

Claims

- [Claim 1] A polypeptide comprising an FcRn binding recombinantly engineered variant of stefin sequence that binds to human FcRn with a K_d of 1×10^{-6} M or less at pH 6.0, and (optionally) a K_d for binding human FcRn at pH 7.4 that is at least half a log greater than the K_d for binding at pH 6.0.
- [Claim 2] A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and has a circulating half-life in human patients of at least 7 days.
- [Claim 3] A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and facilitates transport of the protein across an epithelial tissue barrier.
- [Claim 4] A protein comprising (i) an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn, and (ii) a heterologous polypeptide covalently associated to the FcRn binding recombinantly engineered variant of stefin polypeptide sequence (optionally as a fusion protein or chemically conjugated) which confers a therapeutic activity in human patients.
- [Claim 5] A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and which has an amino acid sequence that is at least 75% identical to a recombinantly engineered variant of stefin polypeptide sequence selected from SEQ ID NOs: 594-887 and 1184.
- [Claim 6] A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and has an amino acid sequence that can be encoded by a nucleic acid having a coding sequence that hybridizes to any one of SEQ ID NOs: 888 to 1181 under stringent conditions of 6X sodium chloride/sodium citrate (SSC) at 45°C followed by a wash in 0.2X SSC at 65°C.
- [Claim 7] The polypeptide of any of the preceding claims, wherein the FcRn binding recombinantly engineered variant of stefin sequence binds to FcRn with a K_d of 1×10^{-7} M or less at pH 6.0, a K_d of 1×10^{-8} M or less at pH 6.0, or K_d of 1×10^{-9} M or less at pH 6.0.
- [Claim 8] The polypeptide of any of the preceding claims, wherein the FcRn binding recombinantly engineered variant of stefin sequence binds to FcRn at pH 7.4 with a K_d that is at least one log greater than the K_d for binding to FcRn at pH 6.0, at least 1.5 logs greater than the K_d for

binding to FcRn at pH 6, at least 2 logs greater than the K_d for binding to FcRn at pH 6, or at least 2.5 log greater than the K_d for binding to FcRn at pH 6.

[Claim 9] The polypeptide of any one of the preceding claims, wherein the polypeptide has a serum half-life in human patients of greater than 10 hours, greater than 24 hours, greater than 48 hours, greater than 72 hours, greater than 96 hours, greater than 120 hours, greater than 144 hours, greater than 168 hours, greater than 192 hours, greater than 216 hours, greater than 240 hours, greater than 264 hours, greater than 288 hours, greater than 312 hours, greater than 336 hours or, greater than 360 hours.

[Claim 10] The polypeptide of any one of the preceding claims, wherein the polypeptide has a serum half-life in human patients of greater than 50%, greater than 60%, greater than 70%, or greater than 80% of the serum half-life of IgG.

[Claim 11] The polypeptide of any one of the preceding claims, wherein the polypeptide has a serum half-life in human patients of greater than 50%, greater than 60%, greater than 70%, or greater than 80% of the serum half-life of serum albumin.

[Claim 12] The polypeptide of any one of the preceding claims, wherein the polypeptide does not inhibit binding of human serum albumin to human FcRn.

[Claim 13] The polypeptide of any one of the preceding claims, wherein the polypeptide does not inhibit binding of IgG to human FcRn.

[Claim 14] The polypeptide of any one of the preceding claims, wherein binding of the polypeptide to human FcRn facilitates transport of the polypeptide from an apical side to a basal side of an epithelial cell layer.

[Claim 15] The polypeptide of any one of the preceding claims comprising an amino acid sequence represented in general formula (I)

FR1-(Xaa)_n-FR2-(Xaa)_m-FR3 (I),

wherein

FR1 is an amino acid sequence having at least 70% identity to MIPGGLSEAK PATPEIQEIV DKVKPQLEEK TNETYGKLEA VQYKTQVLA (SEQ ID NO: 1);

FR2 is an amino acid sequence having at least 70% identity to GT-NYYIKVRA GDNKYMHLKV FKSL (SEQ ID NO: 2);

FR3 is an amino acid sequence having at least 70% identity to EDLVLTGYQV DKNKDDELGT F (SEQ ID NO: 3); and

- Xaa, individually for each occurrence, is an amino acid,
n is an integer from 3 to 20, and m is an integer from 3 to 20.
- [Claim 16] The polypeptide of claim 15, wherein:
FR1 has at least 80%, at least 82%, at least 84%, at least 86%, at least 88%, at least 90%, at least 92%, at least 94%, at least 96%, or at least 98% identity to SEQ ID NO: 1;
FR2 has at least 80%, at least 84%, at least 88%, at least 92%, or at least 96% identity to SEQ ID NO: 2; and/or.
FR3 has at least 80%, at least 85%, at least 90%, or at least 95% identity to SEQ ID NO: 3.
- [Claim 17] The polypeptide of claim 15, wherein:
FR1 comprises the amino acid sequence of SEQ ID NO: 1;
FR2 comprises the amino acid sequence of SEQ ID NO: 2; and/or
FR3 comprises the amino acid sequence of SEQ ID NO: 3.
- [Claim 18] The polypeptide of any one of claims 15-17, wherein (Xaa)_n is an amino acid sequence represented in the general formula
-Xaa-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa-Xaa- (SEQ ID NO: 4)
wherein Xaa, Xaa2, Xaa3, Xaa4, Xaa5, Xaa6 and Xaa7, individually for each occurrence, is an amino acid residue, with the caveat that (i) at least two of Xaa2, Xaa3, Xaa4 or Xaa5 are selected from His, Lys or Arg, or (ii) at least two of Xaa4, Xaa5, Xaa6 or Xaa7 are selected from His, Lys or Arg.
- [Claim 19] The polypeptide of claim 18, wherein wherein at least three, and preferably four of Xaa2, Xaa3, Xaa4, Xaa5, Xaa6 or Xaa7 are selected from His, Lys or Arg.
- [Claim 20] The polypeptide of any of claims 15-19, wherein (Xaa)_n is at least 75% identical to the Loop 2 sequence selected from SEQ ID NOs: 6-299 and 1182.
- [Claim 21] The polypeptide of any one of claims 15-20, wherein (Xaa)_m is an amino acid sequence represented in the general formula
-Xaa-Xaa8-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Xaa14-Xaa- (SEQ ID NO: 5)
wherein Xaa, Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14, individually for each occurrence, is an amino acid residue, with the caveat that at least three of Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14 are selected from His, Lys or Arg, and at least an additional two of Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14 are selected from His, Lys, Arg, Phe, Tyr or Trp.

- [Claim 22] The polypeptide of any of claims 15-18, wherein (Xaa)_m is at least 75% identical to the Loop 4 sequence selected from SEQ ID NOs: 300-593 and 1183.
- [Claim 23] The polypeptide of any one of the preceding claims, wherein the polypeptide includes at least one cysteine, which is (optionally) available for chemical conjugation, and which (optionally) is located at the C-terminal end or the N-terminal end of the polypeptide.
- [Claim 24] The polypeptide of any one of the preceding claims further comprising a heterologous polypeptide covalently linked through an amide bond to form a contiguous fusion protein.
- [Claim 25] The polypeptide of claim 24, wherein the heterologous polypeptide comprises a therapeutic polypeptide.
- [Claim 26] The polypeptide of claim 25, wherein the therapeutic polypeptide is selected from the group consisting of polypeptide hormones, polypeptide cytokines, polypeptide chemokines, growth factors, hemostasis active polypeptides, enzymes, and toxins.
- [Claim 27] The polypeptide of claim 25, wherein the therapeutic polypeptide is selected from the group consisting of receptor traps and receptor ligands.
- [Claim 28] The polypeptide of claim 25, wherein the therapeutic polypeptide sequence is selected from the group consisting of angiogenic agents and anti-angiogenic agents.
- [Claim 29] The polypeptide of claim 25, wherein the therapeutic polypeptide sequence is a neurotransmitter, and optionally wherein the neurotransmitter is Neuropeptide Y.
- [Claim 30] The polypeptide of claim 25, wherein the therapeutic polypeptide sequence is an erythropoiesis-stimulating agent, and optionally wherein the erythropoiesis-stimulating agent is erythropoietin or an erythropoietin mimetic.
- [Claim 31] The polypeptide of claim 25, wherein the therapeutic polypeptide is an incretin, and optionally wherein the incretin is selected from the group consisting of glucagon, gastric inhibitory peptide (GIP), glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2), peptide YY (PYY), and oxyntomodulin (OXM).
- [Claim 32] The polypeptide of claim 25, wherein the therapeutic polypeptide is an anticancer immune enhancing agent, such as a checkpoint inhibitor, a costimulatory receptor agonist or an inducer of innate immunity.
- [Claim 33] The polypeptide of claim 25, wherein the therapeutic polypeptide is an

anti-inflammatory immune inhibiting agent, such as a checkpoint agonist, a costimulatory receptor antagonist or an inhibitor of innate immunity.

- [Claim 34] A pharmaceutical composition suitable for therapeutic use in a human patient, comprising a polypeptide of any of any one of the preceding claims, and a pharmaceutically acceptable excipient.
- [Claim 35] The pharmaceutical composition of claim 34, wherein the pharmaceutical composition is formulated for pulmonary delivery or topical application.
- [Claim 36] The pharmaceutical composition of claim 35, wherein the pulmonary delivery is intranasal delivery.
- [Claim 37] A polynucleotide comprising a sequence encoding the polypeptide of any of any one of the preceding claims.
- [Claim 38] The polynucleotide of claim 37, wherein the sequence encoding the polypeptide is operably linked to a transcriptional regulatory sequence.
- [Claim 39] The polynucleotide of claim 38, wherein the transcriptional regulatory sequence is selected from the group consisting of promoters and enhancers.
- [Claim 40] The polynucleotide of any of claims 37-39, further comprising an origin of replication, a minichromosome maintenance element (MME), and/or a nuclear localization element.
- [Claim 41] The polynucleotide of any of claims 37-40, further comprising a polyadenylation signal sequence operably linked and transcribed with the sequence encoding the polypeptide.
- [Claim 42] The polynucleotide of any of claims 37-40, wherein the sequence encoding the polypeptide comprises at least one intronic sequence
- [Claim 43] The polynucleotide of any of claims 37-42, further comprising at least one ribosome binding site transcribed with the sequence encoding the polypeptide.
- [Claim 44] The polynucleotide of any of claims 37-43, wherein the polynucleotide is a deoxyribonucleic acid (DNA).
- [Claim 45] The polynucleotide of any of claims 37-43, wherein the polynucleotide is a ribonucleic acid (RNA).
- [Claim 46] A viral vector comprising the polynucleotide of any of claims 37-43.
- [Claim 47] A plasmid or minicircle comprising the polynucleotide any of claims 37-43.
- [Claim 48] A cell comprising the polypeptide of any one of claims 1-33, the polynucleotide of any one of claims 37-45, the viral vector of claim 46,

or the plasmid or minicircle of claim 47.

[Claim 49]

A method of increasing serum half-life of a therapeutic molecule, the method comprising conjugating the polypeptide of any one of claims 1-33 to the therapeutic molecule.

[Claim 50]

A polypeptide of any one of claims 1-25 for use in a method for treating an autoimmune disease and/or an inflammatory disease.

[Claim 51]

A polypeptide of any one of claims 1-25 for use in a method for treating cancer.

[Claim 52]

A polypeptide of any one of claims 1-25 for use in a method for treating cardiovascular or metabolic disease or disorder.

[Claim 53]

A method of producing the polypeptide of any one of claims 1-33, the method comprising expressing in a host cell a nucleic acid encoding the polypeptide, and optionally isolating the polypeptide from the host cell.

[Claim 54]

A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and inhibits the binding of human IgG to human FcRn.

[Claim 55]

The protein of claim 54 for use in a method for treating an autoimmune or inflammatory disorder or disease.

[Claim 56]

A pharmaceutical composition suitable for therapeutic use in a human patient, comprising a protein of claim 54, and a pharmaceutically acceptable excipient.

[Claim 57]

The polypeptide of any one of the preceding claims comprising a loop 2 amino acid sequence of any one of SEQ ID NOs: 6-299 and 1182.

[Claim 58]

The polypeptide of any one of the preceding claims comprising a loop 4 amino acid sequence of any one of SEQ ID NOs: 300-593 and 1183.

[Claim 59]

The polypeptide of any one of the preceding claims comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 100% identity to the sequence of any one of SEQ ID NOs: 594-887 or 1184.

[Claim 60]

The polypeptide of any one of the preceding claims encoded by a nucleic acid sequence having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 100% identity to the sequence of any one of SEQ ID NOs: 888-1181.

[Claim 61]

A use of the polynucleotide of any one of the preceding claims for targeting FcRn.

[Claim 62]

A use of the polynucleotide of any one of the preceding claims for increasing serum half-life of a therapeutic molecule.

Claims

1. A polypeptide comprising an FcRn binding recombinantly engineered variant of stefin sequence that binds to human FcRn with a K_d of 1×10^{-6} M or less at pH 6.0, and (optionally) a K_d for binding human FcRn at pH 7.4 that is at least half a log greater than the K_d for binding at pH 6.0.
2. The polypeptide of claim 1, wherein the polypeptide comprising (i) an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn, and (ii) a heterologous polypeptide covalently associated to the FcRn binding recombinantly engineered variant of stefin polypeptide sequence (optionally as a fusion protein or chemically conjugated) which confers a therapeutic activity in human patients.
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3. The polypeptide of claim 1, wherein the polypeptide comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and has an amino acid sequence that can be encoded by a nucleic acid having a coding sequence that hybridizes to any one of SEQ ID NOs: 888 to 1181 under stringent conditions of 6X sodium chloride/sodium citrate (SSC) at 45 °C followed by a wash in 0.2X SSC at 65 °C.
4. The polypeptide of claim 1, wherein the FcRn binding recombinantly engineered variant of stefin sequence binds to FcRn with a K_d of 1×10^{-7} M or less at pH 6.0, a K_d of 1×10^{-8} M or less at pH 6.0, or K_d of 1×10^{-9} M or less at pH 6.0.
5. The polypeptide of claim 1, wherein the FcRn binding recombinantly engineered variant of stefin sequence binds to FcRn at pH 7.4 with a K_d that is at least one log greater than the K_d for binding to FcRn at pH 6.0, at least 1.5 logs greater than the K_d for binding to FcRn at pH 6, at least 2 logs greater than the K_d for binding to FcRn at pH 6, or at least 2.5 log greater than the K_d for binding to FcRn at pH 6.

6. The polypeptide of claim 1, wherein the polypeptide has a serum half-life in human patients of greater than 10 hours, greater than 24 hours, greater than 48 hours, greater than 72 hours, greater than 96 hours, greater than 120 hours, greater than 144 hours, greater than 168 hours, greater than 192 hours, greater than 216 hours, greater than 240 hours, greater than 264 hours, greater than 288 hours, greater than 312 hours, greater than 336 hours or, greater than 360 hours.

7. The polypeptide of claim 1, wherein the polypeptide has a serum half-life in human patients of greater than 50%, greater than 60%, greater than 70%, or greater than 80% of the serum half-life of IgG, and/or

wherein the polypeptide has a serum half-life in human patients of greater than 50%, greater than 60%, greater than 70%, or greater than 80% of the serum half-life of serum albumin.

8. The polypeptide of claim 1, wherein the polypeptide does not inhibit binding of human serum albumin to human FcRn,

wherein the polypeptide does not inhibit binding of IgG to human FcRn, and/or

wherein binding of the polypeptide to human FcRn facilitates transport of the polypeptide from an apical side to a basal side of an epithelial cell layer.

9. The polypeptide of claim 1 comprising an amino acid sequence represented in general formula (I)

FR1-(Xaa)_n-FR2-(Xaa)_m-FR3 (I),

wherein

FR1 is an amino acid sequence having at least 70% identity to MIPGGLSEAK PATPEIQEIV DKVKPQLEEK TNETYGKLEA VQYKTQVLA (SEQ ID NO: 1);

FR2 is an amino acid sequence having at least 70% identity to GTNYYIKVRA GDNKYMHLKV FKSL (SEQ ID NO: 2);

FR3 is an amino acid sequence having at least 70% identity to

EDLVLTGYQV DKNKDELGTG F (SEQ ID NO: 3); and

Xaa, individually for each occurrence, is an amino acid,

n is an integer from 3 to 20, and m is an integer from 3 to 20.

10. The polypeptide of claim 9, wherein:

FR1 has at least 80%, at least 82%, at least 84%, at least 86%, at least 88%, at least 90%, at least 92%, at least 94%, at least 96%, or at least 98% identity to SEQ ID NO: 1;

FR2 has at least 80%, at least 84%, at least 88%, at least 92%, or at least 96% identity to SEQ ID NO: 2; and/or.

FR3 has at least 80%, at least 85%, at least 90%, or at least 95% identity to SEQ ID NO: 3.

11. The polypeptide of claim 9, wherein:

FR1 comprises the amino acid sequence of SEQ ID NO: 1;

FR2 comprises the amino acid sequence of SEQ ID NO: 2; and/or

FR3 comprises the amino acid sequence of SEQ ID NO: 3.

12. The polypeptide of claim 9, wherein (Xaa)_n is an amino acid sequence represented in the general formula

-Xaa-Xaa2-Xaa3-Xaa4-Xaa5-Xaa6-Xaa7-Xaa-Xaa- (SEQ ID NO: 4)

wherein Xaa, Xaa2, Xaa3, Xaa4, Xaa5, Xaa6 and Xaa7, individually for each occurrence, is an amino acid residue, with the caveat that (i) at least two of Xaa2, Xaa3, Xaa4 or Xaa5 are selected from His, Lys or Arg, or (ii) at least two of Xaa4, Xaa5, Xaa6 or Xaa7 are selected from His, Lys or Arg.

13. The polypeptide of claim 12, wherein at least three, and preferably four of Xaa2, Xaa3, Xaa4, Xaa5, Xaa6 or Xaa7 are selected from His, Lys or Arg.

14. The polypeptide of claim 13, wherein (Xaa)_n is at least 75% identical to the Loop 2 sequence selected from SEQ ID NOs: 6-299 and 1182.

15. The polypeptide of claim 13, wherein (Xaa)_m is an amino acid sequence represented in the general formula

-Xaa-Xaa8-Xaa9-Xaa10-Xaa11-Xaa12-Xaa13-Xaa14-Xaa- (SEQ ID NO: 5)

wherein Xaa, Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14, individually for each occurrence, is an amino acid residue, with the caveat that at least three of Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14 are selected from His, Lys or Arg, and at least an additional two of Xaa8, Xaa9, Xaa10, Xaa11, Xaa12, Xaa13 and Xaa14 are selected from His, Lys, Arg, Phe, Tyr or Trp.

16. The polypeptide of claim 13, wherein (Xaa)_m is at least 75% identical to the Loop 4 sequence selected from SEQ ID NOs: 300-593 and 1183.

17. The polypeptide of claim 1, wherein the polypeptide includes at least one cysteine, which is (optionally) available for chemical conjugation, and which (optionally) is located at the C-terminal end or the N-terminal end of the polypeptide, and/or

wherein the polypeptide further comprising a heterologous polypeptide covalently linked through an amide bond to form a contiguous fusion protein.

18. The polypeptide of claim 17, wherein the heterologous polypeptide comprises a therapeutic polypeptide.

19. The polypeptide of claim 18, wherein the therapeutic polypeptide is selected from the group consisting of polypeptide hormones, polypeptide cytokines, polypeptide chemokines, growth factors, hemostasis active polypeptides, enzymes, and toxins,

wherein the therapeutic polypeptide is selected from the group consisting of receptor traps and receptor ligands,

wherein the therapeutic polypeptide sequence is selected from the group consisting of angiogenic agents and anti-angiogenic agents,

wherein the therapeutic polypeptide sequence is a neurotransmitter, and optionally

- wherein the neurotransmitter is Neuropeptide Y,
wherein the therapeutic polypeptide sequence is an erythropoiesis-stimulating agent,
and optionally wherein the erythropoiesis-stimulating agent is erythropoietin
or an erythropoietin mimetic,
wherein the therapeutic polypeptide is an incretin, and optionally wherein the incretin
is selected from the group consisting of glucagon, gastric inhibitory peptide
(GIP), glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2),
peptide YY (PYY), and oxyntomodulin (OXM).
wherein the therapeutic polypeptide is an anticancer immune enhancing agent, such
as a checkpoint inhibitor, a costimulatory receptor agonist or an inducer of
innate immunity, and/or
wherein the therapeutic polypeptide is an anti-inflammatory immune inhibiting agent,
such as a checkpoint agonist, a costimulatory receptor antagonist or an
inhibitor of innate immunity.
20. A pharmaceutical composition suitable for therapeutic use in a human patient,
comprising a polypeptide of claim 1, and a pharmaceutically acceptable excipient.
21. The pharmaceutical composition of claim 20, wherein the pharmaceutical
composition is formulated for pulmonary delivery or topical application.
22. The pharmaceutical composition of claim 21, wherein the pulmonary delivery
is intranasal delivery.
23. A polynucleotide comprising a sequence encoding the polypeptide of claim 1.
24. A viral vector comprising the polynucleotide of claim 23.
25. A plasmid or minicircle comprising the polynucleotide claim 23.
26. A cell comprising the polypeptide of claim 1, the polynucleotide of claim 23,
the viral vector of claim 24, or the plasmid or minicircle of claim 25.

27. A method of increasing serum half-life of a therapeutic molecule, the method comprising conjugating the polypeptide of any one of claims 1-19 to the therapeutic molecule.
28. A polypeptide of claim 1 for use in a method for treating an autoimmune disease and/or an inflammatory disease.
29. A polypeptide of claim 1 for use in a method for treating cancer.
30. A polypeptide of claim 1 for use in a method for treating cardiovascular or metabolic disease or disorder.
31. A method of producing the polypeptide of claim 1, the method comprising expressing in a host cell a nucleic acid encoding the polypeptide, and optionally isolating the polypeptide from the host cell.
32. A protein comprising an FcRn binding recombinantly engineered variant of stefin polypeptide sequence which binds to human FcRn and inhibits the binding of human IgG to human FcRn.
33. The protein of claim 32 for use in a method for treating an autoimmune or inflammatory disorder or disease.
34. A pharmaceutical composition suitable for therapeutic use in a human patient, comprising a protein of claim 32, and a pharmaceutically acceptable excipient.
35. The polypeptide of claim 1 comprising a loop 2 amino acid sequence of any one of SEQ ID NOs: 6-299 and 1182.
36. The polypeptide of claim 1 comprising a loop 4 amino acid sequence of any one of SEQ ID NOs: 300-593 and 1183.

37. The polypeptide of claim 1 comprising an amino acid sequence having at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 100% identity to the sequence of any one of SEQ ID NOs: 594-887 or 1184.
38. The polypeptide of claim 1 encoded by a nucleic acid sequence having at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 100% identity to the sequence of any one of SEQ ID NOs: 888-1181.
39. A use of the polynucleotide of claim 1 for targeting FcRn.
40. A use of the polynucleotide of claim 1 for increasing serum half-life of a therapeutic molecule.