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First Named Inventor	:	Pardis Sabeti, et al.	
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Docket No.	:	BROD-5215US-CON2	
Title	:	ENGINEERED MUSCLE TARGETING COMPOSITIONS	

AMENDMENT AND RESPONSE

FILED VIA EFS-WEB

Commissioner:

In response to the Final Office Action mailed May 27, 2025 ("Office Action"), please enter and consider the following amendments and remarks.

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AMENDMENT

In the Claims

Please amend the claims as follows. This listing of claims will replace all prior versions and listings of claims in this application.

1. (Currently amended) A composition comprising

a modified AAV capsid polypeptide comprising a targeting moiety effective at targeting a muscle cell,

wherein the targeting moiety is inserted after amino acids 453, 587, and 588 of ~~into~~ an AAV9 VP1 capsid polypeptide~~'s surface variable region~~ ,

wherein the targeting moiety comprises one or more n-mer motifs,

each n-mer motif consisting of ~~comprising~~ an amino acid sequence of

$[[X_m]]\ X_{m1}$ RGD $X_1X_2X_3X_4$,

$X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$, or

$X_{m3}X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$,

wherein X_1, X_2, and X_3 are independently selected from any amino acid,

X_4 is L or T, and

(i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or

(ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or

(iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E. ~~m is 1, 2, or 3~~

2. (Previously Presented) The composition of claim 1,

wherein X_4 is L, and

(a) X_1 is Q, H, or Y;

(b) X_2 is T, G, A, or S;

(c) X_3 is T, S, N, R, A;

(d) X_1 is Q, H, or Y, and X_2 is T, G, A, or S;

(e) X_1 is Q, H, or Y, and X_3 is T, S, N, R, A;

(f) X_2 is T, G, A, or S, and X_3 is T, S, N, R, A, or

(g) X_1 is Q, H, or Y, X_2 is T, G, A, or S, and X_3 is T, S, N, R, A.

3. (Previously Presented) The composition of claim 1, wherein

X_4 is L, and

wherein X_1 is Q, X_2 is T or G, and X_3 is T or R; or

wherein X_1 is Q, X_2 is T, and X_3 is T; or

wherein X_1 is Q, X_2 is G, and X_3 is R.

4. (Previously Presented) The composition of claim 1,

wherein X_4 is L, and

wherein X_1 is H, X_2 is G, A, or S, and X_3 is T, S, or A; or

wherein X_1 is H, X_2 is G, and X_3 is T or A; or

wherein X_1 is H, X_2 is G, and X_3 is T; or

wherein X_1 is H, X_2 is G, and X_3 is A.

5. (Previously Presented) The composition of claim 1,

wherein X_4 is L, and

wherein X_1 is H, X_2 is A, and X_3 is S; or

wherein X_1 is H, X_2 is S, and X_3 is S; or

wherein X_1 is Y, X_2 is A, and X_3 is N.

6. (Currently amended) The composition of claim 1,

wherein the one or more n-mer motifs comprise an amino acid sequence chosen from

$GPGRGDX_1X_2X_3X_4$ (SEQ ID NO: 777),

$TSVRGDX_1X_2X_3X_4$ (SEQ ID NO: 778),

$AMSRGDX_1X_2X_3X_4$ (SEQ ID NO: 779),

$GAVRGDX_1X_2X_3X_4$ (SEQ ID NO: 780),

$TPSRGDX_1X_2X_3X_4$ (SEQ ID NO: 781),

$DSRRGDX_1X_2X_3X_4$ (SEQ ID NO: 782),

NASRGDX$_1$X$_2$X$_3$X$_4$ (SEQ ID NO: 783), and

SPVRGDX$_1$X$_2$X$_3$X$_4$ (SEQ ID NO: 784)

wherein X$_1$, X$_2$, and X$_3$ are independently selected from any amino acid, and X$_4$ is L.

7. (Previously Presented) The composition of claim 1, wherein the one or more n-mer motifs comprise an amino acid sequence ENRRGDFNNT (SEQ ID NO: 32).

8. (Canceled)

9. (Currently amended) The composition of claim [[8]] 1, wherein the targeting moiety further comprises one or more linkers comprising one or more glycine or glycine serine linkers.

10. (Canceled)

11. (Canceled)

12. (Original) The composition of claim 1, further comprising a cargo.

13. (Previously Presented) The composition of claim 12, wherein the cargo is

(a) capable of treating or preventing a muscle disease or disorder;

(b) a morpholino, a peptide-linked morpholino, an antisense oligonucleotide, a phosphorodiamidate morpholino oligomer (PMO), a therapeutic transgene, a polynucleotide encoding a therapeutic polypeptide or peptide, a peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO), one or more peptides or polypeptides; one or more polynucleotides encoding a CRISPR-Cas protein, a guide RNA, or both, a ribonucleoprotein, wherein the ribonucleoprotein comprises a CRISPR-Cas system molecule, a therapeutic transgene RNA, or other gene-modifying or therapeutic RNA and/or protein, or any combination thereof; or

(c) both (a) and (b).

14. (Previously Presented) The composition of claim 13, wherein the muscle disease or disorder comprises an autoimmune disease, a cancer, a muscular dystrophy, a neuromuscular disease, a sugar or glycogen storage disease, an expanded repeat disease, a

dominant negative disease, a cardiomyopathy, a viral disease, a progeroid disease, or any combination thereof.

15. (Currently amended) An engineered particle, comprising a modified AAV capsid polypeptide comprising a targeting moiety effective at targeting a muscle cell,

wherein the targeting moiety is inserted after amino acids 453, 587, and 588 of an AAV9 VP1 capsid polypeptide, or any combination thereof, or into an analogous position of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV rh.74, or AAV rh.10 VP1 capsid polypeptide, ~~into an AAV capsid polypeptide's surface variable region~~

wherein the targeting moiety comprises one or more n-mer motifs,

each n-mer motif ~~comprising~~ consisting of an amino acid sequence

$[[X_m]]$ X_{m1} RGD $X_1X_2X_3X_4$,

$X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$, or

$X_{m3}X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$,

wherein X_1, X_2, and X_3 are independently selected from any amino acid,

X_4 is L or T, and

(i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or

(ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or

(iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E. ~~m is 1, 2, or 3~~

16. (Previously Presented) The engineered particle of claim 15, wherein the targeting moiety further comprises one or more linkers comprising one or more glycine or glycine serine linkers.

17. (Currently amended) The engineered particle of claim 16, wherein the targeting moiety is inserted between two amino acids within the AAV capsid polypeptide's surface variable region IV or VIII. ~~X_4 is not L, and m is 0, 1, 2, or 3.~~

18. (Canceled)

19. (Canceled)

20. (Canceled)

21. (Original) The engineered particle of claim 15, further comprising a cargo.

22. (Original) The engineered particle of claim 21, wherein the cargo is

(a) capable of treating or preventing a muscle disease or disorder;

(b) a morpholino, a peptide-linked morpholino, an antisense oligonucleotide, a PMO, a therapeutic transgene, a polynucleotide encoding a therapeutic polypeptide or peptide, a PPMO, one or more peptides or polypeptides; one or more polynucleotides encoding a CRISPR-Cas protein, a guide RNA, or both, a ribonucleoprotein, wherein the ribonucleoprotein comprises a CRISPR-Cas system molecule, a therapeutic transgene RNA, or other gene-modifying or therapeutic RNA and/or protein, or any combination thereof; or

(c) both (a) and (b).

23. (Previously Presented) The engineered particle of claim 22, wherein the muscle disease or disorder comprises an autoimmune disease, a cancer, a muscular dystrophy, a neuromuscular disease, a sugar or glycogen storage disease, an expanded repeat disease, a dominant negative disease, a cardiomyopathy, a viral disease, a progeroid disease, or any combination thereof.

24. (Previously Presented) A vector system comprising a polynucleotide encoding the composition of claim 1.

25. (Canceled)

26. (Currently amended) The vector system of claim [[25]] 24, further comprising a cargo, wherein the cargo ~~polynucleotide~~ is

(a) ~~is~~ capable of treating or preventing a muscle disease or disorder;

(b) ~~is or encodes~~ a morpholino; a peptide-linked morpholino; an antisense oligonucleotide; a PMO, a therapeutic transgene; a polynucleotide encoding

a therapeutic polypeptide or peptide; a PPMO; one or more peptides or polypeptides; one or more polynucleotides encoding a CRISPR-Cas protein, a guide RNA, or both; a ribonucleoprotein, wherein the ribonucleoprotein comprises a CRISPR-Cas system molecule; a therapeutic transgene RNA, or other gene modifying or therapeutic RNA and/or protein; or any combination thereof; or

(c) both (a) and (b).

27. (Withdrawn) A method of treating or preventing a muscle disease or disorder in a subject in need thereof, comprising administering the engineered particle of claim 15 to a subject in need thereof.

28. (Canceled)

29. (Withdrawn – Currently amended) The method of claim [[28]] 27, wherein the engineered particle further comprises a cargo, wherein the cargo is

(a) capable of treating or preventing the muscle disease or disorder;

(b) a morpholino; a peptide-linked morpholino; an antisense oligonucleotide; a PMO, a therapeutic transgene; a polynucleotide encoding a therapeutic polypeptide or peptide; a PPMO; one or more peptides or polypeptides; one or more polynucleotides encoding a CRISPR-Cas protein, a guide RNA, or both; a ribonucleoprotein, wherein the ribonucleoprotein comprises a CRISPR-Cas system molecule; a therapeutic transgene RNA, or other gene modifying or therapeutic RNA and/or protein; or any combination thereof; or

(c) both (a) and (b).

30. (Withdrawn) The method of claim 29, wherein the muscle disease or disorder comprises an autoimmune disease, a cancer, a muscular dystrophy, a neuro-muscular disease, a sugar or glycogen storage disease, an expanded repeat disease, a dominant negative disease, a cardiomyopathy, a viral disease, a progeroid disease, or any combination thereof.

31. (Previously presented) The composition of claim 1, wherein the targeting moiety further comprises one or more linkers comprising one or more glycine or glycine serine linkers.

32. (New) A recombinant AAV VP1 capsid polypeptide comprising an insertion of an n-mer motif consisting of an amino acid sequence of

$X_{m1}RGDX_1X_2X_3X_4$,

$X_{m2}X_{m1}RGDX_1X_2X_3X_4$, or

$X_{m3}X_{m2}X_{m1}RGDX_1X_2X_3X_4$,

wherein X_1, X_2, X_3, and X_4 are independently selected from any amino acid, and

(i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or

(ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or

(iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E.

33. (New) The recombinant AAV VP1 capsid polypeptide of claim 32, wherein X_4 is L or T.

34. (New) The recombinant AAV VP1 capsid polypeptide of claim 32, wherein the recombinant AAV VP1 capsid polypeptide comprises amino acids 1-261 of an AAV9 VP1 capsid polypeptide or analogous amino acids of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV rh.74, or AAV rh.10 VP1 capsid polypeptide.

35. (New) The recombinant AAV capsid polypeptide of claim 32, wherein the n-mer motif is inserted between two amino acids between amino acids 262-269, 327-332, 382-386, 452-460, 488-505, 527-539, 545-558, or 704-714, of an AAV9 VP1 capsid polypeptide, or any combination thereof, or in an analogous position of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV rh.74, or AAV rh.10 VP1 capsid polypeptide.

36. (New) The recombinant AAV capsid polypeptide of claim 32, wherein the n-mer motif is inserted between two amino acids between amino acids 581-593 of an AAV9 VP1 capsid

polypeptide, or in an analogous position of an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV rh.74, or AAV rh.10 VP1 capsid polypeptide.

37. (New) A polynucleotide sequence encoding the amino acid sequence of the recombinant AAV capsid polypeptide of claim 32.

38. (New) A cell comprising the polynucleotide sequence encoding the amino acid sequence of the recombinant AAV capsid polypeptide of claim 32.

REMARKS

Status of the Claims

Claims 1–7, 9, 12–17, 21–24, 26–27, and 29–38 are pending, with claims 1, 15, and 32 being independent. Claims 1, 6, 8–9, 15, 17, 26, and 29 are amended. Claims 8, 10–11, 18–20, 25, and 28 are canceled without prejudice or disclaimer as to the subject matter recited therein. Claims 32–38 are new. Claims 27 and 29–30 are withdrawn pursuant to the Restriction Requirement of November 26, 2024.

Written description for the claim amendments can be found throughout the specification and the claims as originally filed. For example, written description support for the amendments to the amino acid sequences of amended claims 1 and 15 can be found, for example, in TABLES 2-3 of the specification and the sequence listing as filed.

Information Disclosure Statement

Applicants submit herewith an updated Information Disclosure Statement to comply with 37 CFR 1.97 and 1.98(b) for the following references:

1) Stutika et al., Journal of Virology, Vol. 90(3), pp. 1278-1289, February 2016.
2) Wu et al., Journal of Virology, Vol. 74, No. 18, pp. 8635-8647, September 2000.
3) Kelsic, E. D. & Church, G. M. Challenges and opportunities of machine-guided capsid engineering for gene therapy. *Cell Gene Ther. Insights* **5**, 523–536 (published May 16, 2019)

The Applicant respectfully requests consideration of these references.

Sequence Compliance

Claim 6 was considered non-compliant with the requirements of 37 CFR 1.821 through 1.825 because it contains sequence disclosures that are not identified by sequence identifier numbers. In this response, claim 6 is amended to include sequence identifier numbers, and an updated version of the sequence listing is submitted concurrently.

Objections to the Claims

In the Office Action, claim 20 was objected to because of minor informalities. Claim 20 is canceled without prejudice or disclaimer as to the subject matter recited therein.

Withdrawal of the objection is respectfully requested.

Claim Rejection under 35 U.S.C. § 112(b)

In the Office Action, the Examiner rejected claims 8-11 under 35 U.S.C. § 112(b) as allegedly lacking clarity. Applicant respectfully submits that rejection does not apply to the claims as presently presented. Withdrawal of the rejection is respectfully requested.

Claim Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-26 and 31 were rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. At page 5 of the Office Action, the Examiner concedes the specification is at least enabling for a targeting moiety that targets a muscle cell wherein the targeting moiety comprises a 7-10 amino acid motif comprising X_mRGDX_n wherein X_m is 0-3 amino acids and Xn is 1-4 amino acids, and when the n-mer motif is inserted after AAV9 453, 587, and 588 or analogous sites in other AAV serotypes. However, the Examiner alleges the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claims.

Applicant respectfully submits that the rejection does not apply to the claims as presently presented. Withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §102

In the Office Action, the Examiner rejected claims 1, 8, 10-15, 17-19, and 21-26 under 35 U.S.C. §102(a)(2) as being allegedly anticipated by US 20210363193 to Grimm ("Grimm").

According to the Examiner, Grimm teaches

(1) RGD compositions, wherein the RGD peptide comprises $X_mRGDX_1X_2X_3X_4$, where X_m = G or T, X_2 = A, and wherein X_4 can be L (Grimm claim 3).

(2) the peptide is inserted into an AAV capsid, i.e., AAV9 at 588 (see e.g. paragraphs [0016] and [0013]), and

(3) the composition is used to treat, i.e., muscular dystrophy.

The Applicant respectfully disagrees for the following reasons.

Amended claims 1 and 15

Independent claims 1 and 15, and claims dependent therefrom, require *inter alia*:

> … wherein the targeting moiety comprises one or more n-mer motifs,
>
> each n-mer motif ***consisting of*** an amino acid sequence of
>
> X_{m1} RGD $X_1X_2X_3X_4$,
>
> $X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$, or
>
> $X_{m3}X_{m2}X_{m1}$ RGD $X_1X_2X_3X_4$,
>
> wherein X_1, X_2, and X_3 are independently selected from any amino acid, X_4 is L or T, and
>
> (i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or
>
> (ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or
>
> (iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E.
>
> (Emphasis added)

Grimm reference

AAV9S1_P1(SEQ ID NO: 29), AAV9S10_P1 (SEQ ID NO: 30), and AAV9_P1 capsid polypeptides have the same amino acid sequence between Q585 and A600 (see below and FIG. 7).

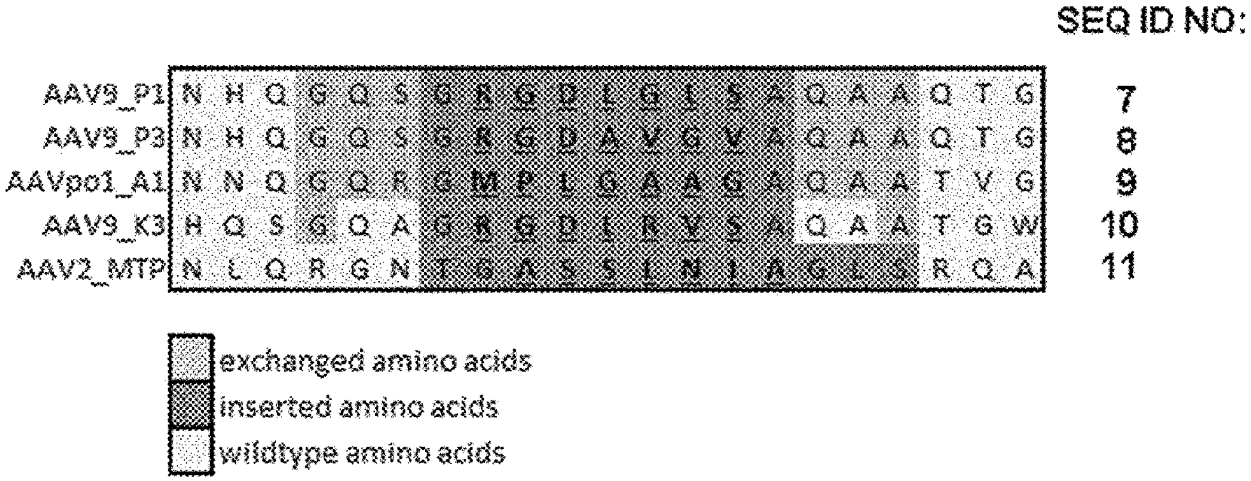

FIG. 7

AMINO ACID SEQUENCE 583-594 (AAV9_P1, AAV9S1_P1 and AAV9S10)

AAV9 WT	**583**	**584**	**585**		**586**	**587**	**588**									**589**	**590**	**591**	**592**	**593**	**594**
	N	H	Q		S	A	Q									A	Q	A	Q	T	G
GRIMM AAV9_P1	N	H	Q	X_{M4}	X_{M3}	X_{M2}	X_{M1}	R	G	D	X_1	X_2	X_3	X_4	X_5	X_6	X_7	A	Q	T	G
	N	H	Q	G	Q	S	G	R	G	D	L	G	L	S	A	Q	A	A	Q	T	G
	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603

The claimed invention is novel over Grimm

Grimm's recombinant AAV capsid polypeptides do not disclose all of the limitations of amended claims 1 and 15, as is evident from the comparison below.

AAV9 WT	**583**	**584**	**585**		**586**	**587**	**588**									**589**	**590**	**591**	**592**	**593**	**594**
	N	H	Q		S	A	Q									A	Q	A	Q	T	G
CLAIMS 1,15	N	H	**Q**		X_{M3}	X_{M2}	X_{M1}	R	G	D	X_1	X_2	X_3	X_4		**A**	Q	A	Q	T	G
	583	584	**585**		586	587	588	589	590	591	592	593	594	595		**596**					
GRIMM AAV9_P1	N	H	Q	X_{M4}	X_{M3}	X_{M2}	X_{M1}	R	G	D	X_1	X_2	X_3	X_4	X_5	X_6	X_7	A	Q	T	G
	N	H	Q	G	Q	S	G	R	G	D	L	G	L	S	A	Q	A	A	Q	T	G
	583	584	585	586	587	588	589	590	591	592	593	594	595	596	597	598	599	600	601	602	603

Claims 1 and 15 require *inter alia*:

> . . . . wherein the targeting moiety comprises one or more n-mer motifs,
>
> each n-mer motif consisting of an amino acid sequence of
>
> $X_{m1}RGDX_1X_2X_3X_4$,
>
> $X_{m2}X_{m1}RGDX_1X_2X_3X_4$, or
>
> $X_{m3}X_{m2}X_{m1}RGDX_1X_2X_3X_4$,
>
> wherein X_1, X_2, and X_3 are independently selected from any amino acid,
>
> **X_4 is L or T**, and
>
> (i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or
>
> (ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or
>
> (iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E.
>
> (Emphasis added)

As the comparison above demonstrates, X_4 of AAV9_P1 capsid polypeptides (and, consequently, also AAV9S1_P1 and AAV9S10_P1) is S, not L or T as required by the claimed invention.

In the Office Action, the Examiner alleges that claim 3 in Grimm discloses X_4 can be L. However, this assumption appears to overlook that claim 3 is dependent on claim 1.

Grimm's claims 1 and 3 require:

> 1. A method for treating and/or preventing a muscular disease and/or for muscle regeneration, the method comprising: contacting a subject with an adeno-associated virus (AAV) capsid polypeptide bonded to a binding peptide comprising an amino acid sequence $RGDX_1X_2X_3X_4$ (SEQ ID NO: 1), with X_1 to X_4 being independently selected amino acids.
>
> 3. The method of claim 1, wherein X_1, X_2, and X_3 are independently selected from L, G, V, and A; and X_4 being S, V, A, G, or L.

Grimm's binding peptide of claim 1, therefore, comprises *inter alia* an amino acid sequence of $RGDX_1X_2X_3X_4$, wherein X_4 can be S, V, A, G, or L. In contrast, the claimed invention requires a targeting moiety comprising an n-mer motif, each n-mer motif ***consisting of*** an amino acid sequence of

$X_{m1}RGDX_1X_2X_3X_4$,

$X_{m2}X_{m1}RGDX_1X_2X_3X_4$, or

$X_{m3}X_{m2}X_{m1}RGDX_1X_2X_3X_4$,

wherein X_1, X_2, and X_3 are independently selected from any amino acid,

X_4 is L or T, and

(i) X_{m3} and X_{m2} are independently selected from any amino acid, and **X_{m1} is G, S, T, N, V, R, I, K, or A**, or

(ii) X_{m3} and X_{m1} are independently selected from any amino acid, and **X_{m2} is N, S, A, P, T, M, or D**, or

(iii) X_{m2} and X_{m1} are independently selected from any amino acid, and **X_{m3} is T, N, S, A, G, D, or E**.

(Emphasis added)

Grimm therefore fails to disclose all the limitations of claims 1, 15, and 32. Specifically, Grimm does not teach an n-motif where X_{m1} can be G, S, T, N, V, R, I, K, or A, or X_{m2} is N, S, A,

P, T, M, or D, or X_{m3} is T, N, S, A, G, D, or E, and where X_4 is L or T. Applicant respectfully submits that the claimed invention is not anticipated by Grimm. Withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. § 103

In the Office Action, the Examiner rejected claims 1, 8-26, and 31 as allegedly being obvious over Grimm in view of Jin et al., bioRxiv, 2019, pages 1-24 ("Jin").

Applicant respectfully traverses that rejection. Jin fails to remedy the deficiencies in the teaching of Grimm. Applicant respectfully submits that the rejection does not apply to the claims as presently presented. Withdrawal of the rejection is respectfully requested.

New claims 32-38

New independent claim 32 requires:

> A recombinant AAV VP1 capsid polypeptide comprising an insertion of an n-mer motif consisting of an amino acid sequence of
>
> $X_{m1}RGDX_1X_2X_3X_4$,
> $X_{m2}X_{m1}RGDX_1X_2X_3X_4$, or
> $X_{m3}X_{m2}X_{m1}RGDX_1X_2X_3X_4$,
>
> wherein X_1, X_2, X_3, and X_4 are independently selected from any amino acid, and
>
> (i) X_{m3} and X_{m2} are independently selected from any amino acid, and X_{m1} is G, S, T, N, V, R, I, K, or A, or
> (ii) X_{m3} and X_{m1} are independently selected from any amino acid, and X_{m2} is N, S, A, P, T, M, or D, or
> (iii) X_{m2} and X_{m1} are independently selected from any amino acid, and X_{m3} is T, N, S, A, G, D, or E.

Claim 32 is a structural claim that is enabled by the specification as filed.

Claim 32 is also novel over Grimm for the same reasons as discussed above.

Obvious-Type Double Patenting

Claims 8-11 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1, 4-8, and 19-21 of co-pending Application No. 17/707,951 in view of Jin.

Claims 1 and 8-26 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-26 of U.S. Patent 11,920,150 from co-pending Application No. 17/707,940 in view of Jin.

Claims 1, and 8-26 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1, 3-8, 11, 13, 16, 18, 19, 21, 23, 31 -35, 37-39, 42, 44, 45, 47, 48, 52, 58, 59, 61, 62, 64, 74, and 77 of co-pending application 17/764,509 in view of Jin.

Claims 1-26 and 31 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-8, 12-14 and 16-26 of co-pending Application No. 17/707,944.

Claims 1-26 and 31 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-4, 6, 8, 10, 14, 16, 21, 30-32, 36, 43-45, 49, 54, 56, 59, 62, 65, 73, 78, 81, 85, 87, 88, 92, 99, 100 and 103 of co-pending Application No. 17/614,327 in view of Jin.

Claims 1-2 and 4-26 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1, 2, 7, 10, 11, 13, 14, 16, 18 and 21 of co-pending Application No. 18/689,897.

Claims 1-3, 6, and 8-26 are rejected on the ground of non-statutory obviousness-type double patenting over claims 1-3, 5, 6, 8, 9, 11, 13, 16, 19, 27, 30, 32, 34, 37, 44-46, 48, 50, 52, 57, 58, 60, 63, 66, 74, 77, 79-81, 91, 92, 93, 105 and 108 of co-pending Application No. 18/698,929.

Claims 1-2 and 7-26 are rejected on the ground of non-statutory obviousness-type double patenting over claims 42-55 of co-pending Application No. 18/287,963.

The issue of whether there is indeed double patenting is contingent upon whether the remarks herewith are indeed considered and entered; and, if so, whether the Examiner believes there is overlap with claims ultimately allowed in the application. Upon a finding of otherwise allowable subject matter, where the provisional double patenting rejection is the only issue remaining in prosecution, and it is believed there is overlap with claims ultimately allowed in the application, a Terminal Disclaimer will be filed for the purposes of expediting prosecution.

No Waiver

All of Applicant's arguments and amendments are without prejudice or disclaimer. Applicant may not have addressed each specific rejection of the independent and dependent claims because Applicant submits that the independent claims are allowable, as discussed above.

Applicant has not acquiesced to any such rejection and reserves the right to address the patentability of any additional claim features in the future.

CONCLUSION

Applicant submits the foregoing as a complete response to the Office Action. Applicant submits that this Amendment and Response place the application in condition for allowance and respectfully requests such action. If any issues can be resolved with an Examiner's Amendment or a telephone conference, please contact Applicant's representative at 478.292.5119.

No additional fees are believed due for consideration of this paper. However, the Commissioner is hereby authorized to charge any fee deemed necessary for consideration of this paper, including any extension of time fees or additional claim fees, or to credit any overpayment to Deposit Account Number 50-5193, reference number BROD-5215US-CON2.

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