoprotein-modifying glycosyltransferase**. 40. A glycoengineered host cell according to claim 1, wherein **at least 45% of the oligosaccharides in the Fc region are complex structures.** 41. A glycoengineered host cell according to claim 1, wherein said recombinant antibody exhibits **at least an 80% increase in maximal ADCC activity** compared to the same antibody produced by the same host cell under identical culture and purification conditions, but which has not been glycoengineered.	
22H	**1998-04-20**	**US8021856 B2** **11/199,232** **US 20050272128 A1** **GLYCOSYLATION ENGINEERING OF ANTIBODIES FOR IMPROVING ANTIBODY-DEPENDENT CELLULAR CYTOTOXICITY** ***FAMILY MEMBERS*** **SEE ABOVE**	**ROCHE GLYCART BIOTECHNOLOGY** (Palo Alto, CA) **PTA: 214 DAYS** **(subject to TD filed 2013-06-13 with respect to US7906329)** **EXPIRES 2019-04-20** **Publication Date: 2005-12-08** **Filing Date: 2005-08-09** **Earliest Effective Filing Date: 1998-04-20**	**Umana; Pablo (Zurich, CH)** **Jean-Mairet; Joel (Zurich, CH)** **Bailey; James E (deceased) (Zurich, CH)**	1. **A method of treating cancer in a mammal in need thereof** comprising administering to said mammal a therapeutically effective amount of a composition comprising a **glycoengineered, recombinant antigen binding molecule** comprising an immunoglobulin Fc region containing N-linked oligosaccharides, produced by a eukaryotic cell line that expresses GnT III, wherein said glycoengineered, recombinant antigen binding molecule **has increased bisecting GlcNAc residues** on said N-linked oligosaccharides and i**ncreased Fc-mediated cellular cytotoxicity** compared to a corresponding antibody that has not been glycoengineered, and wherein said eukaryotic cell is the **CHO cell mutant lec 10.** 2. **A method of treating cancer in a mammal in need thereof** comprising administering to said mammal a therapeutically effective amount of a composition comprising **a glycoengineered, recombinant antigen binding molecule** comprising an immunoglobulin Fc region containing N-linked oligosaccharides, produced by a eukaryotic cell line that expresses GnT III, wherein said glycoengineered, recombinant antigen binding molecule has **increased bisecting GlcNAc residues** on said N-linked oligosaccharides and **increased Fc-mediated cellular cytotoxicity** compared to a corresponding antibody that has not been glycoengineered, and wherein said eukaryotic cell is a **CHO cell**. 3. The method of claim 1 or 2, wherein said GnT III is expressed in an amount sufficient to increase the proportion of said polypeptides carrying bisected hybrid oligosaccharides or	**"UMANA I" FAMILY** ***STATUS*** • EXPIRES 2019-04-20 ***METHODOLOGY*** METHODS OF TREATING CANCER WITH GLYCOENGINEERED ANTIBODIES THAT HAVE INCREASED BISECTING GLCNAC RESIDUES AND NCREASED FC-MEDIATED CELLULAR CYTOTOXICITY

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
			Priority Date: 1999-04-20		galactosylated complex oligosaccharides or mixtures thereof in the Fc region relative to polypeptides carrying bisected complex oligosaccharides in the Fc region. 4. The method of claim 1 or 2, wherein a nucleic acid molecule comprising at least one gene encoding GnT III has been introduced into said eukaryotic cell. 5. The method of claim 2, wherein said eukaryotic cell has been engineered such that an endogenous GnT III gene is activated. 6. The method of claim 5, wherein said endogenous GnT III has been activated by insertion of a DNA element which increases gene expression into the host chromosome. 7. The method of claim 4, wherein said at least one gene encoding GnT HI has been introduced into said host cell chromosome. 8. The method of claim 5, wherein said endogenous GnT III has been activated by insertion of a promoter element, a transposon, or a retroviral element into the host cell chromosome. 9. The method of claim 4, wherein said at least one nucleic acid encoding a GnT III is operably linked to a constitutive promoter element. 10. The method of claim 1 or 2, wherein said recombinant antigen binding molecule is selected from the group consisting of: an antibody, an antibody fragment and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin. 11. The method of claim 10, wherein said recombinant antigen binding molecule is a fusion protein that includes a region equivalent to the Fc region of a human immunoglobulin. 12. The method of claim 10, wherein said recombinant antigen binding molecule is an antibody. 13. The method of claim 12, wherein said antibody is selected from the group consisting of: an anti-CD20 antibody, the chimeric anti-human neuroblastoma monoclonal antibody chCE7, the chimeric anti-human renal cell carcinoma monoclonal antibody chG250, the chimeric anti-human colon, lung, and breast carcinoma monoclonal antibody ING-1, the humanized anti-human 17-1A antigen monoclonal antibody 3622W94, the humanized anti-human colorectal tumor antibody A33, the anti-human melanoma antibody directed against GD3 ganglioside R24, the chimeric anti-human squamous-cell carcinoma monoclonal antibody SF-25, an anti-human EGFR antibody, an anti-human EGFRvIII antibody, an anti-human PSMA antibody, an anti-human PSCA antibody, an anti-human CD22 antibody, an anti-human CD30 antibody, an anti-human CD33 antibody, an anti-human CD38 antibody, an anti-human CD40 antibody, an anti-human CD45 antibody, an anti-human CD52 antibody, an anti-human CD138 antibody, an anti-human HLA-DR variant antibody, an anti-human EpCAM antibody, an anti-human CEA antibody, an anti-human MUC1 antibody, an anti-human MUC1 core protein antibody, an anti-	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					human aberrantly glycosylated MUC1 antibody, an antibody against human fibronectin variants containing the ED-B domain, and an anti-human HER2/neu antibody. 15. The method of claim 1 or 2, wherein said mammal is a human. 16. The method of claim 1 or 2, wherein said composition further comprises a pharmaceutically acceptable carrier. 17. The method of claim 16, wherein said composition further comprises a cytokine. 18. The method of claim 1 or 2, wherein the method of administration is selected from the group consisting of: intravenous infusion, parenteral injection and subcutaneous injection. 19. The method of claim 1 or 2, wherein said increased Fc-mediated cellular cytotoxicity is increased ADCC.	
23A	**1998-12-09**	**US6998267 B1** **09/857,651** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** ***FAMILY MEMBERS*** AT475714T AU200016813A AU771908C BR199917026A BRPI9917026B1 CA2354377C DE69942636D1 DK1137789T3 **EP1137789 B1** EXPIRES 2019-12-08 [see TABLE A - TAB 23B] **EP2264177A1**	**THE DOW CHEMICAL COMPANY** (Midland, MI) PTE: 0 days **EXPIRES 2019-12-08** **Publication Date: 2006-02-14** **Filing Date: 2001-08-27** **Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**	**Seki; Tatsuji (Osaka, JP)** **Fujiyama; Kazuhito (Osaka, JP)**	**1. A method of manufacturing a glycoprotein having a sugar chain**, comprising a step in which a transformed plant cell is produced by introducing to a **plant cell** a gene encoding a **mammalian β 1,4-galactosyltransferase** enzyme and a gene of an exogenous glycoprotein, and a step in which the produced transformed plant cell is cultivated. 3. The method according to claim 1, wherein the glycoprotein sugar chain comprises a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises **a plurality of mannose and acetylglucosamine residues**, and wherein the outer sugar chain contains a terminal sugar portion with a non-reducing terminal galactose. 7. The method according to claim 1, wherein the mammalian β1,4-galactosyltransferase is a **human β1,4-galactosyltransferase**. 8. **A transformed plant cell** having a sugar chain adding mechanism comprising a mammalian β1,4-galactosyltransferase enzyme which transfers a galactose residue to a non-reducing terminal acetylglucosamine residue, wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprise a plurality of mannose and acetylglucosamine residues, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. **12. A method of manufacturing a glycoprotein**, which method includes introducing into a plant cell a gene encoding a **β1,4-galactosyltransferase** of human origin and further introducing a gene encoding an exogenous glycoprotein selected from the group consisting of enzymes, hormones, cytokines, **antibodies**, vaccines, receptors and serum proteins, the glycoprotein produced including a core sugar chain including a plurality of mannose and acetylglucosamine	***STATUS*** • EXPIRES 2019-12-08 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** GLYCOSYLATION OF GLYCOPROTEIN IN PLANT CELLS Claims require a plant cell that expresses a mammalian glycoprotein + mammalian β1,4-galactosyltransferase **AND** β1,3-glucuronyltransferase

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		PENDING ES2350063T3 IL143641A IL143641D0, IL207261D0 JP2002543760A JP2009028054A JP2012223198A JP2014054263A MX2001005778A MX2001PA005778A NZ512185A PT1137789E US20050143564A1 US20080124798A1 US20110070649A1 US20130040391A1 **US7388081 B2** (US20050143564A1) EXPIRES 2020-09-09 [see TABLE A - TAB 23C] **US8241909** B2 (US20110070649A1) EXPIRES 2019-12-08 [see TABLE A - TAB 23D] **US8853370** B2 EXPIRES 2019-12-08 [see TABLE A - TAB 23E] WO2000034490A1 ZA200104695A			residues, and an outer sugar chain containing a terminal sugar chain portion with a non-reducing terminal galactose. 17. The method according to claim 12, wherein the exogenous glycoprotein encoded by the introduced gene is an antibody selected from **immunoglobulin G (IgG)** or single chain variable region antibody fragments (scFv).	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
23B	**1998-12-09**	**EP1137789 B1** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** ***FAMILY MEMBERS*** **SAME ABOVE**	**THE DOW CHEMICAL COMPANY** (Midland, MI) **PTE: 0 days** **EXPIRES 2019-12-08** **Publication Date: 2010-07-28** **Filing Date: 1999-12-08** **Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**	**Seki; Tatsuji (Osaka, JP)** **Fujiyama; Kazuhito (Osaka, JP)**	1. **A method of expressing a glycosyltransferase and an exogenous glycoprotein having a human-type sugar chain in a transformed plant cell**, comprising a step in which a **transformed plant cell** is obtained by introducing into a plant cell the gene of a glycosyltransferase and the gene of an exogenous glycoprotein, and a step in which the obtained transformed plant cell is cultivated. 2. **A method of manufacturing a glycoprotein having a human-type sugar chain**, comprising a step of expressing a glycosyltransferase and an exogenous glycoprotein according to the method of claim 1, and a step in which the exogenous glycoprotein is isolated from the transformed plant cell. 3. A method according to claim 1 or claim 2, wherein the glycosyltransferase is an enzyme capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue. 4. A method according to claim 1 or claim 2, wherein the glycoprotein with a human-type sugar chain comprises a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. 5. A method according to claim 4, wherein the outer sugar chain has a straight chain configuration. 6. A method according to claim 4, wherein the outer sugar chain has a branched configuration. - 7. A method according to claim 6, wherein the branched sugar chain portion has a mono-, bi-, tri-or tetra configuration. 8. A method according to claim 1 through claim 7, wherein the glycoprotein contains neither fucose nor xylose. 9. **A plant cell having a sugar chain adding mechanism** comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and	***STATUS*** • EXPIRES 2019-12-08 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** GLYCOSYLATION OF PROTEINS IN PLANT CELLS Claims require a plant cell that expresses a mammalian glycoprotein + mammalian β1,4-galactosyltransferase **AND** β1,3-glucuronyltransferase

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β-1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. 10. **A recombinant plant, or portion thereof,** comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β -1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), and_ wherein the recombinant plant, or portion thereof, produces mammalian-like glycoproteins comprising neither fucose or xylose. 11. **A transgenic plant** comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β -1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), wherein the transgenic plant produces mammalian-like glycoproteins comprising neither fucose or xylose, and wherein the transgenic plant is regenerated from a plant cell having a sugar chain adding mechanism comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β-1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose.	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
23C	**1998-12-09**	**US7388081 B2** **10/870,635** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** ***FAMILY MEMBERS*** **SAME ABOVE**	**THE DOW CHEMICAL COMPANY** (Midland, MI) **PTA: 276 days** **EXPIRES 2020-09-09** **Publication Date: 2008-06-17** **Filing Date: 2004-06-17** **Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**	**Seki; Tatsuji (Osaka, JP)** **Fujiyama; Kazuhito (Osaka, JP)**	1. **A method of expressing a glycosyltransferase and an exogenous glycoprotein having a human-type sugar chain in a transformed plant cell**, comprising a step in which a transformed plant cell is obtained by introducing into a plant cell the gene of a **glycosyltransferase** and the gene of an exogenous glycoprotein, and a step in which the obtained transformed plant cell is cultivated. 2. **A method of manufacturing a glycoprotein having a human-type sugar chain**, comprising a step of expressing a glycosyltransferase and an exogenous glycoprotein according to the method of claim 1, and a step in which the exogenous glycoprotein is isolated from the transformed plant cell. 3. A method according to claim 1 or claim 2, wherein the glycosyltransferase is an enzyme capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue. 4. A method according to claim 1 or claim 2, wherein the glycoprotein with a human-type sugar chain comprises a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. 5. A method according to claim 4, wherein the outer sugar chain has a straight chain configuration. 6. A method according to claim 4, wherein the outer sugar chain has a branched configuration. - 7. A method according to claim 6, wherein the branched sugar chain portion has a mono-, bi-, tri-or tetra configuration. 8. A method according to claim 1 through claim 7, wherein the glycoprotein contains neither fucose nor xylose. 9. **A plant cell having a sugar chain adding mechanism** comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β-1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. 10. **A recombinant plant, or portion thereof,** comprising:	***STATUS*** • EXPIRES 2020-09-09 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** GLYCOSYLATION OF PROTEINS IN PLANT CELLS

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is Mannosidase I (Man I), Mannosidase II (Man II), β -1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI), and_ wherein the recombinant plant, or portion thereof, produces mammalian-like glycoproteins comprising neither fucose or xylose. 11. **A transgenic plant** comprising: the gene of a first enzyme, wherein the first enzyme is a **glycosyltransferase** capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is **Mannosidase I (Man I), Mannosidase II (Man II), β -1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI),** wherein the transgenic plant produces mammalian-like glycoproteins comprising neither fucose or xylose, and wherein the transgenic plant is regenerated from a plant cell having a sugar chain adding mechanism comprising: the gene of a first enzyme, wherein the first enzyme is a glycosyltransferase capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue; and the gene of a second enzyme which can enhance the first enzyme, wherein the second enzyme is **Mannosidase I (Man I), Mannosidase II (Man II), β-1,4-Galactosyltransferase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI),** wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose.	
23D	**1998-12-09**	**US8241909** **12/795,316** **US 20110070649 A1** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-**	**THE DOW CHEMICAL COMPANY** (Midland, MI) **PTA: 0 days** **EXPIRES 2019-12-08**	**Seki; Tatsuji** (Osaka, JP) **Fujiyama; Kazuhito** (Osaka, JP)	1. **A plant cell comprising a first exogenous gene** encoding a glycosyltransferase and a second exogenous gene encoding an exogenous glycoprotein, in which the exogenous glycoprotein is expressed and the expressed glycoprotein comprises a human-type sugar chain, which has a galactose residue linked to an N-acetylglucosamine residue, wherein the glycosyltransferase is a galactosyltransferase. 2. The plant cell according to claim 1, wherein the galactosyltransferase is a .**beta.1,4-galactosyltransferase** that transfers a galactose residue to a non-reducing terminal acetylglucosamine residue.	***STATUS*** • EXPIRES 2019-12-08 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY***

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		TYPE GLYCOSYLATION ***FAMILY MEMBERS*** **SAME ABOVE**	**Publication Date: 2011-03-24** **Filing Date: 2010-07-07** **Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**		8. The plant cell according to claim 1, wherein the galactosyltransferase is a **human galactosyltransferase,** and the exogenous glycoprotein is an enzyme, a hormone, a cytokine, an **antibody**, a vaccine, a receptor, or a serum protein. 9. The plant cell according to claim 8, wherein the exogenous glycoprotein is horseradish peroxidase, kinase, glucocerebrosidase, .alpha.-galactosidase, tissue-type plasminogen activator (TPA), or 3-hydrorxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. 10. The plant according to claim 8, wherein the exogenous glycoprotein is enkephalin, interferon-alpha, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (C-CSF), chorion, stimulating hormone, interleukin-2, interferon-beta, interferon-gamma, erythropoietin, vascular endothelial growth factor, human choriogonadotropin (HCG), leuteinizing hormone (LH), thyroid stimulating hormone (TSH), prolactin, or ovary stimulating hormone. 11. The plant cell according to claim 8, **wherein the exogenous glycoprotein is an immunoglobulin G (IgG) or a single chain variable region antibody fragments (scFV).** 12. **A plant cell comprising a glycoprotein** comprising a human-type sugar chain, comprising **no fucose or xylose** linked to one or more of the core sugar chain, the outer sugar chain and the terminal sugar chain. 13. **A plant cell comprising an exogenous glycoprotein** that comprises a galactose residue linked to an N-acetylglucosamine residue by a beta 1,4 linkage. 14. **A plant cell comprising an exogenous glycoprotein** that comprises a galactose residue which is added to the glycoprotein by a galactosyltransferase.	GLYCOENGINEERED PLANT CELLS
23E	**1998-12-09**	**US8853370** **13/546,293** **US 2013-0040391 A1** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** ***FAMILY MEMBERS***	**THE DOW CHEMICAL COMPANY** (Midland, MI) **PTA: 0 days** **EXPIRES 2020-09-09** **Publication Date: 2013-02-14** **Filing Date: 2012-07-11**	**Seki; Tatsuji** **(Osaka, JP)** **Fujiyama; Kazuhito** **(Osaka, JP)**	1. **A plant-produced glycoprotein**, comprising (i) a galactosylated sugar chain that comprises **a galactose residue linked to a N-acetylglucosamine residue in .beta.1,4-linkage,** and (ii) a non-galactosylated sugar chain comprising **a xylose residue linked to a mannose residue in .beta.1,2-linkage.** 2. The plant-produced glycoprotein of claim 1, wherein no .alpha.1,3-fucose, and/or no .beta.1,2-xylose is linked to the galactosylated sugar chain. 3. The plant-produced glycoprotein of claim 1, wherein the glycoprotein comprises N-glycans of M7A, M7B, M6B, M3X, M5, GalGNM3, and GalGNM5, wherein M is mannose, X is xylose, Gal is galactose, and N is N-acetylglucosamine, and wherein the structures of M7A, M7B, M6B, M3X, M5, GalGNM3, and GalGNM5 are set forth in FIG. 1.	***STATUS*** • EXPIRES 2020-09-09 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** Claims drawn to a PLANT-PRODUCED GLYCOPROTEIN

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		SAME ABOVE	**Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**		4. The plant-produced glycoprotein of claim 1, wherein the plant-produced glycoprotein is an enzyme, a hormone, a cytokine, an antibody, a vaccine antigen, a receptor, or a serum protein. 5. The plant-produced glycoprotein of claim 4, wherein the plant-produced glycoprotein is an enzyme selected from the group consisting of horseradish peroxidase, kinase, glucocerebrosidase, .alpha.-galactosidase, tissue-type plasminogen activator (TPA), and 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. 6. The plant-produced glycoprotein of claim 4, wherein the plant-produced glycoprotein is selected from the group consisting of enkephalin, interferon-alpha, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), chorion stimulating hormone, interleukin-2, interferon-beta, interferon-gamma, erythropoietin, vascular endothelial growth factor, human choriogonadotropin (HCG), leuteinizing hormone (LH), thyroid stimulating hormone (TSH), prolactin, and ovary stimulating hormone. 7. The plant-produced glycoprotein of claim 4, wherein the plant-produced glycoprotein is an antibody. 8. The plant-produced glycoprotein of claim 1, wherein the galactose residue is a terminal sugar residue in the galactosylated sugar chain. 9. The plant-produced glycoprotein of claim 1, wherein the plant-produced glycoprotein is produced by a process comprising: cultivating a transformed plant cell comprising a first gene encoding a galactosyltranferase, and a second gene encoding the glycoprotein under conditions allowing expression of the galactosyltransferase and the glycoprotein; wherein the transformed plant cell further comprises one or more genes encoding one or more of N-acetylglucosaminyl-transferase I, mannosidase I, and mannosidase II; and isolating the glycoprotein, which comprises a human-type sugar chain comprising a galactose residue linked to a N-acetylglucosamine residue, wherein addition of the galactose residue is catalyzed by the galactosyltransferase. 10. The plant-produced glycoprotein of claim 9, wherein no .alpha.1,3-fucose, nor and/or no .beta.1,2-xylose is linked to the galactosylated sugar chain. 11. The plant-produced glycoprotein of claim 9, wherein the glycoprotein comprises N-glycans of M7A, M7B, M6B, M3X, M5, GalGNM3, and GalGNM5, wherein M is mannose, X is xylose, Gal is galactose, and N is N-acetylglucosamine, and wherein the structures of M7A, M7B, M6B, M3X, M5, GalGNM3, and GalGNM5 are set forth in FIG. 15. 12. The plant-produced glycoprotein of claim 9, wherein glycoprotein is an enzyme, a hormone, a cytokine, an antibody, a vaccine antigen, a receptor, or a serum protein. 13. The plant-produced glycoprotein of claim 12, wherein the plant-produced glycoprotein is an enzyme selected from the group consisting of horseradish peroxidase, kinase,	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					glucocerebrosidase, .alpha.-galactosidase, tissue-type plasminogen activator (TPA), and 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase. 14. The plant-produced glycoprotein of claim 12, wherein the plant-produced glycoprotein is selected from the group consisting of enkephalin, interferon-alpha, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (C-CSF), chorion stimulating hormone, interleukin-2, interferon-beta, interferon-gamma, erythropoietin, vascular endothelial growth factor, human choriogonadotropin (HCG), leuteinizing hormone (LH), thyroid stimulating hormone (TSH), prolactin, and ovary stimulating hormone. 15. The plant-produced glycoprotein of claim 12, wherein the plant-produced glycoprotein is an antibody. 16. The plant-produced glycoprotein of claim 9, wherein the first gene encodes a galactosyltransferase comprising the amino acid sequence of SEQ ID NO:6. 17. The plant-produced glycoprotein of claim 13, wherein the first gene comprises the nucleotide sequence of SEQ ID NO:5.	
24	**1999-03-02**	**US8546105** **12/806,292** **US 20110229931 A1** **ENGINEERING INTRACELLULAR SIALYLATION PATHWAYS** ***FAMILY MEMBERS*** AU200035083A CA2363297A1 CA2363297C EP1399538A2 **EP1399538A4** **WITHDRAWN 2009-01-28** JP2003524395A US20050287637A1 **ABANDONED**	**THE UNIVERSITY OF WYOMING** (Laramie, WY) **THE JOHN HOPKINS UNIVERSITY** (Baltimore, MD) **HUMAN GENOME SCIENCES, INC.** (Rockville, MD) **PTA: 0 days** **EXPIRES 2020-03-01** **Publication Date: 2011-09-22** **Filing Date: 2010-08-09**	**Jarvis; Donald (Laramie, WY)** **Betenbaugh; Michael (Baltimore, MD),** **Lawrence; Shawn (Valley Cottage, NY)** **Lee; Yuan C. (Timonium, MD)** **Coleman; Timothy A. (Derwood, MD)**	**1. A modified eukaryotic cell capable of producing CMP-N-acetylneuraminate (CMP-Neu5Ac) above levels produced before said cell was modified**, when provided N-acetylmannosamine (ManNAc), wherein said cell is modified to comprise and express: i) **at least one copy of a cytidine monophosphate sialic acid synthetase (CMP-SAS) gene**, operably-linked to a promoter functional in the eukaryotic cell, wherein said CMP-SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylneuraminate (Neu5Ac) and cytidine triphosphate (CTP) to CMP-Neu5Ac and PPi; and wherein said polypeptide is (a) a polypeptide having at least 95% identity to SEQ ID NO:4; or (b) a polypeptide having at least 90% identity to SEQ ID NO:4 that contains conservative amino acid substitutions, in which CMP-SAS function is conserved; or (c) a variant of a polypeptide specified in (a) or (b) that contains one or more fusions or truncations, in which CMP-SAS function is conserved; and ii) **at least one copy of a sialic acid phosphate synthetase (SAS) gene**, operably-linked to a promoter functional in the eukaryotic cell, wherein said SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylmannosamine 6-phosphate (ManNAc-6-P) and phosphoenolpyruvate (PEP) to N-acetylneuraminate-9-phosphate (NeuNAc-9-P) and Pi; and wherein said polypeptide is (d) a polypeptide having at least 95% identity to SEQ ID NO: 6; or (e) a polypeptide having at least 90% identity to SEQ ID NO:6 that contains conservative amino acid substitutions and in which SAS function is conserved; or (f) a variant of a polypeptide specified in (d) or (e) that contains one or more fusions or truncations, in which SAS function is conserved. 2. The cell of claim 1, further comprising at least one copy of a gene encoding a **glycosyltransferase**, which is operably linked to a promoter functional in the eukaryotic cell.	***STATUS*** • EXPIRES 2020-03-01 • NO MAINTENANCE FEES DUE • **US6949372B2 (US20020142386A1) - claims drawn to overexpressing sialic acid synthetase (SAS) in a cell.** • **US7776565B2 (US20090226968A1) - claims drawn to overexpressing sialic acid synthetase (SAS) in a cell.** ***METHODOLOGY*** A EUKARYOTIC CELL HAVING AT LEAST ONE COPY OF A CYTIDINE MONO-PHOSPHATE SIALIC ACID SYNTHETASE (CMP−SAS) GENE

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		US20140024812A1 **PENDING** US6949372 B2 (US20020142386A1) US7776565 B2 (US20090226968A1) WO2000052135A2 WO2000052135A3 WO2000052135A9	**Earliest Effective Filing Date: 1999-03-02** **Priority Date: 2000-03-01**		3. The cell of claim 2, wherein the glycosyltransferase gene encodes an enzyme selected from the group consisting of **galactosyltransferase T (Gal T),** N-Acetylglucosamine transferase I (GlcNAc TI), (N-acetylglucosaminyltransferase II (GlcNAc TII). 4. The cell of claim 1, further comprising expression of at least one copy of a gene encoding a **sialyltransferase**, which is operably linked to a promoter functional in the eukaryotic cell. 5. The cell of claim 4, wherein the sialyltransferase gene encodes a sialyltransferase selected from the group consisting of alpha 2-3-sialyltransferase and **alpha 2-6-sialyltransferase**. 31. A stably-transformed eukaryotic cell capable of producing CMP-2-keto-3-deoxy-D-glycero-D-galacto-nononic acid (CMP-KDN) above levels produced before said cell was transformed when provided mannose (Man), wherein said cell is stably-transformed to comprise and express: i) at least one copy of a cytidine monophosphate sialic acid synthetase (CMP-SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said CMP-SAS gene encodes a polypeptide that catalyzes the conversion of deaminoneuraminate and CTP to CMP-Kdn and PPi; and wherein said polypeptide is (a) a polypeptide having at least 95% identity to SEQ ID NO:4; or (b) a polypeptide having at least 90% identity to SEQ ID NO:4 that contains conservative amino acid substitutions, in which CMP-SAS function is conserved; or (c) a variant of a polypeptide specified in (a) or (b) that contains one or more fusions or truncations, in which CMP-SAS function is conserved; and ii) at least one copy of a sialic acid phosphate synthetase (SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said SAS gene encodes a polypeptide that catalyzes the conversion of deaminoneuraminate-6-P and PEP to deaminoneuraminate-9-P and Pi; and wherein said polypeptide is (d) a polypeptide having at least 95% identity to SEQ ID NO: 6; or (e) a polypeptide having at least 90% identity to SEQ ID NO:6 that contains conservative amino acid substitutions and in which SAS function is conserved; or (f) a variant of a polypeptide specified in (d) or (e) that contains one or more fusions or truncations, in which SAS function is conserved. 41. A method for modifying a eukaryotic cell to be capable of producing CMP-N-acetylneuraminate (CMP-Neu5Ac) above levels produced before said cell was modified, when provided N-acetylmannosamine (ManNAc), said method comprising introducing into said cell, in any order: i) at least one copy of a cytidine monophosphate sialic acid synthetase (CMP-SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said CMP-SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylneuraminate (Neu5Ac) and cytidine triphosphate (CTP) to CMP-Neu5Ac and PPi; and wherein said polypeptide is (a) a polypeptide having at least 95% identity to SEQ ID NO:4; or (b) a polypeptide having at least 90% identity to SEQ ID NO:4 that contains conservative amino acid substitutions, in which CMP-SAS function is conserved; or (c) a variant of a polypeptide specified in (a) or (b) that contains one or more fusions or truncations, in which CMP-SAS function is conserved; and ii) at least one copy of a sialic acid phosphate synthetase (SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylmannosamine 6-phosphate (ManNAc-6-P) and phosphoenolpyruvate (PEP) to N-acetylneuraminate-9-phosphate (NeuNAc-9-P) and Pi; and wherein said polypeptide is (d) a polypeptide having at least 95% identity to SEQ ID NO: 6; or (e) a polypeptide having at least 90% identity to SEQ ID NO:6 that contains conservative amino acid substitutions, in which SAS function is conserved; or (f) a variant of a polypeptide specified in (d) or (e) that contains one or more fusions or truncations, in which SAS function is conserved.	AND AT LEAST ONE COPY OF A SIALIC ACID PHOSPHATE SYNTHETASE (SAS) GENE.

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					43. A method for producing CMP-N-acetylneuraminate (CMP-Neu5Ac) in a modified eukaryotic cell above levels produced before said cell was modified, when provided N-acetylmannosamine (ManNAc), said method comprising: i) expressing at least one copy of a cytidine monophosphate sialic acid synthetase (CMP-SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said CMP-SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylneuraminate (Neu5Ac) and cytidine triphosphate (CTP) to CMP-Neu5Ac and PPi; and wherein said polypeptide is (a) a polypeptide having at least 95% identity to SEQ ID NO:4; or (b) a polypeptide having at least 90% identity to SEQ ID NO:4 that contains conservative amino acid substitutions, in which CMP-SAS function is conserved; or (c) a variant of a polypeptide specified in (a) or (b) that contains one or more fusions or truncations, in which CMP-SAS function is conserved; and ii) expressing at least one copy of a sialic acid phosphate synthetase (SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylmannosamine 6-phosphate (ManNAc-6-P) and phosphoenolpyruvate (PEP) to N-acetylneuraminate-9-phosphate (NeuNAc-9-P) and Pi; and wherein said polypeptide is (d) a polypeptide having at least 95% identity to SEQ ID NO: 6; or (e) a variant of a polypeptide having at least 90% identity to SEQ ID NO:6 that contains conservative amino acid substitutions, in which SAS function is conserved; or (f) a variant of a polypeptide specified in (d) or (e) that contains one or more fusions or truncations, in which SAS function is conserved. 44. A method for producing a heterologous protein in a modified eukaryotic cell capable of producing CMP-N-acetylneuraminate (CMP-Neu5Ac) above levels produced before said cell was modified, when provided N-acetylmannosamine (ManNAc), said method comprising: (a) introducing into said modified eukaryotic cell, an expression vector comprising a gene encoding a heterologous protein operably linked to a promoter functional in the eukaryotic cell; (b) expressing the gene encoding a heterologous protein wherein said gene is operably-linked to a promoter functional in the eukaryotic cell; and (c) isolating the heterologous protein from the modified cell or the cell culture media obtained from the modified cell; wherein said cell is modified to comprise and express: i) at least one copy of a cytidine monophosphate sialic acid synthetase (CMP-SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said CMP-SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylneuraminate (Neu5Ac) and cytidine triphosphate (CTP) to CMP-Neu5Ac and PPi; and wherein said polypeptide is (a) a polypeptide having at least 95% identity to SEQ ID NO:4; or (b) a polypeptide having at least 90% identity to SEQ ID NO:4 that contains conservative amino acid substitutions, in which CMP-SAS function is conserved; or (c) a variant of a polypeptide specified in (a) or (b) that contains one or more fusions or truncations, in which CMP-SAS function is conserved; and ii) at least one copy of a sialic acid phosphate synthetase (SAS) gene, operably-linked to a promoter functional in the eukaryotic cell, wherein said SAS gene encodes a polypeptide that catalyzes the conversion of N-acetylmannosamine 6-phosphate (ManNAc-6-P) and phosphoenolpyruvate (PEP) to N-acetylneuraminate-9-phosphate (NeuNAc-9-P) and Pi; and wherein said polypeptide is (d) a polypeptide having at least 95% identity to SEQ ID NO: 6; or (e) a polypeptide having at least 90% identity to SEQ ID NO:6 that contains conservative amino acid substitutions and in which SAS function is conserved; or (f) a variant of a polypeptide specified in (d) or (e) that contains one or more fusions or truncations, in which SAS function is conserved.	

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25	**1999-12-08**	**US7388081 B2** **10/870,635** **US 20050143564 A1** **METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** ***FAMILY MEMBERS***	**DFB BIOTECH, INC.** (Fort Worth, TX) **PTA: 0 days** **EXPIRES 2019-12-08** **Publication Date: 2005-06-30** **Filing Date: 2004-06-17** **Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-08**	**Seki; Tatsuji (Osaka, JP)** **Fujiyama; Kazuhito (Osaka, JP)**	1. **A plant-produced glycoprotein** having a **human-type sugar chain**, obtained from a transformed plant cell, wherein the transformed plant cell was produced by: introducing to a plant cell a gene encoding a **galactosyltransferase enzyme** and **a gene of an exogenenous glycoprotein**; cultivating the transformed plant cell; and when desired separating the resulting glycoprotein. 2. The glycoprotein according to claim 1, wherein the galactosyltransferase enzyme transfers a galactose residue to a non-reducing terminal acetylglucosamine residue. 8. The glycoprotein according to claim 1 wherein the gene encoding an exogenous glycoprotein is selected from one or more of the group consisting of enzymes, hormones, cytokines, **antibodies**, vaccines, receptors and serum proteins. 11. The glycoprotein according to claim 8, wherein the exogenous glycoprotein encoded by the introduced gene is **an antibody selected from immunoglobulin G (IgG) or single chain variable region antibody fragments (scFV)**. 12. The glycoprotein according to claim 1 or 3 wherein the sugar chain is a **human-type sugar chain**.	***STATUS*** • EXPIRES 2019-12-08 • NO MAINTENANCE FEES DUE ***METHODOLOGY*** PLANT-PRODUCED GLYCOPROTEIN HAVING A HUMAN-TYPE SUGAR CHAIN

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Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
26	**2000-06-28**	US7029872 09/892,591 US 20020137134 A1 METHODS FOR PRODUCING MODIFIED GLYCOPROTEINS ***FAMILY MEMBERS*** 317 **FAMILY MEMBERS** ONLY ISSUED US / EP PATENTS and PCT SHOWN EP1297172B1 EP1467615B1 EP1522590B1 EP1597379B1 EP1597380B1 EP1597381B1 EP1597381B2 EP1599595B1 EP1599595B2 EP1599596B1 EP2080809B1 EP2083084B1 EP2088201B1 EP2196540B1 EP2316963B1 EP2333095B1 EP2333096B1 EP2339013B1 EP2359685B1 EP2365089B1 US7326681B2 US7332299B2	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **PTA: 145 DAYS** **EXPIRES 2021-11-19** **Publication Date: 2006-04-18** **Filing Date: 2001-06-27** **Earliest Effective Filing Date: 2000-06-28** **Priority Date: 2001-06-27**	**Gerngross; Tillman U. (Hanover, NH)**	1. **A method for producing a recombinant glycoprotein** comprising an N-glycan structure that comprises a Man5GlcNAc2 glycoform in a **lower eukaryotic host cell** that does not display alpha-2,6 mannosyltransferase activity with respect to the N-glycan on a glycoprotein, the method comprising the step of **introducing into the host cell a nucleic acid encoding an alpha-1,2 mannosidase enzyme** selected to have optimal activity in the ER or Golgi of said host cell, the enzyme comprising: (a) an alpha-1,2 mannosidase catalytic domain having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0; fused to (b) a cellular targeting signal peptide not normally associated with the catalytic domain selected to target the mannosidase enzyme to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, in excess of 30 mole % of the N-glycan structures attached thereto have a Man5GlcNAc2 glycoform that can serve as a substrate for GlcNAc transferase I in vivo. 2**. A method for producing a recombinant glycoprotein** comprising an N-glycan structure that comprises a GlcNAcMan5GlcNAc2 glycoform **in a lower eukaryotic host cell**, the cell genetically modified to produce N-glycan structures having an excess of 30 mole % of a Man5GlcNAc2 glycoform that can serve as a substrate for GlcNAc transferase I in vivo, the method comprising the step of **introducing into said host cell a nucleic acid encoding a GlcNAc transferase I enzyme** selected to have optimal activity in the ER or Golgi of said host cell. the enzyme comprising: (a) a GlcNAc transferase I catalytic domain having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0: fused to (b) a cellular targeting signal peptide not normally associated with the catalytic domain selected to target the GlcNAc transferase I enzyme to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAcMan5GlcNAc2 glycoform is produced. 3. **A method for producing a recombinant glycoprotein** comprising an N-glycan structure that comprises a GlcNAcMan5GlcNAc2 glycoform in **a lower eukaryotic host cell** that does not display alpha-1,6 mannosyltransferase activity with respect to the N-glycan on a glycoprotein, the method comprising the step or steps of introducing into the host cell one or more nucleic acids encoding at least two enzymes, the first enzyme selected to have optimal activity in the ER or Golgi of said host cell, **the enzyme comprising: (a) an alpha-1,2 mannosidase catalytic domain** having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0; fused to **(b) a cellular targeting signal peptide** not normally associated with the catalytic domain of (a) and	**"GERNGROSS I" FAMILY** ***STATUS*** • EXPIRES 2021-11-19 • MAINTENANCE FEES PAID UPTODATE ***METHODOLOGY*** FAMILY DRAWN TO PRODUCING A RECOMBINANT GLYCOPROTEIN IN A FUNGAL OR "LOWER EUKARYOTIC" HOST CELL

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		US7449308B2 US7598055B2 US7625756B2 US7629163B2 US7795002B2 US7863020B2 US7923430B2 US7935513B2 US7981660B2 US8067551B2 US8211691B2 US8268609B2 US8298811B2 US8299228B2 US8445227B2 US8697394B2 US8815544B2 US8877462B2 US8883483B2 US8932825B2 WO2002000879A2 WO2003056914A9 WO2004074458A3 WO2004074461A2 WO2004074497A3 WO2004074498A3 WO2004074499A3 WO2005090552A3 WO2005100584A3 WO2006014679A1 WO2006014683A3 WO2006014685A1 WO2006014725A1 WO2006014726A3 WO2006071280B1 WO2006071856A3 WO2007130638A3			selected to target the first enzyme to the ER or Golgi apparatus of the host cell; the second enzyme selected to have optimal activity in the ER or Golgi of said host cell, the enzyme comprising: **(c) a GlcNAc transferase I catalytic domain** having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0: fused to (d) a cellular targeting signal peptide not normally associated with the catalytic domain of (c) and selected to target the second enzyme to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAcMan5GlcNAc2 glycoform is produced. 4. **A method for producing a recombinant glycoprotein** comprising an N-glycan comprising a GlcNAcMan3GlcNAc2 glycoform in a **lower eukaryotic host cell genetically modified** to produce N-glycan structures having an excess of 30 mole % of a Man5GlcNAc2 glycoform that are converted in vivo to a GIcNAcMan5GlcNAc2 glycoform by GlcNAc transferase I activity localized in the ER or Golgi apparatus of the host cell, the method comprising the step of **introducing into the host cell a nucleic acid encoding a mannosidase II enzyme** selected to have optimal activity in the ER or Golgi of said host cell, the enzyme comprising: (a) a mannosidase II catalytic domain having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0; fused to (b) a cellular targeting signal peptide not normally associated with the catalytic domain selected to target the mannosidase II enzyme to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAcMan3GlcNAc2 glycoform is produced. 5. **A method for producing a recombinant glycoprotein** comprising an N-glycan comprising a GlcNAc2Man3GlcNAc2 glycoform in **a lower eukaryotic host cell genetically modified** to produce N-glycan structures having an excess of 30 mole % of a Man5GlcNAc2 glycoform that are converted in vivo to a GlcNAcMan3GlcNAc2 glycoform by GlcNAc transferase I and mannosidase II localized in the ER or Golgi apparatus of the host cell, the method comprising the step of introducing into the host cell a nucleic acid encoding a GlcNAc transferase II enzyme selected to have optimal activity in the ER or Golgi of said host cell, the enzyme comprising: (a) a GlcNAc transferase II catalytic domain having optimal activity in said ER or Golgi at a pH between 5.1 and 8.0; fused to (b) a cellular targeting signal peptide not normally associated with the catalytic domain selected to target the GlcNAc transferase II enzyme to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAc2Man3GlcNAc2 glycoform is produced.	

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28	**2000-06-28**	**US7449308** **10/371,877** **US 20040018590 A1** **COMBINATORIAL DNA LIBRARY FOR PRODUCING MODIFIED N-GLYCANS IN LOWER EUKARYOTES** ***FAMILY MEMBERS*** SEE ABOVE	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2021-11-11** **PTA: 226 DAYS** **Publication Date: 2008-11-11** **Filing Date: 2003-02-20** **Earliest Effective Filing Date: 2000-06-28** **Priority Date: 2001-06-27**	**Gerngross; Tillman U. (Hanover, NH)** **Wildt; Stefan (Lebanon, NH)** **Choi; Byung-Kwon (Norwich, VT)** **Nett; Juergen Hermann (Grantham, NH)** **Bobrowicz; Piotr (White River Junction, VT)** **Hamilton; Stephen R. (Enfield, NH),** **Davidson; Robert C (Enfield, NH)**	1. **A method for producing a recombinant glycoprotein** comprising complex or hybrid N-glycans **in a yeast or filamentous fungus host cell** that does not display a 1,6 mannosyltransferase activity, the method comprising the step of introducing into the host cell a nucleic acid encoding an alpha-1,2 mannosidase enzyme, the enzyme comprising: a) an alpha-1,2 mannosidase catalytic domain; fused to b) a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the enzyme to the ER or Golgi apparatus of the host cell where the enzyme functions optimally; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, greater than 30 mole percent of the N-glycan structures attached thereto are converted to a Man5GlcNAc2 glycoform that can serve as a substrate for additional glycosylation enzymes so that the glycoprotein comprising complex or hybrid N-glycans can be formed. 29. A **method for producing a recombinant glycoprotein** comprising N-glycan GlcNAcMan5GlcNAc2 glycoforms **in a yeast or filamentous fungus host cell** which produces N-glycan structures having greater than 30 mole percent of a Man5GlcNAc2 glycoform that can serve as a substrate for GlcNAc transferase I in vivo, the method comprising the step of introducing into the host cell a nucleic acid encoding a GlcNAc transferase I enzyme, the enzyme comprising: a) a GIcNAc transferase I catalytic domain; fused to b) a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the catalytic domain to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAcMan5GlcNAc2 glycoform is produced. 30. A **method for producing a recombinant glycoprotein** comprising N-glycan GIcNAcMan3GlcNAc2 glycoforms **in a yeast or filamentous fungus** host cell which produces N-glycan structures having greater than 30 mole percent of a Man5GlcNAc2 glycoform that are converted in vivo to a GlcNAcMan5GlcNAc2 glycoform by GlcNAc transferase I, the method comprising the step of introducing into the host cell a nucleic acid encoding a mannosidase II enzyme, the enzyme comprising: a) a mannosidase II catalytic domain; fused to b) a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the catalytic domain to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAcMan3GlcNAc2 glycoform is produced. 31. A **method for producing a recombinant glycoprotein** comprising N-glycan GlcNAc2Man3GlcNAc2 glycoforms **in a yeast or filamentous fungus host cell** which produces N-glycan structures having greater than 30 mole percent of a Man5GlcNAc2 glycoform that are converted in vivo to a GlcNAcMan3GlcNAc2 by a GlcNAc transferase and	**"GERNGROSS I" FAMILY** ***STATUS*** • MAINTENANCE FEES PAID UPTODATE • EXPIRES 2021-11-11 ***METHODOLOGY*** PRODUCTION OF A GLYCOPROTEIN IN A YEAST OR FILAMENTOUS FUNGUS HOST CELL e.g. PICHIA SP

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					mannosidase II, the method comprising the step of introducing into the host cell a nucleic acid encoding a GlcNAc transferase II enzyme, the enzyme comprising: a) a GlcNAc transferase II catalytic domain; fused to b) a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the catalytic domain to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a GlcNAc2Man3GlcNAc2 glycoform is produced.	
33	**2000-06-28**	**US8067551** **12/291,373** **US 20090155847 A1** **COMBINATORIAL DNA LIBRARY FOR**	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006**	**Gerngross; Tillman U. (Hanover, NH)** **Wildt; Stefan (Lebanon, NH)** **Choi; Byung-Kwon (Norwich, VT)**	1. **A glycoprotein composition** comprising a recombinant human glycoprotein wherein **at least 60 % of the oligosaccharide structures on the glycoprotein consist of a GlcNAcMan.sub.5GlcNAc.sub.2 oligosaccharide structure.** 2. **A glycoprotein composition** comprising a recombinant human glycoprotein wherein at least 60% of the oligosaccharide structures on the glycoprotein in consist of a **$GlcNAcMan_5GlcNAc_2$** oligosaccharide structure, and wherein the glycoprotein is produced in a Pichia pastoris genetically engineered to lack OCH1 activity and to express (a) a chimeric	**"GERNGROSS II" FAMILY** ***STATUS*** • MAINTENANCE FEES - 4TH YEAR FEE WINDOW OPENS: 11/29/2014

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		PRODUCING MODIFIED N-GLYCANS IN LOWER EUKARYOTES ***FAMILY MEMBERS*** SEE ABOVE	**EXPIRES 2021-06-27** **PTA: 0 DAYS** **Publication Date: 2009-06-18** **Filing Date: 2008-11-07** **Earliest Effective Filing Date: 2000-06-28** **Priority Date: 2001-06-27**	**Nett; Juergen Hermann (Grantham, NH)** **Bobrowicz; Piotr (White River Junction, VT)** **Hamilton; Stephen R. (Enfield, NH),** **Davidson; Robert C (Enfield, NH)**	mannosidase I comprising an alpha-1,2 mannosidase catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the enzyme to the ER or Golgi apparatus of the host cell; (b) a chimeric N-acetylglucosamine transferase I (GnT I) comprising a GnT I catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the catalytic domain to the ER or Golgi apparatus of the host cell; and (c) a uridine diphosphate-N-acetylglucosamine (UDP-GlcNAc) transporter. 6. **A glycoprotein composition** comprising a recombinant human glycoprotein wherein at least 50% to 70% of the oligosaccharide structures on the glycoprotein consist of a Man.sub.5GlcNAc.sub.2 oligosaccharide structure. 7. **A glycoprotein composition** comprising a recombinant human glycoprotein wherein at least 50% to 70% of the oligosaccharide structures on the glycoprotein consist of a **$GlcNAcMan_5GlcNAc_2$** oligosaccharide structure, and wherein the glycoprotein is produced in a Pichia pastoris genetically engineered to lack OCH1 activity and to express (a) a chimeric mannosidase I comprising an alpha-1,2 mannosidase catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the enzyme to the ER or Golgi apparatus of the host cell; (b) a chimeric N-acetylglucosamine transferase I (GnT I) comprising a GnT I catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target the catalytic domain to the ER or Golgi apparatus of the host cell; and (c) a uridine diphosphate-N-acetylglucosamine (UDP-GlcNAc) transporter.	• EXPIRES 2021-06-27 ***METHODOLOGY*** GLYCOPROTEINS WHEREIN AT LEAST 60% OF THE OLIGOSACCHARIDE STRUCTURES ON THE GLYCOPROTEIN IN CONSIST OF A $GlcNAcMan_5GlcNAc_2$ OLIGOSACCHARIDE STRUCTURE
34	**2000-06-28**	**US8067551** **12/291,373** **US 20090155847 A1** **N-ACETYL-GLUCOSAMINYL-TRANSFERASE III EXPRESSION IN LOWER EUKARYOTES**	**GLYCOFI, INC*** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2021-06-27** **PTA: 0 DAYS**	**Bobrowicz; Piotr (White River Junction, VT)** **Hamilton; Stephen R. (Enfield, NH),** **Gerngross; Tillman U. (Hanover, NH)** **Wildt; Stefan (Lebanon, NH)**	1. **A method for producing a recombinant glycoprotein** that comprises **a bisected N-glycan** in a yeast host cell, the method comprising: (a) providing a yeast host cell that has been genetically engineered to be diminished or depleted in the activity of an initiating .alpha.-1,6-mannosyltransferase and to comprise a nucleic acid sequence encoding a polypeptide comprising .alpha.-1,2-mannosidase activity, wherein the yeast host cell has the ability to produce a recombinant glycoprotein comprising more than 50 mole % of a Man5GlcNAc2 intermediate which is a productive substrate for GnTI in vivo; (b) transforming the yeast host cell with a nucleic acid sequence encoding a polypeptide comprising N-acetylglucosaminyltransferase I (GnT I) activity, and a nucleic acid sequence	**"BOBROWICZ I" FAMILY** ***STATUS*** • MAINTENANCE FEES - 4TH YEAR FEE WINDOW OPENS: 05/21/2016 • EXPIRES 2021-06-27

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		FAMILY MEMBERS SEE ABOVE	**Publication Date: 2011-11-29** **Filing Date: 2008-11-07** **Earliest Effective Filing Date: 2000-06-28** **Priority Date: 2001-06-27**	**Choi; Byung-Kwon (Norwich, VT)** **Nett; Juergen Hermann (Grantham, NH)** **Davidson; Robert C (Enfield, NH)**	encoding a polypeptide comprising N-acetylglucosaminyltransferase III (GnT III) catalytic activity; (c) transforming the yeast host cell with a nucleic acid sequence encoding the recombinant glycoprotein; and (d) growing the yeast host cell under conditions that allow the host cell to produce the recombinant glycoprotein, wherein the recombinant glycoprotein comprises bisecting N-glycans on Man5GlcNAc2 or a Man3GlcNAc2 core structure. 3. The method of claim 1, wherein the host cell is selected from the group consisting of Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia ptjpert, Pichia stiptis, Pichia methanolica, Pichia sp., Saccharomyces cerevisiae, Saccharomyces sp., Hansenula polymorpha, Kluyveromyces sp., and Candida albicans.	***METHODOLOGY*** METHOD FOR PRODUCING A RECOMBINANT GLYCOPROTEIN THAT COMPRISES A BISECTED N-GLYCAN IN A YEAST HOST CELL
29	**2000-10-06**	**US8329443 B2** **13/102,565** **US 20110250643 A1** **ANTIBODY COMPOSITION-PRODUCING CELL** ***FAMILY MEMBERS*** AU2001294198B2 AU2001294198B9	**KYOWA HAKKO KIRIN CO LTD** (Tokyo, JP) **EXPIRES 2021-10-05** **PTA: 0 DAYS** **Publication Date: 2012-12-11** **Filing Date: 2011-05-06**	**Kanda; Yutaka (Machida, JP)** **Satoh; Mitsuo (Machida, JP)** **Nakamura; Kazuyasu (Machida, JP)** **Uchida; Kazuhisa (Machida, JP)** **Shinkawa; Toyohide (Machida, JP)**	**1. A mammalian cell into which a gene encoding an antibody molecule is introduced,** wherein said mammalian cell produces an antibody composition comprising an antibody molecule having complex N-glycoside-linked sugar chains bound to the Fc region, wherein among the total complex N-glycoside-linked sugar chains bound to the Fc region in the composition, **the ratio of a sugar chain in which fucose is not bound to N-acetylglucosamine in the reducing end in the sugar chain is 20% or more**, and the **cell is resistant to a lectin** which recognizes a sugar chain in which the 1-position of fucose is bound to the 6-position of N-acetyl in the reducing end through an α-bond in the complex N-glycoside-linked sugar chain, wherein said lectin resistance results from decreasing or deleting the activity of an enzyme in said cell, said enzyme being selected from the group consisting of (a)-(d):	**"KANDA" FAMILY** ***STATUS*** • EXPIRES 2021-10-05 • NO MAINTENANCE FEES DUE ***METHODOLOGY*** CELLS PRODUCING ANTIBODY HAVING ENHANCED ANTIBODY-DEPENDENT

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		AU200194198A BR200114475A CA2424602A1 CA2424602C CA2785941A1 CN102311986A CN103333860A CN1894406A EA13224B1 EA13563B1 EP1331266A1 EP1331266A4 EP2314685A1 EP2314686A1 HU200402066A2 HU200402066A3 JP04290423B2 JP04740931B2 JP04741011B2 JP05301525B2 JP05384601B2 JP05384677B2 JP05547754B2 JP2008113663A JP2009142288A JP2011092203A JP2012075441A JP2012085655A JP2012087131A JP2013231032A JP2014043455A KR2003081312A KR877676B1 MX2003002974A MX2003PA002974A PL218428B1 PL362520A1 US6946292 B2 US7393683 B2 US7425446 B2 US7737325 B2 US7741442 B2 US7846725 B2 US8039595 B2	**Earliest Effective Filing Date: 2000-10-06** **Priority Date: 2001-10-05**	**Yamane; Naoko (Machida, JP)** **Hosaka; Emi (Machida, JP)** **Yamano; Kazuya (Machida, JP)** **Yamasaki; Motoo (Machida, JP)** **Hanai; Nobuo (Machida, JP)**	(a) GMD (GDP-mannose 4,6-dehydratase); (b) Fx (GDP-keto-6-deoxymannose 3,5-epimerase, 4-reductase); (c) GFPP (GDP-beta-L-fucose pyrophosphorylase); and (d) α1,6-fucosyltransferase, and wherein said antibody composition has greater **antibody-dependent cellular cytotoxicity (ADCC) activity** than an antibody composition produced by expressing said gene in the parent mammalian cell that has not had the activity of the enzyme selected from the group of (a)-(d) decreased or deleted and that is not resistant to said lectin. 2. The cell according to claim 1, wherein α1,6-fucosylation of the antibody composition is decreased or deleted by a technique selected from the group consisting of the following (a), (b), (c), (d) and (e): (a) a gene disruption technique targeting a gene encoding the enzyme; (b) a technique for introducing a dominant negative mutant of a gene encoding the enzyme; (c) a technique for introducing mutation into the enzyme; (d) a technique for inhibiting transcription or translation of a gene encoding the enzyme; (e) a technique for selecting a cell line resistance to the lectin which recognizes a sugar chain in which the 1-position of fucose is bound to the 6-position of N-acetylglucosamine in the reducing end through an α-bond in the complex N-glycoside-linked sugar chain. 3. The cell according to claim 1, wherein the cell is selected from the group consisting of the following (a) to (i): (a) a CHO cell derived from a Chinese hamster ovary tissue; (b) a rat myeloma cell line, YB2/3HL.P2.G11.16Ag.20 cell; (c) a mouse myeloma cell line, NSO cell; (d) a mouse myeloma cell line, SP2/0-Ag14 cell; (e) a BHK cell derived from a syrian hamster kidney tissue; (f) an antibody-producing hybridoma cell; (g) a human leukemia cell line Namalwa cell; (h) a non-human embryonic stem cell;	CELLULAR CYTOTOXICITY (ADCC) ACTIVITY ***PATENT FAMILY*** **US6946292B2 - claims drawn to an isolated fucosyltransferase knock-out host cell** **US7393683B2- claims drawn to an isolated mammalian host cell in which the expression of the mRNA of .alpha.1,6-fucosyltransferase is inhibited by RNA interference** **US7425446B2- claims drawn to an isolated mammalian host cell which has decreased or no .alpha.1,6-fucosyltransferase activity** **US7737325B2- claims drawn to a non-human knock-out mammal lacking alpha-1,6-fucosylation** **US7741442B2 - claims require 50% or more of the antibodies are non-fucosylated** **US7846725B2 - claims require a CHO in which GDP-mannose 4,6-dehydratase (GMD) is inhibited by RNA interference** **US8039595B2 (US20090191592A1) claims require >50% antibodies do not contain fucose** **US8067232B2 (US20080227196A1) claims drawn to CHO cells having no α1,6-fucosyltransferase activity** **US8101185B2 (US20110052610A1) claims drawn to antibody molecules that bind an interleukin-5 receptor** **US8110195B2 (US20110059115A1) claims drawn to antibody molecules that bind ganglioside GM2** **US8158760B2 (US20090191199 A1) claims**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		US8067232 B2 US8101185 B2 US8110195 B2 US8158760 B2 US8367407 B2 US8895266 B2 WO2002031140A1			(i) a non-human fertilized egg cell. 4. The cell according to claim 1, wherein the lectin is selected from a Lens culinaris lectin (LCA), a pea lectin (PSA), a broad bean lectin (VFA) and an Aleuria aurantia lectin (AAL).	**drawn to CD20 antibodies** **US8329443B2 (US20110250643A1) claims drawn to lectin resistant mammalian cells** **US8367407B2 (US20090228994A1) claims drawn to fucosylation** **US8895266 B2 claims to methods for producing an antibody composition in a mammalian cell that is resistant to a lectin**
30	**2001-10-25**	**EP1443961 B1** **GLYCOPROTEIN COMPOSITIONS** ***FAMILY MEMBERS*** AT430580T AU2002337935B2 BR200213761A CA2463879C CN100423777C CN101357943A,CN1607960A DE60232265D1 DK1443961T3 ES2326964T3 HK1076388A1 HU200600342A2 HU200600342A3 IL161412D0 IL220142D0 JP2005532253A JP2010248228A JP2014076997A	**GENENTECH/ ROCHE** (South San Francisco, CA) **REVOKED 2012-12-12** **Publication Date: 2009-05-06** **Filing Date: 2002-10-22** **Earliest Effective Filing Date: 2001-10-25** **Priority Date: 2002-10-22**	**Presta, Leonard**	**1. A composition comprising a glycoprotein having a human IgG Fc region,** wherein about 51-100% of the glycoprotein in the composition comprises a mature core carbohydrate structure **which lacks fucose**, attached to the Fc region of the glycoprotein, wherein the **Fc region comprises an amino acid sequence that differs from a native sequence human IgG Fc region**, and wherein the **glycoprotein binds FcγRIII with better affinity**, or **mediates antibody-dependent cell-mediated cytotoxicity (ADCC)** more effectively, than the glycoprotein with a mature core carbohydrate structure including fucose attached to the Fc region of the glycoprotein. 2. The composition of claim 1, wherein the Fc region comprises an amino acid substitution at any one or more of amino acid positions 256, 290, 298, 312, 326, 330, 333, 334, 360, 378 or 430, utilizing EU numbering for the Fc region residues. 3. The composition of claim 2, wherein the Fc region comprises amino acid substitutions at any two or three of the residues at positions 298, 333 and 334. 4. The composition of claim 3, wherein the Fc region comprises amino acid substitutions at positions 298, 333 and 334. 5. The composition of claim 4, wherein the replacement residues at postitions 298, 333 and 334 are alanine. 6. A composition according to any of claims 1 to 5, wherein about 80-100% of the glycoprotein in the composition comprises a mature core carbohydrate structure **which lacks fucose**, attached to the Fc region of the glycoprotein.	**"PRESTA" FAMILY** ***STATUS*** • REVOKED 2012-12-12 ***METHODOLOGY*** GLYCOPROTEIN HAVING A HUMAN IGG FC REGION THAT BINDS FCIRIII WITH BETTER AFFINITY, OR MEDIATES ANTIBODY-DEPENDENT CELL-MEDIATED CYTOTOXICITY (ADCC) MORE EFFECTIVELY *PATENT FAMILY* **ALL US/EP PATENT APPLICATIONS ARE ABANDONED**

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		KR2004066105A KR988949B1 MX2004003798A MX2004PA003798A NZ532526A PL213948B1, PL372709A1 US20030157108A1 US20070020260A1 US20080095762A1 US20100255013A1 US20110086050A1 WO2003035835A2 WO2003035835A3 ZA200403000A			7. A composition according to any of claims 1 to 6, wherein the glycoprotein comprises an **antibody**. 8. A composition according to any of the preceding claims, wherein the human IgG Fc region comprises a **human IgG1 IgG2, IgG3 or IgG4 Fc region.** 9. A composition according to claim 7 or claim 8, wherein the antibody is a **chimeric, humanized or human antibody**. 14. A composition according to any of the preceding claims, wherein the glycoprotein has been produced by a **chinese hamster ovary (CHO) cell**. 16. A composition according to any of claims 1 to 14, wherein the glycoprotein is essentially free of **bisecting N-acetylglucosamine** (GlcNAc) attached to the mature core carbohydrate structure. 17. A composition according to any of claims 1 to 14, wherein the glycoprotein **has bisecting N-acetylglucosamine (GlcNAc)** attached to the mature core carbohydrate structure. 18. A composition according o any of claims 1 to 14, 16 or 17, wherein the glycoprotein has **one or more galactose residues** attached to the mature core carbohydrate structure. 20. A composition according to any of claims 1 to 14 or 16 to 19, wherein the glycoprotein has **one or more sialic acid residues attached to the mature core carbohydrate structure.** 26. A composition according to any of claims 1 to 6, wherein the glycoprotein is an **immunoadhesin**. 31. A host cell comprising nucleic acid encoding a glycoprotein which comprises an Fc region as defined in any of claims 1 to 5, 7 to 12, or 16 to 21, wherein about 80-100% of the glycoprotein produced by the host cell comprises a mature core carbohydrate structure **which lacks fucose**, attached to the Fc region of the glycoprotein. 32. The host cell of claim 31 which is a **chinese hamster ovary (CHO) cell**. 34. **A method for producing a glycoprotein** comprising culturing a host cell according to any of claims 31 to 33 so that the nucleic acid is expressed.	

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
31	**2001-12-27**	**EP1467615 B1** **METHOD TO ENGINEER MAMMANLIAN-TYPE CARBOHYDRATE STRUCTURES** ***FAMILY MEMBERS*** SEE ABOVE	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2022-12-24** **Publication Date: 2013-01-23** **Filing Date: 2002-12-24** **Earliest Effective Filing Date: 2001-12-27**	**Wildt Stefan, (Lebanon, Nh)** **Miele Robert (Lebanon, Nh)** **Nett Juergen (Enfield, Nh)** **Davidson Robert (Enfield, NH)**	1. A method for producing a glycoprotein comprising the expression of a nucleic acid encoding the glycoprotein in a lower eukaryotic host cell, which has diminished or depleted activity of one or more enzymes selected from: (a) dolichyl-P-Man:$Man_5GlcNAc_2$-PP-dolichyl alpha-1,3 mannosyltransferase (alg3); (b) dolichyl-P-Man:$Man_6GlcNAc_2$-PP-dolichyl alpha-1,2 mannosyltransferase (alg9); or (c) dolichyl-P-Man:$Man_7GlcNAc_2$-PP-dolichyl alpha-1,6 mannosyltransferase (alg12); said host cell further expressing: (i) an α-1,2-mannosidase catalytic domain fused to a targeting peptide that targets the endoplasmatic reticulum (ER) or Golgi apparatus in the host cell; and (ii) a GlcNAc transferase I (GnT I) catalytic domain fused to a targeting peptide that targets the endoplasmatic reticulum (ER) or Golgi apparatus of the host cell; to produce a glycoprotein having $GlcNAcMan_4GlcNAc_2$ or $GlcNAcMan_3GlcNAc_2$ core structures.	**"WILDT" FAMILY** ***STATUS*** • EXPIRES 2022-12-24 • OPPOSITION filed 10-22-2013 by Novartis AG ***METHODOLOGY*** PRODUCING A HUMAN-LIKE GLYCOPROTEIN IN A NON-HUMAN EUKARYOTIC HOST CELL BY DIMINISHING OR DEPLETING THE ACTIVITY OF ONE OR MORE ENZYMES IN THE HOST CELL THAT TRANSFERS RESIDUE TO THE 1,6 ARM OF A LIPID-LINKED OLIGOSACCHARIDE STRUCTURE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
32A	**2002-07-15**	**US7645609B2** **10/695,243** **US 20040171826 A1** **METHODS AND MEDIA FOR CONTROLLING SIALYLATION OF PROTEINS PRODUCED BY MAMMALIAN CELLS** **FAMILY MEMBERS** AT359358T AU2003249055A1 AU2003249055B2 CA2492267A1 CA2492267C CY1107689T1 DE60313188D1 DE60313188T2 DK1543106T3 EP1543106A2 EP1543106A4 EP1543106B1 ES2285188T3 JP04510938B2 JP2005532813A MX2005000552A MX2005PA000552A PL376381A1 PT1543106E SI1543106T1	**IMMUNEX CORPORATION*** *** acquired by AMGEN** (Thousand Oaks, CA) **EXPIRES 2024-02-15** **PTA: 215 DAYS** **Publication Date: 2010-01-12** **Filing Date: 2003-07-15** **Earliest Effective Filing Date: 2002-07-15** **Priority Date: 2003-07-15**	**Follstad; Brian D. (Seattle, WA)**	1. **A method for increasing the sialic acid content of a protein produced by CHO cells** comprising culturing the CHO cells in a medium comprising mannose, galactose, fructose, and N-acetylmannosamine, wherein culturing the CHO cells in the medium can increase the sialylation of a protein produced by the CHO cells. 2. The method of claim 1, wherein the medium is serum free. 3. The method of claim 1, wherein the CHO cells are cultured in the medium during a production phase. 4. The method of claim 1, wherein the concentrations of galactose, mannose, and fructose in the medium are each from about 1 mM to about 10 mM and the concentration of N-acetylmannosamine in the medium is at least about 0.8 mM. 5. The method of claim 1, wherein the concentrations of galactose, mannose, and fructose in the medium are each from about 1.5 mM to about 4.5 mM. 6. The method of claim 1, wherein the protein is a secreted, recombinant protein. 7. The method of claim 1, wherein the CHO cells are cultured at a temperature from about 29.degree. C. to about 36.degree. C. 8. **A method for increasing the sialic acid content of a protein produced by CHO cells** comprising culturing the CHO cells in a medium comprising galactose and N-acetylmannosamine, wherein culturing the CHO cells in the medium can increase the sialylation of a protein produced by the CHO cells. 9. The method of claim 8, wherein the medium is serum free. 10. The method of claim 8, wherein the CHO cells are cultured in the medium during a production phase. 11. The method of claim 8, wherein the concentration of galactose in the medium, is from about 1 mM to about 10 mM and the concentration of N-acetylmannosamine in the medium is at least about 0.8 mM. 12. The method of claim 8, wherein the concentration of galactose in the medium, is from about 1.5 mM to about 4.5 mM.	***STATUS*** • **EXPIRES** 2024-02-15 • 8TH YEAR FEE WINDOW OPENS: 01/12/2017 ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO A METHOD FOR INCREASING THE SIALIC ACID CONTENT OF A PROTEIN PRODUCED BY CHO CELLS BY SUPPLEMENTING THE CULTURE MEDIA WITH MANNOSE, GALACTOSE, FRUCTOSE, AND N-ACETYLMANNOSAMINE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		US20040115768A1 WO2004008100A2 WO2004008100A3			13. The method of claim 8, wherein the protein is a secreted, recombinant protein. 14. The method of claim 8, wherein the CHO cells are cultured at a temperature from about 29.degree. C. to about 36.degree. C. 15. **A method for increasing the sialic acid content of a protein produced by CHO cells** comprising culturing the CHO cells in a medium comprising mannose, fructose, and galactose, wherein culturing the CHO cells in the medium can increase the sialylation of a protein produced by the CHO cells. 16. The method of claim 15, wherein the medium is serum free. 18. The method of claim 15, wherein the concentrations of galactose, mannose, and fructose in the medium are each from about 1 mM to about 10 mM. 19. The method of claim 18, wherein the concentrations of galactose, mannose, and fructose in the medium are each from about 1.5 mM to about 4.5 mM. 20. The method of claim 15, wherein the protein is a secreted, recombinant protein. 21. The method of claim 15, wherein the CHO cells are cultured at a temperature from about 29.degree. C. to about 36.degree. C. 22. **A method for increasing the sialic acid content of a protein produced by CHO cells** comprising culturing the CHO cells in a medium comprising fructose and galactose, wherein culturing the CHO cells in the medium can increase the sialylation of a protein produced by the CHO cells. 23. The method of claim 22, wherein the medium is serum free. 25. The method of claim 22, wherein the concentrations of galactose and fructose in the medium are each from about 1 mM to about 10 mM. 26. The method of claim 25, wherein the concentrations of galactose and fructose in the medium are each from about 1.5 mM to about 4.5 mM. 27. The method of claim 22, wherein the protein is a secreted, recombinant protein. 28. The method of claim 22, wherein the CHO cells are cultured at a temperature from about 29.degree. C. to about 36.degree. C.	
32B	**2002-07-15**	**EP1543106B1**	**IMMUNEX CORPORATION***	**Follstad; Brian D. (Seattle, WA)**	1. **A method for controlling the sialic acid content of a protein** produced by mammalian cells comprising culturing the cells in a medium comprising galactose and fructose. 2. The method of claim 1, wherein the medium further comprises mannose.	***STATUS*** • **EXPIRES 2023-07-14**

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		METHODS AND MEDIA FOR CONTROLLING SIALYLATION OF PROTEINS PRODUCED BY MAMMALIAN CELLS **FAMILY MEMBERS** SEE ABOVE	*** acquired by AMGEN** (Thousand Oaks, CA) **EXPIRES 2023-07-14** **PTA: 215 DAYS** **Publication Date: 2005-06-22\ Filing Date: 2003-07-14** **Earliest Effective Filing Date: 2002-07-15** **Priority Date: 2003-07-15**		3. The method of claim 2, wherein the medium further comprises N-acetylmanno s amine.; 4. The method of claim 1, wherein the medium is serum free. 5. The method of claim 2, wherein the medium is serum free. 6. The method of claim 2, wherein the concentrations of galactose, mannose, and fructose are each from about 1 mM to about 10 mM. 7. The method of claim 3, wherein the concentration of N-acetyl-mannosamine in the medium is at least about 0.8 mM. 8. The method of claim 1, wherein the protein is a secreted, recombinant protein. 9. The method of claim 1, wherein the mammalian cells are CHO cells. 10. The method of claim 1, wherein the cells are cultured at a temperature from about 29°C to about 36°C. 11. A medium for culturing mammalian cells comprising galactose and fructose. 12. The medium of claim 11, further comprising mannose. 13. The medium of claim 12, further comprising N-acetylmannosamine. 14. The medium of claim 12, wherein the concentrations of galactose, mannose, and fructose are each from about 1 mM to about 10 mM. 15. The method of claim 13, wherein the concentration of N-acetylmannosamine in the medium is at least about 0.8 mM. 16. The medium of claim 11, wherein the medium is serum free. 17. The medium of claim 12, wherein the medium is serum free. 18. The medium of claim 13, wherein the medium is serum free. 19. **A method for controlling the sialic acid content of a protein** comprising culturing a mammalian cell that produces the protein in medium comprising N-acetyl-mannosamine and galactose. 20. The method of claim 19, wherein the medium further comprises fructose and mannose. 21. The method of claim 20, wherein the concentration of fructose in the medium is from about 1.5 mM to about 4.5 mM and wherein the concentration of mannose in the medium is from about 1.5 mM to about 4.5 rnM.	• **NO OPPOSITION FILED** • **ANNUAL FEES PAID UPTODATE** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO A METHOD FOR INCREASING THE SIALIC ACID CONTENT OF A PROTEIN PRODUCED BY CHO CELLS BY SUPPLEMENTING THE CULTURE MEDIA WITH MANNOSE, GALACTOSE, FRUCTOSE, AND N-ACETYLMANNOSAMINE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					22. The method of claim 19, wherein the cell is cultured at a temperature from about 29°C to about 35°C.; 23. The method of claim 19, wherein the concentration of N-acetylmannosamine in the medium is at least about 0.8 mM and wherein the concentration of galactose in the medium is from about 1.5 mM to about 4. 5 mM. 24. The method of claim 19, wherein the protein is a secreted protein. 25. The method of claim 19, wherein the protein is a recombinant protein. 26. The method of claim 19, wherein the cell is a CHO cell. 27. In a medium for culturing mammalian cells, the combination with the medium of galactose and N-acetylmannosamine. 28. The medium of claim 27, wherein the medium further comprises fructose and mannose. 29. The medium of claim 28, wherein the concentration of fructose in the medium is from about 1.5 mM to about 4.5 mM and wherein the concentration of mannose in the medium is from about 1.S mM to about 4.5 mM. 30. The medium of claim 27, wherein the concentration of N-acetyl-mannosanine in the medium is at least about 0.8 mM and wherein the concentration of galactose in the medium is from about 1.S mM to about 4. 5 mM. 31. The medium of claim 27, wherein the mammalian cells are CHO cells. 32. The medium of claim 27, wherein the medium is serum-free. 33. **In a method for producing a protein by culturing mammalian cells that express the protein**, the improvement comprising culturing the mammalian cells at a temperature from about 29°C to about 36°C in a medium comprising N-acetyl-mannosamine. 34. The method of claim 33, wherein the medium further comprises galactose.-25 35. The method of claim 34, wherein the medium further comprises fructose and mannose. 36. The method of claim 35, wherein the concentration of galactose in the medium is from about 1.S mM to about 4.5 mM, wherein the concentration of mannose in the medium is from about 1.5 mM to about 4.5 mM, and wherein the concentration of fructose in the medium is from about 1.S mM to about 4.5 mM. 37. The method of claim 33, wherein the concentration of N-acetyl-mannosamine in the medium is at least about 0.S mM.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					38. The method of claim 33, wherein the medium is serum-free. 39. The method of claim 33, wherein the mammalian cells are CHO cells.; 40. The method of claim 33, wherein the protein is a secreted, recombinant protein. 41. **A method for controlling the static acid content of a recombinant protein** comprising culturing mammalian cells that express the recombinant protein at a temperature from about 29°C to about 36°C in a medium comprising fructose, galactose, mannose, and N-acetylmannosamine, wherein the concentration of fructose in the medium is from about 1.0 mM to about 5.0 mM, wherein the concentration of galactose in the medium is from about 1.0 mM to about 5.0 mM, wherein the concentration mannose in the medium is from about 1.0 mM to about 5.0 mM, and i wherein the concentration N-acetylmannosamine in the medium is at least O.8mM.-26	
	2002-12-23	**US7332303** **10/740645** **US20050084933A1** **PRODUCT QUALITY ENHANCEMENT IN MAMMALIAN CELL CULTURE PROCESSES FOR PROTEIN PRODUCTION** **FAMILY MEMBERS** AT488600T AU2003303394A1	**SQUIBB BRISTOL MYERS (Princeton NJ)** **EXPIRES 2023-12-18** **PTA: 0 days** **Publication Date: 2005-04-21** **Filing Date: 2003-12-18** **Earliest Effective**	**Schilling, Bernhard (Syracuse, NY)** **Gangloff, Scott (Bensalem, PA)** **Kothari, Dharti (Princeton, NJ)** **Leister, Kirk (Fayetteville, NY)** **Matlock, Linda (Parish, NY)** **Zegarelli, Stephen G. (North Syracuse, NY)**	1. **A cell culture process for the production of a soluble CTLA4 molecule**, comprising: a) culturing CHO cells which produce a soluble CTLA4 molecule in cell culture under conditions that allow for protein production; and b) feeding the cells with feeding medium containing D-galactose. 2. The process according to claim 1, further comprising: c) culturing the CHO cells at a temperature at 37.degree. C. under conditions and for a time period that allow for cell growth; d) culturing the CHO cells at a second temperature at 34.degree. C. starting at about day 6 of the culture; and e) culturing the CHO cells at a third temperature at 32.degree. C. starting at about day 10 of the culture. 6. The cell culture process of claim 5, wherein the cell culture contains a glucose level maintained at 3 g/L. 7. The cell culture process of claim 5, wherein sialylation of the soluble CTLA4 molecule is increased compared to sialylation in a culture without feeding the cells with feeding medium containing D-galactose.	**STATUS** • **EXPIRES 2023-12-18** • **EP1575998A4 – WITHDRAWN** • **US20120015438A1 ABANDONED** • **US7541164B2 - claims drawn to the culture host cells which produce soluble cytotoxic T-lymphocyte antigen-4 (CTLA4)** **METHODOLOGY** CLAIMS DRAWN TO THE CULTURE OF HOST CELLS WHICH PRODUCE SOLUBLE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		AU2003303394B2 BR200316882A CA2508925A1 CA2508925C CN100402660C CN1820080A CO5590971A2 DE60335024D1 DK1576182T3 EP1576182A2 EP1576182A4 EP1576182B1 ES2354610T3 HK1075474A1 IL168873A JP04496086B2 JP2006511224A KR1088223B1 KR2005103466A MX2005006522A MX2005PA006522A PL377603A1 PT1576182E SI1576182T1 TWI328614B US20080070280A1 US7332303B2 WO2004058944A2 WO2004058944A3 WO2004058944A8	**Filing Date: 2002-12-23** **Priority Date: 2003-12-18**	**Joosten, Christoph E. (Manlius, NY)** **Basch, Jonathan D. (Dewitt, NY)** **Sakhamuri, Sivakesava (Manlius, NY)** **S. Lee, Steven (Manlius, NY)**	8. The cell culture process of claim 5, further comprising: a) culturing the CHO cells at a temperature at 37.degree. C. under conditions and for a time period that allow for cell growth; b) culturing the CHO cells at a second temperature at 34.degree. C. starting at bout day 6 of the culture; and c) culturing the CHO cells at a third temperature at 32.degree. C. starting at about day 10 of the culture. 9. The cell culture process of claim 8, further comprising purifying the soluble CTLA4 molecule. 11. The cell culture process of claim 1, wherein the soluble CTLA4 molecule comprises the amino acid sequence beginning with methionine at position +1 or alanine at position -1 and ending at aspartic acid at position 124 as shown in SEQ ID NO: 2 joined to an immunoglobulin moiety comprising hinge, CH2 and CH3 domains, wherein the cells are fed daily with a volume of feeding medium that is at least 1% of culture volume and the feeding medium contains D-galactose at a concentration of 3 to 25 g/L, wherein the cell culture volume is at least 500 liters, and wherein the cell culture has an initial seeding density. 32. **A cell culture process for the production of a soluble CTLA4 molecule,** comprising: a. culturing host cells which produce a soluble CTLA4 molecule, wherein the soluble CTLA4 molecule is a CTLA4 fusion protein comprising the amino acid sequence beginning with methionine at position +1 or alanine at position -1 and ending at aspartic acid at position 124 as shown in SEQ ID NO. 2 in cell culture under conditions that allow for protein production; and b. feeding the cells with D-galactose. 33. **A cell culture process for the production of a soluble CTLA4 molecule**, comprising; a. culturing host cells which produce a soluble CTLA4 molecule, wherein the soluble CTLA4 molecule is a CTLA4Ig molecule comprising the amino acid sequence beginning with methionine at position +1 or alanine at position -1 and ending at aspartic acid at position 124 as shown in SEQ ID NO. 2 in cell culture under conditions that allow for protein production; and b. feeding the cells with D-galactose. 34. **A cell culture process for the production of a soluble CTLA4 molecule**, comprising: a. culturing host cells which produce a soluble CTLA4 molecule, wherein the soluble CTLA4 molecule is a CTLA4 mutant molecule comprising the amino acid sequence beginning with methionine at position +1 or alanine at position -1 and ending at aspartic acid at position 124 as shown in SEQ ID NO: 4, in cell culture under conditions that allow for protein production; and b. feeding the cells with D-galactose. 35. **A cell culture process for the production of a soluble CTLA4 molecule**, comprising: a. culturing host cells which produce a soluble CTLA4 molecule, wherein the soluble CTLA4 molecule is L104EA29YIg comprising amino acids -1 to 357 or +1 to 357 as shown in SEQ ID	CYTOTOXIC T-LYMPHOCYTE ANTIGEN-4 (CTLA4)

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					NO: 4, in cell culture under conditions that allow for protein production; and b. feeding the cells with D-galactose.	
32	**2003-02-20**	**US7332299** **10/695,243** **US 20040171826 A1** **ENDO-MANNOSIDASES IN THE MODIFICATION OF GLYCOPROTEINS IN EUKARYOTES** ***FAMILY MEMBERS*** SEE ABOVE	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2023-11-26** **PTA: 279 DAYS** **Publication Date: 2004-09-02** **Filing Date: 2003-10-27** **Earliest Effective Filing Date: 2003-02-20** **Priority Date: 2003-02-20**	**Hamilton; Stephen (Enfield, NH)**	1. **A method for modifying glycosylation structures on glycoproteins expressed in a eukaryotic host cell** comprising: expressing in said host cell a recombinant nucleic acid encoding a polypeptide having an **endomannosidase activity** that is targeted to a vesicular compartment within the host cell, wherein said nucleic acid encoding the polypeptide having an endomannosidase activity is selected from the group consisting of (a) SEQ ID NO: 1 or 3; and (b) a nucleic acid sequence that encodes a polypeptide having the amino acid sequence of SEQ ID NO:2 or 4. 2. **A method for modifying glycosylation structures on glycoproteins expressed in a lower eukaryotic host cell** comprising expressing in the host cell a recombinant nucleic acid encoding a polypeptide having an **endomannosidase activity**, wherein said nucleic acid encoding a polypeptide having an endomannosidase activity is selected from the group consisting of (a) SEQ ID NO: 1 or 3; and (b) a nucleic acid sequence that encodes a polypeptide having the amino acid sequence of SEQ ID NO:2 or 4. NO OTHER CLAIMS	**"HAMILTON I" FAMILY** ***STATUS*** • **EXPIRES** 2023-11-26 • NO MAINTENANCE FEES DUE ***METHODOLOGY*** CLAIMS GENERALLY DRAWN ENDOMANNOSIDASE SEQUENCES AND METHODS FOR MODIFYING GLYCOSYLATION STRUCTURES IN A LOWER EUKARYOTE.

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
35	**2004-02-13**	**US8609370B2** **10/589,447** **US 20080226681 A1** **HIGHLY ACTIVE GLYCOPROTEINS-PROCESS CONDITIONS AND AN EFFICIENT METHOD FOR THEIR PRODUCTION** ***FAMILY MEMBERS***	**GLYCOTOPE GMBH** (Berlin, DE) **EXPIRES 2027-08-24** **PTA: 921 DAYS** **Publication Date: 2008-09-18** **Filing Date: 2008-02-07** **Earliest Effective Filing Date: 2004-02-13** **Priority Date: 2005-02-14**	**Goletz; Steffen (Glienicke-Nordbahn, DE)** **Baumeister; Hans (Berlin, DE)** **Schoeber; Ute (Berlin, DE)**	1. **A process for the production of a highly active sialylation form of a target glycoprotein**, said highly active sialylation form of said target glycoprotein having a sialylation degree that is lower than that of a reference glycoprotein, yet said highly active sialylation form of said target glycoprotein also having an activity that is higher than that of said reference glycoprotein, wherein said sialylation degree also corresponds to a determined concentration of at least one sialic acid precursor additive, said process comprising: (a) **providing a human expression cell line which harbors at least one defect in the sugar nucleotide biosynthetic pathway of sialic acids**, said at least one defect being a defect in at least one enzyme selected from the group consisting of UDP-GlcNAc-2-epimerase, N-acetylmannosamine kinase, N-acetylglucosamine kinase, Neu5Ac-9-P-synthetase, Neu5Ac-9-P-phosphatase, CMP-Neu5Ac synthetase and CMP-sialic acid transporter, and said human expression cell line being transfected with a nucleic acid encoding the target glycoprotein; (b) determining a concentration of said at least one sialic acid precursor additive that is able to reconstitute said defect by a process comprising: (i) **expressing a plurality of different sialylation forms of said target glycoprotein by differential sialylation using different concentrations of said at least one sialic acid precursor additive**; (ii) determining the activity of each of the different sialylation forms in comparison to the reference glycoprotein; and (iii) selecting said highly active sialylation form of said target glycoprotein from among the different sialylation forms expressed, and determining the concentration of the at least one sialic acid precursor additive that correlates with the expression of said highly active sialylation form of said target glycoprotein; and	***STATUS*** • EXPIRES 2027-08-24 • 4TH YEAR MAINTENANCE FEE WINDOW OPENS: 12/17/2016 ***METHODOLOGY*** CLAIMS DRAWN TO A GLYCOPROTEIN EXPRESSED IN A CELL LINE HAVING AT LEAST ONE DEFECT IN THE SUGAR NUCLEOTIDE BIOSYNTHETIC PATHWAY OF SIALIC ACIDS

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					(c) **expressing the highly active sialylation form of said target glycoprotein in said human expression cell line in a medium supplemented with the at least one sialic acid precursor additive at the concentration determined in step (b)(iii)**.	
36	**2005-11-07**	**US8470318** **12/447,204** **US 20100189714 A1** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** ***FAMILY MEMBERS*** AU2006312148A1 AU2006312148B2 AU2007235413B2 AU2007317755A1 AU2008338550A1 CA2627981A1 CA2647524A1 CA2666308A1 CA2666308C CA2707304A1 CN101432301A CN101432301B CN101528774A CN101896202A EA200870411A1 EA200970416A1 EA201070739A1 EP1957099A2 EP1957099A4 EP2010566A2	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **EXPIRES 2028-03-28** **PTA: 518 DAYS** **Publication Date: 2010-07-29** **Filing Date: 2011-12-23** **Earliest Effective Filing Date: 2005-11-07** **Priority Date: 2006-10-27**	**Ravetch; Jeffrey V. (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)** **Kaneko; Yoshikatsu (Niigata, JP)**	1. A method of inhibiting inflammation in a subject, comprising providing a purified preparation of **IgG Fc regions from an IVIG source**, wherein the purified preparation has (i) increased anti-inflammatory activity as compared to the IVIG source, and (ii) a higher content of α2,6 linked sialic acid in the N-linked glycans of the Fc regions than **the IVIG source**, and administering to a subject having inflammation a dose of the purified preparation sufficient to inhibit inflammation in the subject. 2. The method of claim 1, wherein the IgG Fc regions comprise one or more of human IgG1, IgG2, IgG3 or IgG4 Fc regions. 3. The method of claim 1, wherein the IgG Fc regions from the IVIG source are modified by treatment with α2-6 sialyltransferase. 4. The method of claim 1, wherein the IgG Fc regions from the IVIG source are purified from the IVIG source by using one or more of affinity chromatography HPLC, lectin affinity chromatography, high pH anion exchange chromatography, ion-exchange chromatography, and any combination thereof. 5. The method of claim 1, wherein the IgG Fc regions from the IVIG source are purified from the IVIG source by using a lectin having a higher affinity to α2,6 linkages than to α2,3 linkages between sialic acids and galactose. 6. The method of claim 1, wherein the subject has an inflammatory disease. 7. The method of claim 1, wherein the subject has arthritis, thrombocytopenia, or nephritis	**"RAVETCH I" FAMILY** ***STATUS*** • EXPIRES 2028-03-28 • MAINTENANCE FEES: 4TH YEAR FEE WINDOW OPENS: 06/25/2016 ***METHODOLOGY*** CLAIMS REQUIRE IGG FC REGIONS FROM AN IVIG SOURCE

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		EP2010566A4 EP2010566B1 EP2091969A2 EP2091969A4 EP2227255A1 EP2227255A4 EP2455100A2 EP2455100A3 EP2815768A2 EP2815768A3 HK1124074A1 IL194526A IL194526D0 IL197920D0 IL206029D0 JP2009532477A JP2010512306A JP2011506476A MX2008012843A MX2009004399A MX2010006537A NZ572379A US20080206246A1 US20080286819A1 US20090004179A1 US20100189714A1 US20100278808A1 US20110150867A1 US20120134988A1 US20130273040A1 US20140323696A1 WO2007055916A3 WO2007117505A3 WO2008057634A3 WO2009079382A1 ZA200808900A				

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
37	**2006-04-05**	**EP2010566B1** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** ***FAMILY MEMBERS*** SEE ABOVE	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **EXPIRES 2027-04-03** **Publication Date: 2014-09-03** **Filing Date: 2007-04-03** **Earliest Effective Filing Date: 2006-04-05** **Priority Date: 2007-04-03**	**Ravetch; Jeffrey V. (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)** **Kaneko; Yoshikatsu (Niigata, JP)**	1. **A method of increasing the anti-inflammatory activity and lowering the cytotoxicity of a polypeptide containing at least one IgG Fc region**, said method comprising: **providing a source of the polypeptide containing at least one IgG Fc region,** said source of the polypeptide containing at least one IgG Fc region comprising **a plurality of the polypeptide containing at least one IgG Fc region having sialic acid and a plurality of the polypeptide containing at least one IgG Fc region lacking sialic acid**; and **increasing the ratio of the plurality of the polypeptide containing at least one IgG Fc region having sialic acid to the plurality of the polypeptide containing at least one IgG Fc region lacking sialic acid**. 2. The method of claim 1, wherein said source of the polypeptide containing at least **one IgG Fc region comprises a human IgG antibody**. 3. The method of claim 1 or 2, **wherein the source of the polypeptide containing at least one IgG Fc region is provided from expressing a vector comprising a nucleic acid sequence in an expression system**, wherein said nucleic acid sequence is translated into an IgG antibody. 4. The method of claim 3, wherein the expression system comprises modified host expression systems capable of N-linked glycosylation selected from the group consisting of fungal, plant, **vertebrate** and invertebrate expression systems, and any combinations thereof. 5. The method of any one of claims 1-4, wherein the step of increasing the ratio of the plurality of the polypeptides containing at least one IgG Fc region having sialic acid to the plurality of the polypeptides containing at least one IgG Fc region lacking sialic acid is achieved through **a removal of the polypeptides containing at least one IgG Fc region lacking sialic acid**. 6. The method of claim 5, wherein said **removal is achieved by physical or chemical methods**. 7. The method of claim 5 or 6 wherein said removal is achieved by a method selected from the group consisting of **HPLC, lectin affinity chromatography, high pH anion exchange chromatography, and any combination thereof**. 8. The method of any one of claims 1-7, wherein the step of increasing the ratio of the plurality of the polypeptides containing at least one IgG Fc region having sialic acid to the plurality of the polypeptides containing at least one IgG Fc region lacking sialic acid is achieved through an **enrichment of said source of the polypeptide containing at least one IgG Fc region**.	**"RAVETCH II" FAMILY** ***STATUS*** • EXPIRES 2027-04-03 • Renewal fee for patent year 08 paid 2014-04-28 ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF INCREASING THE ANTI-INFLAMMATORY ACTIVITY AND LOWERING THE CYTOTOXICITY OF A POLYPEPTIDE CONTAINING AT LEAST ONE IGG FC REGION BY INCREASING THE RATIO OF THE PLURALITY OF THE POLYPEPTIDE CONTAINING AT LEAST ONE IGG FC REGION HAVING SIALIC ACID TO THE PLURALITY OF THE POLYPEPTIDE CONTAINING AT LEAST ONE IGG FC REGION LACKING SIALIC ACID.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
					9. The method of claim 8 wherein said enrichment is achieved by a method selected from the group consisting of **HPLC, lectin affinity chromatography, high pH anion exchange chromatography,** and any combination thereof. 10. The method of claim 8 or 9 **wherein said sialylation is achieved by a chemical reaction with an enzyme attaching sialic acid to a carbohydrate attached to the polypeptide containing least one IgG Fc region**. 11. The method of claim 10, wherein the enzyme is **α-(2,6) sialyltransferase.**	
38	**2006-04-11**	**US7846724 B2** **11/732,974** **US 20070248600 A1**	**HOFFMANN-LA ROCHE INC** . (Nutley, NJ) **EXPIRES 2028-04-01**	**Hansen; Silke (Iffeldorf, DE)** **Kuenkele; Klaus-Peter (Benediktbeuern, DE)**	**1. A method for the selection of a CHO cell that recombinantly produces a monoclonal antibody comprising human IgG1 or IgG3 heavy chain constant domains,** wherein the heavy chain constant domains are **glycosylated** with a sugar chain at Asn297, wherein the sugar chain comprises **at least 99% fucose**,	**"HANSEN I" FAMILY** ***STATUS***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
		METHOD FOR SELECTING CHO CELL FOR PRODUCTION OF GLYCOSYLATED ANTIBODIES ***FAMILY MEMBERS*** AR60386A1 AU2007236198A1 AU2007236198B2 BRPI0709960A2 CA2647288A1 CA2849203A1 CN101460522A CN101460522B CN103864923A CR10300A EC2008SP8814A EP2007809A1 EP2007809B1 EP2248831A1 ES2395136T3 IL194165D0 IL233150D0 JP05078990B2 JP2009533366A JP2012254996A KR1256257B1 KR1275452B1 KR2008106342A KR2012028397A MA30383B1 MX2008012953A NO200803948A NZ571277A RU2008144293A US20070248600A1 US20100322927A1 US20120128664A1 US20140193404A1 US8703919B2	**PTA: 362 DAYS** **Publication Date: 2010-12-07** **Filing Date: 2007-04-05** **Earliest Effective Filing Date: 2006-04-11** **Priority Date: 2007-04-05**	**Reusch; Dietmar (Munich, DE)** **Schumacher; Ralf (Penzberg, DE)**	wherein **if** the sugar chain comprises N-glycolylneuraminic acid then the amount of N-glycolylneuraminic acid is 1% or less of the sugar chain and wherein **if** the sugar chain comprises N-terminal alpha-1,3-galactose then the amount of N-terminal alpha-1,3-galactose is 1% or less of the sugar chain; the method comprising: (1) cultivating a CHO cell transfected with an expression vector that encodes **the heavy and light chains of a monoclonal antibody** comprising human IgG1 or IgG3 heavy chain constant domains, wherein two DHFR alleles are deleted from the genome of the CHO cell; (2) applying DHFR selection pressure; (3) picking single clones; (4) expanding the clones; (5) producing antibodies from the clones; (6) analyzing glycosylation of the antibodies produced from the clones; and (7) **selecting a clone that produces an antibody wherein the heavy chain constant domains are glycosylated with a sugar chain at Asn297,** **wherein the sugar chain comprises at least 99% fucose**, wherein if the sugar chain comprises N-glycolylneuraminic acid then the amount of N-glycolylneuraminic acid is 1% or less of the sugar chain and wherein if the sugar chain comprises N-terminal alpha-1,3-galactose then the amount of N-terminal alpha-1,3-galactose is 1% or less of the sugar chain. NO OTHER CLAIMS	• EXPIRES 2028-04-01 • Renewal fee for patent year 08 opens on 12/07/2017 ***METHODOLOGY*** CHO CELLS SELECTED FOR GLYCOSYLATION PROFILE OF MONOCLONAL ANTIBODY WHERE SUGAR CHAIN AT ASN297 COMPRISES **AT LEAST 99% FUCOSE**..

Issued US/EP Patents Relating to Antibody Glycosylation

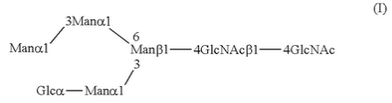
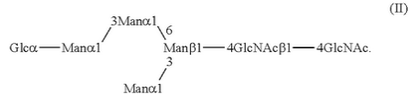
Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
		WO2007115813A1 ZA200808647A				
39	**2006-04-11**	**US8703919 B2** **13/298,553** **US 20120128664 A1** **GLYCOSYLATED ANTIBODIES** ***FAMILY MEMBERS*** SEE ABOVE	**HOFFMANN-LA ROCHE INC** . (Nutley, NJ) **EXPIRES 2027-06-21** **PTA: 77 DAYS** **Publication Date: 2014-04-22** **Filing Date: 2011-11-17** **Earliest Effective**	**Hansen; Silke (Iffeldorf, DE)** **Kuenkele; Klaus-Peter (Benediktbeuern, DE)** **Reusch; Dietmar (Munich, DE)** **Schumacher; Ralf (Penzberg, DE)**	**1. A purified antibody** that binds to the insulin-like growth factor-I receptor IGF-IR, comprising human IgG1 or IgG3 heavy chain constant domains wherein the heavy chain constant domains are glycosylated with a sugar chain at Asn297, wherein the sugar chain comprises at least 99.4% fucose, wherein if the sugar chain comprises N-glycolylneuraminic acid, the amount of N-glycolylneuraminic acid is 1% or less of the sugar chain and wherein if the sugar chain comprises N-terminal alpha-1,3-galactose, the amount of N-terminal alpha-1,3-galactose is 1% or less of the sugar chain and wherein the antibody is produced by the CHO cell line hu Mab<1GF-1R>B1-4E10—9-16 deposited with the Deutsche Sammburg Von Mikroorganismen and Zellkulturen GmbH, Germany, under Accessia No. DSM ACC 2795. NO OTHER CLAIMS	**"HANSEN I" FAMILY** ***STATUS*** • EXPIRES 2027-06-21 • MAINTENANCE FEES: 4th year fee window opens: 04/22/2017 ***METHODOLOGY*** CLAIM 1 DRAWN TO AN ANTIBODY THAT BINDS INSULIN-LIKE GROWTH FACTOR-I RECEPTOR..

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
			Filing Date: 2006-04-11 **Priority Date: 2007-04-05**			
40A	**2006-05-05**	**US7863020** **11/429,672** **US 20060286637 A1** **PRODUCTION OF SIALYLATED N-GLYCANS IN LOWER EUKARYOTES** ***FAMILY MEMBERS*** SEE ABOVE	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2023-02-20** **PTA: 0 DAYS** **Publication Date: 2004-09-02** **Filing Date: 2003-10-27** **Earliest Effective Filing Date: 2003-02-20** **Priority Date:**	**Hamilton; Stephen (Enfield, NH)**	1. **A method for producing a recombinant sialylated glycoprotein in a Pichia pastoris host cell,** the host cell selected or engineered to produce recombinant glycoproteins comprising a glycoform selected from the group consisting of Gal.sub.(1-4) GlcNAc.sub.(1-4) Man.sub.3GlcNAc.sub.2, the method comprising: (a) transforming into the host cell one or more nucleic acid molecules encoding a bifunctional UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase, an N-acetylneuraminate-9-phosphate synthase, and a CMP-Sialic acid synthase; (b) transforming into the host cell a nucleic acid molecule encoding a CMP-sialic acid transporter; and (c) transforming into the host cell a nucleic acid molecule encoding a 2,6-sialyltransferase catalytic domain fused to a cellular targeting signal peptide encoded by nucleotides 1-108 of the S. cerevisiae Mnn2 wherein nucleotides 1-108 encoding the S. cerevisiae Mnn2 have the nucleotide sequence shown by nucleotides 13 to 120 of SEQ ID NO:103; wherein, upon passage of the recombinant glycoprotein through the secretory pathway of the host cell, a recombinant sialylated glycoprotein comprising a glycoform selected from the group consisting of NANA.sub.(1-4)Gal.sub.(1-4)GlcNAc.sub.(1-4)Man.sub.3GlcNAc.sub.2 glycoform is produced. 2. The method of claim 1, wherein said method further comprises the step of transforming into the host cell one or more additional nucleic acids encoding one or more enzymes selected from the group consisting of glycosyltransferases, glycosidases and sugar transporters.	**"HAMILTON III" FAMILY** ***STATUS*** • **EXPIRES** 2023-02-20 • NO MAINTENANCE FEES DUE ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO PRODUCING A RECOMBINANT SIALYLATED GLYCOPROTEIN IN A PICHIA PASTORIS HOST

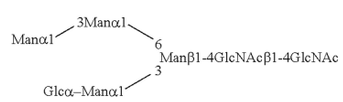
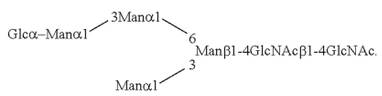
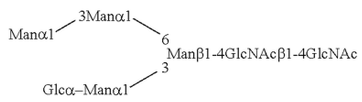
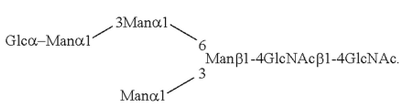
TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY COMMENTS
			2003-02-20		3. The method of claim 1, wherein the 2,6-sialyltransferase is selected from the group consisting of human 2,6-sialyltransferase, rat 2,6-sialyltransferase, and mouse 2,6-sialyltransferase. **4. A method for producing a recombinant sialylated glycoprotein in a Pichia pastoris host cell,** the host cell selected or engineered to produce recombinant glycoproteins comprising a GalGlcNAcMan.sub.5GlcNAc.sub.2 glycoform, the method comprising (a) transforming into the host cell with one or more nucleic acid molecules encoding a bifunctional UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase, an N-acetylneuraminate-9-phosphate synthase, and a CMP-Sialic acid synthase; (b) transforming into the host cell a nucleic acid molecule encoding a CMP-sialic acid transporter; and (c) transforming into the host cell a nucleic acid molecule encoding a 2,6-sialyltransferase catalytic domain fused to a cellular targeting signal peptide encoded by nucleotides 1-108 of the S. cerevisiae Mnn2 wherein nucleotides 1-108 encoding the S. cerevisiae Mnn2 have the nucleotide sequence shown by nucleotides 13 to 120 of SEQ ID NO:103; wherein, upon passage of the recombinant glycoprotein through the secretory pathway of the host cell, a recombinant sialylated glycoprotein comprising a NANAGalGlcNAcMan.sub.5GlcNAc.sub.2 glycoform is produced.	
40B	**2006-05-05**	**US8268609** **12/819,305** **US 2010-0279356 A1** **PRODUCTION OF SIALYLATED N-GLYCANS IN LOWER EUKARYOTES** ***FAMILY MEMBERS*** SEE ABOVE	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2023-08-12** **PTA: 173 DAYS** **Publication Date: 2010-11-04** **Filing Date: 2010-06-21** **Earliest Effective Filing Date: 2003-02-20** **Priority Date: 2003-02-20**	**Hamilton; Stephen (Enfield, NH)**	**1. An yeast host cell capable of producing CMP-sialic acid** comprising: (a) one or more nucleic acid molecules encoding a bifunctional UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase, an N-acetylneuraminate-9-phosphate synthase, and a CMP-Sialic acid synthase, (b) a nucleic acid molecule encoding a CMP-sialic acid transporter, and (c) a nucleic acid molecule encoding a 2,6-sialyltransferase catalytic domain fused to a cellular targeting signal peptide encoded by nucleotides 1-108 of the S. cerevisiae Mnn2 wherein nucleotides 1-108 encoding the S. cerevisiae Mnn2 have the nucleotide sequence shown by nucleotides 13 to 120 of SEQ ID NO:103, wherein the yeast host cell is capable of producing the CMP-sialic acid. 3. The yeast host cell of claim 1, wherein the yeast host cell is a Pichia sp., Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica; Saccharomyces sp., Saccharomyces cerevisiae, Hansenula polymorphs, Kluyveromyces sp., Kluyveromyces lactis, or Candida albicans. 6**. An yeast host cell comprising a CMP-sialic acid biosynthetic pathway** consisting of (a) a bifunctional UDP-N-acetylglucosamine-2-epimerase/N-acetylmannosamine kinase, an N-acetylneuraminate-9-phosphate synthase, and a CMP-Sialic acid synthase, (b) a CMP-sialic acid transporter, and (c) a 2,6-sialyltransferase catalytic domain fused to a cellular targeting signal peptide encoded by nucleotides 1-108 of the S. cerevisiae Mnn2 wherein nucleotides 1-108 encoding the S. cerevisiae Mnn2 have the nucleotide sequence shown by nucleotides 13 to 120 of SEQ ID NO:103, wherein the yeast host cell is capable of producing the CMP-sialic acid.	**"HAMILTON III" FAMILY** ***STATUS*** • **EXPIRES** 2023-08-12 • NO MAINTENANCE FEES DUE - 4TH YEAR FEE WINDOW OPENS: 09/18/2015 ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO YEAST HOST CELL FOR PRODUCING A RECOMBINANT SIALYLATED GLYCOPROTEIN

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					7. The yeast host cell of claim 6, wherein the yeast host cell is genetically engineered to comprise one or more additional nucleic acids encoding one or more enzymes selected from the group consisting of glycosyltransferases, glycosidases, and sugar transporters. 8. The yeast host cell of claim 6, wherein the yeast host cell is a Pichia sp., Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica; Saccharomyces sp., Saccharomyces cerevisiae, Hansenula polymorphs, Kluyveromyces sp., Kluyveromyces lactis, or Candida albicans. 9. The yeast host cell of claim 6, wherein the yeast host cell is a methylotrophic yeast. 10. The yeast host cell of claim 6, wherein the yeast host cell is Pichia pastoris.	
40B	**2007-03-07**	**EP2134834 B1** **PRODUCTION OF GLYCOPROTEINS WITH MODIFIED FUCOSYLATION** ***FAMILY MEMBERS*** AU2008227024A1 CA2679732A1 CN101679934A CN101679934B JP2010519930A KR2009130029A RU2009136982A RU2479629C2 SG187521A1 US20100028951A1 WO2008112092A2 WO2008112092A3 ZA200905728A	**GLYCOFI, INC** (Lebanon, NH) *** acquired by MERCK SHARP & DOHME in 2006** **EXPIRES 2028-03-03** **Publication Date: 2009-12-23** **Filing Date: 2008-03-03** **Earliest Effective Filing Date: 2007-03-07** **Priority Date: 2008-03-03**	**Hamilton; Stephen (Enfield, NH)**	1. **A recombinant lower eukaryote host cell comprising a fucosylation pathway**. 11**. A glycoprotein composition comprising a plurality of glycoforms**, each glycoform comprising at least one -glycan attached thereto, wherein the glycoprotein composition thereby comprises a plurality of -glycans in which greater than 25 mole percent of the plurality of iV-glycans consist essentially of a fucosylated 7V-glycan selected from the group consisting of Man5GlcNAc2, GIcNAcMans GIcNAc2, Man3GlcNAc2, GIcNAcMan3 GIcNAc2, GlcNAc2Man3GlcNAc2, GalGlcNAc2Man3GlcNAc2, Gal2GlcNAc2Man3GlcNAc2, NANAGal2GlcNAc2Man3GlcNAc2, and NANA2Gal2GlcNAc2Man3GlcNAc2. 12. The glycoprotein composition of Claim 11 wherein the fucosylated N- glycans are greater than 50 mole percent of the plurality of -glycans. 13. The glycoprotein composition of Claim 11 wherein the fucosylated N- glycans are greater than 75 mole percent of the plurality of iV-glycans. 14. The glycoprotein composition of Claim 11 wherein the fucosylated N- glycans are greater than 80 mole percent of the plurality of -glycans. 15. The glycoprotein composition of Claim 11 wherein the fucose is in an α1,3-linkage with the GIcNAc at the reducing end of the -glycan. 16. The glycoprotein composition of Claim 11 wherein the fucose is in an αl,6-linkage with the GIcNAc at the reducing end of the -glycan. 17. The glycoprotein composition of Claim 11 wherein the fucose is in an αl ,2-linkage with the Gal at the non-reducing end of the 7V-glycan.	**"HAMILTON IV" FAMILY** ***STATUS*** • **EXPIRES** 2028-03-03 • MAINTENANCE FEES PAID ***METHODOLOGY*** NEW RECOMBINANT LOWER EUKARYOTE HOST CELL, USEFUL FOR PRODUCING GLYCOPROTEINS WITH FUCOSYLATED N-GLYCANS

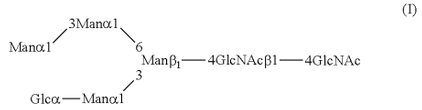
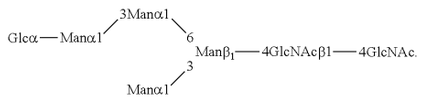
Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
					18. The glycoprotein composition of Claim 11 wherein the fucose is in an α1,3-linkage with the GlcNac at the non-reducing end of the iV-glycan. 19. The glycoprotein composition of Claim 11 wherein the fucose is in an αl,4-linkage with a GIcNAc at the non-reducing end of the 7V-glycan. 20. **A hybrid vector** comprising (a) DNA regulatory elements which are functional in a lower eukaryotic host cell operatively linked to (b) DNA coding sequence encoding a fusion protein encoding (i) a targeting sequence; and (b) a catalytic domain of a fucosylation pathway enzyme. 21. The vector of Claim 17 wherein the fucosylation pathway enzyme is a **fucosyltransferase**.	
41A	**2008-09-26**	**US8025879 B2** **12/507,044** **US 20100081794 A1** **MODIFIED GLYCOPROTEINS AND USES THEREOF** ***FAMILY MEMBERS*** AU2008227024A1 CA2679732A1 CN101679934A CN101679934B JP2010519930A KR2009130029A RU2009136982A RU2479629C2 SG187521A1 US20100028951A1 WO2008112092A2 WO2008112092A3 ZA200905728A	**EUREKA THERAPEUTICS INC** (Emeryville, CA) **EXPIRES 2029-07-21** **PTA: 0 DAYS** **Publication Date: 2010-04-01** **Filing Date: 2009-07-21** **Earliest Effective Filing Date: 2008-09-26** **Priority Date: 2009-07-21**	**Liu; Cheng (Richmond, CA)** **Xiang; Jingyi (Walnut Creek, CA)** **Yan; Su (Albany, CA)** **Wang; Pei (Fremont, CA)** **Tai; Wei Chan (Emeryville, CA)**	**1. An isolated mammalian glycoprotein**, wherein said isolated mammalian glycoprotein exhibits a variant glycosylation pattern, wherein said variant glycosylation pattern comprises an N-linked glycan having a structure of formula (I) or (II): (I)  (II)  2. The isolated mammalian glycoprotein of claim 1, wherein said isolated mammalian glycoprotein is an antibody. 3. The isolated mammalian glycoprotein of claim 2, wherein said antibody exhibits an increased ADCC (antibody-dependent cell-mediated cytotoxicity) activity, as compared to a corresponding wildtype antibody. 4. The isolated mammalian glycoprotein of claim 1, wherein said isolated mammalian glycoprotein has a substantially homogeneous pattern of N-linked glycan, wherein said pattern of N-linked glycan is characterized by a single peak resolved by high performance liquid chromatography (HPLC). 5. The isolated mammalian glycoprotein of claim 1, wherein said isolated mammalian glycoprotein is produced by a host cell comprising a mammalian glycosylation system. 6. The isolated mammalian glycoprotein of claim 1, wherein said isolated mammalian glycoprotein comprises one or more fucose molecules.	***STATUS*** • **EXPIRES** 2029-07-21 • MAINTENANCE FEES - : 4TH YEAR FEE WINDOW OPENS: 09/27/2014 ***METHODOLOGY*** CLAIMS REQUIRE AN N-LINKED GLYCAN HAVING A STRUCTURE OF FORMULA (I) OR (II) THAT INCLUDE A GLUCOSE MOLECULE.

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
41B	**2008-09-26**	**US8080415 B2** **12/507,046** **US 20100081195 A1** **MODIFIED HOST CELLS AND USES THEREOF** ***FAMILY MEMBERS*** AU2008227024A1 CA2679732A1 CN101679934A CN101679934B JP2010519930A KR2009130029A RU2009136982A RU2479629C2 SG187521A1 US20100028951A1 WO2008112092A2 WO2008112092A3 ZA200905728A	**EUREKA THERAPEUTICS INC** (Emeryville, CA) **EXPIRES 2029-12-04** **PTA: 136 DAYS** **Publication Date: 2011-09-27** **Filing Date: 2009-07-21** **Earliest Effective Filing Date: 2008-09-26** **Priority Date: 2009-07-21**	**Liu; Cheng (Richmond, CA)** **Xiang; Jingyi (Walnut Creek, CA)** **Yan; Su (Albany, CA)** **Wang; Pei (Fremont, CA)** **Tai; Wei Chan (Emeryville, CA)**	**1. An isolated host cell** that produces **N-linked glycans** having a structure of Formula I or II: (I)  (II)  **2. An isolated host cell that produces glycoproteins** exhibiting a substantially homogeneous pattern of **N-linked glycan**, wherein the N-linked glycosylation pattern has a structure of Formula I or II: (I)  (II)  6. The isolated host cell of claim 1 or 2, **producing antibodies that exhibit ADCC activity** higher than that of a corresponding host cell lacking said N-linked glycan. 7. The isolated host cell of claim 1 or 2, wherein the host cell is a **Chinese Hamster Ovarian (CHO) cell**.	***STATUS*** • **EXPIRES** 2029-12-04 • MAINTENANCE FEES - : 4TH YEAR FEE WINDOW OPENS: 12/20/2014 ***METHODOLOGY*** CLAIMS REQUIRE AN N-LINKED GLYCAN HAVING A STRUCTURE OF FORMULA (I) OR (II) THAT INCLUDE A GLUCOSE MOLECULE.

Issued US/EP Patents Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	Independent Claims + Selected Dependent Claims	Status Methodology Comments
41C	**2008-09-26**	**US8084222 B2** **12/507,051** **US 20100081150 A1** **METHODS FOR GENERATING HOST CELLS** ***FAMILY MEMBERS***	**EUREKA THERAPEUTICS INC** (Emeryville, CA) **EXPIRES 2029-12-04** **PTA: 136 DAYS** **Publication Date: 2011-12-27** **Filing Date: 2009-07-21** **Earliest Effective Filing Date: 2008-09-26** **Priority Date: 2009-07-21**	**Liu; Cheng (Richmond, CA)** **Xiang; Jingyi (Walnut Creek, CA)** **Yan; Su (Albany, CA)** **Wang; Pei (Fremont, CA)** **Tai; Wei Chan (Emeryville, CA)**	**1. A method of selecting an eukaryotic cell with a variant glycosylation pattern** comprising: (a) providing a plurality of eukaryotic cells; (b) introducing random genetic mutation(s) to said plurality of eukaryotic cells; and (c) selecting from said plurality of cells at least one cell that exhibits a variant glycosylation pattern characterized by a change in the level of at least one type of sugar molecules as compared to a corresponding parental cell that has not been subject to said random genetic mutation, wherein said variant glycosylation pattern is characterized by an N-linked pattern having a structure of Formula I or II: (I)  (II)  	***STATUS*** • **EXPIRES** 2029-12-04 • MAINTENANCE FEES - : 4TH YEAR FEE WINDOW OPENS: 12/27/2014 ***METHODOLOGY*** CLAIMS REQUIRE AN N-LINKED GLYCAN HAVING A STRUCTURE OF FORMULA (I) OR (II) THAT INCLUDE A GLUCOSE MOLECULE.
42	**2008-09-26**	**US8642292 B2** **13/496,997** **US20120214975A1**	**PROBIOGEN AG** (Berlin, DE) **EXPIRES 2029-09-22**	**Sandig; Volker (Berlin, DE)** **von Horsten (Berlin, DE)**	**1. A recombinant vertebrate cell for producing a protein molecule, lacking fucose or with a reduced amount of fucose on its glycomoieties**, said cell comprising a polynucleotide that encodes at least one enzyme which uses GDP-6-deoxy-d-lyxo-4-hexylose as a substrate, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-d-lyxo-4-hexylose into GDP-L-fucose.	***STATUS*** • **EXPIRES 2029-09-22** • NO MAINTENANCE FEES DUE

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		PROCESS FOR PRODUCING MOLECULES CONTAINING SPECIALIZED GLYCAN STRUCTURES **FAMILY MEMBERS** AU2010297580A1 AU2010297580B2 CA2773240A1 CN102648280A CN102648280B EA201200516A1 EP2480671A1 IL218485D0 JP2013505028A KR2012090981A MX2012003404A SG178925A1 US20120214975A1 WO2011035884A1	**PTA: 0 DAYS** **Publication Date: 2011-03-31** **Filing Date: 2010-09-21** **Earliest Effective Filing Date: 2008-09-26** **Priority Date: 2009-09-22**	**Hans Henning (Berlin, DE)** **Ogorek; Christiane (Berlin, DE)**	9. The vertebrate cell of claim 1, wherein the protein molecule is an **antibody**, an antibody fragment, a fusion protein, a virus protein, a virus protein fragment, an antigen, or a hormone. 10. The vertebrate cell of claim 1, wherein the vertebrate cell is a **mammalian**, a fish, an amphibian, a reptilian cell or an avian cell. 11. The vertebrate cell of claim 10, wherein (i). the mammalian cell is a human, **hamster**, canine or monkey cell; (ii). the fish cell is a lectalurus punctatus (channel catfish) ovary (CCO); (iii). the amphibian cell is a xenopus laevis kidney cell; (iv). the reptilian cell is \ iguana heart cells (IGH-2); or the avian cell is an avian retina cell, or an avian somite cell.	***METHODOLOGY*** CLAIMS DRAWN TO PROTEIN WITH REDUCED FUCOSE GLYCOSYLATION

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	1992-03-09	**US5714350A** **08/372,262** **INCREASING ANTIBODY AFFINITY BY ALTERING GLYCOSYLATION IN THE IMMUNOGLOBULIN VARIABLE REGION** **FAMILY MEMBERS**	**PROTEIN DESIGN LABS** (Mountain View, CA) **SLOAN-KETTERING CANCER CENTER** (Mountain View, CA) **EXPIRED 2015-02-03** **Publication Date: 1998-02-03** **Filing Date: 1995-01-13*** ***:PRE-GATT FILING** **Earliest Effective Filing Date: 1992-03-09** **Priority Date: 1992-03-09**	**Co; Man Sung (Cupertino, CA)** **Scheinberg; David A. (New York, NY)** **Queen; Cary L. (Los Altos, CA)**	1. **A method for producing a mutant antibody that comprises a mutant immunoglobulin chain**, the mutant antibody having higher affinity for an antigen than a parent antibody that comprises a parent immunoglobulin chain, the method comprising the steps of: introducing at least one mutation into a parent polynucleotide that encodes the parent immunoglobulin chain to produce a mutant polynucleotide that encodes the mutant immunoglobulin chain, **the mutation introducing into the mutant immunoglobulin chain an amino acid substitution that eliminates a variable region framework glycosylation site of the parent immunoglobulin chain**; and expressing the mutant polynucleotide in a cell as the mutant immunoglobulin chain so as to produce the mutant antibody. 2. The method of claim 1 **wherein the glycosylation site is an N-linked glycosylation site** selected from the group consisting of: (1) -Asn-X-Ser-; and (2) -Asn-X-Thr-; wherein X is an amino acid other than Pro. 3. The method of claim 1 **wherein the glycosylation site is an O-linked glycosylation** site selected from the group consisting of: (1) -Thr-X-X-Pro-; and (2) -Ser-X-X-Pro-; wherein X is an amino acid. 5. The method of claim 1 wherein the mutant polynucleotide encodes a mutant immunoglobulin chain whose variable region framework has no glycosylation sites. 10. The method of claim 1 wherein the mutant immunoglobulin chain is an immunoglobulin heavy chain. 16. The method of claim 9 wherein the cell surface glycoprotein is the CD33 antigen.	***STATUS*** • EXPIRES 2015-02-03 ***METHODOLOGY*** CLAIMS DRAWN TO THE PRODUCTION OF A MUTANT ANTIBODY HAVING AN AMINO ACID SUBSTITUTION THAT ELIMINATES A VARIABLE REGION FRAMEWORK GLYCOSYLATION SITE.

PUBLISHED PCT/US/EP PATENT APPLICATIONS RELATING TO ANTIBODY GLYCOSYLATION

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	1986-3-07	**WO1987005330 A1** **METHOD FOR ENHANCING GLYCOPROTEIN STABILITY** **FAMILY MEMBERS** AU198656271A AU199051336A AU597574B2 AU624487B2 DK198705830A DK198705830D0 EP272253A1 **EP272253A4** **REFUSED** JP63502716A	**MASSACHUSETTS INSTITUTE OF TECHNOLOGY** (Cambridge, MA) **Publication Date: 1987-09-11** **Filing Date: 1986-03-07** **Earliest Effective Filing Date:** **Priority Date: 1986-03-07**	**Bergh, Michel Louis (Sommerville, MA)** **Hubbard, Catherine (Sommerville, MA)** **Rasmussen, James (Ithaca, NY)**	1. **A method for modifying a glycoprotein** comprising: **attaching a galactose residue to a core N acetylglucosamine to form a Gal-GlcNAc sequence**; and **attaching a sialic acid residue to the galactose to form a SAGal-GlcNAc sequence**. 2. The method of claim 1 further comprising first cleaving asparagine- linked oligosaccharide chains of the glycoprotein to remove all sugars other than core N-acetylglucosamine residues bound to the glycoprotein. 12. The method of claim 2 wherein the oligosaccharide chains are cleaved by sequentially digesting the glycoprotein first with an exoglycosidase and secondly with an endoglycosidase. 21. **A method for modifying proteins** comprising: derivatizing amino acids on the protein with a glycoside or thioglycoside S-X, wherein S is a first saccharide selected from the group consisting of N-acetylglucosamine and galactose and X is an aglycone, and enzymatically attaching a second saccharide selected from the group consisting of galactose, N-acetylglucosamine, fucose, and sialic acid. 37. The method of claim 1 wherein the sialic acid residue is attached to the Gal- GlcNAc sequence in a linkage by a **sialyltransferase**. 39. **A method for targeting a protein to a cell having a specific surface receptor for a saccharide**, said method comprising: attaching to the protein an oligosaccharide chain, said oligosaccharide chain having an exposed saccharide and a Gal-->GlcNAc sequence, wherein said exposed saccharide is recognized by the cell surface receptor and said oligosaccharide chain is attached to the protein with a Gal-->GlcNAc sequence. 42. **A protein comprising an oligosaccharide sequence consisting of any of** Galβ1-->4GlcNAc-->; Galβ1-->3GlcNAc-->: SAα2-->6Gal β1-->4G1 cNAc--> ; SAα2-->3Galβ1-->4GlcNAc—>; SAα2-->3Galβ1--->3GlcNAc-->: Gal β1-->4(Fucα1-->3) GlcNAc—> ; Galβ1-->3(Fucα1-->4)GlcNAc-->; SAα2-->3Galβ1-->3 (Fucα1—>4)GlcMAc—>; Galβ1-->4GlcNAcβ1-->4GlcNAc—>; Galβ1-->3G1 cNAcβ1-->4G1 cNAc—>; SAα2-->6Galβ1-->4GlcNAcβ1—>4G! cNAc--> :	***STATUS*** **EP272253A4 – REFUSED** **1992-11-20** (File destroyed) ***METHODOLOGY*** CLAIMS DRAWN TO a METHOD OF GALACTOSYLATION OF A GLYCOPROTEIN

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					SAα2-->3Galβ1-->4Gl cNAcβ1—>4GlcNAc—> ; SAα2-->3Galβ1-->3Gl cNAcβ1—>4GlcNAc-->: Galβ1-->4(Fucα1-->3) GlcNAcβ1—>4G1 cNAc-- > ; Galβ1-->3 (Fucα1-->4)GlcNAcβ1—>4GlcNAc-->; SAα2-->3Galβ1-->3(Fucα1-->4)GlcNAcβ1-->4GlcNAc-->; [GlcNAcβ1-->3Galβ1-->4]nGιcNAc-->, wherein n is between 1 and 10; [GlcNAcβ1—>3Galβ1—>4]n GlcNAcβ1-->4GlcNAc-->, wherein n is between 1 and 10; Galβ1-->4[GlcNAcβ1—>3Galβ1-->4]nGlcNAc-->, wherein n is between 1 and 10; Galβ1-->3[GlcNAcβ1-- 3Galβ1-->4]nGlcNAc—>, wherein n is between 1 and 10: SAα2-->6Galβ1—>4[GlcNAcβ1-->3Galβ1-->4]nGlcNAc-->, wherein n is between 1 and 10: SAα2-->3Galβ1—>4[Gl cNAcβ1-->3Galβ1-->4]nGlcNAc-->, wherein n is between 1 and 10; SAα2-->3Galβ1—>3[GlcNAcβ1-->3GalβI—>4]nGlcNAc—>, wherein n is between 1 and 10; Galβ1-->4(Fucα1—>3)GlcNAcβ1-->3[Galβ1—>4(Fucα1-->3)mGlcNAcβ1-->3]n- Galβ1-- >4GlcNAc-->, wherein m is between 0 and 1, and n is between 1 and 10; Galβ1-->3(Fucα1-->4)Gl cNAcβ1-->3[Gal β1-->4(Fucα1-->3)mGl cNAcβ1-- >3]n- Galβ1-- >4GlcNAc-->, wherein m is between 0 and 1, and n is between 1 and 10; SAα2-->3Galβ1-->3(Fucα1-->4)GlcNAcβ1-->3[Galβ1-->4GlcNAcβ-->3]n- Galβ1-- >4GlcNAc-->, wherein n is between 1 and 10; Galβ1-->4[GlcNAcβ1-->3Galβ1-->4]nGlcNAcβ1—>4GlcNAc—>, wherein n is between 1 and 10; Galβ1-->3[GlcNAcβ1-->3Galβ1-->4]nGlcNAcβ1-->4GlcNAc-->, wherein n is between 1 and 10; SAα2-->6Galβ1-->4[GlcNAcβ1-->3Galβ1-->4]nGlcNAcβ1-->4GlcNAc-->, wherein n is between 1 and 10; SAα2—>3Galβ1—>4[Gl cNAcβ1—>3Galβ1—>4]nG! cNAcβ1— >4GlcNAc—>, wherein n is between 1 and 10; SAα2-->3Galβ1-->3[GlcNAcβ1-->3Galβ1—>4]nGlcNAcβ1—>4GlcNAc—>, wherein n is between 1 and 10; Galβ1-->4(Fucα1-->3)GlcNAcβ1-->3[Galβ1-->4(Fucα1-->3)mGlcNAcβ1-->3]n- Galβ1-->4Gl cNAcβ1-->4GlcNAc-->, wherein m is oetween 0 and 1, and n is between 1 and 10; GaTβ1-->3(Fucα1-->4)GlcNAcβ1-->3[Galβ1-->4(Fucα1-->3)m GlcNAcβ1-->3]n- Galβ1— >4GlcNAcSi— 4GlcNAc-->, wherein m is between 0 and 1, and n is between 1 and 10;	

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					SAα2-->3Galβ1-->3(Fucα1-->4)GlcNAcβ1-->3 [Galβ1-->4GlcNAcβ-->3]n- Galβ1—>4GlcNAcβ1-->4GlcNAc-->, wherein n is between 1 and 10. 43. **A protein comprising an oligosaccnaride sequence consisting of any of**: (GlcNAcβ1-->3Galβ1-->4)nGlcNAcβ1-->3Gal-->, wherein n is between 1 and 10; SAα2-->6Gal-->; SAα2—>6Galβ1-->4(GlcNAcβ1-->3Galβ1-->4)nGlcNAcβ1-->3Gal, wherein n is between 1 and 10; SAα2-->3Gal-->; and SAα2-->3Galβ1-->4(Gl cNAcβ1-->3Galβ1-->4)nGlcNAcβ1-->3Gal-->, wherein n is between 1 and 10. 44. **A glycosylated protein** comprising Gal-GlcNAc-protein, wherein the Gal is attached to the GlcNAc by an enzyme selected from the group consisting of UDP-Gal :GlcNAc-R **β1-- >4 galactosyltransferase** and UDP-Gal :GlcNAc-R β1-- >3 gal actosyltransferase. 45. **A glycosylated protein** comprising SA-Gal -GlcNAc-protein, wherein the SA is attached to the Gal by an enzyme selected from the group consisting of CMP-SA:Galβ1-- >4GlcNAc-R **α2--** **>6 sialyltransferase**; CMP-SA:Galβ1-->3(4)GlcNAc-R α2-->3 sialyltransferase; and CMP-SA:-Galβ1-->4GlcNAc-R α2-->3 sialyltransferase.	
	1988-12-13	**WO1990007000 A2** **NUCLEOTIDES ENCODING HUMAN B1, 4-GALACTOSYL-TRANSFERASE AND USES THEREOF** **FAMILY MEMBERS**	**LA JOLLA CANCER RESEARCH FOUNDATION** (La Jolla, CA) **Publication Date: 1990-06-28** **Filing Date: 1989-11-16**	**FUKUDA, Michiko (US).** **APPERT, Hubert, A.; (US)**	1. **An isolated nucleic acid sequence** which encodes purified **membrane bound human B 1, 4 - galactosyltransferase**, or a functional equivalent thereof. 3. **A cDNA sequence** comprising the sequence identified for membrane-bound human β1,4-galactosyltransferase in Figure 2. 4. **An isolated nucleic acid sequence** having the sequence identified in Figure 2 beginning with adenine at position 1 and ending with cytosine at position 1200. 5. **An isolated nucleic acid sequence** which encodes purified soluble human β 1,4-galactosyltransferase or a functional equivalent thereof.	***STATUS*** • No US or EP **FAMILY MEMBERS** ***METHODOLOGY*** CLAIMS DRAWN TO TO HOST CELL EXPRESSING B4GAL-T1 AND METHODS OF GALACTOSYLATION OF A PEPTIDE

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		AU199047519A CA2003797A1	**Earliest Effective Filing Date: 1988-12-13** **Priority Date: 1988-12-13**		15. **Antibodies reactive with a portion of membrane-bound β1,4-galactosyltransferase identified in Figure 2** beginning with arginine corresponding to nucleotide positions 4 through 6 and ending with arginine corresponding to nucleotide positions 228 through 230. 18. **Antibodies reactive with a portion of both soluble and membrane-bound β 1,4-galactosyltransferase identified in Figure 2** beginning with threonine corresponding to nucleotide positions 231 through 233 and ending with serine corresponding to nucleotide positions 1198 through 1200. 21. **A nucleic acid probe** comprising a nucleotide sequence complementary to a portion of the nucleotide sequence between nucleotides 1 to 411 in Figure 2. 25. **A method of diagnosing an abnormal condition in a subject** comprising: a. detecting the presence of soluble and/or membrane-bound β 1,4-galactosyltransferase; b. quantifying the relative amounts of soluble and/or membrane-bound β 1,4-galactosyltransferase; and c. comparing the amount of soluble and/or membrane-bound β 1,4-galactosyltransferase to the amount in a normal subject; an increase in the normal amount of soluble β 1,4-galactosyltransferase or a decrease in the normal amount of membrane-bound β 1,4--galactosyltransferase being indicative of an abnormal condition.	
	1989-10-24	**WO1991006635 A1** **METHOD FOR PRODUCING SECRETABLE GLYCOSYL-TRANSFERASES AND OTHER GOLGI PROCESSING ENZYMES** **FAMILY MEMBERS** AT161044T AU199066480A	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA (Oakland, CA)** **Publication Date: 1991-05-16** **Filing Date: 1990-10-24** **Earliest Effective Filing Date: 1989-10-24**	**Paulson; James C. (Del Mar, CA)** **Ujita-Lee; Eryn (Redondo Beach, CA)** **Colley; Karen J. (Chicago, IL)** **Adler; Beverly (Newbury Park, CA)** **Browne; Jeffrey K. (Camarillo, CA)**	1. **A method for producing a soluble Golgi processing enzyme** which is secreted by a cell, wherein the naturally occurring enzyme include a retention signal and a membrane anchor, said method comprising the steps of: introducing into said cell at least one gene which is capable of expressing a soluble and secretable enzyme -which lacks said retention signal and anchor domain; expressing said soluble and secretable enzyme is said cell wherein said cell secretes said soluble enzyme; and recovering the soluble enzyme secreted by said cell. 13. **In a method for producing glycosyltransferase wherein said glycosyltransferase is produced within a cell** and remains within said cell, said glycosyltransferase including a membrane anchor and a retention signal which causes said glycosyltransferase to be retained within said cell and an enzymatic domain which provides said glycosyltransferase with enzymatic activity, the improvement comprising: introducing at least one gene into said cell which is capable of a glycosyltransferase which does not have said membrane anchor and retention signal whereby a soluble glycosyltransferase is produced which is secreted by the cell; expressing said soluble glycosyltransferase in said cell in a sufficient amount which is secreted by said cell; and recovering the soluble glycosyltransferase secreted by said cell.	***STATUS*** ***METHODOLOGY*** **CLAIMS DRAWN TO METHOD OF PRODUCING A GLYCOSYLTRANSFERASE IN A CELL AND TO A COMPOSITION OF MATTER COMPRISING A SOLUBLE GLYCOSYLTRANSFERASE**

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		AU646233B CA2065839C DE69031805T2 DK497878T3 **EP497878B1** **EXPIRED 2010-10-24** **[see TABLE A - TAB 4D]** ES2112254T3 GR3026217T3 JP03121342B2 JP5504678A **US5541083** **EXPIRED 2013-07-30** **[see TABLE A - TAB 4B]** **US5776772** **EXPIRED 2009-10-24** **[see TABLE A - TAB 4C]** **WO1991006635A1**	**Priority Date: 1989-10-24**		14. The improved method for producing glycosyltransferase according to claim 13 wherein said **glycosyltransferase** is selected from the group consisting of N-acetylglucosaminyltransferases, N-acetylgalactosaminyltransferases, **sialyltransferase**, **fucosyltransferases**, **galactosyltransferases**, mannosyltransferases sulfotransferases, acetyltransferases and mannosidases. 18. **A composition of matter** comprising a **soluble glycosyltransferase** made by a method comprising the steps of: introducing into a cell at least one gene which is capable of expressing a soluble glycosyltransferase which is secreted by said cell; expressing said soluble glycosyltransferase in said cell in a sufficient amount wherein said cell secretes said soluble glycosyltransferase; and recovering the soluble glycosyltransferase secreted by said cell. 21. **A composition of matter** comprising cells which have been genetically altered to produce a **soluble glycosyltransferase** which is secreted by the cell. 27. **A vector for use in expressing a soluble sialyltransferase in a host cell,** said vector comprising cDNA having a nucleotide sequence which codes for a **sialyltransferase** which lacks the membrane anchor and retention signal of said sialyltransferase. 29. **A method of enzymatically synthesizing an oligosaccharide product** comprising: reacting a starting oligosaccharide with a sugar nucleotide and a homogeneous, soluble glycosyltransferase under conditions in which the glycosyltransferase catalyzes the transfer of a monosaccharide from the sugar nucleotide to the starting oligosaccharide to produce the oligosaccharide product. 33. **A composition comprising a homogenous, soluble glycosyltransferase** in substantially pure form. 34. A composition of claim 33 wherein the glycosyltransferase is a sialyltransferase. 35. A composition of claim 34 wherein the sialyltransferase is β-galactoside α2,6-sialyltransferase. 36. A composition of claim 33 wherein the glycosyltransferase lacks a functional retention signal. 37. A composition of claim 33 wherein the glycosyltransferase consists essentially of a catalytic domain and about three stem region amino acids. 38. **An expression cassette** comprising a promoter operably linked to a DNA sequence encoding a secretable, soluble glycosyltransferase. 47. **A method for producing a sialylated oligosaccharide** comprising: reacting an starting oligosaccharide with CMP-NeuAc and a homogeneous, soluble sialyltransferase under conditions in which the sialyltransferase catalyzes the transfer of a sialic acid from the CMP-NeuAc to the starting oligosaccharide to produce a sialylated oligosaccharide. 48. **A composition comprising a homogeneous soluble sialyltransferase** in substantially pure form which lacks a functional retention signal and a signal anchor domain.	

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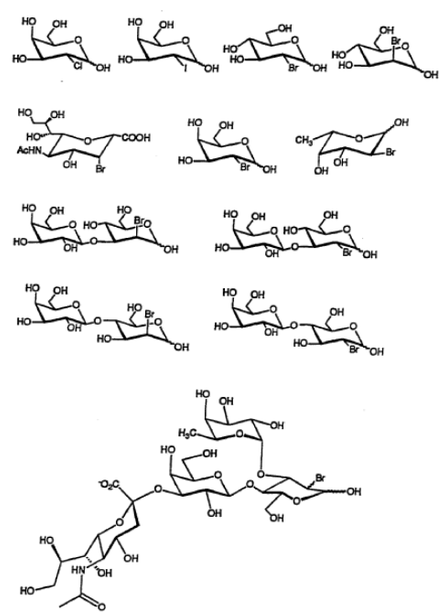
	1990-09-11	**EP0475354 A2** **SIALYSATION OF GLYCOPROTEINS BY GENETIC TECHNOLOGY** ***FAMILY MEMBERS*** **AU199183760A** **AU661824B** **CA2051047A1** **DE4028800A1** **IE19913180A1** **JP6105692A** **PT98917A** **No US counterpart**	**BEHRINGWERKE** (Marburg, Germany) **WITHDRAWN** **1995-11-04** **Issue Date:** **1992-03-18** **Filing Date:** **1991-09-10** **Priority Date:** **1990-09-11**	**Zettlmeissl Gerd** **[DE]** **Grundmann Ulrich** **[DE]** **Becker Achim** **[DE]** **Hermentin Peter** **[DE]**	Claims translated from German 1. **A process for sialylation of glycoproteins**, characterized in that one brings a sequence encoding a sialyltransferase, together with a DNA sequence coding for the glycoprotein to sialylating DNA sequence in a eukaryotic cell for expression of sialylated glycoprotein, and isolating the sialylated glycoprotein. 2. A method according to claim 1, characterized in that one uses the gene coding for α-galactoside a 2,3-sialyltransferase DNA sequence. 3. A method according to claim 1, characterized in that one uses the α-galactoside a 2,6-sialyltransferase-encoding DNA sequence. 4. A method according to claim 1, characterized in that one uses for the N-α-2,6-sialyltransferase Acetylgalactosaminosid coding DNA sequence. 5. A method according to claim 1, characterized in that one uses the gene coding for a human α-2,3-sialyltransferase galactoside DNA sequence. 6. A method according to claim 1, characterized in that one uses the gene coding for a human α-2,6-sialyltransferase galactoside DNA sequence. 7. A method according to claim 1, characterized in that one uses for the human α-N-Acetylgalactosaminosid 2,6-sialyltransferase-encoding DNA.	***STATUS*** • WITHDRAWN 1995-11-04 ***METHODOLOGY*** PRODUCTION OF SIALYLATED GLYCO-PROTEIN(S) BY EXPRESSION OF DNA CODING FOR GLYCOPROTEIN AND SIALYLTRANSFERASE IN EUKARYOTIC CELLS • Appears to be first disclosure of mammalian cells expressing human human α-2,6-sialyltransferase galactoside DNA sequence • EP Register indicates that the file history has been destroyed.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					12. A method according to claim 1, characterized in that there is used as eukaryotic cells are mammalian cells. 13. A method according to claim 1, characterized in that there is used as eukaryotic cells, BHK, C127, CHO, mouse myeloma, Vero or Hela cells. 14. **A process for sialylation of glycoproteins**, characterized in that one introduces a DNA encoding sialyltransferase sequence into a cell which naturally forms a glycoprotein, and the resulting sialylated glycoprotein isolated. 15. A method according to claim 14, characterized in that a monoclonal antibody-producing hybridoma used as the eukaryotic cell. 16. Sialylated glycoproteins obtainable according to any one of claims 1 to 15.	
	1991-10-15	**WO1993008205A1** **PRODUCTION OF FUCOSYLATED CARBOHYDRATES BY ENZYMATIC FUCOSYLATION SYNTHESIS OF SUGAR NUCLEOTIDES; AND IN SITU REGENERATION OF GDP-FUCOSE** **FAMILY MEMBERS** AT174925T AT193551T AU199216680A AU199221459A AU199227854A AU199347833A AU668505B AU672029B AU675209B BG98713A CA2106301A1 CA2106301C CA2121365A1	**SCRIPPS RESEARCH INSTITUTE** (La Jolla, CA) **Publication Date: 1993-04-29** **Filing Date: 1992-10-15** **Earliest Effective Filing Date: 1991-10-15** **Priority Date: 1991-10-15**	**Wong Chi-Huey** **Ichikawa Yoshitaka** **Shen Gwo-Jenn** **Liu Kun-Chin**	1. **A method of producing a fucosylated carbohydrate in a single reaction mixture** comprising the steps of: (a) using a fucosyltransferase to form an 0-glycosidic bond between a nucleoside 5'-diphosphofucose and an available hydroxyl group of a carbohydrate acceptor molecule to yield a fucosylated carbohydrate and a nucleoside 5'- diphosphate, and; (b) recycling in situ the nucleoside 5'diphosphate with fucose to form the corresponding nucleoside 5'-diphospho-fucose. 5. The method of claim 1 wherein the carbohydrate acceptor molecule is **sialylated.** 6. The method of claim 1 for producing a **fucosylated sialylated carbohydrate** molecule through enzymatic formation of glycosidic linkages in a single reaction mixture comprising: (a) forming a first glycosidic linkage between an diphosphonucleoside-activated glycosyl donor and an available hydroxyl group of a carbohydrate acceptor molecule using a first glycosyltransferase; (b) forming a second glycosidic linkage between a monophosphonucleoside-activated **sialyl** donor and an available hydroxyl group of the carbohydrate acceptor molecule using a **sialyltransferase**; and (c) forming a third glycosidic linkage between a diphosphonucleoside-activated fucosyl donor and an available hydroxyl group of the carbohydrate acceptor molecule by the method of claim 1, said glycosidic linkages of steps (a), (b) and (c) being formed in a single reaction mixture. 12. The method of claim 6 wherein the sialy1transferase is selected from the group consisting of a2,3 sialyltransferase, a2,4 sialyltransferase, a2,6 sialyltransferase and a2,8 sialytransferase.	***STATUS*** ***METHODOLOGY*** CLAIMS DRAWN TO IN VITRO METHODS OF PRODUCING FUCOSYLATED SIALYLATED CARBOHYDRATE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		CA2121365C CA2139506A1 CA2139506C CZ199400842A3 DE69228005D1 DE69228005T2 DE69231127D1 EP576592B1 EP642526B1 EP654087A4 ES2129458T3 FI199401732A FI941732A0 HU199401072D0 HU69791T IL106366D0 JP03476455B2 JP6505638A JP7500248A JP8500012A NO199401346A NO199401346D0 NZ255109A RO118132B1 RU2125092C1 SK199400425A3 US20020068331A1 US5276120A US5278299A US5403726A US5461143A US5593887A US5596005A US5759823A US6168934B1 US6319695B1 US6518418B1 US7335500B2 WO1992016640A1 WO1992021657A1 WO1994002624A1			13. The method of claim 6 wherein the fucosyltranferase is selected from the group consisting of al,2-fucosyltransferase, al,3 fucosyltransferase, al,6 fucosyltransferase, al,4 fucosyltransferase and al,3/4 fucosyltransferase. 14. The method of claim 6 wherein the fucosyltransferase is selected from the group consisting of P-galactosidase al,2 fucosyltransferase, N- acetylglucosamine al,3 fucosyltransferase, N-acetylglucosamine al,4 fucosyltransferase, N-acetylglucosamine al,6 fucosyltransferase and N-acetylglucosamine al,3/4 fucosyltransferease. 21. **An in vitro reaction system** comprising a **fucosyltransferase** and a nucleoside-diphospho fucose forming enzyme. 51. **A glycosylhalohydrin** having a formula selected from the group consisting of 	

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	1992-03-09	**WO1993018157** A1 **COMPOSITIONS AND METHODS FOR THE IDENTIFICATION AND SYNTHESIS OF SIALYL-TRANSFERASES** **FAMILY MEMBERS** AT228565T AU199337919A,AU668714B BG62492B1, BG99100A CA2131703C, CA2167521C CZ199402204A3 DE69332520T2, DK632831T3 **EP632831 B1** **LAPSED 2013-03-09** ES2191011T3 FI119692B, FI199404136A FI944136A0,HU199402586D0 HU219260B, HU69933T JP2007020587A JP7505771A, JP9501317A NO199403323D0, NO314666B1, NZ251096A SK199401088A3 **US5858751 A** **EXPIRED 2012-03-09** **[see TABLE A- TAB 7A]** **US5962294** **EXPIRES 2016-10-05** **[see TABLE A- TAB 7A]**	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA (Oakland, CA)** **Publication Date: 1993-09-16** **Filing Date: 1993-03-09** **Earliest Effective Filing Date: 1992-03-09** **Priority Date: 1992-03-09**	**Paulson; James C. (Del Mar, CA)** **Wen; Xiaohong (San Diego, CA)** **Livingston; Brian (San Diego, CA)** **Burlingame; Alma L. (Sausalito, CA)** **Medzihradszky; Katalin (San Francisco, CA)** **Kelm; Sorge (Uiel, DE)** **Gillespie; William (Santa Monica, CA)**	1. **A sialyltransferase** essentially free of substances found in an in vivo physiological milieu with the proviso that the sialyltransferase is other than rat Gal β 1,4 GlcNAc α2,6 sialyltransferase. 8. **A DNA isolate encoding sialyltransferase** with the proviso that said DNA isolate is other than rat Gal β 1,4 GlcNAc α2,6 sialyltransferase. 19. **A recombinant expression vector** comprising DNA encoding sialyltransferase with the proviso that said sialyltransferase is not rat Gal β 1,4 GlcNAc α2,6 sialyltransferase. 22. **A process for producing sialyltransferase** which comprises constructing a vector having DNA encoding sialyltransferase, transforming a host cell with the vector and culturing the transformed cell with the proviso that said sialyltransferase is not Gal β 1,4 GlcNAc α2,6 sialyltransferase. 27. **A DNA isolate encoding a polypeptide** having the amino sequence shown in Fig. 1 or Fig. 2. 28. **A method for producing DNA encoding a sialyltransferase** comprising: a. preparing oligonucleotide probes corresponding to a sialyltransferase conserved region of homology; b. screening by hybridization a DNA library using the oligonucleotide probes; C. detecting the hybridization of step b; and d. recovering a product of step c. 30. **A method for recovering DNA encoding sialyltransferase** comprising: a) constructing a nucleic acid library containing a gene encoding the sialyltransferase; b) amplifying the DNA encoding sialyltransferase use polymerase chain reaction (PCR) by use of a primer which binds to base pairs encoding at least about amino acids from a heptapeptide in the conserved region of homology; C) subcloning PCR products into a suitable vector; d) sequence individual PCR clones to identify conserved region of homology containing clones; e) screening the nucleic acid library using the product of step (d); and f) recovering the product of step e). 38. **A DNA fragment** encoding a conserved region of homology. 39. The DNA fragment of claim 38 having a nucleotide sequence as set forth in Figure 13.	***STATUS*** • **US5962294 expires in 2016** • **has claims drawn to Gal□1,3 GalNAc□2,3 sialyltransferase ("alpha.2,3-0")** ***METHODOLOGY*** CLAIMS DRAWN TO SIALYLTRANSFERASE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		WO199504816 (see below)				
	1992-11-27	**WO1994012646 A1** **PROTEINS HAVING GLYCOSYL-TRANSFERASE ACTIVITY** **FAMILY MEMBERS** AU199456242A AU682837B CA2148929A1 **EP788548A1** **WITHDRAWN 1999-06-01** FI199502574A0 FI199502574A FI952574A0 JP8503373A MX9307465A NO199502039A NO199502039D0 NZ258525A **US5641668 A** **EXPIRED 2001-06-24** **[see TABLE A- TAB 8]**	**CIBA GEIGY CORP (Basel, CH)** **Publication Date: 1994-06-09** **Filing Date: 1993-11-15** **Earliest Effective Filing Date: 1992-11-27** **Priority Date: 1992-11-27**	**Berger; Eric G. (Schofflisdorf, CH)** **Watzele; Manfred (Weilheim, DE)** **Iwanow; Svetoslav X. (Sofia, BG)**	1. **A protein having glycosyltransferase activity** comprising identical or different catalytically active domains of glycosyltransferases. 2. A protein according to claim 1 which is a hybrid protein. 3. A protein according to claim 2 comprising a membrane-bound or soluble glycosyltransferase, linked to a soluble glycosyltransferase. 4. A protein according to claim 2 comprising a suitable linker consisting of genetically encoded amino acids. 5. A protein according to claim 2 selected from the group consisting of the protein having the amino acid sequence depicted in SEQ ID NO. 5 and the protein having the amino acid sequence depicted in SEQ ID NO. 7. 6. A method for preparing a protein according to claim 2 comprising culturing a suitable transformed yeast strain under conditions which allow the expression of said protein. 7. A DNA molecule coding for a protein according to claim 2. 8. A hybrid vector comprising a DNA molecule according to claim 7. 9. A transformed yeast strain comprising a hybrid vector according to claim 8. 10. Use of a protein according to claim 1 for glycosylation.	***STATUS*** • **all US patents have expired** ***METHODOLOGY*** CLAIMS DRAWN TO HYBRID PROTEIN HAVING GLYCOSYLTRANSFERASE ACTIVITY.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	1993-05-17	**WO1994026908 A1** **CHO CELL SIALIDASE BY RECOMBINANT DNA TECHNOLOGY** **FAMILY MEMBERS** AT175239T AT474925T AU199468349A AU199878419A AU200116688A AU771747B2 CA2160458A1 DE69415669D1 DE69415669T2 DE69435304D1 DK700443T3 DK866130T3 **EP700443 B1** **EXPIRED 2014-05-17** **EP866130 B1** **EXPIRED 2014-05-17** ES2128562T3 ES2346941T3 GR3029781T3 JP8510133A NZ266714A PT866130E US20020076791A1 US20030148493A1 **US5928915** **EXPIRED 2013-05-17** **US6562588 B2** **EXPIRED 2013-05-17** **US6916916 B2** **EXPIRED 2013-05-17**	**ROCHE/ GENENTECH (MA)** **Publication Date: 1994-11-24** **Filing Date: 1994-05-17** **Earliest Effective Filing Date: 1993-05-17** **Priority Date: 1993-05-17**	**Warner; Thomas G. (San Carlos, CA)** **Sliwkowski; Mary B. (San Carlos, CA)**	1 A recombinant cell line wherein a constitutive **sialidase gene** is not functionally expressed. 2. The recombinant cell line of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene by any of mutation, addition and deletion of a nucleotide. 3. The recombinant cell line of claim 1 wherein the sialidase gene is not functionally expressed because of deletion of the gene. 4. The recombinant cell line of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene by homologous recombination. 5. The recombinant cell line of claim 1 wherein the sialidase gene is not functionally expressed because of disruption of the gene function by regulation of transcription using antisense RNA. 6. The recombinant cell line of claim 1 which is a Chinese hamster ovary derived cell line. 7. Substantially homogeneous sialidase, obtainable from cell culture fluid of a Chinese hamster ovary cell line. 8. Sialidase according to claim 7 having a molecular weight of about 43 kDa. 9. Sialidase according to claim 7 of which a tryptic fragment has the amino acid sequence CRVQAQSPNSGLDFQDN (SEG. ID. NO. 13). 10. Sialidase according to claim 7 to which binds an antibody obtained using a peptide of amino acid sequence CRVQAQSPNSGLDFQDN (SEG. ID. NO. 13) . 11. **A nucleic acid sequence encoding a sialidase**, obtained by a process comprising: (a) preparing an oligonucleotide probe encoding part or all of the amino acid sequence CRVOAQSPNSGLDFQDN (SEQ. ID. NO. 13); (b) hybridizing the probe with nucleic acid in a mammalian DNA library to form hybrids; (c) isolating hybrids, thereby obtaining a said nucleic acid sequence encoding a sialidase. 12. A nucleic acid sequence according to claim 11 wherein the sialidase is obtainable from cell culture fluid of a Chinese hamster cell line. 13. **An oligonucleotide probe** useful in obtaining a sialidase-encoding gene and having a sequence encoding part of all of the amino acid sequence CRVQAQSPNSGLDFQDN (SEG. ID. NO. 13). 14. **A process for the production of a glycoprotein**, comprising expressing nucleic acid encoding the glycoprotein in a host cell wherein a constitutive sialidase gene is not functionally expressed.	***STATUS*** • **all US and EP patents have expired** ***METHODOLOGY*** CLAIMS DRAWN TO EUKARYOTIC CELL (CHO CELLS) TRANSFORMED WITH AN VECTOR EXPRESSING SIALIDASE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					15. The process according to claim 14 wherein the sialidase gene is not functionally expressed because of disruption of the gene by any of mutation, addition and deletion of a nucleotide. 16. The process according to claim 14 wherein the sialidase gene is not functionally expressed because of deletion of the gene. 17. The process according to claim 14 wherein the sialidase gene is not functionally expressed because of disruption of the gene by homologous recombination. 18. The process according to claim 14 wherein the sialidase gene is not functionally expressed because of disruption of the gene function by regulation of transcription using antisense RNA. 19. The process according to claim 14 which is a Chinese hamster ovary derived cell line. 20. **An isolated DNA** comprising a nucleotide sequence that encodes the amino acid sequence shown in Figure 10 for CHO cell sialidase. 21. **An expression vector** comprising a nucleotide sequence that encodes the amino acid sequence shown in Figure 10 for **CHO cell sialidase**. 22. **A host cell transformed with an isolated DNA** that encodes the amino acid sequence shown in Figure 10 for **CHO cell sialidase.** 23. **A process comprising transforming a host cell with an expression vector** capable, in the host cell transformed with the vector, of expressing a polypeptide having the amino acid sequence shown in Figure 10 for **CHO cell sialidase.** 24. The process of claim 23 that further comprises the steps of culturing the transformed host cell, and recovering the polypeptide from the host cell culture.	
	1993-08-04	**WO199504816** **COMPOSITIONS AND METHODS FOR**	**THE REGENTS OF THE UNIVERSITY OF CALIFORNIA (Oakland, CA)** **Publication Date:**	**Paulson; James C. (Del Mar, CA)** **Wen; Xiaohong (San Diego, CA)** **Livingston; Brian**	1. **A sialyltransferase** essentially free of substances found in an *in vivo* physiological milieu with the proviso that the sialyltransferase is other than rat Gal β 1,4 GIcNAc α2,6 sialyltransferase. 8. **A DNA isolate encoding sialyltransferase** with the proviso that said DNA isolate is other than rat Gal β 1,4 GIcNAc α2,6 sialyltransferase.	***STATUS*** • **US5962294 EXPIRES 2016-10-05** ***METHODOLOGY***

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		PRODUCING SIALYL-TRANSFERASES **FAMILY MEMBERS** AT228565T AU199337919A AU668714B BG62492B1 BG99100A CA2131703A1 CA2131703C CA2167521A1 CA2167521C CZ199402204A3 DE69332520D1 DE69332520T2 DK632831T3 **EP632831B1** **EXPIRED 2012-03-09** **[see TAB 7C]** ES2191011T3 FI119692B FI199404136A0 FI199404136A FI944136A0 HU199402586D0 HU219260B HU69933T JP2007020587A JP7505771A JP9501317A NO199403323A NO199403323D0 NO314666B1 NZ251096A SK199401088A3 **US5858751 A** **EXPIRED 2012-03-09** **[see TABLE A- TAB 7A]** **US5962294** **EXPIRES 2016-10-05** **[see TABLE A- TAB 7A]**	**1995-02-16** **Filing Date: 1994-07-27** **Earliest Effective Filing Date: 1993-08-04** **Priority Date: 1993-08-04**	**(San Diego, CA)** **Burlingame; Alma L. (Sausalito, CA)** **Medzihradszky; Katalin (San Francisco, CA)** **Kelm; Sorge (Uiel, DE)** **Gillespie; William (Santa Monica, CA)**	13. **A recombinant expression vector comprising DNA encoding sialyltransferase** with the proviso that said sialyltransferase is not rat Gal β 1,4 GIcNAc α2,6 sialyltransferase. 16. **A process for producing sialyltransferase** which comprises constructing a vector having DNA encoding sialyltransferase, transforming a host cell with the vector and culturing the transformed cell with the proviso that said sialyltransferase is not Gal β 1,4 GIcNAc α2,6 sialyltransferase. 19. **A method for producing DNA encoding a sialyltransferase** comprising: a. preparing oligonucleotide probes corresponding to a sialyltransferase conserved region of homology; b. screening by hybridization a DNA library using the oligonucleotide probes; C. detecting the hybridization of step b; and d. recovering a product of step c. 21. **A method for recovering DNA encoding sialyltransferase** comprising: a) constructing a nucleic acid library containing a gene encoding the sialyltransferase b) amplifying the DNA encoding sialyltransferase use polymerase chain reaction (PCR) by use of a primer which binds to base pairs encoding at least 5 amino acids from a heptapeptide in the conserved region of homology; c) subcloning PCR products into a suitable vector; d) sequence individual PCR clones to identify conserved region of homology containing clones; e) screening the nucleic acid library using the product of step d) ; and f) recovering the product of step e). 22. **A DNA isolate comprising a DNA sequence encoding rat ST3N sialyltransferase** as defined in Sequence ID No. 4 or its amino acid sequence variants. 27. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding rat ST3N sialyltransferase as defined in Sequence ID No. 4. 28. **An essentially pure rat ST3N sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 4 or its amino acid sequence variants. 33. **A DNA isolate** comprising a DNA sequence encoding porcine ST30 sialyltransferase as defined in Sequence ID No. 2 or its amino acid sequence variants. 38. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding porcine ST30 sialyltransferase as defined in Sequence ID No. 2. 39. **An essentially pure porcine ST30 sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 2 or its amino acid sequence variants. 44. **A DNA isolate** comprising a DNA sequence encoding human ST3N sialyltransferase as defined in Sequence ID No. 10 or its amino acid sequence variants.	PRODUCTION OF MAMMALIAN SIALYLTRANSFERASE(S) USEFUL IN THE ADDITION OF SIALIC ACIDS ON CARBOHYDRATE(S) AND THE IDENTIFICATION OF OTHER MEMBERS OF THE SAME GENE FAMILY

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		WO1993018157 A1 (see above)			49. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding human ST3N sialyltransferase as defined in Sequence ID No. 10. 50. **An essentially pure human ST3N sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 10 or its amino acid sequence variants. 55. **A DNA isolate** comprising a DNA sequence encoding human STZ sialyltransferase as defined in Sequence ID No. 12 or its amino acid sequence variants. 60. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding human STZ sialyltransferase as defined in Sequence ID No. 12. 61. **An essentially pure human STZ sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 12 or its amino acid sequence variants. 66. **A DNA isolate** comprising a DNA sequence encoding human ST30 sialyltransferase as defined in Sequence ID No. 16 or its amino acid sequence variants. 71. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding human ST30 sialyltransferase as defined in Sequence ID No. 16. 72. **An essentially pure human ST30 sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 16 or its amino acid sequence variants. 77. **A DNA isolate** comprising a DNA sequence encoding rat STX sialyltransferase as defined in Sequence ID No. 8 or its amino acid sequence variants. 82. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding rat STX sialyltransferase as defined in Sequence ID No. 8. 83. **An essentially pure rat STX sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 8 or its amino acid sequence variants. 88. **A DNA isolate** comprising a DNA sequence encoding human STX sialyltransferase as defined in Sequence ID No. 14 or its amino acid sequence variants. 89. **A DNA isolate** according to claim 88 wherein said DNA sequence encodes a water soluble human STX sialyltransferase. 93. **A DNA isolate** comprising a first DNA sequence with substantial similarity to a second DNA sequence encoding human STX sialyltransferase as defined in Sequence ID No. 14. 94. **An essentially pure human STX sialyltransferase** comprising the amino acid sequence set forth in Sequence ID No. 14 or its amino acid sequence variants.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1994-12-22	**WO1996020280 A1** **ISOLATED POLYSIALYL TRANSFERASES, NUCLEIC ACID MOLECULES CODING THEREFOR, METHODS OF PRODUCTION AND USE** **FAMILY MEMBERS** AU199646870A AU692355B	**BOEHRINGER MANNHEIM** **LA JOLLA CANCER RESEARCH FOUNDATION (La Jolla, CA)** **Publication Date: 1996-07-04** **Filing Date: 1995-12-21** **Earliest Effective Filing Date:**	**Gerardy-Schahn; Rita (Hiddenhausen, DE)** **Fukuda; Minoru (San Diego, CA)** **Nakayama; Jun (San Diego, CA)** **Eckhardt; Matthias (Hanover, DE)**	1. **Isolated nucleic acid molecule** which encodes a **polysialyl transferase**. 23. **Isolated polysialyl transferase** characterized by a molecular weight of about 34 kilodaltons to about 50 kilodaltons as determined by SDS-PAGE. 27. **Isolated nucleic acid molecule** which hybridizes to a nucleic acid molecule encoding a polysialyl transferase and blocks expression of said polysialyl transferase. 33. **Method for determining expression of polysialyl transferase** in a sample comprising contacting said sample with at least one isolated nucleic acid molecule which hybridizes to a polysialyl transferase coding molecule and determining hybridization as a determination of expression of polysialyl transferase in said sample. 39. **Isolated antibody** which specifically binds to a polysialyl transferase or to a unique, immunogenic portion of a polysialyl transferase.	***STATUS*** • **All patents have expired**. ***METHODOLOGY*** CLAIMS DRAWN TO POLYSIALIC ACID (PSA) THAT IS ADDED TO THE NEURAL CELL ADHESION MOLECULE, NCAM

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		CA2208291A1 **EP871743 A4** **WITHDRAWN – 2001-11-29** JP2002509423A **US5747326A** **EXPIRED – 2002-06-04** **US5849904A** **EXPIRED – 2003-01-15** **US5959078A** **EXPIRED – 2007-10-29** **US6020201A** **EXPIRED – 2014-12-22**	**1994-12-22** **Priority Date:** **1994-12-22**		49. **Fusion protein** comprising: (i) a signal peptide (ii) a polysialyl transferase, and (iii) a non polysialyl transferase protein.	
	1995-04-11	**WO1996032491 A1** **ENZYMATIC SYNTHESIS OF GLYCOSIDIC LINKAGES** **FAMILY MEMBERS** **AT222294T** **AU199653873A** **AU199654453A** **CA2218120C** **CA2218246C** **DE69611442T2** **DE69623005T2** **DK820520T3** **EP820519 B1** **LAPSED in 2009**	**NEOSE TECHNOLOGIES*** (Horsham, PA) (*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **Publication Date:** **1996-10-17** **Filing Date:** **1996-04-10** **Earliest Effective Filing Date:** **1995-04-11** **Priority Date:**	**DeFrees; Shawn (San Marcos, CA)** **Bayer; Robert J. (San Diego, CA)** **Ratcliffe; Murray (Carlsbad, CA)**	1. **A method for the transfer of a monosaccharide from a donor substrate to an acceptor substrate**, comprising: (a) providing a reaction medium comprising at least **one glycosyl transferase**, a donor substrate, an acceptor substrate and a **soluble divalent metal** cation; and (b) supplementing the concentration of said soluble divalent metal cation to achieve a concentration in said reaction medium of between about I mM and about 75 mM for a period of time sufficient to substantially complete said synthesis. 3. A method in accordance with claim 1, wherein said soluble divalent metal cation is a member selected from the group consisting of **Mn^{2+}, Mg^{2+}, Ca^{2+}, Co^{2+}, Zn^{2+}, Cu^{2+}** and combinations thereof. 6. A method in accordance with claim 1, wherein said enzyme is **galactosyl transferase**. 7. A method in accordance with claim 1, wherein said enzyme is **galactosyl transferase** and said reaction medium further comprises **sialyl transferase**. 25. A method for the preparation of NeuAcix(2-3)GalO(l-4)(Fuca l-3) GlcN(R')0(l-3)GalO-OR, wherein R is selected from the group consisting of hydrogen, a saccharide, an oligosaccharide	***STATUS*** • **All US and EP patents have expired** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF IN VITRO GLYCOSYLATION

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		[see TABLE A - TAB 12E] **EP820520 B1** **LAPSED in 2009** **[see TABLE A - TAB 12F]** **ES2180757T3** **JP11503328A** **JP11503329A** **US5876980 A** **EXPIRED 2011-03-02** **[see TABLE A - TAB 12B]** **US5922577A** **EXPIRED 2007-07-13** **[see TABLE A - TAB 12C]** **US6030815A** **EXPIRED 2008-02-29** **[see TABLE A - TAB 12D]** **WO1996032492A1**	**1995-04-11**		and an aglycon group having at least one carbon atom; and R' is selected from the group consisting of acetyl and allyloxycarbonyl; said method comprising: (a) **galactosylating a compound of the formula GlcN(R')0(l-3)GaIO-OR with a galactosyltransferase** in the presence of a UDP-galactose under conditions sufficient to form the compound: GalO(l-4)GlcN(R')0(l-3)GalO-OR; (b) **sialylating said compound formed in (a) with a sialyltransferase** in the presence of a CMP derivative of a sialic acid using a ci(2,3) sialyltransferase under conditions wherein sialic acid is transferred to the non-reducing sugar to form the compound: NeuAca(2-3)GaIO(I--4)GIcN(R') 0(1-3)GaIO-OR; and (c) **fucosylating said compound** formed in (b) to provide said NeuAca(2-3)GalO(l-4)(Fucct l-3)GIcN(R')0(l-3)Gal-OR; wherein said galactosylating and sialylating steps are conducted in a reaction medium comprising a soluble divalent metal cation and said rnedium is supplemented with said soluble divalent metal cation to maintain tile concentration of said divalent metal cation between about I mM and about 75 mM.	
	1996-02-16	**WO1997030087 A1** **PREPARATION OF GLYCOSYLATED ANTIBODIES** **FAMILY MEMBERS** GB199603256D0 NO OTHER **FAMILY MEMBERS**	**GLAXO GROUP LTD** (Greenford, GB) **Publication Date: 1997-08-21** **Filing Date: 1997-02-14** **Earliest Effective Filing Date: 1996-02-16** **Priority Date: 1997-02-14**	**PATEL, Ashvin,** **BOYD, Paul, Nicholas** **LINES, Anne**	1. **An antibody preparation in which a N-glycosylation site of the Fc domain of the antibody is substituted with a biantennary oligosaccharide**, characterised in that at least 20% of the preparation comprises antibody molecules having an oligosaccharide that contains **at least one galactose residue.** **[No other claims]**	***STATUS*** • **No US or EP patent applications filed** ***METHODOLOGY*** NEW ANTIBODY COMPOSITIONS WITH ALTERED GLYCOSYLATION WHICH HAVE INCREASED COMPLEMENT MEDIATED CELL LYSIS ACTIVITY AND ANTIBODY DEPENDENT CELLULAR TOXICITY

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1997-05-27	**WO1998054331** **HIGH LEVEL EXPRESSION OF GLYCOSYL-TRANSFERASES** **FAMILY MEMBERS** AU199876712A NO OTHER **FAMILY MEMBERS**	**NATIONAL RESEARCH COUNCIL OF CANADA (MA)** **Publication Date: 1998-12-03** **Filing Date: 1998-05-26** **Earliest Effective Filing Date: 1997-05-27** **Priority Date: 1998-05-26**	**Wakarchuk, Warren (CA)** **Young, N., Martin (CA)**	1. **A method of expressing a glycosyltransferase in a host cell,** the method comprising introducing into the host cell a nucleic acid encoding the **glycosyltransferase** and incubating the host cell under conditions appropriate for expression of the glycosyltransferase, wherein **the host cell substantially lacks a protease that cleaves polypeptides between two consecutive positively charged amino acid residues**. 19. **A method of expressing a glycosyltransferase in a host cell**, the method comprising introducing into the host cell a nucleic acid comprising a nucleotide sequence encoding a glycosyltransferase polypeptide, wherein the nucleotide sequence lacks one or more occurrences of two adjacent codons for positively charged amino acid residues that are present in a naturally occurring glycosyltransferase polypeptide. 21. **A recombinant nucleic acid comprising a nucleotide sequence encoding a polypeptide having glycosyltransferase activity**, wherein the nucleotide sequence lacks one or more occurrences of two adjacent codons for positively charged amino acid residues that are present in a naturally occurring glycosyltransferase polypeptide. 32. **A method for the transfer of a monosaccharide from a donor substrate to an acceptor substrate**, comprising: (a) providing a reaction medium comprising at least one **glycosyltransferase**, a donor substrate, an acceptor substrate and **a soluble divalent metal cation**; and (b) incubating the reaction medium for a period of time sufficient to complete said transfer; wherein the glycosyltransferase is prepared by the method according to claim 1.	***STATUS*** • **No US or EP patent applications filed** ***METHODOLOGY*** CLAIMS DRAWN TO A "HOST CELL [THAT] SUBSTANTIALLY LACKS A PROTEASE THAT CLEAVES POLYPEPTIDES BETWEEN TWO CONSECUTIVE POSITIVELY CHARGED AMINO ACID RESIDUES." OTHER CLAIMS DRAWN TO EXPRESSION OF GLYCOSYL-TRANSFERASE IN PROKARYOTIC CELLS.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1997-06-24	**WO1998058964** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** **FAMILY MEMBERS** AT296315T AU199881634A AU757627B2 CA2293829A1 CA2293829C DE69830315D1 DE69830315T2 DK994903T3 **EP0994903 B1** **LAPSED** – 2013/2014 ES2244066T3 JP2002506353A PT994903E	**ROCHE/ GENENTECH** (South San Francisco, CA) **Publication Date: 1998-12-30** **Filing Date: 1998-06-23** **Earliest Effective Filing Date: 1997-06-24** **Priority Date: 1997-06-24**	**Raju, T. Shantha (San Mateo, CA)**	1. **A composition comprising a glycoprotein having an inummoglobulin CH2 domain** said CH2 domain having at least one N-linked oligosaccharide wherein substantially all of the oligosaccharide is a **G2 oligosaccharide**. 2. The composition of claim 1 wherein the glycoprotein is an antibody. 3. The composition of claim 2 wherein the antibody is a monoclonal antibody. 4. The composition of claim 3 wherein the antibody is an IgG. 5. The composition of claim 4 wherein the IgG is human IgG1. 6. The composition of claim 5 wherein the monoclonal antibody is selected from the group consisting of an anti-CD20 specific monoclonal antibody, an anti-HER2 specific monoclonal antibody, and antiVEGF specific monoclonal antibody, and an anti-IgE specific monoclonal antibody. 7. The composition of claim 1 wherein the glycoprotein is an immunoadhesin. 8. The composition of claim 7 wherein the immunoadhesin is a tumor necrosis factorimmunoglobulin G I chimera. 9. The composition of claim 1 wherein the glycoprotein is an antibody-immunoadhesin chimera. 10. A method of producing the composition of claim11 comprising the steps of reacting in an aqueous buffered solution at a temperature of about 25-40* C; a) a metal salt at a concentration of about 5 mM to about 25 mM; b) an activated galactose at a concentration of about 5 mM to about 50 mM; c) a galactosyltransferase at a concentration of about I mUnit/ml to about 100 mUnit/ml; d) a substrate glycoprotein; and recovering the glycoprotein. 11. The method of claim 10 wherein the metal salt is selected from the group consisting of Mn2++, Ca2++, and Ba2++.	**"RAJU I" FAMILY** ***STATUS*** • **EP0994903 LAPSED IN 2013/2014** • **US20040191256 ABANDONED** ***METHODOLOGY*** CLAIMS DRAWN TO CH2 IG DOMAIN HAVING G2 OLIGOSACCHARIDE. OTHERWISE THE SPECIFICATION DISCLOSES IN VITRO METHODS OF ADDING GALACTOSE TO THE FC DOMAIN OF PURIFIED RECOMBINANT ANTIBODIES AND ANTIBODY-IMMUNOADHESIN CHIMERAS.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					22. A method for the treatment of a disease state comprising administering to a mammal in need thereof a therapeutically effective dose of the composition of claim 1.	
	1997-06-24	**US20040191256 A1** **10/719603** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** **FAMILY MEMBERS** SEE WO1998058964 ABOVE	**ROCHE/ GENENTECH** (South San Francisco, CA) **ABANDONED** **2011-12-02** **Publication Date:** **2004-09-30** **Filing Date:** **2003-11-21** **Earliest Effective Filing Date:** **1997-06-24** **Priority Date:** **1998-06-23**	**Raju, T. Shantha (San Mateo, CA)**	1. **A composition comprising a glycoprotein having an immunoglobulin CH2 domain** said CH2 domain having at least one N-linked oligosaccharide wherein substantially all of the oligosaccharide is a **G2 oligosaccharide**. 2. The composition of claim 1 wherein the glycoprotein is an antibody. 3. The composition of claim 2 wherein the antibody is a monoclonal antibody. 4. The composition of claim 3 wherein the antibody is an IgG. 5. The composition of claim 4 wherein the IgG is human IgG 1. 6. The composition of claim 5 wherein the monoclonal antibody is selected from the group consisting of an anti-CD20 specific monoclonal antibody, an anti-HER2 specific monoclonal antibody, and anti-VEGF specific monoclonal antibody, and an anti-IgE specific monoclonal antibody. 7. The composition of claim 1 wherein the glycoprotein is an immunoadhesin. 8. The composition of claim 7 wherein the immunoadhesin is a tumor necrosis factor-immunoglobulin G1 chimera. 9. The composition of claim 1 wherein the glycoprotein is an antibody-immunoadhesin chimera. 10. A method of producing the composition of claim 1 comprising the steps of reacting in an aqueous buffered solution at a temperature of about 25-40° C.; a) a metal salt at a concentration of about 5 mM to about 25 mM; b) an activated galactose at a concentration of about 5 mM to about 50 mM; c) a galactosyltransferase at a concentration of about 1 mUnit/ml to about 100 mUnit/ml; d) a substrate glycoprotein; and recovering the glycoprotein. 11. The method of claim 10 wherein the metal salt is selected from the group consisting of Mn2++, Ca2++, and Ba2++. 22. A method for the treatment of a disease state comprising administering to a mammal in need thereof a therapeutically effective dose of the composition of claim 1.	**"RAJU I" FAMILY** ***STATUS*** • **filed on same day as WO1998058964 with identical claims** • **ABANDONED 2011-12-02** ***METHODOLOGY*** CLAIMS DRAWN TO CH2 IG DOMAIN HAVING N-LINKED G2 OLIGOSACCHARIDE. OTHERWISE THE SPECIFICATION DISCLOSES IN VITRO METHODS OF ADDING GALACTOSE TO THE FC DOMAIN OF PURIFIED RECOMBINANT ANTIBODIES AND ANTIBODY-IMMUNOADHESIN CHIMERAS.

PUBLISHED PCT/US/EP PATENT APPLICATIONS RELATING TO ANTIBODY GLYCOSYLATION

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1997-10-31	**WO1999022764** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** **FAMILY MEMBERS** AT419009T AU199910960A AU759779B2 CA2307166A1 DE69840412D1 **EP1028751 B1 LAPSED 2014-02-28** JP2001521909A	**ROCHE/ GENENTECH** (South San Francisco, CA) **Publication Date: 2000-08-23** **Filing Date: 1998-10-16** **Earliest Effective Filing Date: 1997-10-31** **Priority Date: 1997-10-31**	**Raju, T. Shantha (San Mateo, CA)**	**1. A composition comprising glycoprotein** wherein at least one glycoprotein is a glycoprotein having at least one CH2 domain and the composition is substantially free of the glycoprotein having at least one CH2 domain and having an N-linked **G1, G0, or G-1 oligosaccharide in its CH2 domain**. 2. The composition of claim 1 comprising an **antibody glycoprotein**. 20. The composition of claim 1 wherein the composition is further substantially free of the glycoprotein having an N-linked G-2 oligosaccharide in the CH2 domain. **21. A method of producing the composition of claim 20** comprising the steps of reacting in an aqueous buffered solution at a temperature of about 25-40° C.; a) a metal salt at a concentration of about 5 mM to about 25 mM; b) an activated galactose at a concentration of about 5 mM to about 50 mM; c) **a galactosyltransferase** at a concentration of about 1 mUnit/ml to about 100 mUnit/ml; d) a substrate glycoprotein; and recovering the glycoprotein. 22. The method of claim 21 wherein the metal salt is selected from the group consisting of Mn2++, Ca2++, and Ba2++. **24. The method of claim 23 wherein the** galactosyl transferase **is a** mammalian beta.1-4, galactosyl transferase**.**	**"RAJU II" FAMILY** ***STATUS*** • **EP1028751 B1 LAPSED IN 2014** • **US20040136986 ABANDONED** ***METHODOLOGY*** CLAIMS DRAWN TO CH2 IG DOMAIN HAVING N-LINKED G1, G0, or G-1 OLIGOSACCHARIDE.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	1997-10-31	**US20040136986** **10/744,844** **METHODS AND COMPOSITIONS FOR GALACTOSYLATED GLYCOPROTEINS** **FAMILY MEMBERS** SEE **WO1999022764** ABOVE	**ROCHE/ GENENTECH** (South San Francisco, CA) **ABANDONED 2011-01-26** **Publication Date: 2004-07-15** **Filing Date: 2003-12-23** **Earliest Effective Filing Date: 1997-10-31** **Priority Date: 1998-10-30**	**Raju, T. Shantha (San Mateo, CA)**	**1. A composition comprising glycoprotein** wherein at least one glycoprotein is a glycoprotein having at least one CH2 domain and the composition is substantially free of the glycoprotein having at least one CH2 domain and having an n-linked G1, G0, or G-1 oligosaccharide in its CH2 domain. 2. The composition of claim 1 comprising an **antibody glycoprotein**. 20. The composition of claim 1 wherein the composition is further substantially free of the glycoprotein having an N-linked G-2 oligosaccharide in the CH2 domain. **21. A method of producing the composition of claim 20** comprising the steps of reacting in an aqueous buffered solution at a temperature of about 25-40° C.; a) a metal salt at a concentration of about 5 mM to about 25 mM; b) an activated galactose at a concentration of about 5 mM to about 50 mM; c) **a galactosyltransferase** at a concentration of about 1 mUnit/ml to about 100 mUnit/ml; d) a substrate glycoprotein; and recovering the glycoprotein. 22. The method of claim 21 wherein the metal salt is selected from the group consisting of Mn2++, Ca2++, and Ba2++. **24. The method of claim 23 wherein the** galactosyl transferase **is a** mammalian beta.1-4, galactosyl transferase**.**	**"RAJU II" FAMILY** ***STATUS*** • **filed on same day as WO1999022764 with identical claims** • **ABANDONED 2011-01-26** ***METHODOLOGY*** CLAIMS DRAWN TO CH2 IG DOMAIN HAVING N-LINKED G1, G0, or G-1 OLIGOSACCHARIDE.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	1997-10-31	**US20020045207 A1** **09/175202** **GLYCOPROTEIN PRODUCTION PROCESS** **FAMILY MEMBERS** NO OTHER **FAMILY MEMBERS**	**ROCHE/ GENENTECH** (South San Francisco, CA) **ABANDONED 2003-09-26** **Publication Date: 2002-04-18** **Filing Date: 1998-10-19** **Earliest Effective Filing Date: 1997-10-31** **Priority Date: 1998-10-19**	**Krummen, Lynne A. (San Francisco, CA)** **Sliwkowski, Mary B. (San Carlos, CA)** **Warner, Tom (San Carlos, CA)**	1. **A process for producing a glycoprotein in a eukaryotic cell** capable of expressing the glycoprotein comprising the steps of: introducing into the eukaryotic cell at least a first and a second gene capable of being expressed by the eukaryotic cell the first gene comprising a nucleic acid sequence encoding a **galactosyltransferase** and the second gene comprising a nucleic acid sequence encoding a **sialyltransferase**; maintaining the eukaryotic cell under conditions suitable for the expression of the galactosyltransferase, the sialyltransferase and the glycoprotein. 2. The process according to claim 1 wherein the glycoprotein is a heterologous glycoprotein. 3. The process according to claim 2 wherein the eukaryotic cell is a Chinese hamster ovary (CHO) cell. 4. The process according to claim 3 wherein the heterologous glycoprotein is a human glycoprotein. 5. The process according to claim 4 wherein the sialyltransferase is an .alpha.2,3-sialyltransferase. 6. The process according to claim 5 wherein the galactosyltransferase is a .beta.1, 4-galactosyltransferase. 7. The process according to claim 1 wherein the eukaryotic cell is selected for reduced functional expression of a sialidase. 9. The process according to claim 7 wherein the eukaryotic host cell displays a decreased expression of sialidase RNA. 10. The process according to claim 7 wherein the glycoprotein is a heterologous glycoprotein. 11. The process according to claim 10 wherein the eukaryotic cell is a Chinese hamster ovary (CHO) cell. 12. The process according to claim 11 wherein the heterologous glycoprotein is a human glycoprotein. 13. The process according to claim 12 wherein the sialyltransferase is an .alpha.2,3-sialyltransferase. 14. The process according to claim 13 wherein the galactosyltransferase is a .beta.1,4-galactosyltransferase.	***STATUS*** • **ABANDONED 2003-09-26** ***METHODOLOGY*** CLAIMS DRAWN TO METHOD OF PRODUCING A GLYCOPROTEIN IN A EUKARYOTIC CELL THAT EXPRESSES GALACTOSYL-TRANSFERASE AND SIALYLTRANSFERASE

PUBLISHED PCT/US/EP PATENT APPLICATIONS RELATING TO ANTIBODY GLYCOSYLATION

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1998-05-21	**EP1086208 A2** **GALACTOSYL-TRANSFERASE FROM PLANTS INVOLVED IN GALACTOMANNAN BIOSYNTHESIS** **FAMILY MEMBERS** AU199940509A GB199810997D0 WO1999060103A3	**UNILEVER HOUSE [GB]** **WITHDRAWN 2003-12-01** **Publication Date: 2001-03-28** **Filing Date: 1999-05-21** **Earliest Effective Filing Date: 1998-05-21** **Priority Date: 1999-05-21**	**Gidley Michael John [GB]** **Chengappa Sumant [GB]** **Reid John Spence Grant [GB]** **Edwards Mary Elizabeth [GB]** **Dickson Cathryn Anne [GB]**	1. An isolated nucleic acid encoding a polypeptide which is capable of catalysing the biosynthesis of a complex non-cellulosic plant cell wall polysaccharide. 3, A nucleic acid as claimed in claim 1 or claim 2 wherein the polypeptide is a **glycosyltransferase**. 4. A nucleic acid as claimed in claim 3 wherein the polypeptide is a **galactosyltransferase**. 51. **A method for altering the quality or quantity of a polysaccharide in a host cell by influencing the glycosyltransferase activity in that cell**, the method comprising use of any one or more of the following: all or part of the nucleic acid of any one of claims 1 to 16; the polypeptide of claim 44; the antibody or fragment or polypeptide comprising the antigen-binding site thereof of claim 47. 53 A method as claimed in claim 51 or claim 52 wherein the quality altered is **galactose composition of the polysaccharide**. 54 A method as claimed in claim 53 wherein the quality altered is the **mannose:galactose ratio** in a mannose/galactose containing polysaccharide in the cell.	***STATUS*** • **WITHDRAWN 2003-12-01** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO GLYCOSYLATION IN PLANT CELLS USING GALACTOSYLTRANSFERASES FROM FENUGREEK AND GUAR.
	1998-11-18	**EP1131415 A2** **LOW COST MANUFACTURE OF OLIGOSACCHARIDES**	**NEOSE TECHNOLOGIES*** (Horsham, PA)	**Defrees Shawn (North Wales, PA)** **Johnson Karl (Willow Grove, PA)**	1**. A reaction mixture for producing a product saccharide**, wherein the reaction mixture comprises an acceptor saccharide and a first type of plant or microorganism cell that produces: a) a nucleotide sugar, and b) a first recombinant glycosyltransferase that catalyzes the transfer of a sugar from the nucleotide sugar to the acceptor saccharide to form the product saccharide.	***STATUS*** • **WITHDRAWN 2008-01-15** ***METHODOLOGY***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		FAMILY MEMBERS AU200018261A AU2004210567A1 AU773845B2 CA2351022A1 JP2002530087A MX2001004982A MX2001PA004982A US20020001831A1 **ABANDONED** 2005-12-08 WO2000029603A2 WO2000029603A3 WO2000029603A8	(*acquired by NOVO NORDISK and BioGeneriX AG in 2008) **WITHDRAWN** **2008-01-15** **Publication Date:** **2001-09-12** **Filing Date:** **1999-11-18** **Earliest Effective Filing Date:** **1998-11-18** **Priority Date:** **1999-11-18**		2. The reaction mixture of claim 1, wherein the cells are selected from one 2 or more of the group consisting of bacterial cells, yeast cells, fungal cells, and plant cells. 4. The reaction mixture of claim 1, wherein the glycosyltransferase is a **fucosyltransferase** and the nucleotide sugar is GDP-fucose. 5. The reaction mixture of claim 1, wherein the glycosyltransferase is a **sialyltransferase** and the nucleotide sugar is CMP-sialic acid. 40. **A cell** that produces a product saccharide, wherein the cell comprises: a) a recombinant gene that encodes a **glycosyltransferase**; b) an enzymatic system for forming a nucleotide sugar that is a substrate for the glycosyltransferase; and c) an exogenous saccharide acceptor moiety; wherein the glycosyltransferase catalyzes the transfer of a sugar from the nucleotide sugar to the acceptor moiety to produce the product saccharide. 50. **A cell** that produces a sulfated polysaccharide, the cell comprising: a heterologous gene that encodes a sulfotransferase; and an enzymatic system that produces PAPS. 53. **A method of producing a product saccharide**, the method comprising contacting a microorganism or plant cell with an acceptor saccharide, wherein the cell comprises: a) an enzymatic system for forming a nucleotide sugar; and b) a recombinant glycosyltransferase which catalyzes the transfer of a sugar from the nucleotide sugar to the acceptor saccharide to produce the product saccharide. 72. **A method for synthesizing a polysaccharide backbone for heparin, heparan sulfate and related compounds**, the method comprising contacting an acceptor saccharide that comprises a ten-ninal glucuronic acid or GlcNAc residue with a reaction 4 mixture that comprises: a microorganism or plant cell that comprises: a) an enzymatic system for forming LTDP-GIcNAc; and b) a recombinant GlcNAc transferase that catalyzes the transfer of GlcNAc from the UDP-GIcNAc to a terminal glucuronic acid on the acceptor saccharide to produce an acceptor saccharide that comprises a terminal GlcNAc residue; and 11 a microorganism or plant cell that comprises: a) an enzymatic system for fonning LTDP-glucuronic acid; and b) a recombinant glucuronic acid transferase that catalyzes the transfer of glucuronic acid from the UDP-glucuronic acid to a tenninal GlcNAc residue on the acceptor saccharide to produce an acceptor saccharide that	CLAIMS DRAWN TO A CELL THAT PRODUCES A PRODUCT SACCHARIDE

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
					comprises a terminal 17 glucuronic acid residue; and allowing the reaction to proceed until the polysaccharide backbone is synthesized. 76. **A method for synthesizing heparin, heparan sulfate and related compounds**, the method comprising contacting a heparan polysaccharide backbone with a reaction mixture that comprises a microorganism or plant cell which comprises: a) an enzymatic system for forming PAPS; and b) a recombinant sulfotransferase which catalyzes the transfer of a sulfate from the PAPS to the heparan polysaccharide backbone to produce an N-sulfated polysaccharide.	
	1998-12-09	**WO2000034490 A1** **A METHOD FOR MANUFACTURING GLYCOPROTEINS HAVING HUMAN-TYPE GLYCOSYLATION** **FAMILY MEMBERS** AT475714T AU200016813A	**PHYTON HOLDINGS*** ***now DOW CHEMICAL** (Midland, MI) **Publication Date: 2000-06-15** **Filing Date: 1999-12-08**	**Seki; Tatsuji (Osaka, JP)** **Fujiyama; Kazuhito (Osaka, JP)**	1. **A method of manufacturing a glycoproteln having a human-type sugar chain**, comprising a step in which a transf ormed plant cell is obtained by introducing to a plant cell the gene of glycosyltransferase and the gene of an exogenous glycoprotein, and a step in which the obtained transformed plant cell is cultivated. 2. A method according to claim 1, wherein the glycosyltransferase is an enzyme capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamihe residue. 3. A method according to Claim 1, wherein the glycoprotein with a human-type sugar chain comprises a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose.	***STATUS*** **EP1137789 B1 EXPIRES 2019-12-08** **EP2264177A1 PENDING** **US7388081 B2 EXPIRES 2020-09-09** **US8241909 B2 EXPIRES 2019-12-08** **US8853370 B2 EXPIRES 2019-12-08** ***METHODOLOGY***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		AU771908C BR199917026A BRPI9917026B1 CA2354377C DE69942636D1 DK1137789T3 **EP1137789 B1** EXPIRES 2019-12-08 [see TABLE A - TAB 23B] EP2264177A1 **PENDING** ES2350063T3 IL143641A IL143641D0, IL207261D0 JP2002543760A JP2009028054A JP2012223198A JP2014054263A MX2001005778A MX2001PA005778A NZ512185A PT1137789E US20050143564A1 US20080124798A1 US20110070649A1 US20130040391A1 **US7388081 B2** (US20050143564A1) EXPIRES 2020-09-09 [see TABLE A - TAB 23C] **US8241909** B2 (US20110070649A1) EXPIRES 2019-12-08 [see TABLE A - TAB 23D] **US8853370** B2 EXPIRES 2019-12-08 [see TABLE A - TAB 23E] WO2000034490A1 ZA200104695A	**Earliest Effective Filing Date: 1998-12-09** **Priority Date: 1999-12-09**		4. A method according to Claim 3, wherein the outer sugar chain has a straight chain configuration. 5. A method according to Claim 3, wherein the outer sugar chain has a branched configuration. 6. A method according to Claim 5, wherein the branched sugar chain portion has a mono-, bi-, tri-or tetra configuration. 7. A method according to Claim 1 through Claim 6, wherein the glycoprotein contains neither fucose nor xylose. 8. **A plant cell having a sugar chain adding mechanism which can conduct a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue**, wherein the sugar chain adding mechanism adds a sugar chain containing a core sugar chain and an outer sugar chain, wherein the core sugar chain comprises a plurality of mannose and acetylglucosamine, and wherein the outer sugar chain contains a terminal sugar chain portion with a non-reducing terminal galactose. 9. A plant cell according to claim 8, wherein the plant cell is transformed with the gene of a first enzyme capable of conducting a transfer reaction of a galactose residue to a non-reducing terminal acetylglucosamine residue and the gene of a second enzyme which can enhance the f J rst enzyme. 10. A plant cell according to claim 9, wherein the second enzyme is selected from the group consisting of Mannosidase I, Mannosidase II, ~3 1, 4-Galactosyltransf erase (GalT) and N-acetylglucosaminyltransferase I (GlcNAcI). 11. A plant regenerated from the plant cell of claim 8. 12. **A recombinant plant, or portion thereof**, that produces mammalian-like glycoproteins comprising neither fucose or xylose. 13. A glycoprotein with a human-type sugar chain obtained using the method according to Claim 1 through Claim 7. 14. **A plant-produced glycoprotein** comprising neither fucose or xylose.	CLAIMS DRAWN TO METHOD OF MANUFACTURING A GLYCOPROTELN IN A GENETICALLY ENGINEERED PLANT CELL.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1999-10-26	**US8193415B2** **13/458083** **US20120237972 A1** **MAMMALIAN-TYPE GLYCOSYLATION IN PLANTS** **FAMILY MEMBERS** AT365219T AT478150T AU200117383A AU200117384A BR200015031A CA2389217A1 DE60035285D1 DE60035285T2 DE60044858D1 DK1228231T3 DK1772518T3	**STICHTING DIENST LAND-BOUWKUNDIG ONDERZOEK** (Wageningen, NL) **EXPIRES 2020-10-26** **PTA: 0 days** **Publication Date: 2012-09-20** **Filing Date: 2012-04-27** **Earliest Effective Filing Date: 1999-10-26**	**Bakker; Hendrikus Antonius Cornelis; (Hannover, DE)** **Bosch; Hendrik Jan (Wageningen, NL)**	1. **A plant comprising a gene sequence which encodes and expresses a mammalian .beta.1,4-galactosyltransferase and a gene sequence which encodes and expresses a glycoprotein or a functional fragment thereof**, further comprising a gene sequence which encodes and expresses a full-length .beta.1,3-glucuronyltransferase, wherein the plant produces a glycoprotein or a functional fragment thereof comprising a complex N-linked glycan, wherein a galactose residue is attached to a N-acetylglucosamine residue, and wherein the galactose residue is further extended by a glucuronic acid residue. 2. The plant of claim 1, wherein the .beta.1,3-glucuronyltransferase is a rat .beta.1,3-glucuronyltransferase. 3. The plant of claim 1, wherein the mammalian .beta.1,4-galactosyltransferase is a human .beta.1,4-galactosyltransferase. 4. The plant of claim 1, wherein the complex N-linked glycan is devoid of xylose residues. 5. The plant of claim 1, wherein the complex N-linked glycan is devoid of fucose residues. 6. The plant of claim 1, wherein the plant belongs to a genus selected from the group consisting of Nicotiana, Sprirodella, Wolffia, Wolffiella, and Lemna.	***STATUS*** • **EXPIRES 2020-10-26** ***METHODOLOGY*** CLAIMS DRAWN TO GLYOENGINEERED PLANT CELLS

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		EP1228231A1 EP1228231B1 EP1772518A2 EP1772518A3 EP1772518B1 EP2251426A1 ES2288882T3 ES2349427T3 HK1105785A1 IL149271A IL149271D0 IL204883A IL212887D0 IL212888D0 IL212889D0 JP04890712B2 JP2003512076A MX2002004142A MX2002PA004142A NZ518532A PT1228231E PT1772518E TR200201121T2 US20030024012A1 US20040194166A1 US20080003680A1 US20110030108A1 US7781647B2 US8193415B2 US8907163B2 WO2001031044A1 WO2001031045A1 ZA200203227A	**Priority Date: 2000-10-26**		7. The plant of claim 1, wherein the plant is selected from the group consisting of tobacco, Arabidopsis thaliana, duckweed, corn, potato, and tomato. 8. The plant of claim 1, wherein the glycoprotein is a heterologous or recombinant glycoprotein. 9. The plant of claim 8, wherein the glycoprotein is a mammalian glycoprotein. 10. The plant of claim 1, the plant further comprising a gene sequence which encodes and expresses a sulfotransferase that transfers sulfate to glucuronic acid. 11. **A transgenic plant cell which comprises a gene sequence which encodes and expresses a mammalian .beta.1,4-galactosyltransferase and a gene sequence which encodes and expresses a glycoprotein or functional fragment thereof**, further comprising a gene sequence which encodes and expresses a full-length .beta.1,3-glucuronyltransferase, wherein the plant cell produces a glycoprotein or functional fragment thereof comprising a complex N-linked glycan, wherein a galactose residue is attached to a N-acetylglucosamine residue, and wherein the galactose residue is further extended by a glucuronic acid residue. 12. The plant cell of claim 11, wherein the .beta.1,3-glucuronyltransferase is a rat .beta.1,3-glucuronyltransferase. 13. The plant cell of claim 11, wherein the mammalian (.beta.1,4-galactosyltransferase is a human .beta.1,4-galactosyltransferase. 14. The plant cell of claim 11, wherein xylosyltransferase activity is knocked out. 15. The plant cell of claim 11, wherein fucosyltransferase activity is knocked out. 16. The plant cell of claim 11, wherein the plant cell belongs to a genus selected from the group consisting of Nicotiana, Sprirodella, Wolffia, Wolffiella, and Lemna. 17. The plant cell of claim 11, wherein the plant cell is selected from the group consisting of tobacco, Arabidopsis thaliana, corn, duckweed, potato, and tomato. 18. The plant cell of claim 11, wherein the plant cell is capable of regenerating into a whole plant. 19. The plant cell of claim 11, wherein the glycoprotein is a heterologous or recombinant glycoprotein. 20. The plant cell of claim 19, wherein the glycoprotein is a mammalian glycoprotein. 21. The plant cell of claim 11, the plant cell further comprising a gene sequence which encodes and expresses a sulfotransferase that transfers sulfate to glucuronic acid.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	1999-12-09	**WO2001042492 A1** **ENGINEERING INTRACELLULAR SIALYLATION PATHWAYS** **FAMILY MEMBERS** NO **FAMILY MEMBERS**	**HUMAN GENOME SCIENCES INC** **UNIVERSITY OF WYOMING** **UNIV JOHNS HOPKINS** **TEMPLE UNIVERSITY** **Publication Date: 2001-06-14** **Filing Date: 2000-12-07** **Earliest Effective Filing Date: 1999-12-09** **Priority Date: 2000-12-07**	**Betenbaugh, Michael (US)** **Lawrence, Shawn (US)** **Lee, Yuan, C. (US)** **Coleman, Timothy (US)** **Palter, Karen (US)** **Jarvis, Don (US)**	I. **A cell of interest** producing the donor substrate CMP-SA above endogenous levels. 2. **A cell of interest** producing an acceptor substrate, the donor substrate CMP-SA, and expressing the enzyme **sialyltransferase**; wherein said acceptor substrate is a glycan. 3. The cell of claim 2 wherein said glycan is a branched glycan comprising GalGlcNAcMan by at least one branch of said glycan and said Gal is a terminal Gal. 4. The cell of claim 3 wherein said glycan is an asparagine-linked glycan. 5. A cell of interest producing **sialylated glycoprotein** above endogenous levels. 6. The cell of claim 5, wherein said glycoprotein is **asparagine (N)-linked**. 7. The cell of claim 5, wherein said glycoprotein is **heterologous**. 8. The cell of claim 7, wherein said heterologous glycoprotein is **mammalian**. 27. **A method for manipulating glycoprotein production in an insect cell**, said method comprising enhancing expression of at least one enzyme selected from the group consisting of: a) GlcNAc-2 epimerase; b) an enzyme catalyzing conversion of UDP-GlcNAc to ManNAc; c) sialic acid synthetase; d) aldolase; e) CMP-SA synthetase; f) CMP-SA transporter; and	***STATUS*** **ABANDONED - NOT NATIONALIZED** ***METHODOLOGY*** CLAIMS DRAWN TO GLYCOSYLATION IN INSECT CELLS

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					wherein the expression of each enzyme expressed is enhanced to above endogenous levels. 48. **A method for producing a sialylated glycoprotein in a cell of interest** said method comprising: a) determining the carbohydrate substrates in said cell; b) transforming said cell with enzymes to produce necessary precursor substrates; and c) constructing a processing pathway in said cell to produce a sialylated glycoprotein.	
2000-05-12	**2000-05-12**	**US20100322940 A1** **12/820926** **IN VITRO MODIFICATION OF GLYCOSYLATION PATTERNS OF RECOMBINANT GLYCOPEPTIDES** **FAMILY MEMBERS** AU200163149A CA2407707A1 EP1285072A2 HU200302299A2 JP2004528001A MX2002011016A MX2002PA011016A NZ522320A US20020019342A1 ABANDONED US20030003529A1 ABANDONED US20030040037A1 ABANDONED US20030180835A1 ABANDONED	**NOVO NORDISK (Bagsvaerd, DK)** **ABANDONED 2012-04-23** **Publication Date: 2010-12-23** **Filing Date: 2010-06-22** **Earliest Effective Filing Date: 2000-05-12** **Priority Date: 2001-05-14**	**Bayer; Robert J. (San Diego, CA)**	1. **A method for modifying the fucosylation pattern of a recombinant glycopeptide** comprising an acceptor, said method comprising: contacting a full-length recombinant glycopeptide with a reaction mixture that comprises a fucose donor moiety and a **fucosyltransferase** under appropriate conditions in vitro to transfer fucose from the fucose donor moiety to the acceptor moiety, such that the glycopeptide has a substantially uniform fucosylation pattern, wherein said acceptor moiety is Galβ1,4GlcNAc-OR or NeuAcα2,3Galβ1,4GlcNAc-OR, wherein R is an amino acid, a saccharide, an oligosaccharide or an aglycon group having at least one carbon atom and is linked to or is part of a glycopeptide, wherein said fucosyltransferase is an isolated, recombinantly produced human FucT-VI or human FucT-VII **fucosyltransferase lacking a membrane anchoring domain,** **and wherein said fucosyltransferase** provides at least 2-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using an isolated, recombinantly produced FucT-V. 2. The method of claim 1, wherein said isolated, recombinantly produced human fucosyltransferase provides at least 4-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using said isolated, recombinantly produced FucT-V. 3. The method of claim 2, wherein said isolated, recombinantly produced human fucosyltransferase provides at least 8-fold greater fucosylation of said glycopeptide than is achieved under identical conditions using said isolated, recombinantly produced FucT-V. 4. The method of claim 1, wherein the fucosyltransferase is human FucT-VI. 5. The method of claim 2, wherein the fucosyltransferase is human FucT-VI. 6. The method of claim 3, wherein the fucosyltransferase is human FucT-VI.	***STATUS*** • **ALL US APPLICATIONS ABANDONED** ***METHODOLOGY*** CLAIMS DRAWN TO METHOD FOR MODIFYING THE FUCOSYLATION PATTERN OF A RECOMBINANT GLYCOPEPTIDE

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		WO2001088117A2 WO2001088117A3 ZA200208796A			7. The method of claim 1, wherein the fucosyltransferase is human FucT-VII. 8. The method of claim 2, wherein the fucosyltransferase is human FucT-VII. 9. The method of claim 3, wherein the fucosyltransferase is human FucT-VII. 10. The method of claim 1, wherein the concentration of said fucosyltransferase is at least 1 Unit/ml. 11. The method of claim 1, wherein said full-length recombinant glycopeptide is a clotting factor. 12. The method of claim 11, wherein said clotting factor is selected from the group consisting of Factor VIII and Factor IX. 13. The method of claim 1, wherein said clotting factor is present at a concentration of at least 2 mg/ml. 14. The method of claim 1, wherein the concentration of said fucosyltransferase is 50 mU or less of said fucosyltransferase per mg of glycopeptide. 15. A composition comprising a recombinant glycopeptide fucosylated according to the method of claim 1 and a carrier therefor. 16. The composition of claim 15, wherein the recombinant glycopeptide is a clotting factor, a hormone, a growth factor, an enzyme, an enzyme inhibitor, a cytokine, a receptor, a ligand, or a monoclonal antibody. 17. The composition of claim 16, wherein the recombinant glycopeptide is a clotting factor selected from the group consisting of Factor VIII and Factor IX. 18. The composition of claim 16, wherein the recombinant glycopeptide is a growth factor selected from the group consisting of erythropoietin (EPO) and granulocyte colony stimulating factor (G-CSF). 19. The composition of claim 15, wherein at least 80% of the acceptor moieties on the glycopeptide are fucosylated. 20. The composition of claim 15, wherein glycopeptide is attached to a solid support. 21. The composition of claim 20, wherein the solid support is an affinity chromatography medium. 22. The composition of claim 15, wherein the glycopeptide is on a cell.	

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	2003-02-11	**US20060218670A1** **11/212,506** **COMPOSITIONS AND METHODS FOR PRODUCTION OF SIALYLATED GLYOPROTEINS IN PLANTS** **FAMILY MEMBERS** US20060218669A1 ABANDONED 2008-08-06 WO2004071177A3	**ARIZONA STATE** (Phoenix, AZ) **ABANDONED** **2008-11-03** **Publication Date:** **2006-09-28** **Filing Date:** **2005-08-25** **Earliest Effective Filing Date:** **2003-02-11** **Priority Date:** **2004-02-11**	**Joshi; Lokesh** **(Tempe, AZ)** **Shah; Miti M.** **(Scottsdale, AZ)**	1. **A method for producing recombinant sialylated glycoproteins**, comprising administering a nucleic acid encoding the protein to a cell comprising a **plant sialylating enzyme**. 8. The method of claim 1, wherein the plant sialylating enzyme is **plant sialyltransferase**. 9. The method of claim 9, wherein the cell comprises a nucleic acid encoding **plant sialyltransferase**. 12. The method of claim 9, wherein the nucleic acid encodes a polypeptide with at least **70%, 75%, 80%, 85%, 90%, 95% identity to the sequence set forth in SEQ ID NO:8, 9, or 10**. 15. The method of claim 1, wherein the cell is overexpressing a **plant sialylating enzyme**. 19. The method of claim 1, wherein the protein is selected from the group consisting of activin, adenosine deaminase, angiotensinogen I, antithrombin III, antitrypsin, alpha I, apolipoprotein A-I, apolipoprotein A-II, apolipoprotein C-I, apolipoprotein C-II, polipoprotein C-III, apolipoprotein E, atrial natriuretic factor, chorionic gonadotropin, alpha chain, chorionic gonadotropin, beta chain, chymosin, pro, complement, factor B, complement C2, complement C3, complement C4, complement C9, corticotrophin releasing factor, epidermal growth factor, epidermal growth factor receptor, epoxide dehydratase, erythropoietin esterase inhibitor, C1 factor VIII, factor IX, factor X, fibrinogen, gatrin releasing peptide, glucagons, growth hormone, growth hormone RF, somatocrinin, hemopexin, inhibin, insulin, prepro, insulin-like growth factor I, insulin-like growth factor II, interferon alpha, interferon beta, interferon gamma, interleukin-1, interleukin-2, interluekin-3, kininogen, luteinizing hormone beta subunit, luteinizing hormone releasing hormone, lymphotoxin, mast cell growth factor, nerve growth factor beta subunit, oncogene c-sis, PGDF chain A, pancreatic polypeptide, parathyroid hormone, plasminogen, plasminogen activator, prolactin, proopiomelanocortin, protein C, prothrombin, relaxin, rennin, somatostatin, tachykinin, substances P & K, urokinase, vasoactive intestinal peptide, vasopressin, **immunoglobulin**, vaccine epitope, neurotrophic factor, and a hormone. 25. **An isolated nucleic acid** encoding **plant sialyltransferase**. 28. The nucleic acid of claim 25, wherein the nucleic acid encodes a polypeptide with at least **70%, 75%, 80%, 85%, 90%, 95% identity to the sequence set forth in SEQ ID NO:8, 9, or 10**. 31. **A cell comprising the nucleic acid of claim 20 or 25**.	***STATUS*** • **ABANDONED 2008-11-03** ***METHODOLOGY*** CLAIMS DRAWN TO COMPOSITIONS AND METHODS FOR PRODUCTION OF SIALYLATED GLYOPROTEINS IN PLANTS

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
					33. The cell of claim 31, wherein the cell is a human, murine, bacterial, archeal, or fungal cell. 34. **A method for engineering plants to produce recombinant sialylated glycoproteins**, comprising administering to the cell a nucleic acid encoding a plant sialylating enzyme. 37. The method of claim 34, wherein the plant sialylating enzyme is **sialyltransferase**. 41. A sialylated glycoprotein produced by the method of claim 1. 42. The method of claim 41, wherein the protein is selected from the group consisting of activin, adenosine deaminase, angiotensinogen I, antithrombin III, antitrypsin, alpha I, apolipoprotein A-I, apolipoprotein A-II, apolipoprotein C-I, apolipoprotein C-II, polipoprotein C-III, apolipoprotein E, atrial natriuretic factor, chorionic gonadotropin, alpha chain, chorionic gonadotropin, beta chain, chymosin, pro, complement, factor B, complement C2, complement C3, complement C4, complement C9, corticotrophin releasing factor, epidermal growth factor, epidermal growth factor receptor, epoxide dehydratase, erythropoietin esterase inhibitor, C1 factor VIII, factor IX, factor X, fibrinogen, gatrin releasing peptide, glucagons, growth hormone, growth hormone RF, somatocrinin, hemopexin, inhibin, insulin, prepro, insulin-like growth factor I, insulin-like growth factor II, interferon alpha, interferon beta, interferon gamma, interleukin-1, interleukin-2, interluekin-3, kininogen, luteinizing hormone beta subunit, luteinizing hormone releasing hormone, lymphotoxin, mast cell growth factor, nerve growth factor beta subunit, oncogene c-sis, PGDF chain A, pancreatic polypeptide, parathyroid hormone, plasminogen, plasminogen activator, prolactin, proopiomelanocortin, protein C, prothrombin, relaxin, rennin, somatostatin, tachykinin, substances P & K, urokinase, vasoactive intestinal peptide, vasopressin, **immunoglobulin**, vaccine epitope, neurotrophic factor, and a hormone.	
	2003-04-03	**WO2004087757A2** **THERAPEUTIC PRODUCTS WITH**	**LAB FRANCAIS DU FRACTIONNEMENT** (Les Ulis, FR)	**Bourel; Dominique (La Madeleine, FR)** **De Romeuf Christophe**	1. **A method for the preparation of human, humanized or chimeric antibodies or polypeptides** comprising Fc region of human IgG, said antibodies or polypeptides having different binding profiles, wherein said method comprises the steps consisting of a) **providing candidate human, humanized or chimceric antibodies or polypeptides comprising Fc**	***STATUS***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		ENHANCED ABILITY TO IMMUNO-MODULATE CELL FUNCTIONS **FAMILY MEMBERS** AU2004226167A1 CA2520820A1 EP1613654A2 REFUSED 2012-12-07 JP2007527696A US7790399 B2 (US20070135621A1) EXPIRED 2014-10-06 WO2004087757A3	**Publication Date: 2004-10-14** **Filing Date: 2004-04-05** **Earliest Effective Filing Date: 2003-04-03** **Priority Date: 2004-04-05**	**(Lille, FR)** **Siberil; Sophie (Paris, FR)** **Fridman; Wolf Herman (Paris, FR)** **Teillaud; Jean-Luc (Paris, FR)** **Bihoreau; Nicolas (Orsay, FR)** **Nony; Emmanuel (Antony, FR)**	**region of human IgG** produced naturally by or following transfection with a vector comprising the coding sequence for said antibody or polypeptide of cells from animal cell lines comprising hybridoma, heterohybridoma, EBV-transformed human B cell lines or from eukaryotic microorganisms, b) **testing the binding of said antibodies or polypeptides on Fcgamma receptors** including FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB, c) selecting antibodies or polypeptides which: i) bind to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB, or ii) bind to both FcgammaRIIA and FcgammaRIIB but do not bind or bind only weakly to FcgammaRIIIA, or iii) do not bind or bind only weakly to both FcgammaRIIIA, FcgammaRIIA and FcgammaRIIB. 2. A method according to claim 1, wherein said antibodies or polypeptides selected in the step c) i) are produced by cells from lymphoid cell lines or lymphoid-derived cell lines or hybridomas or from epithelial kidney cell lines, said antibodies or polypeptides selected in the step c) ii) are produced by cells from non-lymphoid cell lines and said antibodies or polypeptides selected in the step c) iii) are produced by cells from an heterohybridoma fused to cells from an EBV-transformed cell line or to B lymphocytes from human donors. 3. A method according to claim 2, wherein said lymphoid-derived cell lines are rat myeloma cell lines or the hybridoma YB2/0 cell line (ATCC number CRL-1662) or cell lines derived thereof, and/or the epithelial kidney cell line is VERO (ATCC number CCL-81) or cell lines derived thereof, and/or the non-lymphoid cell line is **CHO (ATCC S number CCL-61) or cell lines derived thereof** and/or said heterohybridoma is K6H6B5 (ATCC number CRL-1823) or cell lines derived thereof. 26. **An antibody or a polypeptide comprising Fc region of human IgG, characterized in that it contains from 70% to 100% of fucose, and from 60% to 98% of galactose.** 31. **An antibody or a polypeptide comprising Fc region of human IgG, characterized in that it contains from 80% to 100% of fucose, from 60% to 98% of galactose and that contains from 30% to 80% of sialylated forms.**	• US7790399 - **EXPIRED DUE TO NONPAYMENT OF MAINTENANCE FEES 2014-10-06** • EP1613654A2 **REFUSED 2012-12-07** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF PREPARING ANTIBODIES OR POLYPEPTIDES HAVING AN FC REGION OF HUMAN IGG MODULATING THE HUMAN TYPE IIB RECEPTORS OF IGG, USEFUL IN TREATING CANCER, AUTOIMMUNE DISORDERS, ALLERGIES AND INFECTIOUS DISEASES
	2003-10-20	**US20070015239 A1** **10/575333** **CORRELATION BETWEEN THE FUCOSE CONTENT GALACTOSE**	**LAB FRANCAIS DU FRACTIONNEMENT (Les Ulis, FR)** **ABANDONED 2014-10-12** **Publication Date:**	**Bihoreau; Nicolas (Orsay, FR)** **De Romeuf Christophe (Lille, FR)** **Jorieux; Sylvie**	1. **A method for preparing a humanized or human chimeric monoclonal antibody, with high effector activity**, comprising: a) producing and purifying monoclonal antibodies obtained from different sources selected from the group consisting of cells, plants and non-human animals, b) measuring **the fucose content** and **the galactose content** of the glycanic structures borne by the glycosylation site of the Fc region of said antibodies, and	***STATUS*** **ABANDONED 2014-10-12** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO "SELECTING ANTIBODIES FOR WHICH THE FUCOSE CONTENT/GALACTOSE

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		CONTENT RATIO OF ANTI-RHESUS-D AND ANTI-HLA-DR ANTIBODIES AND THE ADCC ACTIVITY **FAMILY MEMBERS** AU2004283924A1 AU2004283924B2 BR200415565A CA2542881A1 EP1675873A1 WITHDRAWN 2011-11-04 FR2861080A1 FR2861080B1 IL174896D0 JP2007533299A WO2005040221A1	**2007-01-18** **Filing Date: 2006-04-12** **Earliest Effective Filing Date: 2003-10-20** **Priority Date: 2004-10-20**	**(Villeneuve D'Ascq, FR)** **Nony; Emmanuel (Antony, FR)** **Bourel; Dominique (La Madeleine, FR)**	c) **selecting antibodies for which the fucose content/galactose content ratio is less than or equal 0.6**. 2. The method of claim 1, wherein said antibodies are produced in genetically modified cells by introducing at least one vector allowing the expression of said antibodies, said cells being eukaryotic or prokaryotic cells selected from the group consisting of cells from **mammals**, insects, plants, bacteria and yeasts. 3. The method of claim 1, wherein said cells are genetically modified by introducing at least one vector allowing the expression of at least one polypeptide having a **glycosyl transferase activity**. 4. The method of claim 3, wherein said glycosyl transferase activity is a **galactosyl transferase activity**. 5. The method of claim 4, wherein said galactosyl transferase activity is a **beta(1,4)-galactosyl transferase** activity or a beta(1,3)-galactosyl transferase activity.	CONTENT RATIO IS LESS THAN OR EQUAL 0.6."
	2004-02-13	**WO2005080585A1** **HIGHLY ACTIVE GLYCOPROTEINS-PROCESS CONDITIONS AND AN EFFICIENT METHOD FOR THEIR PRODUCTION** **FAMILY MEMBERS** AU2005215889A1 AU2005215889B2 AU2005215889B9	**GLYCOTOPE GMBH** (Berlin, DE) **Publication Date: 2005-09-01** **Filing Date: 2005-02-14** **Earliest Effective Filing Date: 2004-02-13** **Priority Date:**	**Goletz; Steffen (Glienicke-Nordbahn, DE)** **Baumeister; Hans (Berlin, DE)** **Schoeber; Ute (Berlin, DE)**	1. **Highly active glycoprotein produced by a process** comprising: expression of said highly active glycoprotein in an expression cell line, **harboring at least one defect in the sugar nucleotide biosynthetic pathway of sialic acids** and which is transfected with nucleic acid encoding the glycoprotein, in a medium supplemented with a concentration of at least one sialic acid precursor additive, the concentration being determined by a process comprising: (i) expression of a plurality of different sialylation forms of said glycoprotein by differential sialylation using different concentrations of at least one sialic acid precursor; and (ii) determination of the activity of the different sialylation forms in comparison with a reference glycoprotein in (a) suitable bioassay(s); and (iii) selection of the sialylation form with the higher/highest activity and determination of the concentration of the sialic acid precursor additive(s) which is correlated with the higher/highest activity level of said glycoprotein.	***STATUS*** • **US8609370B2 (US20080226681A1) EXPIRES 2027-08-24** • **EP1725673A1 - Announcement of Intention To Grant 2013-10-11** ***METHODOLOGY*** CLAIMS DRAWN TO A GLYCOPROTEIN EXPRESSED IN A CELL LINE HAVING AT LEAST ONE DEFECT IN THE SUGAR

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		CA2557725A1 CN103627670A CN1926242A CN1926242B EP1725673 A1 JP04913604B2 JP05506759B2 JP2007522179A JP2012087123A US8609370B2 (US20080226681A1) EXPIRES **2027-08-24**	**2005-02-14**		12. **Process for the generation of an expression cell line with a defect in the sugar nucleotide biosynthetic pathway of sialic acids** comprising the selection of expression cell line from primary cells or cell lines with a recognition molecule that binds to desialylated structures which can be sialylated by at least two enzymes.	NUCLEOTIDE BIOSYNTHETIC PATHWAY OF SIALIC ACIDS
	2004-04-15	**WO2005100584 A2** **PRODUCTION OF GALACTOSYLATED GLYCOPROTEINS IN LOWER EUKARYOTES** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia Filed: 20.10.2006 2005233387 Published: 16.11.2006 Canada Filed: 12.10.2006 2562772	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2005-10-27** **Filing Date: 2005-04-15** **Earliest Effective Filing Date: 2004-04-15** **Priority Date: 2004-04-15**	**Davidson; Robert C (Enfield, NH)** **Gerngross; Tillman U. (Hanover, NH)** **Wildt; Stefan (Lebanon, NH)** **Choi; Byung-Kwon (Norwich, VT)** **Nett; Juergen Hermann (Grantham, NH)** **Bobrowicz; Piotr (White River Junction, VT)**	1. A **recombinant lower eukaryotic host cell** producing human- like glycoproteins characterized as having a terminal p- galactose residue and essentially lacking fucose and static acid residues on the glycoprotein. 5. A **recombinant lower eukaryotic host cell** producing human-like glycoproteins, ; the host comprising an isolated nucleic acid molecule encoding p-galactosyltra nsferase activity and at least an isolated nucleic acid molecule encoding UDP galactose transport activity, UDP-galactose C4 epimerase activity or galactokinase activity or galactose-l- phosphate uridyl transferase activity. 8. A **recombinant lower eukaryotic host cell** producing human-like glycoproteins, the host cell capable of transferring p-galactose residue onto an N-linked oligosaccharide branch of a glycoprotein comprising a terminal GlcNAc residue, I the N-linked oligosaccharide branch selected from the group consisting of GlcNAcp 1,2- Manal,3; GlcNAcp 1,4-Manal,3; GlcNAcp 1,2-Manal,6; GlcNAcp1,4-Manal,6; and GlcNAcp1,6-Manal,6 on a trimannose core. 15. A **composition comprising a human-like glycoprotein** characterized as having a **terminal p-galactose residue and essentially lacking fucose and sialic acid residues** on the	**DAVIDSON FAMILY** ***STATUS*** **EP1737969 – see below** ***METHODOLOGY*** CLAIMS DRAWN TO RECOMBINANT YEAST OR FILAMENTOUS FUNGUS HOST CELL

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		China Filed: 15.04.2005 200580011116.4 Germany Withdrawn: 17.10.2006 European Patent Office (EPO) Filed: 27.10.2006 2005732293 Published: 03.01.2007 India Filed: 08.11.2006 6595/DELNP/2006 Published: 31.08.2007 Japan Filed: 13.10.2006 2007507921		**Hamilton; Stephen R. (Enfield, NH),**	glycoprotein. 18. **A method for producing human-like glycoproteins in a lower eukaryotic host cell** the method comprising the step of producing UDP- galactose above endogenous levels. 35. A **recombinant lower eukaryotic host cell** expressing GalNAc Transferase activity.	
	2004-04-15	**EP1737969 A1** **PRODUCTION OF GALACTOSYLATED GLYCOPROTEINS IN LOWER EUKARYOTES** **FAMILY MEMBERS** SEE ABOVE	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **INTENTION TO GRANT** **Publication Date: 2011-03-03** **Filing Date: 2010-07-21** **Earliest Effective Filing Date: 2004-04-15** **Priority Date: 2004-04-15**	**Davidson; Robert C (Enfield, NH)** **Gerngross; Tillman U. (Hanover, NH)** **Wildt; Stefan (Lebanon, NH)** **Choi; Byung-Kwon (Norwich, VT)** **Nett; Juergen Hermann (Grantham, NH)** **Bobrowicz; Piotr (White River Junction, VT)** **Hamilton; Stephen R. (Enfield, NH),**	1. **A recombinant lower eukaryotic host cell** producing human-like glycoproteins characterized as having a terminal 13-galactose residue and essentially lacking fucose and sialic acid residues on the glycoprotein; wherein the host cell expresses: nucleic acid molecule encoding β1,4-galactosyltransferase activity and nucleic acid molecule encoding UDP-galactose C4 epimerase activity. 2. The host cell of claim 1, wherein the 131,4-galactosyltransferase activity is selected from uman Ga1TI, Ga1TII, Ga1TIII, Ga1TIV, Ga1TV, Ga1TVI, Ga1TVII, bovine Ga1TI, X leavis Ga1T elegans Ga1TII. 3. The host of claim 1 or 2 wherein the UDP-galactose C4 epimerase activity is encoded by a gene selected from SpGALE, ScGAL10 and hGALE. 4. The host cell of claim 1, 2 or 3 which expresses UDP-galactose transport activity. 5. The host of claim 4 wherein the UDP-galactose transport activity is encoded by a gene from SpUGT, hUGT1, hUGT2, and DmUGT. 6. The host cell of any preceding claim which exhibits an elevated level of UDP-galactose. 7. The host of any preceding claim which is impaired in initiating 1,6 mannosyltransferase activity with respect to the glycan on the glycoprotein.	**DAVIDSON FAMILY** ***STATUS*** • **EP1737969** **INTENTION TO GRANT** ***METHODOLOGY*** CLAIMS DRAWN TO RECOMBINANT YEAST OR FILAMENTOUS FUNGUS HOST AND A COMPOSITION COMPRISING A HUMAN-LIKE GLYCOPROTEIN

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
					8. The host of any preceding claim which is selected from Pichia pastoris, Pichia finlandica, Pichia trehalophila, Pichia koclamae, Pichia membranaefaciens, Pichia minuta (Ogataea minuta, Pichia lindneri), Pichia opuntiae, Pichia thermotolerans, Pichia salictaria, Pichia guercuum, Pichia pijperi, Pichia stiptis, Pichia methanolica, Pichia sp., Saccharomyces cerevisiae, Saccharomyces sp., Hansenula polymorpha, Kluyveromyces sp., Kluyveromyces lactis, Candida albicans, Aspergillus nidulans, Aspergillus niger, Aspergillus oryzae, Trichoderma reesei, Chrysosporium lucknowense, Fusarium sp., Fusarium gramineum, Fusarium venenatum, Physcomitrella patens and Neurospora crassa. 9. A method for producing human-like glycoproteins in a lower eukaryotic host cell as defined in any one of claims 1 to 8. 10. The method of claim 9 which produces a glycoprotein selected from G1eNAcMan3GleNAc2, G1eNAc2Man3GleNAc2, G1eNAe3Man3GleNAc2, G1eNAc4Man3GleNAc2, G1eNAc5Man3GleNAc2, G1eNAe6Man3GleNAc2, G1eNAcMan4GleNAc2, G1eNAcMan5GleNAc2, G1eNAc2Man5GleNAc2 and G1eNAc3Man5GleNAc2. 11. The method of claim 9 or 10 wherein at least 60 mole % of the glycoproteins comprise galactose. 12. **A composition comprising a human-like glycoprotein characterized as having a terminal β-galactose residue and essentially lacking fucose and sialic acid residues on the glycoprotein** wherein the glycoprotein comprises N-linked oligosaccharides selected from Ga1G1eNAcMan3GleNAc2, Ga1G1eNAc2Man3GleNAc2, Gal2GleNAe2Man3GleNAc2, Ga1G1eNAc3Man3GleNAc2, Gal2GleNAc3Man3GleNAc2, Ga13G1eNAe3Man3GleNAc2, Ga1G1eNAc4Man3GleNAc2, Gal2GleNAc4Man3GleNAc2, Ga13G1eNAe4Man3GleNAc2, Ga14G1eNAc4Man3GleNAe2Ga1G1eNAcMan5GleNAc2, Ga1G1eNAe2Man5GleNAc2, Gal2GleNAc2Man5GleNAc2, Ga1G1eNAc3Man5GleNAc2, Gal2GleNAc3Man5GleNAc2, and Ga13G1eNAe3Man5GleNAc2. 13. A composition comprising a human-like glycoprotein obtainable by a method of claim 9, 10 or 11.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2004-07-21	**WO2006014679** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A GLCNAC2MAN3 GLCNAC2 GLYCOFORM** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia Filed: 24.01.2007 2005269759 Published: 22.02.2007 Canada Filed: 12.01.2007 2573745 China Filed: 19.07.2005 200580024584.5 European Patent Office (EPO) Filed: 19.01.2007 2005790298 Published: 25.04.2007 Withdrawn: 19.02.2008	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **WITHDRAWN 2008-11-07** **Publication Date: 2006-02-09** **Filing Date: 2005-07-19** **Earliest Effective Filing Date: 2004-07-21** **Priority Date: 2004-07-21**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1. **A composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N- glycan consists essentially of at least 75 mole percent GlcNAc2Man3GlcNAc2. 20. **A eukaryotic host cell comprising an exogenous gene encoding an immunoglobulin or fragment thereof**, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of at least 75 mole percent GlcNAc2Man3GlcNAc2. 22. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of at least 75 mole percent GIcNAc2Man3GlcNAc2.	**"GERNGROSS FAMILY II"** ***STATUS*** • **NO US COUNTERPART** • **EP1776385** **WITHDRAWN 2009-02-19** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF AT LEAST 75 MOLE PERCENT GlcNAC2MAN3GlcNAC2.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		India Filed: 14.02.2007 1208/DELNP/2007 Published: 27.04.2007 Japan Filed: 19.01.2007 2007522673				
	2004-07-21	**WO2006014683 A2** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A GLCNAC2MAN3 GLCNAC2 GLYCOFORM** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 24.01.2007 2005269763 Published: 22.02.2007 Canada 12.01.2007 2573842 China 19.07.2005 200580024664.0 European Patent Office (EPO) 18.01.2007 2005790299 Published: 11.04.2007 Withdrawn: 05.08.2008 India 14.02.2007	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **WITHDRAWN 2008-11-07** **Publication Date: 2006-02-09** **Filing Date: 2005-07-19** **Earliest Effective Filing Date: 2004-07-21** **Priority Date: 2004-07-21**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1. **A composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N- glycan **consists essentially of Gal2GlcNAc2Man3GlcNAc2 lacking fucose**. 17. **A eukaryotic host cell** comprising an exogenous gene encoding an immunoglobulin or fragment thereof, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a **plurality of N-glycans in which the predominant N-glycan consists essentially of Gal2GlcNAc2Man3GlcNAc2 lacking fucose**. 19**. A method for producing in a eukaryotic host** a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan **consists essentially of Gal2GlcNAc2Man3GlcNAc2 lacking fucose.**	**"GERNGROSS FAMILY IIb"** ***STATUS*** • **NO US COUNTERPART** • **EP1771477** **WITHDRAWN 2009-01-16** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF GAL2GLCNAC2MAN3GLCNAC2 LACKING FUCOSE. AND METHODS OF MAKING

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		1206/DELNP/2007 Published: 03.08.2007 Japan 19.01.2007 2007522676				
	2004-07-21	**WO06014685 A1** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A MAN3GLCNAC2 GLYCOFORM** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 16.01.2007 2005269765 Published: 08.02.2007 Canada 11.01.2007 2573541 China 19.07.2005 200580024582.6 European Patent Office (EPO) 16.01.2007 2005791012 Published: 11.04.2007 Withdrawn: 05.08.2008 India 14.02.2007 1205/DELNP/2007 Published: 03.08.2007 Japan 19.01.2007	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2006-02-09** **Filing Date: 2005-07-19** **Earliest Effective Filing Date: 2004-07-21** **Priority Date: 2004-07-21**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1**. A composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N- glycan consists essentially of Man3GlcNAc2. 10. The composition of claim l, wherein said immunoglobulins exhibit increased antibody-dependent **cellular cytotoxicity (ADCC) activity**. 21. **A eukaryotie host cell** comprising an exogenous gene encoding an immunoglobulin or fragment thereof, said eukaryotie host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of Man3GlcNAc2. 23. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan wherein the composition thereby comprises a plurality of N- glycans in which the predominant N-glycan consists essentially of Man3GlcNAc2.	**"GERNGROSS FAMILY IIc"** ***STATUS*** • **NO US COUNTERPART** • **EP1771480** **WITHDRAWN 2008-08-05** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF MAN3GlcNAC2 AND METHODS OF MAKING

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		2007522677				
	2004-07-21	**WO06014725 A1** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A GlcNAcMAN5GLCNAC 2 GLYCOFORM** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 24.01.2007 2005269712 Published: 22.02.2007 Canada 12.01.2007 2573864 China 19.07.2005 200580024782.1 European Patent Office (EPO) 19.01.2007 2005790979 Published: 11.04.2007 Withdrawn: 04.03.2008 India 14.02.2007 1207/DELNP/2007 Published: 03.08.2007 Japan 19.01.2007 2007522695	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2006-02-09** **Filing Date: 2005-07-19** **Earliest Effective Filing Date: 2004-07-21** **Priority Date: 2004-07-21**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1. A **composition** comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant **N- glycan consists essentially of GlcNAcMan5GlcNAc2**. 21. A **eukaryotic host cell** comprising an exogenous gene encoding an immunoglobulin or fragment thereof, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan **consists essentially of GlcNAcMan5GlcNAc2**. 23. **A method for producing in a eukaryotic host** a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a **plurality of N-glycans in which the predominant N-glycan consists essentially of GlcNAcMan5GlcNAc2**.	**"GERNGROSS FAMILY IId"** ***STATUS*** • **NO US COUNTERPART** • **EP1771479** **WITHDRAWN 2008-03-04** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF GlcNAcMan5GlcNAc2 AND METHODS OF MAKING

PUBLISHED PCT/US/EP PATENT APPLICATIONS RELATING TO ANTIBODY GLYCOSYLATION

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2004-12-23	**WO06014726 A2** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A MAN5GLCNAC2 GLYCOFORM** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 22.01.2007 2005269713 Published: 15.02.2007 Canada 11.01.2007 2573554 China 19.07.2005 200580024712.6 European Patent Office (EPO) 18.01.2007 2005790364 Published: 11.04.2007 Withdrawn: 04.03.2008 India 14.02.2007 1209/DELNP/2007 Published: 27.04.2007 Japan 19.01.2007 2007522696	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2006-07-06** **Filing Date: 2005-12-22** **Earliest Effective Filing Date: 2004-12-23** **Priority Date: 2004-12-23**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1. **A composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the **predominant N- glycan consists essentially of Man5GlcNAc2** having the structure Manal-6-(Manal,2- Manal,2-Manal,3)-Manh3 1,4-G1cNAc3 1,4-GlcNAc. 28. **A eukaryotic host cell** comprising an exogenous gene encoding an * immunoglobulin or fragment thereof, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of Man5GlcNAc2 having the structure Mana 1 -6-(Mana 1,2-Manal,2-Manal,3)- Man3 1,4-G1cNAc 1,4- G1cNAc. 30. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of Man5GlcNAc2 having the structure Manu 1 -6- (Manctl,2-Manal, 2-Manal,3)-Man I,4-G1cNAc 1,4-GIcNAc.	**"GERNGROSS FAMILY IIe"** ***STATUS*** • **NO US COUNTERPART** • **EP1771478**https://register.epo.org/application?number=EP05790979 **WITHDRAWN 2008-03-04** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF MAN5GlcNAC2 HAVING THE STRUCTURE MANAL-6-(MANAL,2- MANAL,2-MANAL,3)-MANH3 1,4-GlcNAC3 1,4-GlcNAC AND METHODS OF MAKING
	2004-12-23	**WO06071856 A2** **IMMUNOGLOBULINS COMPRISING**	**GLYCOFI, INC.*** (Lebanon, NH)	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)**	1. **A composition** comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the **predominant N- glycan consists essentially of Man5GlcNAc2** having the structure Manal-6-(Manal,2- Manal,2-Manal,3)-Manh3 1,4-G1cNAc3 1,4-GlcNAc.	**"GERNGROSS FAMILY IIf"**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		PREDOMINANTLY A MAN5GLCNAC2 GLYCOFORM **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) NONE	* acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2006-07-06** **Filing Date: 2005-12-22** **Earliest Effective Filing Date: 2004-12-23** **Priority Date: 2004-12-23**	**Wildt; Stefan (Lebanon, NH)**	28. **A eukaryotic host cell** comprising an exogenous gene encoding an * immunoglobulin or fragment thereof, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of Man5GlcNAc2 having the structure Mana 1 -6-(Mana 1,2-Manal,2-Manal,3)- Man3 1,4-G1cNAc 1,4- G1cNAc. **30**. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of Man5GlcNAc2 having the structure Manu 1 -6- (Manctl,2-Manal, 2-Manal,3)-Man I,4-G1cNAc 1,4-GIcNAc.	***STATUS*** • **ABANDONED** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF MAN5GlcNAC2 GLYCOFORM AND METHODS OF MAKING
	2004-12-23	**WO06071280 A1** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A GALGLCNACMAN5GL CNAC2 GLYCOFORM** **FAMILY MEMBERS**	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2006-07-06**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	**1. A composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N- glycan consists essentially of GalGlcNAcMan5G1cNAc2. **21. A eukaryotic host cell comprising an exogenous gene encoding an immunoglobulin or fragment thereof**, said eukaryotic host cell engineered or selected to express said immunoglobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant	**"GERNGROSS FAMILY IIg"** ***STATUS*** • **NO US COUNTERPART**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		NATIONAL PHASE APPS FILED (FROM WIPO) Australia 06.06.2007 2005322617 Published: 05.07.2007 Canada 01.06.2007 2590441 China 19.07.2005 200580044453.3 European Patent Office (EPO) 15.06.2007 2005790215 Published: 12.09.2007 Withdrawn: 25.11.2008 India 19.06.2007 4685/DELNP/2007 Published: 17.08.2007 Japan 22.06.2007 2007548187	**Filing Date: 2005-07-19** **Earliest Effective Filing Date: 2004-12-23** **Priority Date: 2004-12-23**		N-glycan consists essentially of GalGlcNAcMan5GlcNAc2. 23. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins,** each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan within said plurality of N-glycans consists essentially of GalGlcNAcMan5G1cNAc2.	• **EP1831256**https://register.epo.org/application?number=EP05790979 **WITHDRAWN 2008-11-25** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF GalGlcNAcMan5G1cNAc2 GLYCOFORM AND METHODS OF MAKING
19		**WO2007005786 A2** **METHODS AND COMPOSITIONS WITH ENHANCED THERAPEUTIC ACTIVITY** **FAMILY MEMBERS** AU2006265676A1 AU2006265676B2 CA2614046A1 CN101506238A	**CENTOCOR (Malvern, PA)** **Publication Date: 2007-01-11** **Filing Date: 2006-06-30** **Earliest Effective Filing Date: 2005-06-30** **Priority Date:**	**Cai, Ann (West Chester, PA)** **Ngo, Cam (Philadelphia, PA)** **Raju, T. Shantha (West Chester, PA)** **Scallon, Bernard (Wayne, PA)**	1. **A method for controlling the properties of an Fc-containing molecule**, comprising altering the **sialylation** of the oligosaccharjdes in the Fc region. 2. The method of claim 1, wherein the **sialylation is increased in the Fc region**. 3. The method of claim 1, wherein the properties controlled are selected from the group consisting of affinity for one or more of the FcyRJ, Fc'RHA, and FcyRIIIA receptors, ADCC activity, macrophage or monocyte activation, **serum half-life**, and avidity. 4. The method of claim 1, wherein the sialylation is altered from the wild type Fc region by at least one method selected from the group consisting of enzymatic treatment, enzymatic modification of the molecule, genetic manipulation of the molecule, lectin chromatography, affinity chromatography, ion exchange chromatography, hydrophobic interaction chromatography, size-exclusion chromatography, **changing the cell line used for expression**	***STATUS*** • **NO US FILING** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD FOR CONTROLLING THE PROPERTIES OF AN FC-CONTAINING MOLECULE BY ALTERING THE SIALYLATION OF THE OLIGOSACCHARJDES IN THE FC REGION.

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		CN101506238B EP1896071A2 EP1896071A4 (see below) IL188420D0 JP2009504569A SG163548A1 WO2007005786A3	**2006-06-30**		**of the protein**, culturing host cells used to produce the Fc-containing protein in serum, and exposing protein to a varied pH environment. 5. The method of claim 4, wherein the enzymatic treatment comprises treating with sialidase or **sialyltransferase**. 8. The method of claim 1, wherein the Fc-containing molecule is an **antibody**. 9. **A method for controlling the properties of an Fc-containing therapeutic protein** characterized as having the **biantennary oligosaccharide** covalently attached to an **asparagine residue in the CH2 immunoglobujjn domain** of said protein, comprising converting an Fc-containing therapeutic protein **not of the G2S2 glycoform** into an oligosaccharjde being substantially of the **G2S2 sialylated glycoform**. 11. The method of claim 9, wherein the converting step comprises at least one of enzymatically engineering a recombinanfly expressed monoclonal antibody, using chromatography to enrich particular glycoforms, using **sialyltransferases to add sialic acid residues**, and **changing the cell line used for expression of the protein**. 12. The method of claim 11, wherein the chromatography comprises lectin affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography, or size-exclusion chromatography. 13. The method of claim 12, wherein the genetic engineering incorporates **glycosyltransferases**. 14. A method for controlling the properties of an Fc-containing therapeutic protein characterized as having the biantennary oligosaccharide covalently attached to an asparagine residue in the CH2 immunoglobulin domain of said protein, comprising converting an Fc-containing therapeutic protein of the **G2S2 glycoform into an oligosaccharide being substantially of the G2, G1, or G0 non-sialylated glycoforms**. 15. The method of claim 14, wherein said Fc-containing protein has one or more of the properties selected from the group consisting of enhanced affinity for Fc7RJIA and FcyRIIIA, enhanced activity in NK cell-mediated ADCC assays, reduced affinity for FcyRI, reduceded ability to activate macrophages, and **longer serum half-life as compared to the same Fc-containing therapeutic protein substantially of the sialylated G2S2 glycoform**. **16. An Fc-containing protein produced or altered by the method of any of claims 1-15.** 40. **A method for controlling a binding affinity for a target of an Fc-containing molecule having a binding domain specific for the target**, comprising altering the **sialylation** of the oligosaccharides in the Fc region.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					41. The method of claim 40, wherein the **sialylation is increased in the Fc region and the avidity is decreased.** 42. The method of claim 40, wherein **the sialylation is decreased in the Fc region** and the avidity is increased. 43. The method of claim 40, wherein the sialylation is altered from the wild type Fc region by at least one method selected from the group consisting of enzymatic treatment, enzymatic modification of the molecule, genetic manipulation of the molecule, lectin chromatography, affinity chromatography, ion exchange chromatography, hydrophobic interaction chromatography, size-exclusion chromatography, **changing the cell line used for expression of the protein**, culturing host cells used to produce the Fc-containing protein in serum, and exposing protein to a varied pH environment. 44. The method of claim 43, wherein the enzymatic treatment comprises treating with sialidase or **sialyltransferase**. 47. The method of claim 40, wherein the Fc-containing molecule is an **antibody**.	
2005-06-30	**EP1896071** **METHODS AND COMPOSITIONS WITH ENHANCED THERAPEUTIC ACTIVITY** **FAMILY MEMBERS** SEE ABOVE	**CENTOCOR (Malvern, PA)** **INTENTION TO GRANT 2014-07-31** **Publication Date: 2011-02-09** **Filing Date: 2006-06-30** **Earliest Effective Filing Date: 2005-06-30** **Priority Date: 2006-06-30**	**Cai, Ann (West Chester, PA)** **Ngo, Cam (Philadelphia, PA)** **Raju, T. Shantha (West Chester, PA)** **Scallon, Bernard (Wayne, PA)**	1. **An in vitro method for controlling the properties of an Fc-containing molecule**, comprising altering the sialylation of the oligosaccharides in the Fc region to the G2S2 sialylated glyco form, wherein the sialylation is increased in the Fc region, wherein the sialylation is altered from the wild type Fc region by enzymatic treatment or enzymatic modification of the molecule by an **α-(2,3)-sialyltransferase**, and wherein the properties controlled are selected from the group consisting of affinity for one or more of the FcγRI, FcγRIIA, and FcγRIIIA receptors, ADCC activity, macrophage or monocyte activation, serum half-life, and avidity. 2. The method of claim 1, wherein the Fc-containing molecule has a binding domain specific for a target, said target being an immobilized target. 3. The method of claim 1, wherein the Fc-containing molecule has a binding domain specific for a target, said target being expressed on the surface of a cell. 4. The method of claim 1, wherein the Fc-containing molecule is an antibody. 5. **An in vitro method for controlling the properties of an Fc-containing therapeutic protein characterized as having a biantennary oligosaccharide covalently attached to an asparagine residue in the CH2 immunoglobulin domain of said protein**, comprising converting an Fc-containing therapeutic protein **not of the G2S2 glycoform** into an oligosaccharide being of the G2S2 sialylated glycoform, wherein the converting step comprises using an **α-(2,3)-sialyltransferase** to add sialic acid residues, and wherein said Fc-containing protein has one or more of the properties selected from the group consisting of **reduced**	***STATUS*** • **NO US COUNTERPART** • **INTENTION TO GRANT 2014-07-31** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD FOR CONTROLLING THE PROPERTIES OF AN FC-CONTAINING MOLECULE BY ALTERING THE SIALYLATION OF THE OLIGOSACCHARJDES IN THE FC REGION. METHODS REQUIRE □-(2,3)-SIALYLTRANSFERASE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					affinity for FcyRIIA and FcyRIIIA, **reduced activity in NK cell-mediated ADCC assays**, **enhanced affinity for FcyRI**, **enhanced ability to activate macrophages**, and **shorter serum half-life** as compared to the same Fc-containing therapeutic protein not of the G2S2 glycoform. 6. An Fc-containing protein produced or altered by the method of any of claims 1-5. 7. **An Fc-containing therapeutic protein characterized as having a biantennary oligosaccharide covalently attached to an asparagine residue in the CH2 immunoglobulin domain of said protein being of the G2S2 a-(2,3)-sialylated glycoform**, wherein said Fc-containing protein has reduced affinity for FcyRIIA and FcyRIIIA, reduced activity in NK cell-mediated ADCC assays, enhanced affinity for FcyRI, enhanced ability to activate macrophages, and shorter serum half-life compared to a preparation of the same Fc-containing therapeutic protein in the non-sialylated GO, Gl, or G2 glycoforms. 8. The protein of claim 7, wherein the target bound by the target binding domain of the protein is an immobilized target. 9. The protein of claim 7, wherein the target bound by the binding domain of the protein is expressed on the surface of a cell. 10. The protein of any one of claims 7-9, wherein the protein is indicated for the treatment of oncology-related disorders, chronic diseases, or infectious diseases. 11. The protein of claim 10, wherein the infectious diseases involve FcR mediated clearance of antibody-opsonized cells or particles comprising one or both of viruses and bacteria and the chronic diseases requiring long term treatment. 12. The protein of claim 7, wherein the protein comprises a recombinantly expressed monoclonal antibody or an antibody modified enzymatically using sialyltransferases. 13. The protein of claim 7, wherein the protein is selected from the group consisting of Abl, Ab2, Ab3, or Ab5. 14. **An in vitro method for preparing a batch of therapeutic recombinant Fc-containing protein of the G2S2 sialylated glycoform** characterized as comprising an immunoglobulin IgG isotype domain of at least a hinge region, a CH2, and a CH3 domain, wherein the method comprises treating the batch with an **α-(2,3)-sialyltransferase enzyme to add sialic acid residues to the polysaccharide chains attached to said protein.** 15. A pharmaceutical composition comprising a protein produced by the method of claim 14 in combination with a pharmaceutically acceptable carrier.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					16. The protein produced by the method of claim 14 for use in treatment of a disease or condition. 17. The protein produced by the method of claim 14 for use in vivo in diagnosis of a disease or condition. 18. The protein of claim 16, wherein said protein is used to treat a neoplastic disease selected from the group consisting of a carcinoma, a lymphoma, a sarcoma, and a myeloma. 19. The protein of claim 16, wherein said protein is used to treat an inflammatory disorder selected from the group consisting of psoriasis, rheumatoid arthritis, ulcerative colitis, inflammatory bowel disease, Crohn's disease, and systemic lupus erythematosus. 20. The protein of claim 16, wherein the protein is used to treat disorders involving corneal or retinal neovascularization. 21. **An in vitro method for controlling a binding affinity for a target of an Fc-containing molecule having a binding domain specific for the target**, comprising altering the sialylation of the oligosaccharides in the Fc region to the G2S2 sialylated glycoform, wherein the sialylation is increased in the Fc region and the avidity is decreased, and wherein the sialylation is altered from the wild type Fc region by **enzymatic treatment or enzymatic modification of the molecule with an α-(2,3)-sialyltransferase.** 22. The method of claim 21, wherein the target is an immobilized target. 23. The method of claim 21, wherein the target is expressed on the surface of a cell 24. The method of claim 21, wherein the Fc-containing molecule is an antibody. 25. An in vitro method comprising the protein produced by the method of claim 14 for diagnosis of a disease or condition.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2005-06-30	**WO2007024743 A3** **PROTEOLYSIS RESISTANT ANTIBODY PREPARATIONS** **FAMILY MEMBERS** AU2006283560A1 AU2006283560B2 BRPI0614850A2 CA2619825A1 CN101557825A CN102628074A EP1937306A2 EP1937306A4 (see below) IL189542D0 JP2009526746A US20070041979A1 ABANDONED US20110124024A1 (see below) WO2007024743A3	**CENTOCOR (Malvern, PA)** **Publication Date: 2007-03-01** **Filing Date: 2006-08-18** **Earliest Effective Filing Date: 2005-08-19** **Priority Date: 2006-08-18**	**Raju, T. Shantha (West Chester, PA)** **Scallon, Bernard (Wayne, PA)**	1. **A method of treatment of a human disease** characterized by the release of a protease, comprising administering a glycosylated Fc-containing protein preparation, wherein the antibody preparation is substantially homogeneous for a **single glycoform**. 2. The method of claim 1, wherein the Fc-containing protein is an antibody. 3. The method of claim 2, wherein the antibody is a therapeutic monoclonal antibody. 4. The method of claim 1, wherein the protease is selected from the group consisting of pepsin, a matrix metalloproteinase, trypsin, chymotrypsin, and a glycosylation modification enzyme. 5. The method of claim 4, wherein the matrix metalloproteinase is selected from the group consisting of matrix metalloproteinase-7 (MMP-7), neutrophil elastase (liNE), stromelysin (MMP-3), and macrophage elastase (MMP-12). 6. The method of claim 4, wherein the glycosylation modification enzyme comprises J3-galactosidase or sialidase A. 7. The method of claim 2, **wherein the glycoform of the antibody is substantially in the GO glycoform.** 8. The method of claim 2, **wherein the glycoform of the antibody is substantially in the G2 glycoform.** 9. The method of claim 2, **wherein the glycoform of the antibody is substantially in the G2S2 glycofonn.** 10. The method of claim 1, wherein the disease to be treated is characterized by the invasion of neutrophils into an affected site in the body. [1. The method of claim 1, wherein the disease to be treated is an autoimmune disease. 12. The method of claim 11, wherein the autoimmune disease is **rheumatoid arthritis.**	***STATUS*** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF ADMINISTERING A GLYCOSYLATED Fc-CONTAINING PROTEIN PREPARATION, THAT IS SUBSTANTIALLY ***HOMOGENEOUS FOR A SINGLE GLYCOFORM***.

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					13. **A method of altering the stability of an Fc-containing protein to cleavage by a protease**, comprising modifying the amount of sialylated glycoforms in the Fc-containing protein.	
	2005-06-30	**US20110124024 A1** **12/952,663** **PROTEOLYSIS RESISTANT ANTIBODY PREPARATIONS** **FAMILY MEMBERS** SEE ABOVE	**CENTOCOR (Malvern, PA)** **PENDING** **Publication Date: 2007-03-01** **Filing Date: 2006-08-18** **Earliest Effective Filing Date: 2005-08-19** **Priority Date: 2006-08-18**	**Raju, T. Shantha (West Chester, PA)** **Scallon, Bernard (Wayne, PA)**	**PUBLISHED AND PENDING CLAIMS:** 1. **A method of altering the stability of an Fc-containing protein** to cleavage by a protease, comprising **modifying the amount of sialylated glycoforms** in the Fc-containing protein. 2. The method of claim 1, wherein the Fc-containing protein comprises an **antibody** in an antibody preparation. 3. The method of claim 2, wherein the altering step comprises modifying the antibody preparation so that the antibody is **substantially free of sialylated glycoforms and the stability of the antibody is increased**. 4. The method of claim 3, wherein the step of modifying the antibody preparation is selected from the group consisting of culturing an antibody host cell with serum, preparing the antibody at low pH, **use of a specific host cell, and treatment with a glycosylation modification enzyme**. 5. The method of claim 4, further comprising the step of modifying the antibody preparation so that the antibody is **substantially homogeneous for glycoform G0**. 8. The method of claim 3, wherein the protease is selected from the group consisting of papain, ficin, bromolein, pepsin, matrix metalloproteinase-7 (MMP-7), neutrophil elastase (HNE), stromelysin (MMP-3), macrophage elastase (MMP-12), trypsin, chymotrypsin, and glycosylation modification enzymes. 9. The method of claim 8, wherein the protease contacts the antibody preparation in vitro. 10. The method of claim 8, wherein the protease is papain. 11. The method of claim 8, wherein the protease contacts the antibody preparation in vivo. 14. The method of claim 5, further comprising the steps of contacting the protein with a protease and testing cleavage of the protein. 15. The method of claim 14, wherein the protease is selected from the group consisting of papain, ficin, bromolein, pepsin, matrix metalloproteinase-7 (MMP-7), neutrophil elastase (HNE), stromelysin (MMP-3), macrophage elastase (MMP-12), trypsin, chymotrypsin, and glycosylation modification enzymes.	***STATUS*** • **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF ALTERING THE STABILITY OF AN FC-CONTAINING PROTEIN TO CLEAVAGE BY A PROTEASE, COMPRISING MODIFYING THE AMOUNT OF SIALYLATED GLYCOFORMS IN THE FC-CONTAINING PROTEIN

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					16. The method of claim 15, wherein the protease is papain.	
	2005-06-30	**EP1937306 A2** **PROTEOLYSIS RESISTANT ANTIBODY PREPARATIONS** **FAMILY MEMBERS** SEE ABOVE	**CENTOCOR (Malvern, PA)** **PENDING** **Publication Date: 2008-07-02** **Filing Date: 2006-08-18** **Earliest Effective Filing Date: 2005-08-19** **Priority Date: 2006-08-18**	**Raju, T. Shantha (West Chester, PA)** **Scallon, Bernard (Wayne, PA)**	PENDING CLAIMS (as of 2014-02-21): 1**. A method of altering the stability of an Fc-containing protein to cleavage by a protease**, comprising **modifying the sialylation of glycoforms in the Fc-containing protein**. 2 The method of claim 1, wherein the Fc-containing protein comprises an antibody in an antibody preparation. 3. The method of claim 2, wherein the altering step comprises modifying the antibody preparation so that the antibody is substantially free of sialylated glycoforms and the stability of the antibody is increased. 4. The method of claim 3, wherein the step of modifying the antibody preparation is treatment with a glycosylation modification enzyme. 5. The method of claim 4, further comprising the step of modifying the antibody preparation so that the antibody is substantially homogeneous for glycoform GO. 6. The method of claim 4, wherein the modification step comprises treating the antibody preparation with sialidase A. 7. The method of claim 6, further comprising the step of treating the antibody preparation with 13-galactosidase after treatment with sialidase A. 8. The method of any preceding claim, wherein the protease is selected from the group consisting of papain, ficin, bromolein, pepsin, matrix metalloproteinase-7 (MMP-7), neutrophil elastase (HNE), stromelysin (MMP-3), macrophage elastase (MMP-12), trypsin and chymotrypsin. 9. The method of claim 8, wherein the protease contacts the antibody preparation in vitro. 10. The method of claim 8, wherein the protease is papain. 11. The method of claim 8, wherein the protease contacts the antibody preparation in vivo. 12. The method of claim 11, wherein the protease is associated with a pathologic condition. 13. The method of claim 12, wherein the pathologic condition is cancer. 14**. A method for detecting or diagnosing a disease state in a cell or subject**, comprising: determining the state of glycosylation of Fc-containing proteins in the cell or subject; correlating	***STATUS*** • **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF ALTERING THE STABILITY OF AN FC-CONTAINING PROTEIN TO CLEAVAGE BY A PROTEASE, COMPRISING MODIFYING THE AMOUNT OF SIALYLATED GLYCOFORMS IN THE FC-CONTAINING PROTEIN

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					the state of glycosylation with the presence or levels of a protease; and correlating the presence or levels of the protease with a disease state indicated by the presence or levels of the protease. 15. The method of claim 14, wherein the Fc-containing protein is an antibody. 16. **A method for evaluating glycosylation of an antibody,** comprising: contacting the antibody with an protease, and monitoring the activity of the protease, further comprising comparing the activity of the protease to a known activity of the protease in connection with a known antibody composition. 17. The method of claim 16, wherein the activity monitored is the resistance to cleavage by the antibody. 18. The method of claim 17, wherein the resistance is determined by the presence of Fab, F(ab')2, Fv, facb, or Fc fragments. 19. The method of claim 16, wherein the protease is selected from the group consisting of papain, pepsin, a matrix metalloproteinase including MMP-7, neutrophil elastase (HNE), stromelysin (MMP-3), macrophage elastase (MMP-12), trypsin and chymotrypsin. 20. The method of claim 16, wherein the glycosylation evaluated comprises the amount of glycosylation. 21. The method of claim 16, wherein the glycosylation evaluated comprises the glycoform content.	
	2004-12-23	**WO07029054 A1** **IMMUNOGLOBULIN COMPRISING PREDOMINANTLY A**	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)**	1. **A composition comprising a plurality of immunoglobulins**, each im-munoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan is selected from the group consisting of **Man7GlcNAc2 and Man8GlcNAc2**	**"GERNGROSS FAMILY IIh"** ***STATUS***

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		MAN7GLCNAC2, MAN8GLCNAC2 GLYCOFORM **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 05.03.2008; 2005336263 Published: 03.04.2008 Canada 28.02.2008; 2620713 China 09.09.2005; 200580051541.6 Germany Withdrawn: 11.03.2008 European Patent Office (EPO) 04.03.2008; 2005786499 Published: 02.07.2008 Withdrawn: 19.11.2008 India 31.03.2008; 2647/DELNP/2008 Published: 04.07.2008 Japan 07.03.2008; 2008529704 United States of America 14.02.2008; 11990588 Published: 10.09.2009 ABANDONED	in 2006 **Publication Date: 2007-03-15** **Filing Date: 2005-09-09** **Earliest Effective Filing Date: 2005-09-09** **Priority Date: 2005-09-09**	**Wildt; Stefan (Lebanon, NH)**	21. **A eukaryotic host cell** comprising an exogenous gene encoding an im-munoglobulin or fragment thereof, said eukaryotic host cell engineered or selected to express said immunogiobulin or fragment thereof, thereby producing a composition comprising a plurality of immunoglobulins, each immunoglobulin comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan is selected from the group consisting of **Man7GlcNAc2 and Man8G1cNAc2.** 23. **A method for producing in a eukaryotic host a composition comprising a plurality of immunoglobulins**, each immunoglobulin comprising at least one N-glycan wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan is selected from the group consisting of **Man7G1cNAc2 and Man8 G1cNAc2.**	• **EP1937305** **WITHDRAWN 2009-08-07** • **US2009136525** **ABANDONED 2012-10-11** ***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF GalGlcNAcMan5G1cNAc2 GLYCOFORM AND METHODS OF MAKING
	2005-09-09	**WO07028144 A1** **IMMUNOGLOBULINS COMPRISING PREDOMINANTLY A GLCNACMAN$_3$GLCNAC$_2$ GLYCOFORM**	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date:**	**Gerngross; Tillman U. (Hanover, NH)** **Li, Huijan (Lebanon, NH)** **Wildt; Stefan (Lebanon, NH)**	1. **A composition comprising a plurality of immunoglobulins or fragments**, each immunoglobulin or fragment comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of **GlcNAcMan3 GlcNAc2**. 2. The composition of claim 1, wherein greater than 50 mole percent of said plurality of N-glycans consists essentially of GlcNAcMan3GlcNAc2.	**"GERNGROSS FAMILY IIi"** ***STATUS*** • **EP1942935** **REFUSED 2012-08-31** **ABANDONED 2012-10-11**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		FAMILY MEMBERS NATIONAL PHASE APPS FILED (FROM WIPO) Australia 03.03.2008 2006287173 Published: 03.04.2008 Canada 26.02.2008 2620515 China 01.09.2006 200680031862.4 Germany Withdrawn: 04.03.2008 European Patent Office (EPO) 28.02.2008 2006802932 Published: 16.07.2008 Refused: 31.08.2012 Withdrawn: 07.12.2012 India 27.02.2008 1743/DELNP/2008 Published: 25.07.2008 Japan 29.02.2008 2008529366 United States of America 20.02.2008 11990722 Published: 28.05.2009 ABANDONED	**2007-03-08** **Filing Date: 2006-09-01** **Earliest Effective Filing Date: 2005-09-09** **Priority Date: 2005-09-09**		3. The composition of claim 1 , wherein greater than 75 mole percent of said plurality of N-glycans consists essentially of GlcNAcMan3GlcNAc2. 4. The composition of claim 1, wherein greater than 90 mole percent of said plurality of N-glycans consists essentially of GlcNAcMan3 GlcNAc2. 5. The composition of claim 1, wherein the GlcNAcMan3GlcNAc2 N-glycan is present at a level from about 5 mole percent to about 50 mole percent more than the next most predominant N-glycan structure of said plurality of N-glycans. 6. The composition of claim 1, wherein the immunoglobulins or fragments exhibit decreased binding affinity for an FcγRII receptor. 7. The composition of claim 6, wherein the FcγRII receptor is a FcγRTIa receptor. 8. The composition of claim 7, wherein the immunoglobulins or fragments exhibit decreased phagocytosis (clearance of immunocomplexes by macrophages). 9. The composition of claim 6, wherein the FcγRJI receptor is a FcγRIIb receptor. 10. The composition of claim 9, wherein the immunoglobulins or fragments activate B cells. 11. The composition of claim 1, wherein the immunoglobulins or fragments exhibit increased binding affinity for an FcγRIII receptor. 12. The composition of claim 11, wherein the FcγRm receptor is a FcγREIa receptor. 13. The composition of claim 11, wherein the FcγRm receptor is a FcγRHIb receptor. 14. The composition of claim 1, wherein the immunoglobulins or fragments exhibit increased antibody-dependent cellular cytotoxicity (ADCC) activity. 15. The composition of claim 1, wherein the immunoglobulins or fragments are essentially free of fucose. 16. The composition of claim 1, wherein the immunoglobulins or fragments lack fucose. 17. The composition of claim 1, wherein the immunoglobulins or fragments bind to an antigen selected from the group consisting of growth factors, FGFR, EGFR, VEGF, leukocyte antigens, CD20, CD33, cytokines, **TNF-α,** and TNF-β. 18. The composition of claim 1, wherein the immunoglobulins or fragments comprise an Fc region selected from the group consisting of an IgGl, IgG2, IgG3, and IgG4 Fc regions.	***METHODOLOGY*** CLAIMS DRAWN TO AN IMMUNOGLOBULIN COMPRISING AT LEAST ONE N-GLYCAN IN WHICH THE PREDOMINANT N- GLYCAN CONSISTS ESSENTIALLY OF GlcNAcMan3 GlcNAc2 AND METHODS OF MAKING

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					19. A pharmaceutical composition comprising the composition of claim 1 and a pharmaceutically acceptable carrier. 20. The pharmaceutical composition of claim 19, wherein the immunoglobulins or fragments are essentially free of fucose. 21. The pharmaceutical composition of claim 19, wherein the immunoglobulins or fragments lack fucose. 22. The pharmaceutical composition of claim 19, wherein the immunoglobulins or fragments comprise an antibody which binds to an antigen selected from the group consisting of growth factors, FGFR, EGFR, **VEGF**, leukocyte antigens, CD20, CD33, cytokines, **TNF-α**, and TNF-β. 25. **A eukaryotic host cell** comprising an exogenous gene encoding an immunoglobulin or fragment thereof, wherein the eukaryotic host cell is genetically modified or selected to express the immunoglobulin composition of Claim 1. 27. A method for producing a composition comprising a plurality of immunoglobulins or fragments, each immunoglobulin or fragment comprising at least one N-glycan attached thereto wherein the composition thereby comprises a plurality of N-glycans in which the predominant N-glycan consists essentially of GlcNAcMan3GlcNAc2 comprising: (a) providing the eukaryote host cell of Claim 25; (b) growing the eukaryote host cell in a culture medium for a time sufficient for the eukaryote host cell to produce the immunoglobulins or fragments; and, (c) isolating the immunoglobulins or fragments to produce the composition.	
	2005-11-07	**WO2007055916 A3** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** **FAMILY MEMBERS**	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **Publication Date: 2007-05-18** **Filing Date: 2006-10-27** **Earliest Effective Filing Date: 2005-11-07**	**Ravetch; Jeffrey V. (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)**	1. **A method of predicting the cytotoxic activity of an antibody or variant thereof** comprising: determining a binding affinity of the antibody or variant thereof to a Fc activating receptor; determining a binding affinity of the antibody or variant thereof to a Fc inhibitory receptor, and calculating the ratio of said activating binding affinity to said inhibitory binding affinity, wherein the magnitude of said ratio is an indication of the cytotoxic activity of the antibody or variant thereof. 2. **A method of selecting a cytotoxic antibody or variant thereof out of a plurality of antibodies** comprising: comparing the A/1 ratios of the plurality of antibodies; and selecting the cytotoxic antibody or variant thereof with the greater A/I ratio.	***STATUS*** **EP1957099 A4 INTENTION TO GRANT ANNOUNCED 2014-09-03** **claims drawn to modified antibodies having enhanced cytotoxicity and having a higher A/I ratio than unmodified antibody (see below)** **EP2010566 B1 – GRANTED (seeTABLE A)** **EP2091969A4 – REFUSED 2013-05-10** **Original claims drawn to: "1. An isolated polypeptide containing at least one IgG Fc**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		AU2006312148A1 AU2006312148B2 AU2007235413A1 AU2007235413B2 AU2007317755A1 AU2008338550A1 CA2627981A1 CA2647524A1 CA2666308A1 CA2666308C CA2707304A1 CN101432301A CN101432301B CN101528774A CN101896202A EA200870411A1 EA200970416A1 EA201070739A1 EP1957099A4 EP2010566B1 EP2091969A4 EP2227255A4 EP2455100A3 EP2815768A3 HK1124074A1 IL194526A IL194526D0 IL197920D0 IL206029D0 JP2009532477A JP2010512306A JP2011506476A MX2008012843A MX2009004399A MX2010006537A NZ572379A US20080206246A1 US20080286819A1 US20090004179A1 US20100189714A1 US20100278808A1 US20110150867A1 US20120134988A1	**Priority Date: 2006-10-27**		3. **A method of selecting one or more antibodies or variants thereof** comprising determining the A/1 ratio of a plurality of antibodies or variants thereof and selecting those antibodies or variants thereof with a A/I ratio of less than 1. 4. **A method of selecting one or more cytotoxic antibodies or variants thereof** comprising etermining the A/I ratio of a plurality of cytotoxic antibodies or variants thereof and selecting those cytotoxic antibodies or variants thereof with a A/I ratio of 1 or greater. 5. The method of claim 4 wherein the A/I ratio of the cytotoxic antibodies or variants thereof is between about 10 to less than 500. 6. The method according to claim 2 wherein the cytotoxic antibody is a human cytotoxic antibody. 7. The method according to claim 1 wherein an Fc activating receptor is selected from the group consisting of FcγRII, FcγRIII, and an Fc inhibitory receptor is FcγRIIB. 8. The method of claim 7, wherein the human FcγRII activating receptor is FcγRIIA or FcγRIIC, wherein the humanFcγRIII activating receptor is FcγRIIIA, and wherein the human FcγRII inhibitory receptor is FcγRIIB. 9. The method of claim 6 wherein the cytotoxic antibody is a chimeric antibody. 10. The method according to claim 6 wherein the cytotoxic antibody is a humanized antibody. 11. The method according to claim 2 wherein the A/I ratio is determined by an assay selected from the group consisting of a competition or sandwich ELISA, a radioimmunoassay, a dot blot assay, a fluorescence polarization assay, a scintillation proximity assay, a homogeneous time resolved fluorescence assay, a resonant mirror biosensor analysis, and a surface plasmon resonance analysis . 12. **A purified modified antibody comprising an IgG Fc region**, the modified antibody having a greater A/I ratio as compared to the unmodified antibody. 13. **A purified modified antibody comprising an IgG Fc region**, the modified antibody having a lower A/I ratio as compared to the unmodified antibody. 14. The purified modified antibody of claim 12 comprising a human IgGl, IgG2 , IgG3 or IgG4 Fc region, wherein the modified antibody binds to a human Fc activating receptor selected from the group consisting of FcγRII and FcγRIII, and wherein the modified antibody binds to a human FcγRII inhibitory receptor.	**region, having altered properties compared to an unpurified antibody preparation, wherein sialylation of the isolated polypeptide is higher than the sialylation of the unpurified antibody preparation."** **EP2227255 A4 – WITHDRAWN** **EP2455100 A3 - WITHDRAWN** **US20080206246A1– PENDING (see below)** **US20080286819A1– PENDING** **claims drawn to methods of identifying Abs with reduced cytotoxicity** **US20100278808A1– PENDING (see below)** **US20110150867A1 – ABANDONED** **US20120134988 –PENDING (see below)** **US20130273040A1 – PENDING** **claims drawn to method of inhibiting inflammation in a patient.** **US20140323696A1–PENDING (see below)** **US8470318 B2 (US20100189714A1)-GRANTED- (see TABLE A)** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF SELECTING A CYTOTOXIC ANTIBODY OR VARIANT THEREOF

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		US20130273040A1 US20140323696A1 US8470318B2 WO2007055916A3 WO2007117505A2 WO2007117505A3 WO2008057634A2 WO2008057634A3 WO2009079382A1 ZA200808900A			15. The modified antibody of claim 14, wherein the modified antibody has an increased cytotoxicity activity in vi trσ. 16. The purified modified antibody of claim 14, wherein the human FcγRII activating receptor is FcγRIIA or FcγRIIC, wherein the human FcγRIII activating receptor is FcγRIIIA, and wherein the human FcγRII inhibitory receptor is FcγRIIB. 17. The purified modified antibody of claim 12, wherein the modified antibody has a lower amount of sialic acid compared to an unmodified antibody. 18. The purified modified antibody of claim 17, wherein the modified antibody is derived from a naturally occurring antibody source. 19. The purified modified antibody of claim 18, wherein the modified antibody has less than 20 percent sialic acid content. 20. The purified modified antibody of claim 17, wherein the modified antibody is expressed in a cell line having a protein sialylation deficiency. 21. The purified modified antibody of claim 20, wherein the modified antibody has less than 4 percent sialic acid content . 22. The purified modified antibody of claim 17, wherein the antibody is modified by treatment with sialidase . 23. The purified modified antibody of claim 17, wherein the antibody is purified by affinity chromatography.	
	2006-04-05	**US20120134988 A1** **13/336199** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** **FAMILY MEMBERS**	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **PENDING** **Publication Date: 2012-05-31** **Filing Date: 2011-12-23** **Earliest Effective Filing Date: 2006-04-05**	**Ravetch; Jeffrey V. (New York, NY)** **Kaneko; Yoshikatsu (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)**	**PUBLISHED AND PENDING CLAIMS:** 1. **A pharmaceutical composition comprising:** (a) a purified preparation of a modified protein that (i) comprises **a sialylated human Fc region having a higher content of α 2,6 linkages relative to α 2,3 linkages between sialic acids and galactose**, and (ii) has a **higher anti-inflammatory activity compared to a parent** of the protein that does not have a higher content of α 2,6 linkages relative to α 2,3 linkages, and (b) a pharmaceutically acceptable carrier. 20. The pharmaceutical composition of claim 1, wherein the **sialic acids and galactose** are attached to an asparagine residue in a CH.sub.2 immunoglobulin domain of the **sialylated human Fc region**.	***STATUS*** • **PENDING – RESPONSE TO RESTRICTION FILED 2014-12-03** ***METHODOLOGY*** CLAIMS DRAWN TO A MODIFIED PROTEIN HAVING A SIALYLATED HUMAN FC REGION HAVING A **HIGHER** CONTENT OF A 2,6 LINKAGES RELATIVE TO A 2,3 LINKAGES BETWEEN SIALIC ACIDS AND GALACTOSE

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		SEE ABOVE	**Priority Date: 2007-04-03**		21. The pharmaceutical composition of claim 1, wherein the sialylated human Fc region are substantially of the **G2S2 sialylated glycoform**. 28. The pharmaceutical composition of claim 1, wherein the modified protein is obtained by increasing the sialic acid content of the parent of the protein. 29. The pharmaceutical composition of claim 28, wherein the increasing step is performed by expressing a nucleic acid encoding the parent of the protein in a **genetically engineered host cell** having an activity of creating .alpha. 2,6 linkages between at least one galactose moiety and a respective terminal sialic acid in an N-linked biantennary oligosaccharide. 30. The pharmaceutical composition of claim 29, wherein the genetically engineered host cell expresses an .**alpha. 2,6 sialyltransferase**.	
	2006-04-05	**US20080206246A1** **11/957015** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** **FAMILY MEMBERS** SEE ABOVE	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **PENDING** **Publication Date: 2008-08-28** **Filing Date: 2007-12-14** **Earliest Effective Filing Date: 2006-04-05** **Priority Date: 2007-04-03**	**Ravetch; Jeffrey V. (New York, NY)** **Kaneko; Yoshikatsu (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)**	**PENDING CLAIMS (of 2011-06-09):** 50. (Currently Amended) A method of increasing anti-inflammatory activity of a human Fc-containing polypeptide preparation, the method comprising increasing sialylation of a first Fc-containing polypeptide preparation to form a purified or modified Fc-containing polypeptide preparation, wherein the purified or modified Fc-containing polypeptide preparation is characterized as having a higher content of N-linked biantennary oligosaccharides having terminal sialic acids connected to galactose by an α 2,6 linkage as compared to the first Fc-containing polypeptide preparation, such that the anti-inflammatory activity of the purified or modified Fc-containing polypeptide preparation is increased as compared to the first Fc-containing protein preparation ~~The method of claim 11~~, wherein the purified or modified Fc-containing polypeptide preparation is a preparation of human IgG antibody Fc fragments.	***STATUS*** • **PENDING – NON FINAL OFFICE ACTION MAILED 2014-08-14** ***METHODOLOGY*** PENDING CLAIMS DRAWN TO SIALYLATION OF OF A PREPARATION OF HUMAN IGG ANTIBODY FC FRAGMENTS HAVING VARYING DEGREES OF SIALYLATION

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					54. (Currently Amended) The method of claim 46 or 50 ~~claim 11~~, wherein the purified or modified Fc-containing polypeptide preparation comprises sialylated Fc-containing polypeptides ~~N-linked biantennary oligosaccharides having terminal sialic acids connected to galactose by an α 2,6 linkage~~ in an amount of about 30% or more . 55. (Currently Amended) The method of claim 46 or 50 ~~claim 11~~, wherein the purified or modified Fc-containing polypeptide preparation comprises sialylated Fc-containing polypeptides ~~N-linked biantennary oligosaccharides having terminal sialic acids connected to galactose by an α 2,6 linkage~~ in an amount of about 50% or more. 56. (Currently Amended) The method of claim 46 or 50 ~~claim 11~~, wherein the purified or modified Fc-containing polypeptide preparation comprises sialylated Fc-containing polypeptides ~~N-linked biantennary oligosaccharides having terminal sialic acids connected to galactose by an α 2,6 linkage~~ in an amount of about 100%.	
	2006-04-05	**US20100278808A1** **12/294883** **POLYPEPTIDES WITH ENHANCED ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS** **FAMILY MEMBERS** SEE ABOVE	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **PENDING** **Publication Date: 2010-11-04** **Filing Date: 2010-06-30** **Earliest Effective Filing Date: 2006-04-05** **Priority Date: 2007-04-03**	**Ravetch; Jeffrey V. (New York, NY)** **Kaneko; Yoshikatsu (New York, NY)** **Falk, Nimmerjahn (Thumau, DE)**	**PENDING CLAIMS (as of 2015-01-07)**	***STATUS*** • **PENDING – RESPONSE TO NON FINAL OFFICE ACTION MAILED 2014-08-14** ***METHODOLOGY*** CLAIMS DRAWN TO MODIFIED IGG POLYPEPTIDE HAVING A HIGHER A 2,6 LINKED N-ACETYLNEURAMINIC ACID CONTENT IN THE N LINKED GLYCANS OF THE FC REGION AND A HIGHER ANTI INFLAMMATORY ACTIVITY AND A LOWER CYTOTOXIC ACTIVITY

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
					1. **(Currently amended)** A modified IgG polypeptide preparation from an unmodified source, said preparation containing IgG polypeptides comprising a higher α2,6 linked N-acetylneuraminic acid ~~sialic acid~~ content in the N-linked glycans of the Fc regions of said IgG polypeptides relative to said unmodified source, wherein the modified IgG polypeptide preparation has a higher anti-inflammatory activity and a lower cytotoxic activity as compared to said unmodified source. 2. **(Currently amended)** The modified IgG polypeptide preparation of claim 1, wherein the IgG Fc region is a human IgG1, IgG2, IgG3 or IgG4 Fc region. 3. **(Currently amended)** The modified IgG polypeptide preparation of claim 1 having an increased anti-inflammatory activity *in vitro*. 4. **(Currently amended)** The modified IgG polypeptide preparation of claim 1, having an increased anti-inflammatory activity *in vivo*. 5. – 7. **(Cancelled)** 6. **(Currently amended)** The modified IgG polypeptide preparation of claim 1, from a recombinant antibody source. 8. **(Currently amended)** ~~The polypeptide preparation of claim 1,~~ A modified IgG polypeptide preparation from an unmodified source, said preparation containing IgG polypeptides comprising a higher α2,6 linked N-acetylneuraminic acid content in the N-linked glycans of the Fc regions of said IgG polypeptides relative to said unmodified source, wherein	

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					the modified IgG polypeptide preparation has a higher anti-inflammatory activity and a lower cytotoxic activity as compared to said unmodified source, wherein the modified IgG polypeptide preparation is produced from a cell line having an enhanced protein sialylation activity. 9. (**Currently amended**) ~~The polypeptide preparation of claim 1,~~ A modified IgG polypeptide preparation from an unmodified source, said preparation containing IgG polypeptides comprising a higher α2,6 linked N-acetylneuraminic acid content in the N-linked glycans of the Fc regions of said IgG polypeptides relative to said unmodified source, wherein the modified IgG polypeptide preparation has a higher anti-inflammatory activity and a lower cytotoxic activity as compared to said unmodified source, wherein the modified IgG polypeptide preparation is modified by treatment with sialyltransferase. 10. (**Currently amended**) The modified IgG polypeptide preparation of claim 1, which is purified. 11. (**Currently amended**) A pharmaceutical formulation comprising the modified IgG polypeptide preparation of claim 1 in combination with a suitable carrier or diluent. 12. – 22. (**Cancelled**) 23. (**Currently amended**) The modified IgG polypeptide preparation of claim 1, wherein the preparation contains polypeptides lacking a Fab region.	
	2006-04-05	**US20140323696A1** **14/280181** **POLYPEPTIDES WITH ENHANCED**	**THE ROCKEFELLER UNIVERSITY** (New York, NY) **PENDING**	**Ravetch; Jeffrey V.** (New York, NY) **Kaneko; Yoshikatsu** (New York, NY) **Falk, Nimmerjahn**	**PENDING CLAIMS** (as of 2015-02-02) 1-22. Canceled 23. **A method of preparing a pharmaceutical preparation having anti-inflammatory activity**, comprising:	*STATUS* • **PENDING - NON FINAL ACTION MAILED 2015-02-02**

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		ANTI-INFLAMMATORY AND DECREASED CYTOTOXIC PROPERTIES AND RELATING METHODS **FAMILY MEMBERS** SEE ABOVE	**Publication Date: 2014-10-30** **Filing Date: 2014-05-16** **Earliest Effective Filing Date: 2006-04-05** **Priority Date: 2007-04-03**	**(Thumau, DE)**	expressing, in a host cell, **a recombinant IgG antibody**; subjecting the expressed recombinant **IgG antibody** to **one or more purification steps** to produce a preparation comprising the recombinant **IgG antibody**; **treating the composition comprising the recombinant IgG antibody with an alpha-(2,6) sialylatransferase** and a donor of sialic acid to increase the fraction of recombinant **IgG antibody** in the composition having alpha-2,6-linked sialic acid on N-glycans of the Fc region of the recombinant **IgG antibody** thereby preparing a composition enriched for sialylated recombinant **IgG antibody**, wherein the enriched composition has increased anti-inflammatory activity relative to the un-enriched composition, and **processing the composition enriched for sialylated recombinant IgG antibody** to produce a pharmaceutical preparation, wherein the processing comprises combining the recombinant **IgG antibody** with a physiologically acceptable carrier, excipient or stabilizer, thereby preparing a pharmaceutical preparation having increased anti-inflammatory activity. 24 -26 Canceled 27. The method of claim 23 wherein the recombinant IgG antibody is a **monoclonal antibody**. 28. The method of claim 26 wherein the recombinant IgG antibody is **chimeric antibody**. 29. The method of claim 26 wherein the recombinant IgG antibody is a **humanized antibody**. 30. The method of claim 23 further comprising subjecting the composition enriched for sialylated recombinant IgG antibody to affinity chromatography to produce a composition further **enriched for sialylated recombinant** IgG antibody. 31. The method of claim 23 where in the host cell is a **mammalian cell line** 32. The method of claim 31 wherein the mammalian cell line is a **CHO cell line**. 33. The method of claim 23 further comprising **measuring the sialic acid content of the composition enriched for sialylated recombinant** IgG antibody. 34. The method of claim 32 **wherein the step of measuring comprises one or more of: affinity chromatography, HPLC, and mass spectrometry**. 35. The method of claim 23 further comprising measuring the anti-inflammatory activity of the composition enriched for sialylated recombinant IgG antibody. 36. The method of claim 23 further comprising measuring the antibody dependent cell cytotoxicity of the composition enriched for sialylated recombinant IgG antibody.	***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF PREPARING A RECOMBINANT IgG ANTIBODY THAT IS TREATED WITH AN ALPHA-(2,6) SIALYLATRANSFERASE THEREBY INCREASING ITS ANTI-INFLAMMATORY ACTIVITY

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					37. The method of claim 23 wherein the purification step comprises ion-exchange chromatography or affinity chromatography. 38. The method of claim 23 wherein the composition enriched for sialylated recombinant IgG antibody exhibits an increased protective effect in a K/B×N serum-induced arthritis mouse model relative to the un-enriched composition. 39. The method of claim 23 **wherein the host cell harbors a recombinant sialyltransferase.** 40. A pharmaceutical preparation made by the method of claim 23.	
	2006-05-05	**WO2007130638 A2** **PRODUCTION OF SIALYLATED N-GLYCANS IN LOWER EUKARYOTES** **FAMILY MEMBERS** SEE ABOVE	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2007-11-15** **Filing Date: 2007-05-04** **Earliest Effective Filing Date: 2006-05-05**	**Hamilton; Stephen (Enfield, NH)**	1. **A method for producing a recombinant sialylated glycoprotein** in a host cell, the host cell selected or engineered to produce glycoproteins comprising a Gal(i-4)GlcNAc(1-4)Man3GlcNAc2 glycoform, the method comprising the step of **introducing into the host cell a nucleic acid encoding an enzyme having sialyltransferase activity**, the enzyme comprising a sialyltransferase catalytic domain and a cellular targeting signal peptide to target the sialyltransferase catalytic domain to the secretory pathway of the host cell; wherein, upon passage of the recombinant glycoprotein through the secretory pathway of the host cell, a recombinant glycoprotein comprising aNANA(i^)Gal(1-4)GlcNAC(i-4)Man3GlcNA2 glycoform is produced. 4. A **method for producing a recombinant sialylated glycoprotein** in a host cell, the host cell selected or engineered to produce glycoproteins comprising a Gal(i-4)GlcNAc(1-4)Man3GlcNAc2 glycoform, the method comprising the step of **introducing into the host cell: (a) a nucleic acid encoding an enzyme having sialyltransferase activity**; and (b) a nucleic acid encoding one or more enzymes involved in the biosynthesis or transport of CMP-Sia; wherein upon passage of the recombinant glycoprotein through the secretory pathway of the	**"HAMILTON III" FAMILY** ***STATUS*** • **US7863020 (US20060286637A1) (see TABLE A)** • **US8268609 (US20100279356A1) (see TABLE A)** • **US20130018177 A1 – PENDING Claims drawn to a method for producing a recombinant sialylated**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
			Priority Date: 2006-05-05		host cell, a recombinant glycoprotein comprising glycoform is produced. 6. **A method for producing a recombinant sialylated glycoprotein in a eukaryotic host cell** comprising **introducing into the host cell a nucleic acid encoding a trans-sialidase enzyme**. 10. **A method for producing a recombinant sialylated glycoprotein in a host cell**, the host cell selected or engineered to produce glycoproteins comprising a GalGlcNAcMan5GlcNAc2 glycoform, the **method comprising the step of introducing into the host cell a nucleic acid encoding an enzyme having sialyltransferase activity**, the enzyme comprising a sialyltransferase catalytic domain and a cellular targeting signal peptide to target the sialyltransferase catalytic domain to the secretory pathway of the host cell; wherein, upon passage of the recombinant glycoprotein through the secretory pathway of the host cell, a recombinant glycoprotein comprising a NANAGaIGIcNAcMa^GIcNA glycoform is produced. 11. **A method for producing a recombinant sialylated glycoprotein in a host cell,** the host cell selected or engineered to produce glycoproteins comprising a GaIGIcNAcMa^GIcNAc glycoform, the method comprising the step of **introducing into the host cell: (a) a nucleic acid encoding an enzyme having sialyltransferase activity**; and (b) a nucleic acid encoding one or more enzymes involved in the biosynthesis or transport of CMP-Sia; wherein upon passage of the recombinant glycoprotein through the Golgi apparatus of the host cell, a recombinant glycoprotein comprising a NANAGalGlcNAcMansGlcNA 2 glycoform is produced. 25. **A nucleic acid encoding an enzyme comprising a sialyltransferase catalytic domain** operatively linked to a cellular targeting signal peptide to target the sialyltransferase catalytic domain to the Golgi apparatus of the host cell. 26. A **nucleic acid encoding a fusion protein comprising a trans-sialidase catalytic domain** and a cellular targeting signal peptide to target the trans-sialidase catalytic domain to the secretory pathway, cell wall or cell membrane of the host cell. 31. **A method for producing a sialylated glycoprotein in a recombinant non-human eukaryotic host cell** comprising **introducing into medium used for growing the host a trans- sialidase enzyme** and a sialic acid donor. 32. **A method of enhancing the production of CMP-sialic acid in a host cell** comprising the step **of introducing into the host cell a nucleic acid encoding an enzyme having GIcNAc**	**glycoprotein in a lower eukaryotic host cell** • **EP2365089 A1 –-PENDING Claims drawn to a method for producing CMP-sialic acid in a yeast host cell** • **EP2027281 A2 –PENDING Claims drawn to a method for producing a recombinant sialylated glycoprotein in a host cell** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO PRODUCTION OF SIALYLATED GLYCOPROTEINS BY HOST CELLS TRANSFECTED WITH ENZYMES OF THE SIALYLATION PATHWAY (E.G., SIALYLTRANSFERASES, TRANS-SIALIDASES, SIALATE ALDOLASE, GLCNAC EPIMERASE)

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					epimerase activity. 33. **A method of enhancing the production of CMP-sialic acid in a host cell** comprising the step of **introducing into the host cell a nucleic acid encoding an enzyme having sialate aldolase activity**.	
	2006-06-09	**WO2007146847 A3** **GLYCOSYLATION ENGINEERED ANTIBODY THERAPY** **FAMILY MEMBERS** CA2655246A1 CN101466402A EP2035034A2 EP2035034A4 WITHDRAWN 2012-02-24 US20100173323A1 ABANDONED 2012-03-01 WO2007146847A3	**UNIVERSITY OF MARYLAND** (Baltimore, MD) **Publication Date: 2007-12-21** **Filing Date: 2007-06-09** **Earliest Effective Filing Date: 2006-06-09** **Priority Date: 2006-06-09**	**Strome Scott (Reisterstown, MD)** **Wang Lai-Xi (Ellicott City, MD)**	1**. A method of producing an antibody having a desired glycosylation state** comprising the steps of a) removing one or more sugars, b) chemically synthesizing a sugar, and c) enzymatically attaching the chemically synthesized sugar to (i) the antibody or (ii) a sugar attached to the antibody. 14. **A method of evaluating a biological activity of a glycopolypeptide** comprising the steps of a) producing a substantially pure population of glycopolypeptides having a selected glycosylation state, and b) measuring the biological activity of the glycopolypeptide. 21. **A method of selecting the glycosylation state for a monoclonal antibody** comprising the steps of a) determining a Fcg Receptor allele on an immune cell, and b) selecting a glycosylation state which modulates, relative to a source monoclonal antibody having a heterogeneous glycosylation state, i) Antibody Dependent Cell Cytotoxicity, ii) Complement Dependent Cytotoxicity, iii) an Fc g receptor binding affinity, or iv) a monoclonal antibody induced cell signaling event. 25. **A method of creating a substantially pure glycoform of a pre-existing monoclonal antibody having a heterogeneous glycosylation state** comprising the steps of a) using the method of claims 1 - 4 to create two or more of the glycoforms present in the pre-existing monoclonal antibody, b) testing the two or more glycoforms for a biological activity or a toxicity to determine a preferred glycoform of the pre-existing monoclonal antibody having a higher	***STATUS*** • **EP2035034 – WITHDRAWN 2012-02-24** • **US20100173323A1 – ABANDONED 2012-03-01** ***METHODOLOGY*** CLAIMS DRAWN TO IN VITRO ENZYMATIC MODIFICATION OF IMMUNOGLOBULIN GLYCOSYLATION PROFILE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					biological activity or a lower toxicity, and c) using the method of claim 1-4 to produce a monoclonal antibody glycoform having a substantially pure preferred glycosylation state identified in step b) as having a higher biological activity or a lower toxicity.	
	2006-09-10	**WO2008028686A2** **FULLY HUMAN HIGH YIELD PRODUCTION SYSTEM FOR IMPROVED ANTIBODIES AND PROTEINS** **FAMILY MEMBERS** AU2007294122A1 AU2007294122B2 BRPI0716997A2 CA2662226A1 CN101588817A CN101588817B CN103436574A CU23791A3 EA17622B1 EA200970263A1 EP1900750A1 EP1911766A1 EP2073842B1 EP2428223A3 EP2428224A3 EP2428225A3	**GLYCOTOPE GMBH** (Berlin, DE) **Publication Date: 2008-03-13** **Filing Date: 2007-09-10** **Earliest Effective Filing Date: 2006-09-10** **Priority Date: 2007-09-10**	**Goletz; Steffen; (Glienicke-Nordbahn, DE)** **Danielczyk; Antje (Panketal, DE)** **Baumeister; Hans (Berlin, DE)** **Stahn; Renate (Berlin, DE)** **Loffler; Anja (Eichhorst, DE)** **Stockl; Lars (Berlin, DE)**	1. **A method for producing a protein molecule composition**, comprising (a) **introducing in a host cell which is an immortalized human blood cell at least one nucleic acid encoding at least a part of said protein;** and (b) culturing said host cell under conditions which permit the production of said protein molecule composition; and (c) isolating said protein molecule composition. 2. A method according to claim 1 for producing a protein molecule composition, preferably an **antibody molecule composition**, comprising the following steps: (a) introducing in a host cell which is an **immortalized human blood cell** at least one nucleic acid encoding a protein or at least one part thereof; wherein said host cell is selected to produce a protein composition having at least one of the following **glycosylation characteristics**: (i) it comprises no detectable NeuGc; and/or (ii) it has a **galactosylation degree on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition**, that is **increased compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096]** when expressed therein; and/or (iii) it has an amount of **G2 structures** on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same	***STATUS*** **EP1900750 A1 - WITHDRAWN** **EP1911766 A1 - WITHDRAWN** **EP2073842 B1 GRANTED** **EP2428223 A3 - PENDING** **EP2428224 A3 – PENDING (see below)** **EP2428225 A3 - PENDING** **US20100028947A1 – ALLOWED 2015-02-04** **Generally, claims drawn to the use of human cells of myeloid leukaemia origin for expression of antibodies** ***METHODOLOGY*** CLAIMS DRAWN TO THE GLYCOSYLATION OF A PROTEIN IN AN IMMORTALIZED BLOOD CELL

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		IL197459D0 JP2010502204A KR2009077911A MX2009002388A NZ575974A SG174792A1 US20100028947A1 WO2008028686A3 WO2008135259A2 WO2008135259A3 ZA200901912A			protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or (iv) it has an amount of GO structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or (v) it comprises no detectable terminal Galalpha1-3Gal; and/or (vi) it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or (vii) it comprises at least one carbohydrate structure containing bisecting GIcNAc; and/or (viii) **it has a sialylation pattern which is altered compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein**, (b) culturing said host cell under conditions which permits the production of said protein molecule composition; and (c) isolating said protein molecule composition, wherein the protein molecules have at least one of the glycosylation characteristics (i) to (viii). 10. The method of at least one of the claims 1 to 9, wherein a host cell is used, which is selected from the following groups 1 to 4: (a) group 1, comprising **host cells having a high sialylation activity such as K562** or cell lines derived therefrom; (b) group 2, comprising **host cells having due to a genetic deficiency or an expression suppression system a low or no sialylation** activity, comparable to and including NM- F9 [DSM ACC2606], NM-D4 [DSM ACC2605] and GT-2X or cell lines derived therefrom; (c) group 3, comprising host **cells having a higher sialylation degree than K562** such as NM-H9 and NM-H9D8 or cell lines derived therefrom; (d) group 4, comprising **host cells having a low or no fucosylation activity** such as NM-H9D8-E6 and NM-H9D8-E6Q12 or cell lines derived therefrom.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2006-09-10	**EP2428224 A2** **USE OF HUMAN CELLS OF MYELOID LEUKAEMIA ORIGIN FOR EXPRESSION OF ANTIBODIES** **FAMILY MEMBERS** AU	**GLYCOTOPE GMBH** (Berlin, DE) **PENDING** **Publication Date: 2012-03-14** **Filing Date: 2007-09-10** **Earliest Effective Filing Date: 2006-09-10** **Priority Date: 2007-09-10**	**Goletz; Steffen; (Glienicke-Nordbahn, DE)** **Danielczyk; Antje (Panketal, DE)** **Baumeister; Hans (Berlin, DE)** **Stahn; Renate (Berlin, DE)** **Loffler; Anja (Eichhorst, DE)** **Stockl; Lars (Berlin, DE)**	**PENDING CLAIMS (as of 2015-01-07)** 1. **A method for selecting a host cell for producing a protein composition having at least one of the following glycosylation characteristics**: (i) **it has an amount of G2 structures** on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or (ii) **it comprises more than 35% G2 structures** present on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein composition; and/or (iii) **it has an amount of GO structures** on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or (iv) **it comprises less than 22% GO structures** present on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein composition; and/or (v) **it comprises an amount of fucose** on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule	***STATUS*** • **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF SELECTING A HOST CELL FOR PRODUCING A PROTEIN COMPOSITION BASED ON THE GLYCOSYLATION OF A PROTEIN IN AN IMMORTALIZED BLOOD CELL

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or it comprises at least 2% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition containing bisecting GIcNAc; and/or (vi) **it has a sialylation pattern which is altered** compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein, wherein (vii) **it has an increased sialylation degree** with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which is at least 15% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; or (viii) **it has a decreased sialylation degree** with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which is at least 15% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; by the following steps (a) introducing in at least two different host cells providing a diverging glycosylation pattern at least one nucleic acid encoding a protein or at least one part thereof; wherein said host cells are immortalized human blood cells; and (b) culturing said at least two different host cells, wherein each different host cell produces a protein composition having a glycosylation pattern diverging from the glycosylation pattern produced by the other host cell; (c) isolating said expressed protein compositions carrying a different glycosylation pattern from the at least two different host cells; and (d) selecting said host cell producing a protein composition which has at least one of the glycosylation characteristics defined in (i) to (vii). 10. The method according to any one of the claims 1 to 9, wherein said protein is an **antibody or a fragment thereof.**	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					11. The method according to claim 10, wherein the antibody is selected from the group consisting of antibodies against ganglioside GD3, antibodies against human interleukin-5 receptor alpha—chain, antibodies against HER2, antibodies against CC chemokine receptor 4, antibodies against CD20, antibodies against CD22, antibodies against neuroblastoma, antibodies against MUC1, antibodies against epidermal growth factor receptor; in particular an antibody selected from the group consisting of Pankomab, Muromomab, Daclizumab, Basiliximab, Abciximab, Rituximab, Herceptin, Gemtuzumab, Alemtuzumab, Ibritumomab, Cetuximab, Bevacizumab, Tositumomab, Pavlizumab, Infliximab, Eculizumab, Epratuzumab, Omalizumab, Efalizumab, **Adalimumab**, OKT3, anti-CC chemokine receptor 4 antibody KM2160, and anti-neuroblastoma antibody chCE7. 12. The method according to claim 10, wherein the antibody is selected from the group consisting of an antibody against MUC1; **an antibody against HER2; and an antibody against EGFR.** 13. The method according to any one of claims 1 to 12, wherein said protein (i) is fused to another peptide or polypeptide sequence such as a linker, an activating molecule or a toxin; or (ii) is an antibody fragment fused to another protein sequence, in particular a protein sequence selected from the group consisting of cytokines, co-stimulatory factors, toxins, antibody fragments from other antibodies, multimerisation sequences, and sequences for detection, purification, secretion or stabilization such as tags, localization signals or linkers; or (iii) is an antibody or antibody fragment coupled to an effector molecule which mediates a therapeutic effect, such as an immune effector molecule, a toxin or a radioisotope. 14. The method according to any one of claims 10 to 13, wherein the antibody is of the IgG class, preferably a a human, humanized or chimeric IgG which comprises a human Fc region. 15. The method according to any one of claims 10 to 14, wherein the antibody composition comprises at least one glycoform of an antibody molecule with at least one carbohydrate chain attached to another glycosylation site of the antibody molecule than the amino acid Asn-297 in the second domain of the Fc region.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2007-03-02	**US20090068705A1** **USE OF COPPER GLUTAMATE IN CELL CULTURE FOR PRODUCTION OF POLYPEPTIDES** **FAMILY MEMBERS** AU2008223133A1 CA2679941A1 CN101679941A EP2115126A1 INTENTION TO GRANT IL200622D0 JP05586235B2 JP2010519909A KR2009127326A MX2009009240A RU2009132986A WO2008109410A1 ZA200906061A	**WYETH*** (Madison, NJ) ***now Pfizer** **PENDING** **Publication Date: 2009-03-12** **Filing Date: 2008-02-29** **Earliest Effective Filing Date: 2007-03-02** **Priority Date: 2008-02-29**	**Drapeau; Denis (Salem, NH)** **Snow; Jessica (Sterling, MA)** **Hiller; Gregory (Wakefield, MA)** **Luan; Yen Tung (Chelmsford, MA)**	29. **A method of producing a polypeptide in a cell culture** comprising steps of: culturing mammalian cells that contain a gene encoding a polypeptide of interest in a cell culture medium comprising **between approximately 0.5 and 5 μM copper and between approximately 1.7 and 33 mM glutamate** under conditions and for a time sufficient to permit expression of the polypeptide, wherein the **glycosylation pattern of the expressed polypeptide is increased** relative to the glycosylation pattern that would be observed on the expressed polypeptide under otherwise identical conditions in an otherwise identical medium that lacks copper and glutamate. 31. The method of claim 29, wherein the increased glycosylation pattern of the expressed polypeptide **comprises an increase in total sialylation**.	***STATUS*** • **PENDING** • **EP2115126 A1 – GRANT INTENDED – similar claims as in US but require in addition that the polypeptide is TNFR-Ig.** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF INCREASING THE GLYCOSYLATION PATTERN OF AN PROTEIN EXPRESSED IN MAMMALIAN CELLS CULTURED IN MEDIA SUPPLEMENTED WITH COPPER AND GLUTAMATE
	2007-03-07	**WO2008112092 A2**	**GLYCOFI, INC.*** (Lebanon, NH)	**Hamilton; Stephen (Enfield, NH)**	1. **A recombinant lower eukaryote host cell comprising a fucosylation pathway.** 2. The host cell of Claim 1 which is yeast or filamentous fungus.	**"HAMILTON IV" FAMILY**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		PRODUCTION OF GLYCOPROTEINS WITH MODIFIED FUCOSYLATION **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 01.09.2009 2008227024 Published: 24.09.2009 Canada 01.09.2009 2679732 China 03.03.2008 200880014608.2 European Patent Office (EPO) 08.09.2009 2008726344 Published: 23.12.2009 Granted: 17.04.2013 India 25.08.2009 4999/CHENP/2009 Published: 06.11.2009 Japan 04.09.2009 2009552704 Republic of Korea 07.10.2009 1020097020933 Published: 17.12.2009 Russian Federation 07.10.2009 2009136982 United States of America 20.08.2009 12528029 Published: 04.02.2010	* acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2008-09-18** **Filing Date: 2008-03-03** **Earliest Effective Filing Date: 2007-03-07** **Priority Date: 2008-03-03**		3. The host cell of Claim 2 wherein the yeast is a Pichia sp. 4. The host cell of Claim 3 wherein the Pichia sp. is Pichia pastor is. 5. The host cell of claim 1 wherein the host cell further does not display αl,6-mannosyltransferase activity with respect to the N-glycan on a glycoprotein and includes an αl,2-mannosidase catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target αl,2-mannosidase activity to the ER or Golgi apparatus of the host cell whereby, upon passage of a recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a fucosylated Man5GlcNAc2 glycoform is produced. 6. The host cell of Claim 5 further including a GIcNAc transferase I catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain of and selected to target GIcNAc transferase I activity to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a fucosylated GIcN AcMan5 GIcN Ac2 glycoform is produced. 7. The host cell of Claim 6 further including a mannosidase II catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target mannosidase II activity to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a fucosylated GIcN AcMan3 GIcN Ac2 glycoform is produced. 8. The host cell of Claim 7 further including a GIcNAc transferase II catalytic domain fused to a cellular targeting signal peptide not normally associated with the catalytic domain and selected to target GIcNAc transferase II activity to the ER or Golgi apparatus of the host cell; whereby, upon passage of the recombinant glycoprotein through the ER or Golgi apparatus of the host cell, a recombinant glycoprotein comprising a fucosylated GlcNAc2Man3GlcNAc2 glycoform is produced. 11. **A glycoprotein composition comprising a plurality of glycoforms,** each glycoform comprising at least one N-glycan attached thereto, wherein the glycoprotein composition thereby comprises a plurality of N-glycans in which greater than 25 mole percent of the plurality of iV-glycans consist essentially of a fucosylated 7V-glycan selected from the group consisting of Man5GlcNAc2, GIcN AcMans GIcN Ac2, Man3GlcNAc2, GIcN AcMan3 GIcN Ac2, GlcNAc2Man3GlcNAc2, GalGlcNAc2Man3GlcNAc2, Gal2GlcNAc2Man3GlcNAc2, NANAGal2GlcNAc2Man3GlcNAc2, and NANA2Gal2GlcNAc2Man3GlcNAc2.	***STATUS*** • **EP2134834 GRANTED** **NO OPPOSITION FILED** **EXPIRES 2028-03-03** **2014 ANNUAL FEES PAID IN DE, CH, AT, FR, GB – LAPSED ELSEWHERE** **Claims drawn to a recombinant Pichia host cell** • **US20100028951 A1 – PENDING** **Similar claims as in PCT** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO RECOMBINANT LOWER EUKARYOTE HOST CELL COMPRISING A FUCOSYLATION PATHWAY AND TO GLYCOPROTEIN COMPOSITIONS HAVING A PLURALITY OF GLYCOFORMS

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
					12. The glycoprotein composition of Claim 11 wherein the fucosylated N-glycans are greater than 50 mole percent of the plurality of N-glycans. 13. The glycoprotein composition of Claim 11 wherein the fucosylated N-glycans are greater than 75 mole percent of the plurality of iV-glycans. 14. The glycoprotein composition of Claim 11 wherein the fucosylated N-glycans are greater than 80 mole percent of the plurality of N-glycans. 15. The glycoprotein composition of Claim 11 wherein the fucose is in an α 1,3 -linkage with the GIcNAc at the reducing end of the N-glycan. 16. The glycoprotein composition of Claim 11 wherein the fucose is in an αl,6-linkage with the GIcNAc at the reducing end of the N-glycan. 17. The glycoprotein composition of Claim 11 wherein the fucose is in an αl ,2-linkage with the Gal at the non-reducing end of the 7V-glycan. 18. The glycoprotein composition of Claim 11 wherein the fucose is in an α 1,3 -linkage with the GlcNac at the non-reducing end of the iV-glycan. 19. The glycoprotein composition of Claim 11 wherein the fucose is in an αl,4-linkage with a GIcNAc at the non-reducing end of the 7V-glycan. 20. A hybrid vector comprising (a) DNA regulatory elements which are functional in a lower eukaryotic host cell operatively linked to (b) DNA coding sequence encoding a fusion protein encoding (i) a targeting sequence; and (b) a catalytic domain of a fucosylation pathway enzyme. 21. The vector of Claim 17 wherein the fucosylation pathway enzyme is a fucosyltransferase.	
	2007-04-16	**WO2008128228 A1** **METHODS RELATED TO CELL SURFACE GLYCOSYLATION** **FAMILY MEMBERS**	**MOMENTA PHARMACEUTICALS** (Cambridge, MA) **Publication Date: 2008-10-23** **Filing Date:**	**Collins; Brian Edward (Arlington, MA)** **Bosques; Carlos J (Arlington, MA)** **Zhu; Xiangping (North Grafton, MA)**	1. **A method of determining one or more characteristics of the glycosylation pattern of a glycoprotein produced by a cell,** the method comprising steps of: a) determining a difference in glycosylation pattern between: (i) a first surface glycosylation pattern present under a first set of conditions on the surface of a cell that produces a glycoprotein of interest; and (ii) a second surface glycosylation pattern present under a second set of conditions on the surface of the cell; and b) based on the determined difference, establishing one or more characteristics of the glycosylation pattern of the glycoprotein of interest produced by the cell.	***STATUS*** • **US8338088 B2 EXPIRES 2028-02-24 see below** • **EP2135081 B1 EXPIRES 2028-04-15 similar claims as in PCT**

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
		AU2008240081A1 BRPI0810472A2 CA2682744A1 CN101675339A CN101675339B DK2135081T3 EP2135081A1 EP2135081B1 EP2511705A1 WITHDRAWN ES2399940T3 JP05175336B2 JP2010525328A RU2009141980A RU2475751C2 US8338088B2 US20100196940A1 (See below)	**2008-04-15** **Earliest Effective Filing Date: 2007-04-16** **Priority Date: 2008-04-15**	**Bulik; Dorota A. (Malden, MA)** **Thiruneelakantapillai; Lakshmanan (Boston, MA)** **Parsons; Ian Christopher (Belmont, MA)** **Shriver; Zachary (Cambridge, MA)** **Chillakuru; Rajeev (Cambridge, MA)** **Venkataraman; Ganesh (Bedford, MA)**	7. **A method comprising steps of** a) determining a difference in glycosylation pattern between: (i) a first surface glycosylation pattern present on the surface of cells in a first culture of cells; and (ii) a second surface glycosylation pattern present on the surface of cells in culture, wherein the first culture and second culture differ from one another with respect to at least one parameter; and b) based on the determined difference, establishing effects of the at least one parameter on glycosylation of glycoproteins produced by cells in culture. 36. **A method of determining one or more characteristics of the glycosylation pattern of a glycoprotein of interest produced by a cell**, the method comprising: a) providing a cell that produces a glycoprotein of interest, which cell has at least one cell-surface glycan attached to the surface of the cell, so that the cell has a cell surface glycosylation pattern; and b) determining at least one characteristic of the cell surface glycosylation pattern; and c) based on the determined characteristic, establishing one or more characteristics of the glycosylation pattern of the glycoprotein of interest, wherein the determined characteristic correlates with the one or more characteristics of the glycosylation pattern of the glycoprotein of interest. 60. **A method of determining one or more differences in the glycosylation pattern of a glycoprotein of interest** comprising: a) providing a first cell comprising at least one first cell-surface glycan attached to the surface of the first cell, which first cell produces the glycoprotein of interest; b) characterizing the at least one first cell-surface glycan; c) providing a second cell comprising at least one second cell-surface glycan attached to the surface of the second cell, which second cell produces the glycoprotein of interest; d) characterizing the at least one second cell-surface glycan; e) determining one or more differences between the first cell-surface glycan and the second cell-surface glycan; and f) establishing one or more differences in the glycosylation pattern of the glycoprotein of interest, wherein the determined difference or differences between the first cell-surface glycan and the second cell-surface glycan correlate with the one or more differences in the glycosylation pattern of the glycoprotein of interest. 90. **A method of determining one or more characteristics of the glycosylation pattern of a glycoprotein of interest** comprising steps of: a) providing a cell comprising at least one cell-surface glycan attached to the surface of the cell, which cell produces the glycoprotein of interest; and b) characterizing the at least one cell-surface glycan; and c) determining one or more characteristics of the glycosylation pattern of the glycoprotein of interest, wherein the characterized at least one glycan correlates with the one or more characteristics of the glycosulation pattern of the glycoprotein of interest. 91. The method of claim 90, wherein the cell-surface glycoprotein is liberated from the cell by subjecting the cell to protease treatment such that the glycoprotein is liberated from the cell, wherein the protease treatment does not substantially rupture the cell membrane.	***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF DETERMINING THE GLYCOSYLATION OF RECOMBINANT PROTEINS BASED ON THE GLYCOSYLATION OF AT LEAST ONE CELL-SURFACE GLYCAN

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					92. The method of claim 90, wherein the cell-surface glycoprotein is liberated from the cell by subjecting the cell to one or more proteolytic enzymes selected from the group consisting of: proteinase K, trypsin, and combinations thereof. 93. The method of claim 92, wherein the step of subjecting comprises subjecting the cell to one or more proteolytic enzymes at a concentration of about 0.1 to 2.0 mg/mL. 94. The method of claim 92, wherein the step of subjecting comprises subjecting the cell to protease treatment for about 15 minutes at a temperature of about 37°C. 95. The method of claim 90, wherein the step of determining comprises subjecting the cell-surface glycoprotein to a characterization method selected from the group consisting of: NMR, mass spectrometry, liquid chromatography, 2-dimensional chromatography, SDS-PAGE, antibody staining, lectin staining, monosaccharide quantitation, fluorophore-assisted carbohydrate electrophoresis (FACE), micellar electrokinetic chromatography (MEKC), exoglycosidase or endoglycosidase treatments, and combinations thereof.	
	2007-04-16	**US8338088B2** **12/595,902** **US20100196940A1** **METHODS RELATED TO CELL SURFACE GLYCOSYLATION** **FAMILY MEMBERS** SEE ABOVE	**MOMENTA PHARMACEUTICALS** (Cambridge, MA) **EXPIRES 2028-02-24** **PTA: 315 days** **Publication Date: 2008-08-05** **Filing Date: 2008-04-15** **Earliest Effective Filing Date:**	**Collins; Brian Edward (Arlington, MA)** **Bosques; Carlos J (Arlington, MA)** **Zhu; Xiangping (North Grafton, MA)** **Bulik; Dorota A. (Malden, MA)** **Thiruneelakantapillai; Lakshmanan (Boston, MA)** **Parsons; Ian**	1. **A method of determining one or more characteristics of the glycosylation pattern of a recombinant non-cell surface glycoprotein of interest** produced by a cell, the method comprising: a) **providing a cell that produces the recombinant non-cell surface glycoprotein of interest**, which cell has at least one cell-surface glycan attached to the surface of the cell, so that the cell has a cell surface glycosylation pattern; b) **liberating at least one cell surface glycan from the cell**; c) **determining at least one characteristic of the cell surface glycosylation pattern** selected from the group consisting of degree of glycosylation site occupancy, identity of at least one linked glycan, relative amounts of linked glycans, complete or partial composition of linked glycans, and combinations thereof; and d) **based on the at least one determined characteristic, establishing one or more characteristics of the glycosylation pattern of the recombinant non-cell surface**	***STATUS*** • **EXPIRES 2028-02-24** • **4th year fee window opens: 12/25/2015** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF DETERMINING ONE OR MORE CHARACTERISTICS OF THE GLYCOSYLATION PATTERN OF A RECOMBINANT NON-CELL SURFACE GLYCOPROTEIN

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			2007-04-16 **Priority Date: 2008-04-15**	**Christopher (Belmont, MA)** **Shriver; Zachary (Cambridge, MA)** **Chillakuru; Rajeev (Cambridge, MA)** **Venkataraman; Ganesh (Bedford, MA)**	**glycoprotein of interest**, wherein the determined characteristic correlates with the one or more characteristics of the glycosylation pattern of the non-cell surface glycoprotein of interest. 2. The method of claim 1, wherein the at least one characteristic of the glycosylation pattern comprises a change in glycosylation pattern of the recombinant non-cell surface glycoprotein of interest. 3. The method of claim 1, wherein the step of establishing one or more characteristics comprises establishing an extent of sialylation present in the glycosylation pattern of the recombinant non-cell surface glycoprotein of interest. 4. The method of clam 1, wherein the step of liberating comprises exposing the cell to a protease. 5. The method of claim 4, wherein the step of exposing comprises subjecting the cell to protease treatment such that at least one cell surface glycoprotein is liberated, wherein the protease treatment does not substantially rupture cell membranes. 6. The method of claim 1, wherein the step of liberating comprises: a) cleaving one or more protein-linked cell-surface glycans from cell surface glycoproteins; and b) characterizing the one or more cleaved protein-linked cell-surface glycans. 7. The method of claim 6, wherein the protein-linked cell-surface glycan is an N-linked glycan. 8. The method of claim 6, wherein the protein-linked cell-surface glycan is an O-linked glycan. 9. The method of claim 6, wherein the protein-linked cell-surface qlycans comprise at least one sialic acid residue. 10. The method of claim 1, further comprising a step of recording information about at least one of the glycosylation patterns in a fixed medium. 11. The method of claim 1, wherein the recombinant non-cell surface glycoprotein of interest is selected from the group consisting of human somatropin, coagulation factor VIIa, coagulation IX, interferon alphacon-1, insulin glargine, and insulin. 12. The method of claim 1, wherein the recombinant non-cell surface glycoprotein of interest is a recombinant antibody.	

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					13. The method of claim 12, wherein the recombinant antibody is selected from the group consisting of etanercept, infliximab, adalimumab, basiliximab, daclizumab, omalizumab, gemtuzumab, alemtuzumab, rituximab, cetuximab, bevacizumab, palivizumab, and abciximab. 14. The method of claim 1, wherein the recombinant non-cell surface glycoprotein of interest is a therapeutic protein product. 15. The method of claim 1, wherein the recombinant non-cell surface glycoprotein of interest is a commercial glycoprotein that is produced industrially. 16. The method of claim 14, wherein the therapeutic protein product is or comprises a product selected from the group consisting of: a hematologic agent, an interferon, a colony stimulating factor, an antibody, an enzyme, and a hormone. 17. The method of claim 16, wherein the therapeutic protein product is or comprises an antibody. 18. The method of claim 14, wherein the therapeutic protein of interest is characterized in that it has undergone regulatory review in one or more countries. 19. The method of claim 14, wherein the at least one characteristic of the glycosylation pattern of the therapeutic protein of interest is compared to a reference sample that is a pharmaceutical product which has an established glycosylation pattern. 20. The method of claim 19, wherein the surface glycosylation pattern of the cell has at least a 75% correlation to the established glycosylation pattern of the reference sample. 21. The method of claim 1, wherein the step of determining the at least one characteristic of the cell surface glycosylation pattern includes a mass spectrometry technique. 22. The method of claim 1, wherein the glycosylation pattern includes one or more glycan structures selected from the group consisting of high mannose structures, hybrid structures, phosphorylated high mannose, sialylated termini, N-acetylneuraminic acid, N-glycolylneuraminic acid, extension on .alpha.1,6 mannose branches, extension on .alpha.1,3 mannose branches, core fucosylation, sulfated glycans, phosphorylated glycans, sialic acid linked to an N-acetylglucosamine, and acetylated glycans.	

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	2008-02-29	**US20100226912 A1** **12/601178** **RECOMBINANT PROTEIN PRODUCTION IN AVIAN EBX® CELLS** **FAMILY MEMBERS** AU2008252902A1 AU2008252902B2 BRPI0810322A2 CA2687493A1 CN101688179A EA17964B1 EA200971056A1 EP1995309A1 WITHDRAWN 2009-05-27 EP2152855A1 PENDING IL202213D0 JP2010529833A KR2010016540A MX2009012747A	**VIVALIS** (Roussay, FR) **ABANDONED 2014-07-15** **Publication Date: 2010-09-09** **Filing Date: 2008-05-21** **Earliest Effective Filing Date: 2008-02-29** **Priority Date: 2008-05-21**	**Mehtali; Majid (Coueron, FR)**	1. **An avian EBx® cell transfected with at least one expression vector** comprising at least one expression cassette comprising nucleic acid sequence encoding a recombinant protein of interest operably linked to a promoter sequence capable of effecting expression of said protein in said cell. 17. **A method for producing at least one biological product of interest in avian EBx® cell**, said method comprising the steps of: a) preparing EBx® cell according to claims 1 to 16 by transfection with at least one expression vector; b) culturing said EBx® cell under suitable conditions and in suitable medium; and c) harvesting the biological product of interest from the EBx® cell, the suitable medium, or both said EBx® cell and said medium. 18. The method according to claim 17, wherein the EBx® cells are transfected by electroporation with at least one expression vector in adherent culture in a serum free medium. 19. The method according to claim 17, wherein the EBx® cells are transfected by liposome-mediated transfection with at least one expression vector in suspension culture in a serum-free medium. 20. The method of claims 17 to 19 wherein the biological product of interest is an antibody molecule, an antibody fragment or a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said biological product of interest is having an increased Fc-mediated cellular toxicity. 21. **A biological product of interest having chicken or duck EBx® glycosylation**.	***STATUS*** • **ABANDONED 2014-07-15** • **EP2152855 A1 PENDING** **Similar claims as in US20100226912** ***METHODOLOGY*** CLAIMS DRAWN TO ANTIBODY POPULATION PRODUCED IN EBX® CELLS AND HAVING EBX® GLYCOSYLATION

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		NZ580820A WO2008142124A1 ZA200908195A			22. **An antibody population produced in EBx® cells and having EBx® glycosylation** wherein said antibody population, or fragment thereof, comprises Fc region comprising a large proportion of antibodies carrying a common N-linked fucosylated-oligosaccharide structure of a biantennary-type that comprises long chains with terminal GlcNac that are highly galactosylated, and which confer strong ADCC activity to said antibodies. 23. The antibody according to claim 22 of IgG1 or IgG3 subtypes, produced in EBx® cells, and having an increased ADCC activity compared to the same antibody produced in hybridoma or CHO cells.	
	2008-05-30	**WO2009146362 A2** **YEAST STRAIN FOR THE PRODUCTION OF PROTEINS WITH TERMINAL ALPHA-1,3-LINKED GALACTOSE** **FAMILY MEMBERS** NATIONAL PHASE APPS FILED (FROM WIPO) Australia 17.11.2010 2009251328 Published: 09.12.2010 Canada 26.11.2010 2725947 China 28.05.2009 200980129646.7 European Patent Office (EPO) 15.11.2010 2009755723 Published: 23.02.2011 India 22.11.2010 7514/CHENP/2010 Japan	**GLYCOFI, INC.*** (Lebanon, NH) * acquired by MERCK SHARP & DOHME in 2006 **Publication Date: 2009-12-03** **Filing Date: 2009-05-28** **Earliest Effective Filing Date: 2008-05-30** **Priority Date: 2009-05-28**	**Hamilton; Stephen (Enfield, NH)**	1. **A yeast or filamentous fungus host cell that can produce recombinant glycoproteins having N-glycans that have at least one terminal α-galactosyl epitope.** 11. **A method for producing a host cell capable of producing N-glycans that have terminal α-galactosyl residues**, comprising: (a) providing a recombinant yeast or filamentous fungus host cell capable of producing N-glycans that have at least one terminal α-galactose on the non-reducing end of the N-glycan; and (b) introducing a nucleic acid encoding an fusion protein comprising the catalytic domain of an α-galactosyltransferase linked to a targeting peptide that targets the fusion protein to the ER or Golgi of the host cell into the host cell to provide the host cell producing N-glycans that have terminal α-galactosyl residues. 12. **A method for producing a polypeptide having N-glycans that have at least one terminal α-galactosyl residue**, comprising (a) providing a recombinant yeast or filamentous fungus host cell capable of producing N-glycans that have at least one terminal α-galactose on the non-reducing end ofthe N-glycan; (b) introducing a nucleic acid encoding the polypeptide into the host cell; (c) expressing the polypeptide in the host cell; and (d) recovering the polypeptide from the host cells wherein the polypeptide has at least one N-glycan thereon that has terminal α-galactosyl residue. 13. **A recombinant lower eukaryotic, yeast or fungal host cell producing human-like glycoproteins**, the host cell comprising a nucleic acid encoding a fusion protein capable of transferring an α-galactose residue onto a terminal β-galactose residue of an N-linked oligosaccharide branch of an N-glycan having a trimnannose core of a glycoprotein produced by the host cell, wherein the N-linked oligosaccharide branch has a structure selected from the group consisting of: Galβl 4-GlcNAcβls2-Manαl ,3; Galβl,4-GlcNAcβl,4-Man αl,3; Galβ1,4-GlcNAcβl ,2-Manαl ,6; Galβl,4-GlcNAc βl,4Manαl,6; and Galβ1,4-GlcNacβ1,6-Manαl ,6 14. **A recombinant glycoprotein produced by a yeast or filamentous fungal host cell, wherein the N-glycans of said glycoprotein comprises a predominant N-glycan comprising a terminal α- galactosyl epitope.**	**"NATARAJAN FAMILY"** ***STATUS*** • **EP2285404 PENDING** • **US20110086054 A1 ABANDONED** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO METHOD FOR PRODUCING A HOST CELL CAPABLE OF PRODUCING N-GLYCANS THAT HAVE TERMINAL α-GALACTOSYL RESIDUES

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		29.11.2010 2011511812 United States of America 30.11.2010 12995284 Published: 14.04.2011			16. **A vaccine composition** comprising a vaccine glycoprotein produced by a yeast or filamentous fungal host cell, wherein the glycoprotein comprises a predominant N-glycan comprising a terminal α-galactosyl epitope.	
	2008-05-30	**WO2010007214A1** **ENZYMATICAL MODIF ICATION OF CELL GLYCOSYLATION USING SERUM ALBUMIN AND DIVALENT CATIONS** **FAMILY MEMBERS** AU2009272654A1 AU2009272654B2 EP2166085 A1 WITHDRAWN 2010-09-25 EP2318540A1 EP2318540 A4 PENDING US20110136203A1 PENDING	**GLYKOS FINLAND** (Helsinki, FI) **SUOMEN PUNAINEN RISTI, VERIPALVELU** (Helsinki, FI) **Publication Date: 2010-01-21** **Filing Date: 2009-07-16** **Earliest Effective Filing Date: 2008-07-16** **Priority Date: 2009-07-16**	**Nystedt; Johanna; (Helsinki, FI)** **Anderson; Heidi; (Helsinki, FI)** **Valmu; Leena; (Helsinki, FI)** **Natunen; Jari; (Vantaa, FI)** **Satomaa; Tero; (Helsinki, FI)**	1. **Method for in vitro enzymatic modification of cell glycosylation**, the method comprising the step of contacting cells in culture medium with a glycosyltransferase or glycosidase, wherein said culture medium contains **divalent cations Mg2+ and Ca2+** and a non-glycoprotein substantially without acceptor glycans for said glycosyltransferase or glycosidase. 8. **A kit for in vitro enzymatic modification of cell glycosylation** comprising culture medium for cell cultures and glycosyltransferase or glycosidase. 11. **A cell population derived from human stem cells**, wherein the cell population comprises in vitro enzymatically-modified glycosylation taking place in the presence of divalent cations Mg2+ and Ca2+, and wherein the cells are adherent cells detached from cell culture surface and modified in the presence of condition that prevents adhesion of the cells, especially clustering and surface adherence. 19. **A cell population produced spontaneously by glycan modification by endogenously-induced sialylation or fucosylation under cell maintaining conditions, preferably comprising Ca2+ and/or Mg2+.** 23. **A method for in vitro enzymatic modification of cell glycosylation including the presence of divalent cations Mg2+ and Ca2+ and where the cells are adherent cells detached from cell culture surface and modified in the presence of condition that prevents adhesion of the cells**, especially clustering and surface adherence and where the cells are modified for at least 0.5 hours, more preferably over 1 hour, and most preferably 2 hours or longer. 36. **A cell population derived from isolated early human cells,** wherein the cell population comprises in vitro enzymatically modified glycosylation comprising A) enzymatic in vitro glycan modification a) in vitro increased sialylation by Neu5Ac, and/or b) in vitro increased fucosylation, and/or c) in vitro reduced sialylation, and/or B) spontaneous glycan modification by exogenously-induced sialylation and/or fucosylation under cell maintaining conditions, and optionally C) further modification of cell surface glycoprotein content by proteolytic treatment wherein the cells are glycan modified in the presence of divalent cations Mg2+ and/or Ca2+ and optionally any modification enzyme is removed from the cell preparation by using at least one reagent selected from the group consisting of a) a glycan linked tag, not essentially reducing the enzymatic activity of the protein	***STATUS*** **EP2318540A1 – PENDING (see below)** **Pending claims drawn to a method of in vitro enzymatic modification of the glycosylation of viable cells.** **US20110136203 A1 - PENDING** **Pending claims as of 11-19-2014 drawn to methods of in vitro enzymatic modification of the fucosylation of cells in culture** ***METHODOLOGY*** CLAIMS DRAWN TO THE IN VITRO MODIFICATION OF THE GLYCOSYLATION OF VIABLE CELLS BY CONTACTING THE CELLS WITH A GLYCOSYLTRANSFERASE OR GLYCOSIDASE AND ADDING DIVALENT CATIONS TO THE CULTURE MEDIA

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					and b) a protein specifically linked tag, not essentially reducing the enzymatic activity of the enzyme protein and c) a specific substrate inhibitor binding effectively to the active site of the enzyme and releasing the enzyme from the cells, preferably being acceptor substrate analog of glycosyltransferase or substrate analog for protease. 38. **A controlled reagent for cell modification that is recombinant human sialyltransferase or fucosyltransferase comprising biantennary N-glycan with terminal structures NeuAccc3/α6Gal or a sialidase(neuraminidase) enzyme,** which is preferably glycosylation controlled for use in the production of the cell population as defined in claim 11 or in the method as defined in claim 23. 39. **A method for removing a glycosyltransferase or sialidase modification enzyme from modified cells involving a step of incubation of the cells with an inhibitor or substrate of the enzyme**.	

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	2008-09-26	**WO2010036443 A1** **CELL LINES AND PROTEINS WITH VARIANT GLYCOSYLATION PATTERN** **FAMILY MEMBERS** CN102216452A CN102216452B EP2340305A1 JP2012503656A KR2011084196A US20100081150A1 US20100081172A1 US20100081195A1 US20100081794A1 US20120107874A1 US8025879B2 US8080415B2 US8084222B2	**EUREKA THERAPEUTICS INC** (Emeryville, CA) **Publication Date: 2010-04-01** **Filing Date: 2009-07-21** **Earliest Effective Filing Date: 2008-09-26** **Priority Date: 2009-07-21**	**Liu; Cheng (Richmond, CA)** **Xiang; Jingyi (Walnut Creek, CA)** **Yan; Su (Albany, CA)** **Wang; Pei (Fremont, CA)** **Tai; Wei Chan (Emeryville, CA)**	**1. A glycoprotein modified to exhibit a variant glycosylation pattern**, wherein said variant glycosylation pattern is characterized by a change in levels of at least two types of sugar molecules as compared to a corresponding wildtype glycoprotein. 2. The glycoprotein of claim 1, wherein said variant glycosylation pattern is evidenced by a change in level of glucose, **galactose**, or both. 4. The glycoprotein of claim 1, **wherein said change in level of glucose is an increase**. 8. **An antibody produced by a modified host cell**, the antibody comprising an N-linked glycan, wherein the antibody has increased binding affinity to an Fc gamma receptor Ilia (FcγRIIIa), and/or decreased binding affinity to an Fc gamma receptor lib (FcγRIIb), as compared to a corresponding antibody produced by an unmodified host cell, thereby enhancing ADCC (antibody-dependent cell-mediated cytotoxicity) activity against effector cells expressing FcγRIIIa and/or FcγRIIb. 9. **An antibody produced by a modified host cell**, the antibody comprising an N-linked glycan, wherein the antibody exhibits an increased ADCC activity, as compared to a corresponding antibody produced by a corresponding unmodified host cell, and wherein the increased ADCC activity is against effector cells expressing a high affinity Fc gamma receptor, FcγRIIIa 158V/V, and effector cells expressing a low affinity Fc gamma receptor, FcγRIIIa 158F/F or FcγRIIIa 158F/V. 20. The antibody of claim 8 or 9, wherein the host cell is a **Chinese Hamster Ovarian (CHO) cell.** **41. A method of producing a modified glycoprotein comprising**: (a) providing a heterologous polynucleotide sequence that encodes said modified glycoprotein; and (b) causing said modified glycoprotein to be expressed in a host cell, wherein the host cell produces **N-linked glycan** having a variant glycosylation pattern characterized by **a change in the level of one or more sugar moieties** selected from the group consisting of glucose, **galactose**, **mannose**, and glucosamine. **46. A modified host cell that produces N-linked glycans having a variant glycosylation pattern** characterized by a change in the level of one or more sugar moieties selected from the group consisting of glucose, galactose, mannose, and glucosamine as compared to an unmodified parental host cell.	***STATUS*** **EP2340305 A1- WITHDRAWN** **US20100081172A1 - ABANDONED** **US20120107874- PENDING** **Claims require an N-linked glycan having a glucose molecule.** **US8025879 B2 (US20100081794A1)** **Claims require an N-linked glycan having a structure of formula (I) or (II) that include a glucose molecule.** **US8080415 B2 (US20100081195A1)** **Claims require an N-linked glycan having a structure of formula (I) or (II) that include a glucose molecule.** **US8084222 B2 (US20100081150A1)** **Claims require an N-linked glycan having a structure of formula (I) or (II) that include a glucose molecule.** ***METHODOLOGY*** CURRENTLY PENDING CLAIMS REQUIRE AN N-LINKED GLYCAN HAVING A GLUCOSE MOLECULE.
	2009-03-27	**EP2411417A1**	**DEUTSCHES RHEUMA FORSCHUNGSZEN**	**Ehlers; Marc (Berlin, DE)** **Hess; Constanze**	1. **Method of producing an sialylated antibody specific for a human autoimmune antigen, allergen or human Rhesus factor D antigen, comprising an Fc-portion of IgG type, and exhibiting a sialic acid residue at the Fc-portion**, comprising the following steps:	***STATUS*** **PENDING - Renewal fee for year 05**

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		PROPHYLAXIS OF UNWANTED INFLAMMATORY IMMUNE REACTIONS AND METHODS OF PRODUCING THEM **FAMILY MEMBERS** EP2233502 A1 WITHDRAWN 2011-03-30 US20120058111 A1 ABANDONED 2013-12-19 WO2010109010A1	(Berlin, DE) **PENDING** **Publication Date: 2012-02-01** **Filing Date: 2010-03-26** **Earliest Effective Filing Date: 2009-03-27** **Priority Date: 2010-03-26**	**(Berlin, DE)** **Lorenz; Alexandra Katharina (Berlin, DE)** **Winkler; Andre (Potsdam, DE)**	a) isolation of B cells from an individual suffering from an autoimmune disease, allergy or exhibiting an immune response to human Rhesus factor D antigen and individualisation of isolated B cells; b) optionally, cloning of selected B cells; c) optionally, selection of B cell clone that provides native antibody specific for human Rhesus factor D antigen or an antigen associated with autoimmune disease or allergy of donor of B cells; d) isolation of the whole or part of the nucleic acid coding sequence encoding the native antibody provided by an individualized B cell or a cell clone originating from an individualized B cell and being specific for human Rhesus factor D antigen or an antigen associated with autoimmune disease or allergy of donor of B cells; e) use of isolated native antibody nucleic acid coding sequence as a whole or in part to provide a nucleic acid coding sequence encoding an antibody with specificity for the same antigen as the respective native antibody and exhibiting an Fc-portion of IgG type, preferably of human IgG type; f) **expression of antibody encoded by the nucleic acid coding sequence of step e)**; and g) **addition of sialic acid residue to the Fc-portion of the expressed antibody**. 2. Method of claim 1, wherein the sialic acid residue is added by the host used for expression of the antibody or is added to the expressed antibody in vitro. 3. Method of anyone of claims 1 to 2, **wherein expression is performed in a host that expresses β1,4-galactosyltransferase and /or α2,6-sialyltransferase, preferably human β1,4-galactosyltransferase and/or human α2,6-sialyltransferase**. 4. **Method of producing a sialylated antibody specific for a human autoimmune antigen, allergen or human Rhesus factor D antigen, comprising an Fc-portion of IgG type, and exhibiting a sialic acid residue at the Fc-portion**, comprising the following steps: i) providing blood sample from an individual suffering from an autoimmune disease, allergy or exhibiting an immune response to human Rhesus factor D antigen or an autoimmune antigen or allergen; ii) isolation of IgG antibody specific for human Rhesus factor D antigen or an autoimmune antigen or allergen from blood sample; and iii) **addition of sialic acid residue to the Fc-portion of the isolated IgG antibody**.	**paid 2014-02-20** **EP2233502 A1 WITHDRAWN 2011-03-30** **US20120058111 A1 ABANDONED 2013-12-19** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF PRODUCING AN **SIALYLATED** ANTIBODY SPECIFIC FOR A HUMAN AUTOIMMUNE ANTIGEN, ALLERGEN OR HUMAN RHESUS FACTOR D ANTIGEN

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					5. Method of anyone of claims 1 to 4, **wherein the sialic acid residue is added to amino acid Asn 297 or a homologous position of the Fc-portion**. 6. Method of anyone of claims 1 to 5, wherein the antigen is selected from table 1. 7. **Sialylated antibody obtainable by a method of anyone of claims 1 to 6**. 8. Sialylated isolated antibody specific for an antigen selected from autoimmune antigens, allergens or Rhesus factor D antigen, comprising an Fc-portion of IgG type, and exhibiting a sialic acid residue at the Fc-portion. 9. Sialylated antibody according to claims 7 or 8, wherein the antibody exhibits a binding affinity of ≤ 10<-6>M for the antigen or allergen. 10. **Sialylated antibody according to anyone of claims 7 to 9, wherein the sialic acid residue is positioned at amino acid Asn<297> or a homologous position of the Fc-portion**. 11. Antibody according to anyone of claims 7 to 10, wherein the antigen is selected from table 1. 12. Immune complex comprising an antibody according to one of the claims 7 to 11 specifically bound to its antigen. 13. Pharmaceutical composition comprising an antibody according to one of claims 7 to 11 or an immune complex of claim 12 and a pharmaceutically acceptable excipient. 14. Kit comprising an antibody according to one of claims 7 to 11, an immune complex of claim 12, a pharmaceutical composition of claim 13. 15. Antibody according to anyone of claims 7 to 11, immune complex of claim 12, pharmaceutical composition of claim 13 or a kit of claim 14 for treatment and/or prophylaxis of autoimmune disease, allergy or Rhesus factor D reactivity.	
	2009-04-20	**WO2010122460 A1** **CONTROL OF PROTEIN GLYCOSYLATION AND COMPOSITIONS AND METHODS RELATING THERETO** **FAMILY MEMBERS**	**PFIZER** (New York, NY) **Publication Date: 2010-10-28** **Filing Date: 2010-04-15** **Earliest Effective**	**Combs; Rodney G.; (Wildwood, MO)** **Roe; Susanna; (Wentzville, MO)** **Ruble; Derrick L. (Wentzville, MO)**	1. **A method for decreasing the glycosylation level of a protein**, said method comprising expressing a protein comprising at least one glycosylation site in a host cell grown in culture in the presence of a **glycosylation inhibiting amount of a glycosylation inhibitor**, wherein said protein comprises a lower level of glycosylation compared with an otherwise identical protein produced in an otherwise identical host cell grown under otherwise identical conditions in the absence of said inhibitor, thereby controlling the glycosylation level of said protein. 2. The method of claim 1 , wherein said glycosylation site is in a ligand binding site or an antigen binding site.	***STATUS*** **EP2421892 A1 – PENDING – similar claims as in PCT** **US20120039908 A1 - ALLOWED** **Claims drawn to a fusion protein comprising a RAGE polypeptide** ***METHODOLOGY***

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		AU2010240569A1 CA2757079A1 CN102803292A EP2421892 A1 PENDING IL215480D0 JP2010246541A KR2011139292A MX2011010989A RU2011142230A US20120039908 A1 ALLOWED 2015-01-0-5	**Filing Date:** **2009-04-20** **Priority Date:** **2010-04-15**		3. The method of claim 2, wherein said glycosylation level is selected from the group consisting of glycan site occupancy at said glycosylation site and the extent of glycosylation at said glycosylation site. 4. The method of claim 3, wherein said glycosylation site is selected from the group consisting of an O-linked glycosylation site and an N-linked glycosylation site. 5. The method of claim 4, wherein said glycosylation site is an N-linked glycosylation site, and further wherein said glycosylation site comprises the amino acid sequence asparagine-X-serine or asparagine-X-threonine where X is any amino acid except praline. 6. The method of claim 5, **wherein said glycosylation inhibitor** is at least one inhibitor selected from the group consisting of tunicamycin, a tunicaymycin homolog, streptovirudin, mycospocidin, amphomycin, tsushimycin, antibiotic 24010, antibiotic MM 19290, bacitracin, corynetoxin, showdomycin, duimycin, 1-deoxymannonojirimycin, deoxynojirimycin, N-methyl-1-dexoymannojirimycin, brefeldin A, a glucose analog, a mannose analog, 2-deoxy-D-glucose, 2-deoxyglucose, D-(+)-mannose, D-(+) galactose, 2-deoxy-2-fluoro-D-glucose, 1 ,4-dideoxy-1 ,4-imino-D-mannitol (DIM), fluoroglucose, fluoromannose, UDP-2-deoxyglucose, GDP-2-deoxyglucose, a hydroxymethylglutaryl-CoA reductase inhibitor, 25-hydroxycholesterol, hydroxycholesterol, swainsonine, cycloheximide, puromycin, actinomycin D, monensin, m-Chlorocarbonyl-cyanide phenylhydrazone (CCCP), compactin, dolichyl-phosphoryl-2-deoxyglucose, N-Acetyl-D-Glucosamine, hygoxanthine, thymidine, cholesterol, glucosamine, mannosamine, castanospermine, glutamine, bromoconduritol, conduritol epoxide, a conduritol derivative, a glycosylmethyl-p-nitrophenyltriazene, β-Hydroxynorvaline, threo-β-fluoroasparagine, D-(+)-Gluconic acid δ-lactone, di(2-ethyl hexyl)phosphate, tributyl phosphate, dodecyl phosphate, 2-dimethylamino ethyl ester of (diphenyl methyl)-phosphoric acid, [2-(diphenyl phosphinyloxy)ethyl]trimethyl ammonium iodide, iodoacetate, and fluoroacetate. 7. The method of claim 6, wherein said glycosylation inhibitor is 2-deoxy-D-glucose. 8. The method of claim 7, wherein said glycosylation inhibiting amount ranges from about 0.5 g/L to 3 g/L . 9. The method of claim 8, said method further comprising maintaining the glucose concentration in said culture in an amount ranging from about 0.05 g/L to 10 g/L. 10. The method of claim 8, wherein the host cell is selected from the group consisting of a yeast cell, an insect cell, and a mammalian cell. 11. The method of claim 10, wherein said mammalian host cell is selected from the group consisting of a CHO cell, an NSO cell, NS0/1 , Sp2/0, a human cell, HEK 293, BHK, COS,	CLAIMS DRAWN TO AN INHIBITOR OF GLYCOSYLATION e.g. TUNICAMYCIN

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					Hep G2, PER.C6, COS-7, TM4, CV1 , VERO-76, MDCK, BRL 3A, W138, MMT 060562, TR1 , MRC5, and FS4. 12. The method of claim 11 , wherein said host cell is a CHO cell. 13. The method of claim 12, wherein said glycosylation site is at least one glycosylation site comprising an amino acid sequence selected from the group consisting of asparagine-isoleucine-threonine (NIT), asparagine-glycine-serine (NGS), asparagine-serine-threonine (NST), and asparagine-threonine-serine (NTS). 31. **A composition comprising an amount of a fusion protein**, wherein the fusion protein comprises a RAGE polypeptide linked to an immunoglobulin polypeptide, a) wherein the RAGE polypeptide comprises a fragment of human RAGE (SEQ ID NO: 3) wherein the fragment of human RAGE comprises a ligand binding site and at least one amino acid residue that may be glycosylated, b) wherein the immunoglobulin polypeptide comprises a C_H2 domain or a portion of a C_H2 domain of an immunoglobulin and a C_H3 domain of an immunoglobulin, and c) wherein the N-terminal residue of the immunoglobulin polypeptide is linked to the C-terminal residue of the RAGE polypeptide; and wherein at least 0.5% of the amount of the fusion protein is aglycosylated. 35. **A composition comprising a protein comprising at least one potential glycosylation site**, wherein the amount of fully glycosylated protein is less than the amount of less than fully glycosylated protein, and further comprising a pharmaceutically acceptable carrier.	
	2007-04-16	**US20120329709** **13/322049** **PRODUCTION OF GLYCOPROTEINS** **FAMILY MEMBERS** AU2010254215A1 CA2761817A1 **EP2435577** PENDING WO2010138502A2 WO2010138502A3	**MOMENTA PHARMACEUTICALS** (Cambridge, MA) **PENDING** **Publication Date: 2008-08-05** **Filing Date: 2008-04-15** **Earliest Effective Filing Date: 2007-04-16**	**Collins; Brian Edward (Arlington, MA)** **Bosques; Carlos J (Arlington, MA)** **Zhu; Xiangping (North Grafton, MA)** **Bulik; Dorota A. (Malden, MA)** **Thiruneelakantapillai; Lakshmanan (Boston, MA)** **Parsons; Ian**	**PENDING CLAIM (filed 2014-07-22)** 1. **A method of inhibiting the addition of a galactosyl moiety from a UDP-galactose glycosyl donor to an acceptor glycoprotein or protein,** comprising: providing a mammalian cell or batch of cultured mammalian cells having or subject to a manipulation, that decreases the level of the activity of a UDP nucleoside diphosphatase, and increases the proportion of mono-galactosylated glycans; wherein the manipulation comprises culturing the cells in cell culture media supplemented with uridine, separating said glycoprotein or protein having a target glycan structure, resulting from said inhibiting from at least one component with which said cell or batch of cells was cultured; and optionally, analyzing said glycoprotein to confirm the presence of the target glycan structure, thereby inhibiting the addition of a galactosyl moiety to an acceptor glycoprotein or protein.	***STATUS*** • **PENDING – Final Office Action mailed 2014-11-19** • **EP2435577 A2 - PENDING (see below)** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS FOR ASSESSING THE GLYCOSYLATION OF A TARGET GLYCOPROTEIN PRODUCED BY A CELL THROUGH ANALYSIS OF CELL-SURFACE GLYCANS ON THE CELL. THE PRESENT DISCLOSURE THEREFORE

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			Priority Date: 2008-04-15	**Christopher (Belmont, MA)** **Shriver; Zachary (Cambridge, MA)** **Chillakuru; Rajeev (Cambridge, MA)** **Venkataraman; Ganesh (Bedford, MA)**	2. The method of claim 1, further comprising one or more selected from the group consisting of: selecting a target glycan structure; selecting the cell on the basis of the cell having or subject to a manipulation that decreases the level of the activity of a UDP nucleoside diphosphatase; and analyzing said glycoprotein to confirm the presence of the target glycan structure. 3. The method of claim 1, further comprising evaluating a glycan on the surface of said cell or batch of cultured cells in order to determine if said target glycan structure is present on a glycoprotein produced by said cell or batch of cultured cells. 4. The method of claim 3, wherein said evaluation comprises evaluating a glycan on the surface of said cell or batch of cultured cells, to determine a property of said glycan, comparing the property to a reference, to thereby determine if said target glycan structure is present on the product.	TEACHES THAT GLYCOSYLATION OF CELL SURFACE PROTEINS CAN SERVE AS A PROXY FOR GLYCOSYLATION OF OTHER PROTEINS.
	2007-04-16	**EP2435577** **PRODUCTION OF GLYCOPROTEINS** **FAMILY MEMBERS** SEE ABOVE	**MOMENTA PHARMACEUTICALS** (Cambridge, MA) **PENDING** **Publication Date: 2008-08-05** **Filing Date: 2008-04-15** **Earliest Effective Filing Date: 2007-04-16** **Priority Date: 2008-04-15**	**Collins; Brian Edward (Arlington, MA)** **Bosques; Carlos J (Arlington, MA)** **Zhu; Xiangping (North Grafton, MA)** **Bulik; Dorota A. (Malden, MA)** **Thiruneelakantapillai; Lakshmanan (Boston, MA)** **Parsons; Ian Christopher (Belmont, MA)** **Shriver; Zachary (Cambridge, MA)** **Chillakuru; Rajeev**	1. **A method of inhibiting or promoting the addition of a monosaccharide moiety to an acceptor glycoprotein or protein,** comprising: providing a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and, e.g., which manipulation optionally promotes the formation of a target glycan structure; culturing said cell, e.g., to provide a batch of cultured cells, e.g., to provide a glycoprotein or protein; optionally, separating said glycoprotein or protein having a target glycan structure resulting from said inhibiting or promoting from at least one component with which said cell or batch of cells was cultured; and optionally, analyzing said glycoprotein to confirm the presence of the target glycan structure, thereby inhibiting or promoting the addition of a glycan moiety to an acceptor glycoprotein or protein. 2. The method of claim 1, further comprising one or more of: optionally, selecting a target glycan structure; optionally, selecting a cell on the basis of the cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; and optionally, analyzing said glycoprotein to confirm the presence of the target glycan structure.	***STATUS*** • **PENDING** • **currently not examined** • **5th year renewal fee paid 2014-05-27** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS FOR ASSESSING THE GLYCOSYLATION OF A TARGET GLYCOPROTEIN PRODUCED BY A CELL THROUGH ANALYSIS OF CELL-SURFACE GLYCANS ON THE CELL. THE PRESENT DISCLOSURE THEREFORE TEACHES THAT GLYCOSYLATION OF CELL SURFACE PROTEINS CAN SERVE AS A PROXY FOR GLYCOSYLATION OF OTHER PROTEINS Antibodies listed in TABLE 1 include interferon gamma-lb

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				(Cambridge, MA) **Venkataraman; Ganesh (Bedford, MA)**	3. The method of claim 1, further comprising evaluating a glycan on the surface of said cell or batch of cultured cells in order to determine if said target glycan structure is present on a glycoprotein produced by said cell or batch of cultured cells. 100. The method of claim 1, where the manipulation is, or is the product of, a selection for the production of a target glycan structure, e.g., GalGlcNAc2Man3GlcN Ac2FuC-ASn, a decreased glycosylation, e.g., sialylation or galactosylation, e.g., decreased mono- galactosylation or di-galactosylation, or a target decreased level of glycosylation, e.g., sialylation or galactosylation. 110. The method of claim 1, wherein the target glycan structure is increased, remains the same, or is decreased, as compared to what would be seen in the absence of the manipulation. 111. The method of claim 1 , wherein a component of the target glycan structure is transferred by a glycosyltransferase from a glycosyl donor to a protein acceptor or glycoprotein acceptor to provide said glycoprotein and a nucleoside diphosphate, and the glycosyl donor is UDP-galactose, UDP-N-acetylglucosamine, UDP-N- acetylgalactosamine, GDP-fucose or GDP-mannose. 112. **A method of making, or providing, a glycoprotein having a target glycan structure, e.g., by inhibiting or promoting the addition of a monosaccharide moiety to a protein or glycoprotein**, comprising: providing a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; culturing said cell, e.g., to provide a batch of cultured cells; optionally, separating the glycoprotein or protein having a target glycan structure from at least one component with which said cell or batch of cells was cultured; optionally, analyzing said glycoprotein to confirm the presence of the target glycan structure; and optionally, comparing the structure of said target glycan structure present on a glycoprotein from said cultured cell or batch of cells to a reference, and determining if said target glycan structure present on a glycoprotein from said cultured cell or batch of cells differs from the corresponding glycan structure formed by a cell that lacks the manipulation thereby providing a glycoprotein having a target glycan structure. 223. **A method of monitoring a process, e.g., a process of culturing cells, e.g., cells of a selected type, to produce a product,** comprising: optionally, selecting a target glycan structure; optionally, selecting a cell on the basis of the cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; providing a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi; culturing said cell, e.g., to provide a batch of cultured cells; and evaluating (directly or indirectly)	alteplase; tissue plasminogen activator Recombinant antihemophilic factor human albumin Laronidase interferon alfa-N3, human leukocyte derived human antihemophilic factor virus-filtered human coagulation factor IX Alefacept; recombinant, dimeric fusion protein LFA3-Ig Bivalirudin darbepoetin alfa Bevacizumab interferon beta-la; recombinant coagulation factor IX Interferon beta-lb Tositumomab antihemophilic factor human growth hormone botulinum toxin type A Alemtuzumab acritumomab; technetium-99 labeled alglucerase; modified form of beta-glucocerebrosidase imiglucerase; recombinant form of beta-glucocerebrosidase crotalidae polyvalent immune Fab, ovine digoxin immune fab [ovine] Rasburicase Etanercept epoietin alfa Cetuximab algasidase beta Urofollitropin follitropin beta Teriparatide human somatropin Glucagon follitropin alfa antihemophilic factor Antihemophilic Factor; Factor XIII adefovir dipivoxil Trastuzumab Insulin

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					a glycan complement, glycan component or glycan structure produced by the cell or the batch of cultured cells, to thereby monitor the process. 239. **A method of controlling a process for making a glycoprotein having a target glycan structure**, comprising: (1) providing a glycoprotein made by the process of: optionally, selecting a target glycan structure; optionally, selecting a cell on the basis of the cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; providing a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi; and culturing the cell to provide a glycoprotein and, e.g., to form a batch of cultured cells; (2) evaluating (directly or indirectly) the glycan structure of the glycoprotein, (3) responsive to said evaluation, selecting a production parameter, e.g., a culture condition, e.g., a level of a nutrient or other component in the culture medium, to thereby control the process for making a glycoprotein having a target glycan structure. 243. **A method of making a glycoprotein**, comprising: (a) providing, acknowledging, selecting, accepting, or memorializing a defined, desired or preselected target glycan structure for the glycoprotein, (b) optionally providing a cell manipulated to increase or decrease the level of a nucleoside diphosphatase activity, (c) culturing a cell manipulated to increase or decrease the level of a nucleoside diphosphatase activity, e.g., to form a batch of cultured cells, and (d) isolating from the cell or batch of cultured cells a glycoprotein having the desired target glycan structure, thereby making a glycoprotein. 244. **A method of making a glycoprotein**, comprising: (a) providing, acknowledging, selecting, accepting, or memorializing a defined, desired or preselected target glycan structure for the glycoprotein, chosen, e.g., from Table 1; (b) optionally, providing, acknowledging, selecting, accepting, or memorializing a manipulation from Table 2; (c) culturing a cell having the manipulation, e.g., to form a batch of cultured cells;	antihemophilic factor/von Willebrand factor complex-human Somatotropin Adalimumab human insulin recombinant human hyaluronidase interferon alfacon-1 eptifibatide alpha-interferon Palifermin Anakinra antihemophilic factor insulin glargine granulocyte macrophage colony-stimulating factor lutropin alfa for injection OspA lipoprotein Ranibizumab gemtuzumab ozogamicin Galsulfase Nesiritide Pegfilgrastim Oprelvekin Filgrastim Fanolesomab somatropin [rDNA] Mitoxantrone insulin; zinc suspension; insulin; isophane suspension insulin, regular; Insulin coagulation factor VIIa Somatropin immunoglobulin intravenous PEG-L-asparaginase abatacept, fully human soluable fusion protein muromomab-CD3 high-molecular weight hyaluronan human chorionic gonadotropin live attenuated Bacillus Calmette-Guerin peginterferon alfa-2a pegylated version of interferon alfa-2b

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					(d) isolating from the cell or batch of cultured cells a glycoprotein having the desired target glycan structure, thereby making a glycoprotein. 245. A method of formulating a pharmaceutical composition comprising: contacting a glycoprotein made by a method described herein with a pharmaceutically acceptable substance, e.g., an excipient or diluent. 246. A reaction mixture comprising a manipulated cell described herein and a culture medium, optionally including secreted glycoprotein having a target glycan structure. 247. **A pharmaceutical preparation of a glycoprotein described herein or made by a method described herein, wherein the glycoprotein is selected from Table 1**. 248. **A glycoprotein selected from Table 1** having a target glycan structure selected from Table 2. 249. **A method of making, or providing, a glycoprotein having a target glycan structure, e.g., by inhibiting or promoting the addition of a monosaccharide moiety to a protein or glycoprotein**, comprising: optionally, selecting a target glycan structure; selecting a cell, preferably on the basis that it produces a protein having the primary amino acid sequence of said glycoprotein but which protein when provided by said cell lacks said target glycan structure; optionally, selecting a manipulation, e.g., selecting the manipulation on the basis that the manipulation increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure providing said manipulation to said cell to provide a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; culturing said selected cell, e.g., to provide a batch of cultured cells; optionally, separating the glycoprotein having a target glycan structure from at least one component with which the cell or said batch of cultured cells was cultured; optionally, analyzing said glycoprotein to confirm the presence of the target glycan structure thereby making, or providing, a glycoprotein having a target glycan structure, e.g., by inhibiting or promoting the addition of a monosaccharide moiety to a protein or glycoprotein. 250. **A method of providing a cell that makes a glycoprotein having a target glycan structure**, comprising: optionally, selecting a target glycan structure; selecting a cell, preferably on the basis that it produces a protein having the primary amino acid sequence of said glycoprotein but which protein lacks said target glycan structure; optionally, selecting a manipulation, e.g., selecting the manipulation on the basis that the manipulation increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure;	Abarelix (injectable suspension); gonadotropin-releasing hormone antagonist epoietin alfa Aldesleukin Somatrem dornase alfa Efalizumab; selective, reversible T-cell blocker combination of ribavirin and alpha interferon Interferon beta la antihemophilic factor antihemophilic factor Lepirudin Infliximab Abciximab Reteplase Rituxima interferon alfa-2a Somatropin synthetic porcine secretin Basiliximab Eculizumab

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					providing said manipulation to said cell to provide a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure; optionally producing glycoprotein from said cell and determining if said glycoprotein has said target glycan structure, thereby providing a cell that makes a glycoprotein having a target glycan structure. 251. **A method of selecting a cell suitable for the production of protein having a target gylcan,** comprising: optionally, selecting a target glycan structure, e.g., from a list comprising a plurality of target glycan structures (in embodiments the list is also provided), and optionally memorializing said selected target glycan structure; optionally, selecting a cell on the basis of the cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi, and which manipulation thereby promotes the formation of said target glycan structure (in embodiments the manipulation is from a list comprising a plurality of manipulations, and in embodiments the list is also provided); providing a cell having or subject to a manipulation that increases or decreases the level of the activity of a nucleoside diphosphatase, e.g., the level of activity in the Golgi; culturing said cell to provide a plurality of progeny cells; and selecting one of said progeny cells.	

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	2009-09-22	**WO2011035884 A1** **PROCESS FOR PRODUCING MOLECULES CONTAINING SPECIALIZED GLYCAN STRUCTURES** **FAMILY MEMBERS** AU2010297580A1 AU2010297580B2 CA2773240A1 CN102648280A CN102648280B EA201200516A1 EP2480671A1 PENDING IL218485D0 JP2013505028A KR2012090981A MX2012003404A SG178925A1 US8642292 B2 (US20120214975A1)	**PROBIOGEN AG** (Berlin, DE) **Publication Date: 2012-08-01** **Filing Date: 2010-09-21** **Earliest Effective Filing Date: 2009-09-22** **Priority Date: 2010-09-21**	**Sandig; Volker (Berlin, DE)** **VON HORSTEN Hans Henning (Berlin, DE)** **OGOREK Christiane (Berlin, DE)**	1. **A vertebrate cell for producing a molecule**, which naturally comprises fucose on its glycomoieties, lacking fucose or with a reduced amount of fucose on its glycomoieties comprising at least one enzyme which uses GDP-6-deoxy-D-lyxo-4-hexulose as a substrate, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo-4-hexulose into GDP-L-fucose. 10. The vertebrate cell of claims 1 to 9, wherein the vertebrate cell is a mammalian, a fish, an amphibian, a reptilian cell or an avian cell. 11. The vertebrate cell of claim 10, wherein i) the mammalian cell is a human, hamster, canine or monkey cell, preferably a Chinese hamster ovary cell (CHO), an African green monkey kidney cell (VERO- 76) (ATCC CRL-1587), a human cervical carcinoma cell (HELA) (ATCC CCL 2), a Madin Darbin canine kidney cell (MDCK) (ATCC CCL 34), a human PER.C6 cell, or a human AGE1.HN cell; ii) the fish cell is a Ictalurus punctatus (channel catfish) ovary (CCO) cell (ATCC CRL-2772), iii) the amphibian cell is a Xenopus laevis kidney cell (ATCC CCL- 102); iv) the reptilian cell is a Iguana iguana heart cells (IgH-2) (ATCC CCL- 108); or v) the avian cell is an avian retina cell, preferably a AGE1.CR.PIX cell, or an avian somite cell. 13. **A method for producing a molecule**, which naturally comprises fucose on its glycomoieties, lacking fucose or with a reduced amount of fucose on its glycomoieties comprising the steps of: i) providing a vertebrate cell according to claims 1 to 12, ii) isolating the molecule which is capable of being a substrate for a fucosy transferase, preferably a protein or lipid, from the cell in i). 16. **A composition comprising glycoproteins** which comprise i) between 70 and 95% of GO -GlcNac, GO, Gl , and/or G2 complex type N-glycans, and ii) between 5 and 30% high mannose type N-glycans, wherein the complex type N-glycans of the glycoproteins are free of fucose or substantially free of fucose. 17. The composition of claim 16, **wherein of the complex type N-glycans 75% are GO and 25% are GO -GlcNac, Gl and/or G2 complex type N-glycans.** 18. The composition of claim 16, **wherein of the high mannose type N-glycans 50% are man5 glycans and 50% are man6, man7 and/or man8 N-glycans**. 19. The composition of claims 16 to 18, wherein the glycoproteins are **antibodies**, preferably, IgGls. 20. **A protein or lipid** which comprises glycomoieties containing D-rhamnose, D-perosamine, deoxy-D-talose, 6-deoxy-D-altrose, 4-keto-3,6-dideoxy-D-mannose, and/or L-colitose.	***STATUS*** **EP2480671A1 - PENDING** **US8642292 B2 – EXPIRES 2030-09-21** **See below** ***METHODOLOGY*** CLAIMS DRAWN TO

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
					21. **An expression unit** comprising one or more vertebrate expression control sequences operably linked to a polynucleotide comprising a nucleic acid sequence encoding an enzyme which uses GDP-6-deoxy-D-lyxo-4-hexulose as a substrate, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo-4-hexulose into GDP-L-fucose. 23. **An eukaryotic cell for producing a protein**, which normally comprises fucose on its glycomoieties, lacking fucose or with a **reduced amount of fucose** on its glycomoieties comprising: i) a first polynucleotide comprising a nucleic acid sequence encoding an enzyme which uses GDP-6-deoxy-D-lyxo-4-hexulose as a substrate, and ii) a second polynucleotide comprising a nucleic acid sequence encoding a protein, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo- 4-hexulose into GDP-L-fucose. 26. **A method for producing a protein**, which normally comprises fucose on its glycomoieties, lacking fucose or with a reduced amount of fucose on its glycomoieties comprising the steps of: i) providing an eukaryotic cell according to claims 23 to 25, ii) expressing the enzyme encoded by the first polynucleotide and the protein encoded by the second polynucleotide in said cell, and iii) isolating the protein from said cell. 27. A protein lacking fucose or with a reduced amount of fucose on its glycomoieties obtainable by the method of claim 26.	
	2009-09-22	**US8642292 B2** **13/496,997** **US 20120214975 A1**	**PROBIOGEN AG** (Berlin, DE) **EXPIRES 2030-09-21** **PTA: 0 days**	**Sandig; Volker (Berlin, DE)** **Von Horsten Hans Henning (Berlin, DE)** **Ogorek Christiane**	1. **A recombinant vertebrate cell for producing a protein molecule**, lacking fucose or with a reduced amount of fucose on its glycomoieties, said cell comprising a polynucleotide that encodes at least one enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo-4-hexylose into GDP-L-fucose. 2. The vertebrate cell of claim 1, wherein the enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate is selected from the group consisting of GDP-6-deoxy-D-lyxo-4-hexylose	***STATUS*** • **EXPIRES 2030-09-21** • **4th year fee window opens: 02/04/2017**

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		PROCESS FOR PRODUCING MOLECULES CONTAINING SPECIALIZED GLYCAN STRUCTURES **FAMILY MEMBERS** AU2010297580A1 AU2010297580B2 CA2773240A1 CN102648280A CN102648280B EA201200516A1 EP2480671A1 PENDING IL218485D0 JP2013505028A KR2012090981A MX2012003404A SG178925A1 US8642292 B2 (US20120214975A1)	**Publication Date:** **2012-08-01** **Filing Date:** **2010-09-21** **Earliest Effective Filing Date:** **2009-09-22** **Priority Date:** **2010-09-21**	**(Berlin, DE)**	reductase (RMD), GDP-perosamine synthetase (Per), GDP-6-deoxy-D-talose synthetase (GTS), GDP-Fucose synthetase Cys109Ser-(GTS-Cys109Ser) mutant, GDP-4-keto-6-deoxymannose-3-dehydratase (ColD), and GDP-4-keto-6-deoxymannose-3-dehydratase (ColD) in combination with GDP-L-colitose synthase (ColC). 3. The vertebrate cell of claim 2, wherein the GDP-6-deoxy-D-lyxo-4-hexylose reductase (RMD) is from Pseudornonas aeruginosa (SE) ID NO: 1). 4. The vertebrate cell of claim 1 further comprising GDP-D-rhamnose, GDP-D-perosamine, GDP-deoxy-D-talose, GDP-6-deoxy-D-altrose, GDP-4-keto-3,6-dideoxy-D-mannose, and/or GDP-L-colitose. 5. The vertebrate cell of claim 1, wherein the polynucleotide is transiently present or stably maintained in said cell. 6. The vertebrate cell of claim 1, wherein the cell comprises said protein molecule which is capable of being a substrate for a fucosyltransferase. 7. The vertebrate cell of claim 6, wherein the molecule is a substrate protein. 8. The vertebrate cell of claim 1, wherein the protein molecule is an endogenous or an exogenous protein. 9. The vertebrate cell of claim 1, wherein the protein molecule is an antibody, an antibody fragment, a fusion protein, a virus protein, a virus protein fragment, an antigen, or a hormone. 10. The vertebrate cell of claim 1, wherein the vertebrate cell is a mammalian, a fish, an amphibian, a reptilian cell or an avian cell. 11. The vertebrate cell of claim 10, wherein i) the mammalian cell is a human, hamster, canine or monkey cell; ii) the fish cell is a lectalurus punctatus (channel catfish) ovary (CCO); iii) the amphibian cell is a Xenopus laevis kidney cell; iv) the reptilian cell is a Iguana iguana heart cells (IgH-2); or v) the avian cell is an avian retina cell, or an avian somite cell. 12. The vertebrate cell according to claim 1 which further comprises at least one glycosyltransferase for GDP-D-rhamnose, GDP-D-perosamine, GDP-deoxy-D-talose, GDP-6-deoxy-D-altrose, GDP-4-keto-3,6-dideoxy-D-mannose, or GDP-L-colitose. 13. **A method for producing a protein molecule**, lacking fucose or with a reduced amount of fucose on its glyconioieties comprising the steps of: i) providing a vertebrate cell according to claim 1, ii) isolating the protein molecule which is capable of being a substrate for a fucosyltransferase from the cell in i).	***METHODOLOGY*** CLAIMS DRAWN TO A RECOMBINANT VERTEBRATE CELL FOR PRODUCING A PROTEIN MOLECULE, LACKING FUCOSE OR WITH A REDUCED AMOUNT OF FUCOSE ON ITS GLYCOMOIETIES

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					14. A protein molecule lacking fucose or with a reduced amount of fucose on its glycomoieties obtainable by the method of claim 13. 15. A composition of protein molecules according to claim 14. 16. **A protein molecule which comprises glycomoieties** containing D-rhamnose, D-perosamine, deoxy-D-talose, 6-deoxy-D-altrose, 4-keto-3,6-dideoxy-D-mannose, and/or L-colitose, wherein said protein molecule is obtainable by the method of claim 13. 17. **An expression unit** comprising one or more vertebrate expression control sequences operably linked to a polynucleotide comprising a nucleic acid sequence encoding an enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo-4-hexylose into GDP-L-fucose. 18. The expression unit of claim 17, wherein the enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate is selected from the group consisting of GDP-6-deoxy-D-lyxo-4-hexylose reductase (RMD), GDP-perosamine synthetase (Per), GDP-6-deoxy-D-talose synthetase (GTS), GDP-Fucose synthetase Cys109Ser-(GFS-Cys109Ser) mutant, GDP-4-keto-6-deox:/mannose-3-dehydratase (ColD), and GDP-4-keto-6-dcoxymannose-3-dehydratase (ColD) in combination with GDP-L-colitosc synthase (ColC). 19. **A recombinant eukaryotic cell for producing a protein**, lacking fucose or with a reduced amount of fucose on its glycomoieties comprising: i) a first polynucleotide comprising a nucleic acid sequence encoding an enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate, and ii) a second polynucleotide comprising a nucleic acid sequence encoding a protein, wherein the enzyme does not catalyze the reaction which converts GDP-6-deoxy-D-lyxo-4-hexylose into GDP-L-fucose. 20. The eukaryotic cell of claim 19, wherein the enzyme which uses GDP-6-deoxy-D-lyxo-4-hexylose as a substrate is selected from the group consisting of GDP-6-deoxy-D-lyxo-4-hexylose reductase (RMD), GDP-perosamine synthetase (Per), GDP-6-deoxy-D-talose synthetase (GTS), GDP-Fucose synthetase Cys109Ser-(GFS-Cys109Ser) mutant, GDP-4-keto-6-deoxymannose-3-dehydratase (ColD), and GDP-4-keto-6-deoxymannose-3-dehydratase (ColD) in combination with GDP-L-colitose synthase (ColC). 21. The eukaryotic cell of claim 19, wherein the protein is antibody, an antibody fragment, a fusion protein comprising the Fc region of an antibody, a virus protein, a virus protein fragment, an antigen, or a hormone. 22. **A method for producing a protein lacking fucose or with a reduced amount of fucose on its glycomoieties** comprising the steps of: i) providing an eukaryotic cell according to claim	

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					19, ii) expressing the enzyme encoded by the first polynucleotide and the protein encoded by the second polynucleotide in said cell, and iii) isolating the protein from said cell. 23. A protein lacking fucose or with a reduced amount of fucose on its glycomoieties obtainable by the method of claim 22. 24. The vertebrate cell of claim 8, wherein the protein molecule is an antibody, an antibody fragment, a fusion protein, a virus protein, a virus protein fragment, an antigen, or a hormone.	
	2010-10-25	**WO2011059684 A1** **ANTIBODY GLYCOSYLATION VARIANTS** **FAMILY MEMBERS** AU2010318542A1 CA2778809A1 CN102770554A EA201290241A1 EP2494061 A1 EP2494061 A4 IL219289D0 JP2013509415A KR2012101404A	**CENTOCOR ORTHO BIOTECH INC** (Horsham, PA) **Publication Date: 2011-05-19** **Filing Date: 2010-10-25** **Earliest Effective Filing Date: 2009-10-29** **Priority Date: 2010-10-25**	**Luo; Jinquan (Radnor, PA)** **McCarthy; Stephen (Radnor, PA)** **Raju; T. Shantha (Radnor, PA)** **Scallon; Bernard (Radnor, PA)** **Spinka-Doms; Tracy (Radnor, PA)**	1. **An Fc-containing molecule with increased resistance to protease** comprising an antibody Fc domain with N-glycosylation sites at the ends of loop structures. 2. The Fc-containing molecule of claim 1 , wherein Fc domain is IgG4 and the N- glycosylation sites are in the CH3 domain. 3. The Fc-containing molecule of claim 1, wherein the N-glycosylation sites are distal from proteolytic cleavage sites. 4. The Fc-containing molecule of claim 1, wherein the Fc domain is from any of IgGl, IgG2, IgG3, and IgG4 molecule. 5. The Fc-containing molecule of claim 1, wherein the Fc-containing molecule is an antibody or Fc fusion protein. 19. **A method for treating a disease** characterized by the release of a protease, comprising administering to a subject or patient a glycosylated Fc-containing protein preparation, wherein the antibody preparation has residues altered from wild-type, the residues being distant from the	***STATUS*** **EP2494061 A4 – PENDING – see below** **US20120276092 A1 ABANDONED 2014-11-20** **NO PENDING US APPLICATIONS** ***METHODOLOGY*** CLAIMS DRAWN TO

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		MX2012005006A US20120276092 A1			FcyR binding site in the lower hinge or distant from the FcRn binding site at the CH2-CH3 junction region. 20. **A method of increasing resistance of an Fc-containing protein to cleavage by a protease**, comprising adding N-glycosylation sites to the Fc-containing protein correlative to the EU numbering at at least one of positions 359, 382, and 419. 21. The method of claim 20, comprising adding N-glycosylation sites to the Fc-containing protein correlative to the EU numbering at positions 359, 382, and 419. 22. The method of claim 21 , further comprising removing the N-glycosylation site correlative to the EU numbering at position 297. 23. A method of changing the susceptibility of an Fc-containing protein to cleavage by a protease, comprising altering N-glycosylation sites of the sequence of the Fc-containing protein correlative to the EU numbering at residues 359, 382, and 419. 24. The method of claim 23, comprising adding N-glycosylation sites to the Fc-containing protein correlative to the EU numbering at positions 359, 382, and 419.	
	2010-10-25	**EP2494061 A4** **ANTIBODY GLYCOSYLATION VARIANTS** **FAMILY MEMBERS** SEE ABOVE	**CENTOCOR ORTHO BIOTECH INC*** (Horsham, PA) **(* JANSSEN BIOTECH)** **Publication Date: 2012-09-05** **Filing Date: 2010-10-25** **Earliest Effective Filing Date: 2009-10-29** **Priority Date: 2010-10-25**	**Luo; Jinquan (Radnor, PA)** **McCarthy; Stephen (Radnor, PA)** **Raju; T. Shantha (Radnor, PA)** **Scallon; Bernard (Radnor, PA)** **Spinka-Doms; Tracy (Radnor, PA)**	**PENDING CLAIMS (as of 2014-03-09)** 1. **An Fc-containing molecule comprising an antibody Fc domain with N- glycosylation sites at the ends of loop structures in the CH3 domain**, wherein the Fc-containing molecule has increased resistance to protease, as compared to Fc-containing molecules having the analogous unmodified antibody Fc domain. 2. The Fc-containing molecule of claim 1, wherein: (i) Fc domain is IgG4 and the N-glycosylation sites are in the CH3 domain; (ii) the N-glycosylation sites are distal from proteolytic cleavage sites; (iii) the Fc domain is from any of an IgG1, IgG2, IgG3, and IgG4 molecule; or (iv) the Fc-containing molecule is an antibody or Fc fusion protein. 3. The Fc-containing molecule of claim 1 or claim 2, wherein the protease is selected from the group consisting of pepsin, plasmin, trypsin, chymotrypsin, a matrix metalloproteinase, a serine endopeptidase, and a cysteine protease, optionally wherein the protease is a matrix metalloproteinase selected from the group consisting of gelatinase A (MMP2), gelatinase B	***STATUS*** **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO A METHOD OF INCREASING RESISTANCE OF AN FC-CONTAINING PROTEIN TO CLEAVAGE BY A PROTEASE, AND TO A FC-CONTAINING MOLECULE COMPRISING AN ANTIBODY Fc DOMAIN WITH N-GLYCOSYLATION SITES AT THE ENDS OF LOOP STRUCTURES IN THE CH3 DOMAIN

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					(MMP-9), matrix metalloproteinase-7 (MMP-7), stromelysin (MMP-3), and macrophage elastase (MMP-12). 4. The Fc-containing molecule of any preceding claim, wherein the Fc domain exhibits N-glycosylation sites correlative to EU numbering at at least one of residues 359, 382, and 419. 5. The Fc-containing molecule of claim 4, wherein: (i) the Fc domain exhibits N-glycosylation sites correlative to EU numbering at residues 359, 382, and 419 of the Fc domain; or (ii) the Fc domain exhibits N-glycosylation sites correlative to EU numbering at residues 359, 382, and 419 of the Fc domain, and an N-glycosylation site at residue 297 of the Fc domain is removed, optionally wherein residue 299 is changed from Thr to Asn, residue 359 is changed from Thr to Asn, residue 361 is changed from Asn to Thr, residue 419 is changed from Thr to Asn, and residue 421 is changed from Asn to Thr. 6. The Fc-containing molecule of claim 4, wherein the Fc domain has a change from wild-type at at least one of residue 359, 361, 419, and 421. 7. The Fc-containing molecule of claim 6, wherein: (i) residue 359 is changed from Thr to Asn and residue 361 is changed from Asn to Thr, and/or residue 419 is changed from Thr to Asn and residue 421 is changed from Asn to Thr; or (ii) the Fc domain has a change from wild-type at residues 359, 361, 419, and 421, optionally wherein residue 359 is changed from Thr to Asn, residue 361 is changed from Asn to Thr, residue 419 is changed from Thr to Asn, and residue 421 is changed from Asn to Thr. 8. The Fc-containing molecule of claim 1, wherein correlative to EU numbering at least one of residues 228, 234, and 235 in the hinge region is altered. 9. An Fc-containing molecule with increased resistance to protease according to claim 1, comprising an antibody Fc domain with N-glycosylation sites correlative to EU numbering at residues 359, 382, and 419 of the Fc domain and an N-glycosylation site at residue 297 of the Fc domain is removed, wherein the Fc domain has a change from wild-type at residues 299, 359, 361, 419, and 421. 10. The Fc-containing molecule of claim 9, wherein correlative to EU numbering at least one of residues 228, 234, and 235 in the hinge region is altered.	

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					11. The Fc-containing molecule of any preceding claim, for use in a method for treating a disease associated with the presence of elevated levels of proteases. 12. **A method of increasing resistance of an Fc-containing protein to cleavage by a protease,** comprising adding N-glycosylation sites to the Fc-containing protein correlative to the EU numbering at at least one of positions 359, 382, and 419. 13. The method of claim 12, comprising adding N-glycosylation sites to the Fc-containing protein correlative to the EU numbering at positions 359, 382, and 419, optionally further comprising removing the N-glycosylation site correlative to the EU numbering at position 297. 14. The method of claim 12, further comprising altering from wild type correlative to EU numbering at least one of residues 228, 234, and 235 in the hinge region.	
	2009-12-02	**US20110263828 A1** **12/959351** **METHODS FOR MODIFYING HUMAN ANTIBODIES BY GLYCAN ENGINEERING** **FAMILY MEMBERS** NO OTHER FAMILY MEMBERS	**ACADEMIA SINICA** (Taipei, TW) **PENDING** **Publication Date: 2011-10-27** **Filing Date: 2010-12-02** **Earliest Effective Filing Date: 2009-12-02** **Priority Date: 2010-12-02**	**WONG; Chi-Huey (La Jolla, CA)** **WU; Chung-Yi (Taipei, TW)**	**PENDING CLAIMS (as of 2014-04-28)** 7. (Currently amended) A method for modifying the Fc region glycosylation pattern of a human, chimeric or humanized antibody, the method comprising: (a) providing a glycosylated Fc region of a human, chimeric or humanized antibody attached to an oligosaccharide at one or more sites; (b) contacting the glycosylated Fc region with ~~an endo-glycosylase~~ one or more endo-glycosylases and ~~an exo-glycosylase~~ α-fucosidase under conditions wherein the oligosaccharide is digested by the one or more endoglycosylases to a single ~~sugar~~ GlcNAc unit at each site, and wherein any fucose residue attached to the single GlcNAc unit is removed by the α-fucosidase ~~wherein the endo-glycosylase is selected from the group consisting of Endo F3, Endo F2, endo-ß-N-acetylglucosaminidase (NAG), endo-H, endo-A and endo-M, and wherein the exo-glycosylase is selected from the group consisting of α-mannosidase, α-fucosidase, sialidase and galactosidase or a mixture thereof~~, and (c) contacting the defucosylated single sugar glycosylated Fc region with a glycosyl transferase under conditions suitable for elongating the defucosylated GlcNAc ~~single sugar~~ unit to form a homogeneous oligosaccharide at each site by glycosylation~~; and~~ ~~(d) optionally, contacting the homogeneous oligosaccharide with alpha-2,6-sialytransferase under conditions suitable for adding a terminal sialylic acid~~, thereby producing a modified homogeneously glycosylated Fc region.	***STATUS*** **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO TO IN VITRO ENZYMATIC MODIFICATION OF A FC REGION'S GLYCOSYLATION PROFILE USING AN ENDOGLYCOSIDASE AND FUCOSIDASE

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					16. (Currently amended) A method for modifying the Fc region glycosylation pattern of a human, chimeric or humanized antibody, the method comprising: (a) providing a glycosylated Fc region of a human, chimeric or humanized antibody attached to heterogeneous oligosaccharides at one or more sites; (b) contacting the glycosylated Fc region with ~~an endo-glycosylase~~ one or more endo-glycosylases and ~~an exo-glycosylase~~ α-fucosidase under conditions wherein the oligosaccharide is digested by the one or more endoglycosylases to a single ~~sugar~~ GlcNAc unit at each site, and wherein any fucose residue attached to the single GlcNAc unit is removed by the α-fucosidase ~~wherein the endo-glycosylase is selected from the group consisting of Endo F3, Endo F2, endo-ß-N-acetylglucosaminidase (NAG), endo-H, endo-A and endo-M, and wherein the exo-glycosylase is selected from the group consisting of α-mannosidase, α-fucosidase, sialidase and galactosidase or a mixture thereof~~; (c) contacting the defucosylated single sugar glycosylated Fc region with a glycosyl transferase under conditions suitable for elongating the defucosylated GlcNAc single sugar unit to form a first homogeneous oligosaccharide at each site by glycosylation; and (d) contacting the first homogeneous oligosaccharide with β-1,4-galactosyltransferase to produce a second oligosaccharide having a terminal galactose~~; and~~ ~~(e) optionally, contacting the second oligosaccharide with alpha-2,6-sialytransferase under conditions suitable for adding a terminal sialylic acid to the terminal galactose, thereby producing a modified glycosylated Fc region~~.	

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	2011-02-24	**US20140046032 A1** **14/000035** **METHOD OF PRODUCTION OF SIALYLATED ANTIBODIES** **FAMILY MEMBERS** AR85302A1 EP2678357 A1 JP2014508759A TW201241182A WO2012113863A1	**SANOFI** (Paris, FR) **PENDING** **Publication Date: 2014-02-13** **Filing Date: 2012-02-23** **Earliest Effective Filing Date: 2011-02-24** **Priority Date: 2012-02-23**	**Blanche; Francis (Paris, FR)** **Cameron; Beatrice (Paris, FR)** **Genet; Bruno (Paris, FR)** **Soubrier; Fabienne (Paris, FR)**	**PENDING CLAIMS (as of 2013-08-16)** 1**. A method for producing an IgG antibody, wherein at least 80% of the said antibody comprises a complex, bi-antennary oligosaccharide, which contains two sialic acid residues**, attached to each Fc domain of the antibody, said method comprising the steps of: a) **introducing a mutation in the said Fc domain of the said antibody**, and b) **expressing the mutant antibody obtained in step a) in a cell line expressing a β-galactosyltransferase and a sialyltransferase activity**. 2. The method of claim 1, wherein the β-galactosyltransferase is a β-1,4-galactosyltransferase and the sialyltransferase is a **α-2,6-sialyltransferase**. 3. The method of claim 1, wherein the β-1,4-galactosyltransferase is encoded by the polynucleotide sequence represented by SEQ ID NO: 35 and the α-2,6-sialyltransferase is encoded by the polynucleotide sequence represented by SEQ ID NO: 33. 4. The method of claim 1, wherein the said sialic acid residues are linked to the antibody through an α-2,6-linkage. 5. The method of claim 1 wherein the antibody is a monoclonal antibody. 6. The method of claim 1, wherein the antibody is a humanized antibody. 7. The method of claim 1, **wherein the said mutation affects an amino acid selected from the group consisting of F243, V264, and D265**. 8. The method of claim 1, wherein the said mutation is a **substitution of the said amino acid by an amino acid selected from the group consisting of alanine (A), glycine (G), leucine (L), and lysine (K)**. 9. The method of claim 1, wherein the said mutation is selected from the group consisting of D265L, D265K, and D265A.	***STATUS*** **PENDING – as of 2015-02-06 not yet examined** **EP2678357 A1 - PENDING** **Renewal fee patent year 03 paid 2014-12-02** ***METHODOLOGY*** CLAIMS DRAWN TO IGG ANTIBODY WHEREIN AT LEAST 80% OF THE SAID ANTIBODY COMPRISES A COMPLEX, BI-ANTENNARY OLIGOSACCHARIDE, WHICH CONTAINS TWO SIALIC ACID RESIDUES AND THAT HAS A MUTANT FC DOMAIN

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					10. The method of claim 1, wherein the said antibody comprises a human IgG4 Fc domain. 11. The method of claim 1, wherein the said antibody comprises **a human IgG1 Fc domain**. 12. The method of claim 1, wherein said cell line expressing a β-galactosyltransferase and a sialyltransferase activity is a cell line that is stably transfected with one or two vectors encoding beta-galactosyltransferase and sialyltransferase. 13. The method of claim 1, wherein said cell line expressing a β-galactosyltransferase and a sialyltransferase activity is a cell line that is stably transfected with one or two vectors encoding said antibody. 14. **An antibody produced by the method of claim 1**. 15. A pharmaceutical composition comprising the antibody of claim 14. 16. (canceled) 17. **A composition comprising an IgG antibody, wherein at least 80% of the said antibody comprises a complex, bi-antennary oligosaccharide attached to each Fc domain of the said antibody**, said oligosaccharide comprising two sialic acid residues, wherein the Fc domain comprises an amino sequence which differs from a native sequence human IgG Fc domain. 18. The composition of claim 17 wherein the said sialic acid residues are linked to the antibody through an α-2,6-linkage. 19. The composition of claim 17, wherein the antibody of the composition of the invention comprises an amino acid substitution at any one or more of amino acid positions 243, 264 and 265. 20. The composition of claim 19, wherein the said substitution is a substitution of the said amino acid by an amino acid selected from the group consisting of alanine (A), glycine (G), leucine (L), and lysine (K). 21. The composition of claim 20, wherein the said substitution is selected from the group consisting of D265L, D265K, and D265A.	

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
	2011-02-25	**WO2012115904A2** **PRODUCTION OF N- AND O-SIALYLATED TNFRII-FC FUSION PROTEIN IN YEAST** **FAMILY MEMBERS** EP2678030 A2 PENDING US20130330340 A1 ALLOWED 2015-01-29 WO2012115904A3	**MERCK SHARP & DOHME** (Kenilworth, NJ) **Publication Date: 2012-08-30** **Filing Date: 2012-02-20** **Earliest Effective Filing Date: 2011-02-25** **Priority Date: 2012-02-20**	**Hamilton; Stephen R. (Enfield, NH)** **Cook; W. James (Hanover, NH)** **Gomathinayagam; Sujatha (Hanover, NH)**	1. A composition comprising **a fragment of recombinant human tumor necrosis factor receptor fused to the constant region of an antibody (TNFRII-Fc)** wherein the TNFRII-Fc has N-glycans and O-glycans and wherein the O-glycans are of the dystroglycan- or O-mannose reduced glycans, and pharmaceutically acceptable salts thereof. 2. The composition of claim 1 , wherein the N-glycans and O-glycans on the TNFRII-Fc are predominantly sialylated with **a2,6** or **a2,3 sialic acid residues**. 4. The composition of claim 1, wherein the N-glycans and -glycans on the TNFRII-Fc which are sialylated comprise N-acetylneuraminic acid (NANA) and no N- glycolylneuraminic acid (NGN A). 5. The composition of claim 1 , wherein a ratio of mole sialic acid to mole of the TNFRII-Fc is at least 10. 6. The composition of claim 5, wherein a ratio of mole sialic acid to mole of the TNFRII-Fc is about 10 to 21. 7. The composition of claim 5, wherein a ratio of mole sialic acid to mole of the TNFRII-Fc is greater than 21. 8. The composition of claim 1 , wherein the N-glycans on the TNFRII-Fc are predominantly mono-, bi-, tri-, or tetra-sialylated N-glycans N-glycans .	***STATUS*** **US20130330340 A1 - ALLOWED 2015-01-29** **Claims drawn to a composition comprising a fragment of recombinant human tumor necrosis factor receptor fused to the constant region of an antibody (TNFRII-Fc) and methods of making the same.** **EP2678030 A2 – PENDING** **Similar claims as in PCT** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO A COMPOSITION COMPRISING A FRAGMENT OF RECOMBINANT HUMAN TUMOR NECROSIS FACTOR RECEPTOR FUSED TO THE CONSTANT REGION OF AN ANTIBODY (TNFRII-Fc) AND METHODS OF MAKING THE SAME.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	2011-04-13	**EP2697251A1** **A METHOD FOR CONTROLLING THE MAIN COMPLEX N-GLYCAN STRUCTURES AND THE ACIDIC VARIANTS AND VARIABILITY IN BIOPROCESSES PRODUCING RECOMBINANT PROTEINS** **FAMILY MEMBERS** CA2829061A1 EP2511293 A1 WITHDRAWN 2013-04-18 US20140087423 A1 PENDING WO2012140138A1	**LEK PHARMACEUTICALS** (Ljubljana, SI) **PENDING** **Publication Date: 2012-10-17** **Filing Date: 2011-04-13** **Earliest Effective Filing Date: 2011-04-13** **Priority Date: 2011-04-13**	**Koncilja; Matjaz (Menges, SI)** **Spudic; Vatroslav (Menges, SI)** **Stojkovic; Sasa (Menges, SI)** **Tisu; Matjaz (Menges, SI)**	**1. A method of controlling quality and quantity of posttranslational modification of a recombinantly produced polypeptide/protein (glycoprotein),** wherein the posttranslational modification affects the **glycosylation profile** and/or the acidic variants profile, as manifested in CEX profiles, wherein the polypeptide/protein (glycoprotein) production is in eukaryotic host cells, the method comprising the following steps: a) **cultivating the eukaryotic cells** in a suitable medium under conditions which allow the expression of the polypeptide/protein, wherein the content of the dissolved CO2 (PCO2) in the medium is at a first value during the initial growth phase of the eukaryotic cells, allowing the eukaryotic cells to grow, and b) **increasing or decreasing the content of the dissolved CO2 (PCO2)** in the medium during the production phase of the eukaryotic cells to a second value. 2. The method of claim 1, wherein the glycosylation profiles are selected from (i) bGO structures such as bG0(-N), bG0(-F), and bG0, and from (ii) bG1 structures such as bG1(-N), bG1(1-6), and bG1(1-3). 4. The method of any of claims 1 to 3, wherein the acidic variants are selected from deamidated, isomerised, glycated, and **sialylated variants** of the recombinantly produced polypeptide/ protein. 8. The method of any of the aforementioned claims, wherein the cell is an insect or **mammalian cell.** 9. The method of claim 8, wherein the mammalian cell is a **CHO cell** or a hybridoma. 10. The method of any of the aforementioned claims, **wherein the glycosylated polypeptide is an antibody, or a fragment or derivative thereof**. 11. The method of claim 10, wherein said antibody, or fragment or derivative thereof, is selected from: a) a hybridoma-derived antibody, or a fragment or derivative thereof, b) a chimerised antibody, or a fragment or derivative thereof, c) **a humanised antibody, or a fragment or derivative thereof,** and/or d) a human antibody, or a fragment or derivative thereof. 12. The method of claims 10 or 11, wherein said antibody, or fragment or derivative thereof, is an IgG, an IgG fragment, or IgG derivative, and in particular **an anti-TNFa-,** anti-VEGF-, anti-HER2-, anti-CD20-, or anti-EGFR-antibody, or a fragment or derivative thereof.	***STATUS*** **PENDING** **EP2511293 A1 - WITHDRAWN 2013-04-18** **US20140087423 A1 - PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO METHODS OF CONTROLLING QUALITY/QUANTITY OF POSTTRANSLATIONAL MODIFICATION OF RECOMBINANTLY PRODUCED POLYPEPTIDE/PROTEIN E.G. ANTIBODY, INVOLVES CULTIVATING EUKARYOTIC CELLS IN MEDIUM, AND INCREASING/DECREASING CONTENT OF DISSOLVED CARBON DIOXIDE.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	2011-07-21	**WO2013013013 A2** **COMPOSITIONS AND METHODS FOR PRODUCING MODIFIED GLYCOPROTEINS** **FAMILY MEMBERS** WO2013013017A3 WO2013013019A3	**ALNYLAM PHARMACEUTICALS** (Cambridge, MA) **Publication Date: 2013-01-24** **Filing Date: 2012-07-19** **Earliest Effective Filing Date: 2011-07-21** **Priority Date: 2012-07-19**	**ROSSOMANDO, Anthony (US)** **MARAGANORE, John M. (US)** **THILL, Gregory P. (US)** **BETTENCOURT Brian (US)**	1. **A composition comprising an antibody or a fusion protein that comprises the Fc domain of an antibody**, (a) wherein **at least about 70% of the antibody or the fusion protein molecules comprise a complex N-glycan**; and (b) wherein **about 40% to about 100% of the N-glycans are afucosyl glycans**. 2. The composition of claim 1 , wherein said **N-glycans comprise a mixture of glycoforms**, and wherein i) **about 20% to about 100%** of the GO glycans are afucosyl GO glycans: **or** ii) **about 1% to about 80%** of the Gl and Gl glycans are afucosyl Gl and G1 glycans; **or** iii) **about 1% to about 80% of the G2 glycans are afucosyl G2 glycans**; or iv) a combination of (i), (ii), or (iii). 3. The composition of claim 1 or 2, wherein: i) about 20% to about 100% of the GO glycans are afucosyl GO glycans; and ii) about 1% to about 80% of the Gl and Gl ' glycans are afucosyl Gl and Gl ' glycans. 4. The composition of any one of claims 1 -3, wherein: **(i) about 20% to about 100% of the GO glycans are afucosyl GO glycans; (ii) about 1% to about 80% of the Gl and Gl glycans are afucosyl Gl and Gl glycans; and (iii) about 1% to about 80% of the G2 glycans are afucosyl G2 glycans.** 5. The composition of any one of claims 1-4, wherein said **N-glycan is linked to the Fc domain of the antibody or the fusion protein.** 6. The composition of any one of claims 1-5, wherein said composition comprises an antibody and wherein said **antibody is an IgG**. 7. The composition of claim 6, **wherein said IgG is IgG1**.	***STATUS*** **NOT YET NATIONALIZED** ***METHODOLOGY*** CLAIMS DRAWN TO ANTIBODIES HAVE "ABOUT 1% TO ABOUT 80% OF THE G2 GLYCANS ARE AFUCOSYL G2 GLYCANS."
	2011-08-10	**WO2013021279**	**LABORATOIRE FRANCAIS DU FRACTIONNEMENT**	**Faid; Valegh (Les Ulis, FR)** **Chevreux; Guillaume**	1. **A composition, comprising: a population of antibodies wherein the population of antibodies is highly galactosylated**.	***STATUS*** **NOT YET NATIONALIZED** **EP2741769 A2 – PENDING – see below**

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		HIGHLY GALACTOSYLATED ANTIBODIES **FAMILY MEMBERS** NONE	**ET DES BIOTECHNOLOGIES** (Les Ulis, FR) **Publication Date: 2013-02-14** **Filing Date: 2012-08-10** **Earliest Effective Filing Date: 2011-08-10** **Priority Date: 2012-08-10**	**(Paris, FR)**	7. A composition, comprising: **a population of antibodies**, wherein the level of galactosylation of the antibodies in the population is **at least 70%,** wherein the population of antibodies comprises antibodies that comprise mono-galactosylated N-glycans, and wherein antibodies in the population are encoded by the same nucleic acid sequence. 8. The composition of any one of claims 1-7, wherein the level of galactosylation of the antibodies in the population is **at least 80%.** 9. The composition of claim 8, wherein the level of galactosylation of the antibodies in the population is **at least 90%.** 13. The composition of any one of claims 1-12, wherein the population of antibodies comprises antibodies that comprise **bi-galactosylated N-glycans**. 14. The composition of any one of claims 1-13, wherein the **population** of antibodies comprises antibodies that comprise both **mono-galactosylated N-glycans and bi-galactosylated N-glycans.**	***METHODOLOGY*** CLAIMS DRAWN TO A POPULATION OF ANTIBODIES WHEREIN THE POPULATION OF ANTIBODIES IS HIGHLY GALACTOSYLATED AND WHEREIN THE LEVEL OF GALACTOSYLATION OF THE ANTIBODIES IN THE POPULATION IS AT LEAST 70%
	2011-08-10	**EP2741769 A2** **HIGHLY GALACTOSYLATED ANTIBODIES** **FAMILY MEMBERS**	**LABORATOIRE FRANCAIS DU FRACTIONNEMENT ET DES BIOTECHNOLOGIES** (Les Ulis, FR)	**Faid; Valegh** **(Les Ulis, FR)** **Chevreux; Guillaume** **(Paris, FR)**	1. A composition, comprising: **a population of antibodies wherein the population of antibodies is highly galactosylated**. 5. The composition of any one of claims 1- 4, wherein the level of galactosylation of the antibodies in the population is **at least 70%.**	***STATUS*** **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO A POPULATION OF ANTIBODIES WHEREIN THE

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		AU2012293420A1 CA2844435A1 CN104168913A IL230719D0 JP2014525395A KR2014101331A US20140296490A1 PENDING WO2013021279A2 WO2013021279A3	**Publication Date:** **2014-06-018** **Filing Date:** **2012-08-10** **Earliest Effective Filing Date:** **2011-08-10** **Priority Date:** **2012-08-10**		8. The composition of any one of claims 1-7, wherein the level of galactosylation of the antibodies in the population is **at least 80%.** 9. The composition of claim 8, **wherein the level of galactosylation of the antibodies in the population is at least 90%.** 29. The composition of any one of claims 1-28, wherein the antibodies in the population are **chimeric, humanized or fully human antibodies**.	POPULATION OF ANTIBODIES IS HIGHLY GALACTOSYLATED AND WHEREIN THE LEVEL OF GALACTOSYLATION OF THE ANTIBODIES IN THE POPULATION IS AT LEAST 70%
	2011-08-10	**US20140296490A1** **14/237,751** **HIGHLY GALACTOSYLATED ANTIBODIES** **FAMILY MEMBERS** SEE ABOVE	**LABORATOIRE FRANCAIS DU FRACTIONNEMENT ET DES BIOTECHNOLOGIES** (Les Ulis, FR) **Publication Date:** **2014-06-018** **Filing Date:**	**Faid; Valegh** **(Les Ulis, FR)** **Chevreux; Guillaume** **(Paris, FR)**	**PUBLISHED AND PENDING CLAIMS (as of 2014-06-05):** 1. A composition, comprising: **a population of antibodies wherein the population of antibodies is highly galactosylated**. 7. **A composition, comprising: a population of antibodies, wherein the level of galactosylation of the antibodies in the population is at least 70%,** wherein the population of antibodies comprises antibodies that comprise mono-galactosylated N-glycans, and wherein antibodies in the population are encoded by the same nucleic acid sequence. **12. A composition, comprising: a population of antibodies, wherein the ratio of the level of galactosylation of the antibodies in the population to the level of fucosylation of the**	***STATUS*** **PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO A POPULATION OF ANTIBODIES WHEREIN THE POPULATION OF ANTIBODIES IS HIGHLY GALACTOSYLATED AND WHEREIN THE LEVEL OF GALACTOSYLATION OF THE

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			2012-08-10 **Earliest Effective Filing Date: 2011-08-10** **Priority Date: 2012-08-10**		**antibodies in the population is between 0.8 and 1.2,** wherein the population of antibodies comprises antibodies that comprise mono- galactosylated N-glycans, and wherein antibodies in the population are encoded by the same nucleic acid sequence. 21. The composition of claim 12, wherein the antibodies of the population of antibodies have an **increased level of complement dependent cytotoxicity (CDC) activity** when compared to a population of antibodies not produced in mammary gland epithelial cells. 39. **A method for producing a highly galactosylated population of antibodies**, comprising: producing the population of antibody in mammary gland epithelial cells such that a highly galactosylated population of antibodies is produced.	ANTIBODIES IN THE POPULATION IS AT LEAST 70%
	19	**US20130149300 A1** **13/628,439** **MONOCLONAL ANTIBODIES WITH ALTERED AFFINITIES FOR HUMAN FCyRI, FCyRIIIa, AND C1q PROTEINS** **FAMILY MEMBERS** WO2013095738A3	**MAPP BIO-PHARMACEUTICAL** (San Diego, CA) **ICON GENETICS GMBH (Halle/Saale, DE)** **PENDING** **Publication Date: 2013-06-13** **Filing Date: 2012-09-27**	**Hiatt; Andrew (San Diego, CA)** **Zeitlin; Larry (Poway, CA)**	**PUBLISHED CLAIMS:** **1. An antibody, or antigen binding fragment thereof**, wherein the antibody is present in a substantially homogeneous composition represented by the presence of the **GNGN glycoform** and wherein the antibody has a **binding affinity for human FcγRI and FcγRIIIa** and said binding affinities for FcγRI and FcγRIIIa of the GNGN antibody, are greater than the binding affinities for FcγRI and FcγRIIIa of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF glycoforms**. **5. An antibody, or antigen binding fragment thereof**, wherein the antibody is present in a substantially homogeneous composition represented by the presence of the G1/G2 glycoform and wherein the antibody has a **binding affinity for human FcγRI and FcγRIIIa** and said binding affinities for FcγRI and FcγRIIIa of the G1G2 antibody, are greater than the binding affinities for FcγRI and FcγRIIIa of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF glycoforms**.	***STATUS*** **PENDING – RCE filed 2014-12-29** **No EP patent application** ***METHODOLOGY*** PENDING CLAIMS DRAWN TO AN ANTIBODY THAT BINDS TO EBOLA

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			Earliest Effective Filing Date: 2011-09-27 **Priority Date: 2012-09-27**		**6. An antibody, or antigen binding fragment thereof**, wherein the antibody is present in a substantially homogenous composition represented by the presence of the G1/G2 glycoform and a. wherein the antibody, or antigen binding fragment thereof, has a **binding affinity for human C1q and FcγRIIIa** and b. wherein said binding affinities for C1q of the G1/G2 antibody, or antigen binding fragment thereof, is less than the binding affinities for C1q of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF glycoforms** and c. wherein said binding affinity for FcγRIIIa of the G1/G2 antibody, or antigen binding fragment thereof, is **greater** than the binding affinity for **FcγRIIIa** of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF** glycoforms. **7. An antibody, or antigen binding fragment thereof**, wherein the antibody is present in a substantially homogenous composition represented by the presence of the G1/G2 glycoform and a. wherein the antibody, or antigen binding fragment thereof, has a **binding affinity for C1q and FcγRI** and b. wherein said binding affinities for C1q of the G1/G2 antibody, or antigen binding fragment thereof, is less than the binding affinities for C1q of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF glycoforms** and c. wherein said binding affinity for FcγRI of the G1/G2 antibody, or antigen binding fragment thereof, is **greater** than the binding affinity for **FcγRI** of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF** glycoforms. **8. An antibody, or antigen binding fragment thereof**, wherein the antibody is present in a substantially homogenous composition represented by the presence of the G1/G2 glycoform and a. wherein the antibody, or antigen binding fragment thereof, has a **binding affinity for human FcγRI, FcγRIIIa and C1q**, and b. wherein said binding affinities for **FcγRI and FcγRIIIa** of the G1/G2 antibody, or antigen binding fragment thereof, are greater than the binding affinities for FcγRI and FcγRIIIa of the antibody, or antigen binding fragment thereof present in a composition containing **G0, G1F, G2F or GNGNF** glycoforms and	

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					c. wherein said binding affinity for C1q of the G1/G2 antibody, or antigen binding fragment thereof, is less than the binding affinity for C1q of the antibody, or antigen binding fragment thereof present in a composition containing G0, G1F, G2F or GNGNF glycoforms. 13. The antibody, or antigen binding fragment thereof, of claims 1-8 wherein said antibody is produced in a **mammalian cell.** 15. The antibody, or antigen binding fragment thereof, of claim 13 wherein said antibody is produced in a **CHO cell**. PENDING CLAIMS (as of 2014-12-29) 7. (Currently Amended) An antibody or antigen binding fragment within a substantially homogenous glycan composition represented by the presence of greater than 80% of the G1/G2 glycoform, ~~and~~ a. wherein the antibody or antigen binding fragment has a binding affinity for C1q and FcγRI,~~and~~ b. wherein said binding affinities for C1q of the G1/G2 antibody or antigen binding fragment is less than the binding affinities for C1q of the antibody or antigen binding fragment present in a composition containing ~~more than~~ a ~~trace~~ detectable amount of G0, G1F, G2F or GNGNF glycoforms,~~and~~ c. wherein said binding affinity for FcγRI of the G1/G2 antibody or antigen binding fragment is greater than the binding affinity for FcγRI of the antibody or antigen binding fragment present in a composition containing ~~more than~~ a ~~trace~~ detectable amount of G0, G1F, G2F or GNGNF glycoforms, and d. wherein said antibody or antigen binding fragment binds to an Ebola virus.	

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	2011-10-05	**US20140234899** **14/348822** **PROCESS FOR ANTIBODY G1 GLYCOFORM PRODUCTION** **FAMILY MEMBERS** EP2764020 A1 PENDING JP2014531215A WO2013050335 A1	**HOFFMANN-LA ROCHE INC. (Nutley, NJ)** **PENDING** **Publication Date: 2014-08-21** **Filing Date: 2014-03-31** **Earliest Effective Filing Date: 2011-10-05** **Priority Date: 2012-10-02**	**Hueller; Martina (Achmuehle, DE)** **Reusch; Dietmar (Muenchen, DE)**	1. **Method for producing an immunoglobulin or immunoglobulin fragment or fusion polypeptide with Gl glycostructure** comprising the following steps: incubating an affinity chromatography column eluate containing the immunoglobulin or immunoglobulin fragment or fusion polypeptide with a **galactosyltransferase**, incubating the galactosyltransferase reaction product with a **sialyltransferase**, incubating the sialyltransferase reaction product with a beta- 1 ,4-galactosidase, removing or inactivating the beta-l,4-galactosidase, and incubating the beta-l,4-galactosidase reaction product, in which the beta-l,4-galactosidase has been removed or inactivated, with a sialidase and thereby producing an immunoglobulin or immunoglobulin fragment or fusion polypeptide with Gl glycostructure. 2. Method according to claim 1, characterized in that the **galactosyltransferase** is added during the incubating in two or more aliquots. 3. Method according to any one of claims 1 or 2, characterized in that the **galactosyltransferase** is added during the incubating in three to six aliquots. 4. Method according to any one of the preceding claims, characterized in that the first aliquot of the **galactosyltransferase** is added after zero to two hours incubation time. 5. Method according to any one of the preceding claims, characterized in that an aliquot of the galactosyltransferase is added each after six to twelve hours incubation time.	***STATUS*** **PENDING** **EP2764020 A1 - PENDING** ***METHODOLOGY*** CLAIMS DRAWN TO THE IN VITRO GLYCOSYLATION OF PURIFIED ANTIBODIES.

Published PCT/US/EP Patent Applications Relating to Antibody Glycosylation

Tab No.	Earliest Effective Priority Date	Patent No. (Hyperlinked to USPTO/EP Database) Title Family Members	Assignee Dates	Inventors	All Independent Claims + Selected Dependent Claims	Status Methodology/Comments
	2011-11-10	**US20140286946A1** **14/354931** **METHOD FOR PREPARING ANTIBODIES HAVING IMPROVED PROPERTIES** **FAMILY MEMBERS** AU2012332840A1 CA2853809A1 CN104011076A EP2773661 A1 PENDING JP2014532661A KR2014097245A WO2013066761A1	**MERCK SHARP & DOHME** (Kenilworth, NJ) **PENDING** **Publication Date: 2014-09-25** **Filing Date: 2014-04-29** **Earliest Effective Filing Date: 2011-02-25** **Priority Date: 2012-10-26**	**Stadheim; Terrance A. (Lyme, NH)** **Cua; Daniel (Palo Alto, CA)** **Zha; Dongxing (Etna, NH))**	9) A pharmaceutical formulation comprising an Fc-containing polypeptide, wherein the Fc-containing polypeptide comprises sialylated N-glycans, wherein the sialic acid residues in the sialylated N-glycans contain α-2,3 linkages, and wherein at least 30%, 40%, 50%, 60%, 70%, 80% or 90% of the *N*-glycans on the Fc-containing polypeptide comprise an N-linked oligosaccharide structure selected from the group consisting of SA(1-4)Gal(1-4)GlcNAc(2-4)Man3GlcNAc2. 10) The pharmaceutical formulation of claim 9, wherein at least 30%, 40%, 50%, 60%, 70%, 80% or 90% of the *N*-glycans on the Fc-containing polypeptide comprise an N-linked oligosaccharide structure selected from the group consisting of $NANA_2Gal_2GlcNAc_2Man_3GlcNAc_2$, 11) The pharmaceutical formulation of any one of claims 9-10, wherein the Fc-containing polypeptide has one or more of the following properties when compared to a parent Fc-containing polypeptide: (a) increased effector function; (b) increased ability to recruit immune cells; and (c) increased inflammatory properties.	***STATUS*** **PENDING** **EP2773661 A1 - PENDING** **Claims drawn to a method of enhancing an immune response in a subject by administering to the subject a therapeutically effective amount of an Fc-containing polypeptide comprising sialylated N-glycans, wherein the sialic acid residues in the sialylated N-glycans contain a-2,3 linkages, and wherein at least 30%, 40%, 50%, 60%, 70%, 80% or 90% of the N-glycans on the Fc-containing polypeptide comprise an N-linked oligosaccharide structure selected from the group consisting of SA(1,4)Gal(1-4)GlcNAc(2-4)Man3GlcNAc2.** ***METHODOLOGY*** CLAIMS GENERALLY DRAWN TO DRAWN TO FC-CONTAINING POLYPEPTIDE HAVING SIALYLATED N-GLYCAN CONTAINING α-1,3 LINKAGES.
	2011-11-18	**WO2013074598A1**	**MERCK SHARP & DOHME** (Kenilworth, NJ)	**Stadheim; Terrance A. (Lyme, NH)** **Cua; Daniel**	1) **An Fc-containing polypeptide comprising mutations at amino acid positions 252, 254, 256, 433, 434, 243 and 264 of the Fc region**, wherein the numbering is according to the EU index as in Kabat, wherein the Fc-containing polypeptide comprises N-glycans, and wherein **at**	***STATUS*** **NOT YET NATIONALIZED**

TAB NO.	EARLIEST EFFECTIVE PRIORITY DATE	PATENT NO. (HYPERLINKED TO USPTO/EP DATABASE) TITLE FAMILY MEMBERS	ASSIGNEE DATES	INVENTORS	ALL INDEPENDENT CLAIMS + SELECTED DEPENDENT CLAIMS	STATUS METHODOLOGY/COMMENTS
		METHOD FOR PREPARING ANTIBODIES HAVING IMPROVED PROPERTIES **FAMILY MEMBERS**	**NOT YET NATIONALIZED** **Publication Date: 2013-05-23** **Filing Date: 2012-11-14** **Earliest Effective Filing Date: 2011-11-18** **Priority Date: 2012-11-14**	**(Palo Alto, CA)** **Zha; Dongxing (Etna, NH))**	**least 30%, 40%, 50%, 60%, 70%, 80% or 90% of the N-glycans on the Fc-containing polypeptide comprise an N-linked oligosaccharide structure** selected from the group consisting of SA(1-4)Gal(1-4)GlcNAc(2-4)Man3GlcNAc2. 2) The Fc-containing polypeptide of claim 1 , **wherein the sialic acid residues in the sialylated N- glycans are attached via a-2,6 linkages**. 3) The Fc-containing polypeptide of any one of claims 1-2, wherein the Fc-containing polypeptide is an **antibody or an antibody fragment**. 4) The Fc-containing polypeptide of any one of claims 1-3, wherein the Fc-containing polypeptide has increased FcRn binding and has one or more of the following properties when compared to a parent Fc-containing polypeptide: a) reduced effector function, b) increased anti-inflammatory properties, c) increased sialylation, d) increased bioavailability when administered parenterally, e) reduced binding to FcyRI, FcyRIIa and FcyRTfla, f) increased binding to FcyRIIb; and g) increased affinity to human FcRn at pH6 and pH7.	***METHODOLOGY*** CLAIMS CURRENTLY DRAWN TO FC-CONTAINING POLYPEPTIDE COMPRISING MUTATIONS AT AMINO ACID POSITIONS 252, 254, 256, 433, 434, 243 AND 264 OF THE FC REGION

KEYWORD SEARCH STRINGS

Antibody Glycosylation

Keyword Searches Relating to Antibody Glycosylation

SEARCH	SEARCH STRING	CRITERIA/DATABASES	HITS (INPADOC FAMILIES)
	METHODS OF GLYCOENGINEERING – GALACTOSYLATION AND/OR SIALYLATION IN CHO CELLS		
1	**CTB**=(Galactosyltransferase or UDP-Gal ADJ BetaGlcNAc ADJ Beta ADJ 1 adj 4- ADJ Galactosyltransferase adj Polypeptide ADJ 1 adj GGTB2 adj .Beta-1 adj 4-Galactosyltransferase ADJ 1 adj Beta-1 adj 4-GalTase adj beta4Gal-T1 adj UDP-Gal ADJ Beta-GlcNAc ADJ Beta-1 adj 4-Galactosyltransferase adj Glycoprotein-4-Beta-Galactosyltransferase or UDP-Galactose ADJ Beta-N-Acetylglucosamine ADJ Beta-1 adj 4-Galactosyltransferase or Lactose ADJ Synthase or CDG2D or Beta4Gal-T1 or GT1 or EC ADJ 2.4.1 or GTB2) **AND** PRD>=(19700101) AND AD>=(19000101);	claims/ title/abstract US/EP (granted) & US & EP patapps/ PCT	**1478 (503)**
2	**CTB**=(Galactosyltransferase or UDP-Gal ADJ BetaGlcNAc ADJ Beta ADJ 1 adj 4- ADJ Galactosyltransferase adj Polypeptide ADJ 1 adj GGTB2 adj .Beta-1 adj 4-Galactosyltransferase ADJ 1 adj Beta-1 adj 4-GalTase adj beta4Gal-T1 adj UDP-Gal ADJ Beta-GlcNAc ADJ Beta-1 adj 4-Galactosyltransferase adj Glycoprotein-4-Beta-Galactosyltransferase or UDP-Galactose ADJ Beta-N-Acetylglucosamine ADJ Beta-1 adj 4-Galactosyltransferase or Lactose ADJ Synthase or CDG2D or Beta4Gal-T1 or GT1 or EC ADJ 2.4.1 or GTB2) **AND** **CTB**=(antibod* OR Ig OR IgG* OR immunoglobul* OR mAb OR immuno-globul* OR immun* ADJ globul* OR moAb OR monoclon*) **AND** PRD>=(19700101) AND AD>=(19000101);	claims/ title/abstract US/EP (granted) & US & EP patapps/ PCT	**574 (191)**
3	**CTB**=(mannose SAME galactose SAME ratio) AND CTB=(antibody) AND PRD>=(19700101) AND AD>=(19000101);	claims/ title/abstract US/EP (granted) & US & EP patapps/ PCT	**22 (10)**
4	**CTB**=("CHO cell" SAME (glyco* or galactos*)) AND PRD>=(19700101) AND AD>=(19000101);	claims US/EP (granted) & US & EP patapps/ PCT	**194 (62)**
5	Patent documents citing US5047335 (Univ California, Paulson)	-	**195**
6	**CLE**=(glycoprotein AND (mannose SAME galactose)) AND PRD>=(19700101) AND AD>=(19000101);	claims US/EP (granted) & US & EP patapps/ PCT	**315**
7	**CLE**=(glycoprotein SAME (mannose SAME galactose)) AND PRD>=(19700101) AND AD>=(19000101);	claims US/EP (granted) & US & EP patapps/ PCT	**151 (55)**
8	**ALL**=(Asn297 and galactosylation and CHO) AND PRD>=(19700101) AND AD>=(19000101);	US/EP (granted) & US & EP patapps/ PCT	**291 (71)**
9	**CLE**=(glycoform SAME antibody) AND PRD>=(19700101) AND AD>=(19000101);	claims/ title/abstract US/EP (granted) & US & EP patapps/ PCT	**112 (22)**
10	**ALL**=(antibod* OR Ig OR IgG* OR immunoglobul* OR mAb OR immuno-globul* OR immun* ADJ globul* OR moAb OR monoclon*) **AND** **PA**=("A+ Science Invest" OR Abbott OR "AB Enzymes" OR Amgen OR "Bayer Bioscience" OR Biowa OR Celltech OR Centocor OR "Centre National de la Recherche Scientifique" OR Cetus or "Chesapeake Perl" OR "Chugai" OR "Columbia University" OR "Cornell Research Foundation" OR "LFB Biotech" OR Enzon OR Eukarion OR "Flanders Interuniversity" OR Genencor OR Genentech OR Genmab OR Glaxo OR GlycArt OR GlycoFi OR Glycotope OR Greenovation OR Kyowa OR Neose OR Roche OR "University of Ghent" OR Immunomedics OR "Institut Français de Recherche Pour L'Exploitation de la mer" OR Introgene OR Invitrogen OR Isis OR "Korea Research Institute of Bioscience and Biotechnology" OR MacroGenics OR MIT OR Medexgen OR Medicago OR Merck OR Novozymes OR "Novo Nordisk" OR Oxyrane OR Pfizer OR "Plant Research International" OR "Protein Design Labs" OR "Research Corporation Technologies" OR "Rockefeller University" OR "Sangamo BioSciences" OR "Scripps Research Institute" OR "Seattle Genetics" OR "Smithkline Beecham" OR "Dow Chemical" OR Unilever OR "Universitat fur Bodenkultur Wien" OR "Universite de Rouen" OR "Universite Joseph Fourier" OR "University of Maryland" OR "University of Wyoming" OR "University of York" OR VIB OR Wyeth OR Xencor OR ZymoGenetics) **AND** **ALL**=(Galactosyltransferase or UDP-Gal ADJ BetaGlcNAc ADJ Beta ADJ 1 adj 4- ADJ Galactosyltransferase adj Polypeptide ADJ 1 adj GGTB2 adj .Beta-1 adj 4-Galactosyltransferase ADJ 1 adj Beta-1 adj 4-GalTase adj beta4Gal-T1 adj UDP-Gal ADJ Beta-GlcNAc ADJ Beta-1 adj 4-Galactosyltransferase adj Glycoprotein-4-Beta-Galactosyltransferase or UDP-Galactose ADJ Beta-N-Acetylglucosamine ADJ Beta-1 adj 4-Galactosyltransferase or Lactose ADJ Synthase or CDG2D or Beta4Gal-T1 or GT1 or EC ADJ 2.4.1 or GTB2) AND PRD>=(19700101) AND AD>=(19000101);	US/EP (granted) & US & EP patapps/ PCT	**1402 (358)**
11	SEARCH 10 **AND NOT** (SEARCH 1)	US/EP (granted) & US & EP patapps/ PCT	**1089**

Keyword Searches Relating to Antibody Glycosylation

SEARCH	SEARCH STRING	CRITERIA/DATABASES	HITS (INPADOC FAMILIES)
			(286)
12	PA=(LFB ADJ BIOTECHNOLOGIES) AND PRD>=(19700101) AND AD>=(19000101);	US/EP (GRANTED) & US & EP PATAPPS/ PCT	**198 (68)**
13	CTB=((G2 OR G2S2 OR G1) SAME GLYCOFORM) AND PRD>=(19700101) AND AD>=(19000101);	US/EP (GRANTED) & US & EP PATAPPS/ PCT	**14 (6)**
GLYCOENGINEERED ANTIBODIES			
1	CTB=((ANTIBOD* OR IG OR IGG* OR IMMUNOGLOBUL* OR MAB OR IMMUNO-GLOBUL* OR IMMUN* ADJ GLOBUL* OR MOAB OR MONOCLON*)) AND CTB=(GLYCOFORM) AND PRD>=(19700101) AND AD>=(19000101);	CLAIMS/ TITLE/ABSTRACT US/EP (GRANTED)	**27 (10)**
2	CL=(((ANTIBOD* OR IGG* OR IMMUNOGLOBUL*) SAME (MANNOS* OR GLUCOS* OR GLYCOS* OR GALACTOS* OR SIAL*))) AND PRD>=(19700101) AND AD>=(19000101);	CLAIMS US/EP (GRANTED) & US & EP PATAPPS/ PCT	**1227 (926)**