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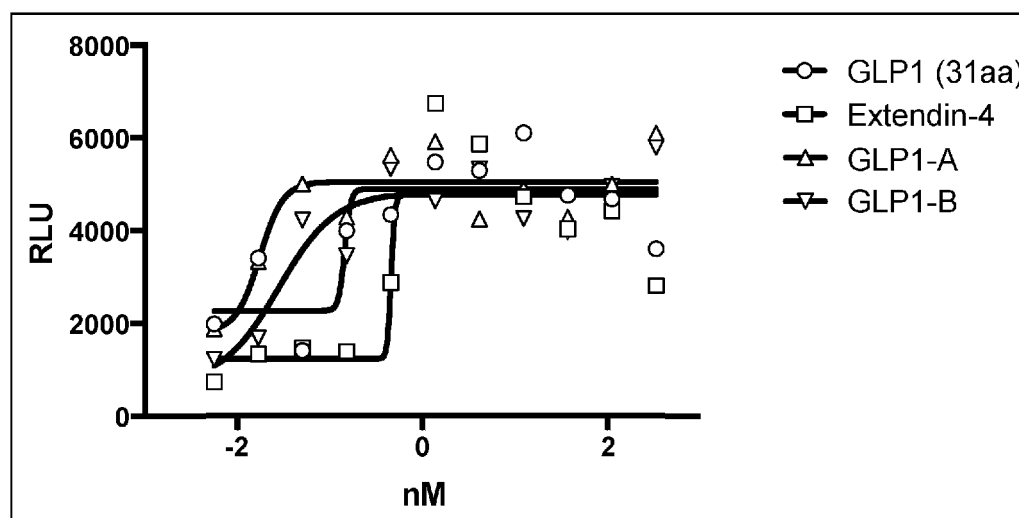


Fig. 3

(57) Abstract: Provided are various embodiments relating to variant IgG Fc polypeptides of companion animals having increased Protein A binding for ease of purification, decreased C1q binding for reduced complement-mediated immune responses, decreased CD16 binding (e.g., for reduced antibody-dependent cellular cytotoxicity (ADCC) induction, increased stability, and/or the ability to form heterodimeric proteins. In addition, various embodiments relating to antibodies and fusion proteins comprising such variant IgG Fc polypeptides are provided. Also provided are various embodiments relating to contiguous polypeptides comprising one or more variant GLP1 polypeptide(s) having improved serum half-life. Further provided are various embodiments relating to contiguous polypeptides or heterodimeric polypeptides comprising a GLP1 polypeptide and a glucagon polypeptide as a dual GLP1 receptor and glucagon receptor agonist. In various embodiments, such polypeptides may be used to treat, for example, diabetes, obesity, or related indications, in companion animals, such as canines, felines, and equines.



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IGG FC VARIANTS FOR VETERINARY USE

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of US Provisional Application No. 62/545,858, filed August 15, 2017, which is incorporated by reference herein in its entirety for any purpose.

FIELD

[0002] The present disclosure relates to variant IgG Fc polypeptides of companion animals with enhanced features, including increased Protein A binding (e.g., for ease of purification), decreased C1q binding (e.g., for reduced complement-mediated immune responses), decreased CD16 binding (e.g., for reduced antibody-dependent cellular cytotoxicity (ADCC) induction, increased stability, and/or the ability to form heterodimeric proteins. The variant IgG Fc polypeptides of the present disclosure may have broad applicability in companion animal therapeutics. For example, variant IgG Fc polypeptides may be used in the design and production of long-acting GLP1 polypeptides for treating, for example, diabetes, obesity, or related indications, in companion animals, such as canines, felines, and equines. In addition, variant IgG Fc polypeptides may be used in the design and production of antibodies or fusion proteins for treating various disorders in companion animals.

BACKGROUND

[0003] IgG Fc plays an important role in Fc-mediated functions through interactions with FcRn, Fc receptor, and C1q. In companion animals, various IgG subtypes possess differences in these functions, which are often considered when choosing a particular IgG antibody or IgG Fc fusion protein for therapeutic or diagnostic applications. For example, the ability of an IgG subtype to have weak or no measurable binding affinity to C1q or CD16 may be advantageous. In addition, IgG Fc's ability to bind Protein A may be useful for purification using a Protein A affinity purification platform.

[0004] However, most IgG Fc subtypes of canine, feline, and equine do not possess Protein A binding properties, weak or no measurable binding affinity to CD16, and weak or no measurable binding affinity to C1q. For example, of the four canine IgG Fc subtypes (IgG-A, IgG-B, IgG-C, and IgG-D), only canine IgG-B Fc has appreciable affinity to Protein A. Meanwhile only canine IgG-A Fc and IgG-D Fc have no or weak C1q binding or CD16 binding. Antibodies

and Fc fusion proteins comprising variant IgG Fc polypeptides that have reduced binding to C1q and/or CD16, and/or that able to bind Protein A are desirable.

[0005] Glucagon-like peptide-1 (GLP1) is a potent antihyperglycemic hormone, which plays an important role in regulating blood glucose level. Native GLP1 has an in vivo half-life of approximately 2 minutes. Long-acting GLP1 polypeptides can be used to treat diabetes and obesity, prevent diabetes, control hyperglycemic conditions, lower lipids, treat conditions that would benefit from lowered blood glucose levels, suppress gastric or intestinal movement, slow gastric emptying, and/or decrease food intake. There remains a need for long-acting GLP1 polypeptides for treating high blood glucose or uncontrollable blood glucose-induced conditions in companion animals, such as canines, felines, and equines.

SUMMARY OF THE INVENTION

Embodiment 1. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification relative to a wild-type IgG Fc polypeptide of a companion animal species, wherein the variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.

Embodiment 2. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification relative to a wild-type IgG Fc polypeptide of a companion animal species, wherein the variant IgG Fc polypeptide has reduced binding affinity to C1q and/or CD16 relative to the wild-type IgG Fc polypeptide.

Embodiment 3. The polypeptide of embodiment 1 or embodiment 2, wherein the variant IgG Fc polypeptide binds to C1q and/or CD16 with a dissociation constant (K_d) of greater than 5×10^{-6} M, greater than 1×10^{-5} M, greater than 5×10^{-5} M, greater than 1×10^{-4} M, greater than 5×10^{-4} M, or greater than 1×10^{-3} M, as measured by biolayer interferometry.

Embodiment 4. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.

Embodiment 5. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide binds to Protein A with a dissociation constant (K_d) of less than 5×10^{-6} M, less than 1×10^{-6} M, less than 5×10^{-7} M, less than 1×10^{-7} M, less than 5×10^{-8} M, less than 1×10^{-8} M, less than 5×10^{-9} M, less than 1×10^{-9} M, less than 5×10^{-10} M, less than 1×10^{-10} M, less than 5×10^{-11} M, less than 1×10^{-11} M, less than 5×10^{-12} M, or less than 1×10^{-12} M, as measured by biolayer interferometry.

Embodiment 6. The polypeptide of any one of the preceding embodiments, wherein the companion animal species is canine, feline, or equine.

Embodiment 7. The polypeptide of any one of the preceding embodiments, wherein the wild-type IgG Fc polypeptide is

- a) a canine IgG-A Fc, IgG-B Fc, IgG-C Fc, or IgG-D Fc;
- b) an equine IgG1 Fc, IgG2 Fc, IgG3 Fc, IgG4 Fc, IgG5 Fc, IgG6 Fc, or IgG7 Fc; or
- c) a feline IgG1a Fc, IgG1b Fc, or IgG2 Fc.

Embodiment 8. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification to a hinge region relative to a wild-type feline or equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide has increased recombinant production and/or increased hinge disulfide formation relative to the wild-type IgG Fc polypeptide, as determined by SDS-PAGE analysis under reducing and/or nonreducing conditions.

Embodiment 9. The polypeptide of any one the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;
- b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 3 of SEQ ID NO: 129; and/or
- c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 20 of SEQ ID NO: 129.

Embodiment 10. The polypeptide of any one the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;
- b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 3 of SEQ ID NO: 129; and/or
- c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 20 of SEQ ID NO: 129.

Embodiment 11. The polypeptide of any one the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a proline at a position corresponding to position 16 or at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;

b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a serine at a position corresponding to position 3 or at position 3 of SEQ ID NO: 129; and/or

c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a proline at a position corresponding to position 20 or at position 20 of SEQ ID NO: 129.

Embodiment 12. The polypeptide of any one the preceding embodiments, wherein the variant IgG Fc polypeptide comprises a hinge region or a portion of a hinge region from an IgG Fc polypeptide of a different isotype.

Embodiment 13. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises a hinge region or a portion of a hinge region from a wild-type feline IgG-1a Fc polypeptide, from a wild-type feline IgG-1b Fc polypeptide, or from a wild-type equine IgG1 Fc polypeptide.

Embodiment 14. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises SEQ ID NO: 19, SEQ ID NO: 125 or SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135.

Embodiment 15. A polypeptide comprising an amino acid sequence of SEQ ID NO: 19, SEQ ID NO: 125 or SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135.

Embodiment 16. A polypeptide comprising a variant IgG2 Fc polypeptide comprising at least one amino acid substitution relative to a wild-type feline IgG2 Fc polypeptide, wherein the at least one amino acid substitution is a cysteine, and wherein the variant IgG2 Fc polypeptide is capable of forming at least one additional inter-chain disulfide linkage relative to the wild-type feline IgG2 Fc polypeptide.

Embodiment 17. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises at least one amino acid substitution relative to

a wild-type feline IgG Fc polypeptide, wherein the at least one amino acid substitution is a cysteine, and wherein the variant IgG Fc polypeptide is capable of forming at least one additional inter-chain disulfide linkage relative to the wild-type feline IgG Fc polypeptide.

Embodiment 18. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises a cysteine at a position corresponding to position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, or position 16 of SEQ ID NO: 16.

Embodiment 19. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises a cysteine at a position corresponding to position 14 of SEQ ID NO: 16.

Embodiment 20. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises a cysteine at position 14 of SEQ ID NO: 16.

Embodiment 21. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide is at least 90% identical, at least 95% identical, at least 97% identical, or at least 99% identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 100, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

Embodiment 22. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises SEQ ID NO: 17.

Embodiment 23. A polypeptide comprising an amino acid sequence of SEQ ID NO: 17.

Embodiment 24. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 205 of SEQ ID NO: 1, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 1;

b) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 24 of SEQ ID NO: 3;

c) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 4, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 4;

d) an amino acid substitution at a position corresponding to position 15 of SEQ ID NO: 64, and/or an amino acid substitution at a position corresponding to position 203 of SEQ ID NO: 64;

e) an amino acid substitution at a position corresponding to position 199 of SEQ ID NO: 67, and/or an amino acid substitution at a position corresponding to position 200 of SEQ ID NO: 67; and/or

f) an amino acid substitution at a position corresponding to position 199 of SEQ ID NO: 68, an amino acid substitution at a position corresponding to position 200 of SEQ ID NO: 68, an amino acid substitution at a position corresponding to position 201 of SEQ ID NO: 68, and/or an amino acid substitution at a position corresponding to position 202 of SEQ ID NO: 68.

Embodiment 25. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) an amino acid substitution at position 21 of SEQ ID NO: 1, an amino acid substitution at position 23 of SEQ ID NO: 1, an amino acid substitution at position 25 of SEQ

ID NO: 1, an amino acid substitution at position 80 of SEQ ID NO: 1, an amino acid substitution at position 205 of SEQ ID NO: 1, and/or an amino acid substitution at position 207 of SEQ ID NO: 1;

b) an amino acid substitution at position 21 of SEQ ID NO: 3, an amino acid substitution at position 23 of SEQ ID NO: 3, and/or an amino acid substitution at position 24 of SEQ ID NO: 3;

c) an amino acid substitution at position 21 of SEQ ID NO: 4, an amino acid substitution at position 23 of SEQ ID NO: 4, an amino acid substitution at position 25 of SEQ ID NO: 4, an amino acid substitution at position 80 of SEQ ID NO: 4, and/or an amino acid substitution at position 207 of SEQ ID NO: 4;

d) an amino acid substitution at position 15 of SEQ ID NO: 64, and/or an amino acid substitution at position 203 of SEQ ID NO: 64;

e) an amino acid substitution at position 199 of SEQ ID NO: 67, and/or an amino acid substitution at position 200 of SEQ ID NO: 67; and/or

f) an amino acid substitution at position 199 of SEQ ID NO: 68, an amino acid substitution at position 200 of SEQ ID NO: 68, an amino acid substitution at position 201 of SEQ ID NO: 68, and/or an amino acid substitution at position 202 of SEQ ID NO: 68.

Embodiment 26. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a threonine at a position corresponding to position 21 of SEQ ID NO: 1, a leucine at a position corresponding to position 23 of SEQ ID NO: 1, an alanine at a position corresponding to position 25 of SEQ ID NO: 1, a glycine at a position corresponding to position 80 of SEQ ID NO: 1, an alanine at a position corresponding to position 205 of SEQ ID NO: 1, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 1;

b) a threonine at a position corresponding to position 21 of SEQ ID NO: 3, a leucine at a position corresponding to position 23 of SEQ ID NO: 3, and/or an isoleucine at a position corresponding to position 24 of SEQ ID NO: 3;

c) a threonine at a position corresponding to position 21 of SEQ ID NO: 4, a leucine at a position corresponding to position 23 of SEQ ID NO: 4, an alanine at a position corresponding to position 25 of SEQ ID NO: 4, a glycine at a position corresponding to position 80 of SEQ ID NO: 4, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 4;

d) a threonine or a valine at a position corresponding to position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at a position corresponding to position 203 of SEQ ID NO: 64;

e) a leucine at a position corresponding to position 199 of SEQ ID NO: 67, and/or a histidine at a position corresponding to position 200 of SEQ ID NO: 67; and/or

f) a leucine at a position corresponding to position 199 of SEQ ID NO: 68, a histidine at a position corresponding to position 200 of SEQ ID NO: 68, an asparagine at a position corresponding to position 201 of SEQ ID NO: 68, and/or a histidine at a position corresponding to position 202 of SEQ ID NO: 68.

Embodiment 27. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a threonine at position 21 of SEQ ID NO: 1, a leucine at position 23 of SEQ ID NO: 1, an alanine at position 25 of SEQ ID NO: 1, a glycine at position 80 of SEQ ID NO: 1, an alanine at position 205 of SEQ ID NO: 1, and/or a histidine at position 207 of SEQ ID NO: 1;

b) a threonine at position 21 of SEQ ID NO: 3, a leucine at position 23 of SEQ ID NO: 3, and/or an isoleucine at position 24 of SEQ ID NO: 3;

c) a threonine at a position 21 of SEQ ID NO: 4, a leucine at position 23 of SEQ ID NO: 4, an alanine at position 25 of SEQ ID NO: 4, a glycine at position 80 of SEQ ID NO: 4, and/or a histidine at position 207 of SEQ ID NO: 4;

d) a threonine or a valine at position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at position 203 of SEQ ID NO: 64;

e) a leucine at position 199 of SEQ ID NO: 67, and/or a histidine at position 200 of SEQ ID NO: 67; and/or

f) a leucine at position 199 of SEQ ID NO: 68, a histidine at position 200 of SEQ ID NO: 68, an asparagine at position 201 of SEQ ID NO: 68, and/or a histidine at position 202 of SEQ ID NO: 68.

Embodiment 28. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of:

a) SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 84; or

b) SEQ ID NO: 19, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 75, or SEQ ID NO: 76.

Embodiment 29. A polypeptide comprising an amino sequence of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 84, SEQ ID NO: 19, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 75, or SEQ ID NO: 76.

Embodiment 30. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 2, or an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 3;
- b) an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 63, an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 65, an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 66, or an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 69; or
- c) an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 80, or an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 81.

Embodiment 31. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 93 of SEQ ID NO: 2, or an amino acid substitution at position 93 of SEQ ID NO: 3;
- b) an amino acid substitution at position 87 of SEQ ID NO: 63, an amino acid substitution at position 87 of SEQ ID NO: 65, an amino acid substitution at position 87 of SEQ ID NO: 66, or an amino acid substitution at position 87 of SEQ ID NO: 69; or
- c) an amino acid substitution at position 198 of SEQ ID NO: 80, or an amino acid substitution at position 198 of SEQ ID NO: 81.

Embodiment 32. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an arginine at a position corresponding to position 93 of SEQ ID NO: 2, or an arginine at a position corresponding to position 93 of SEQ ID NO: 3;
- b) a serine at a position corresponding to position 87 of SEQ ID NO: 63, a serine substitution at a position corresponding to position 87 of SEQ ID NO: 65, a serine at a position corresponding to position 87 of SEQ ID NO: 66, or a serine at a position corresponding to position 87 of SEQ ID NO: 69; or
- c) an alanine at a position corresponding to position 198 of SEQ ID NO: 80, or an alanine at a position corresponding to position 198 of SEQ ID NO: 81.

Embodiment 33. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an arginine at position 93 of SEQ ID NO: 2, or an arginine at position 93 of SEQ ID NO: 3;
- b) a serine at position 87 of SEQ ID NO: 63, a serine at position 87 of SEQ ID NO: 65, a serine at position 87 of SEQ ID NO: 66, or a serine at position 87 of SEQ ID NO: 69; or
- c) an alanine at position 198 of SEQ ID NO: 80, or alanine at position 198 of SEQ ID NO: 81.

Embodiment 34. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises the amino acid sequence of:

- a) SEQ ID NO: 78, SEQ ID NO: 79, or SEQ ID NO: 84; or
- b) SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, or SEQ ID NO: 77; or
- c) SEQ ID NO: 82 or SEQ ID NO: 83.

Embodiment 35. A polypeptide comprising an amino sequence of SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 84, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77, SEQ ID NO: 82, or SEQ ID NO: 83.

Embodiment 36. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 2, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 2; or
- b) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 3.

Embodiment 37. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 5 of SEQ ID NO: 2, an amino acid substitution at position 38 of SEQ ID NO: 2, an amino acid substitution at position 39 of SEQ ID NO: 2, an amino acid substitution at position 97 of SEQ ID NO: 2, and/or an amino acid substitution at position 98 of SEQ ID NO: 2; or

b) an amino acid substitution at position 5 of SEQ ID NO: 3, an amino acid substitution at position 38 of SEQ ID NO: 3, an amino acid substitution at position 39 of SEQ ID NO: 3, an amino acid substitution at position 97 of SEQ ID NO: 3, and/or an amino acid substitution at position 98 of SEQ ID NO: 3.

Embodiment 38. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a proline at a position corresponding to position 5 of SEQ ID NO: 2, a glycine at a position corresponding to position 38 of SEQ ID NO: 2, an arginine at a position corresponding to position 39 of SEQ ID NO: 2, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 2, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 2; or

b) a proline at a position corresponding to position 5 of SEQ ID NO: 3, a glycine at a position corresponding to position 38 of SEQ ID NO: 3, an arginine at a position corresponding to position 39 of SEQ ID NO: 3, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 3, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 3.

Embodiment 39. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a proline at position 5 of SEQ ID NO: 2, a glycine at position 38 of SEQ ID NO: 2, an arginine at position 39 of SEQ ID NO: 2, an isoleucine at position 97 of SEQ ID NO: 2, and/or a glycine at position 98 of SEQ ID NO: 2; or

b) a proline at position 5 of SEQ ID NO: 3, a glycine at position 38 of SEQ ID NO: 3, an arginine at position 39 of SEQ ID NO: 3, an isoleucine at position 97 of SEQ ID NO: 3, and/or a glycine at position 98 of SEQ ID NO: 3.

Embodiment 40. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of:

a) SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, or SEQ ID NO: 147; or

b) SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

Embodiment 41. A polypeptide comprising an amino sequence of SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO:

149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

Embodiment 42. A polypeptide comprising a variant IgG Fc polypeptide comprising:

a) a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 1, a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 2, a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 3, or a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 4; or

b) a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 16, a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118.

Embodiment 43. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a tyrosine or a tryptophan at position 138 of SEQ ID NO: 1, a tyrosine or a tryptophan at position 137 of SEQ ID NO: 2, a tyrosine or a tryptophan at position 137 of SEQ ID NO: 3, or a tyrosine or a tryptophan at position 138 of SEQ ID NO: 4; or

b) a tyrosine or a tryptophan at position 154 of SEQ ID NO: 16, a tyrosine or a tryptophan at position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118.

Embodiment 44. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

Embodiment 45. A polypeptide comprising an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

Embodiment 46. A contiguous polypeptide comprising the polypeptide of any one of the preceding embodiments and a glucagon-like peptide-1 (GLP1) polypeptide.

Embodiment 47. A contiguous polypeptide comprising the polypeptide of any one of the preceding embodiments and a glucagon polypeptide.

Embodiment 48. A polypeptide comprising a variant IgG Fc polypeptide comprising:

a) a serine at a position corresponding to position 138 of SEQ ID NO: 1, a serine at a position corresponding to position 137 of SEQ ID NO: 2, a serine at a position corresponding to position 137 of SEQ ID NO: 3, a serine at a position corresponding to position 138 of SEQ ID NO: 4, a serine at a position corresponding to position 154 of SEQ ID NO: 16, a serine at a position corresponding to position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a serine at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118;

b) an alanine at a position corresponding to position 140 of SEQ ID NO: 1, an alanine at a position corresponding to position 139 of SEQ ID NO: 2, an alanine at a position corresponding to position 139 of SEQ ID NO: 3, an alanine at a position corresponding to position 140 of SEQ ID NO: 4, an alanine at a position corresponding to position 156 of SEQ ID NO: 16, an alanine at a position corresponding to position 156 of SEQ ID NO: 80 or SEQ ID NO: 117, or an alanine at a position corresponding to position 156 of SEQ ID NO: 81 or SEQ ID NO: 118; and/or

c) a threonine at a position corresponding to position 181 of SEQ ID NO: 1, a threonine at a position corresponding to position 180 of SEQ ID NO: 2, a threonine at a position corresponding to position 180 of SEQ ID NO: 3, a threonine at a position corresponding to position 181 of SEQ ID NO: 4, a threonine at a position corresponding to position 197 of SEQ ID NO: 16, a threonine at a position corresponding to position 197 of SEQ ID NO: 80 or SEQ ID NO: 117, or a threonine at a position corresponding to position 197 of SEQ ID NO: 81 or SEQ ID NO: 118.

Embodiment 49. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises:

a) a serine at position 138 of SEQ ID NO: 1, a serine at position 137 of SEQ ID NO: 2, a serine at position 137 of SEQ ID NO: 3, a serine at position 138 of SEQ ID NO: 4, a serine at position 154 of SEQ ID NO: 16, a serine at position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a serine at position 154 of SEQ ID NO: 81 or SEQ ID NO: 118;

b) an alanine at position 140 of SEQ ID NO: 1, an alanine at position 139 of SEQ ID NO: 2, an alanine at position 139 of SEQ ID NO: 3, an alanine at position 140 of SEQ ID NO: 4, an alanine at position 156 of SEQ ID NO: 16, an alanine at position 156 of SEQ ID NO: 80 or SEQ ID NO: 117, or an alanine at position 156 of SEQ ID NO: 81 or SEQ ID NO: 118; and/or;

c) a threonine at position 181 of SEQ ID NO: 1, a threonine at position 181 of SEQ ID NO: 2, a threonine at position 181 of SEQ ID NO: 3, a threonine at position 181 of SEQ ID NO: 4, a threonine at position 197 of SEQ ID NO: 16, a threonine at position 197 of SEQ ID NO: 80 or SEQ ID NO: 117, or a threonine at position 197 of SEQ ID NO: 81 or SEQ ID NO: 118.

Embodiment 50. The polypeptide of any one of the preceding embodiments, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 124.

Embodiment 51. A polypeptide comprising an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 124.

Embodiment 52. The polypeptide of any one of the preceding embodiments, wherein the polypeptide is glycosylated.

Embodiment 53. The polypeptide of any one of embodiments 1 to 51, wherein the polypeptide is aglycosylated.

Embodiment 54. A contiguous polypeptide comprising the polypeptide of any one of embodiments 48 to 53 and a glucagon-like peptide-1 (GLP1) polypeptide.

Embodiment 55. A contiguous polypeptide comprising the polypeptide of any one of embodiments 48 to 53 and a glucagon polypeptide.

Embodiment 56. A heterodimeric protein comprising the contiguous polypeptide of embodiment 46 and the contiguous polypeptide of embodiment 54.

Embodiment 57. A heterodimeric protein comprising the contiguous polypeptide of embodiment 47 and the contiguous polypeptide of embodiment 55.

Embodiment 58. The contiguous polypeptide or heterodimeric protein of any one of embodiments 46, 47, or 54 to 57, wherein the GLP1 polypeptide is a wild-type GLP1 polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 85.

Embodiment 59. The contiguous polypeptide or heterodimeric protein of any one of embodiments 46, 47, or 54 to 58, wherein the GLP1 polypeptide is a variant GLP1 polypeptide.

Embodiment 60. The contiguous polypeptide or heterodimeric protein of any one of embodiments 46, 47, or 54 to 59, wherein the GLP1 polypeptide comprises the amino acid sequence of SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 98, or SEQ ID NO: 99.

Embodiment 61. The contiguous polypeptide or heterodimeric protein of any one of embodiments 46, 47, or 54 to 60, wherein the glucagon polypeptide is a wild-type glucagon polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 21.

Embodiment 62. The contiguous polypeptide or heterodimeric protein of any one of embodiments 46, 47, or 54 to 61, wherein the glucagon polypeptide is a variant glucagon polypeptide.

Embodiment 63. A heterodimeric protein comprising:

i) a first variant canine IgG Fc polypeptide comprising at least one amino acid modification relative to a first wild-type canine IgG Fc polypeptide and a second variant canine IgG Fc polypeptide comprising at least one amino acid modification relative to a second wild-type canine IgG Fc polypeptide; or

ii) a first variant feline IgG Fc polypeptide comprising at least one amino acid modification relative to a first wild-type feline IgG Fc polypeptide and a second variant feline IgG Fc polypeptide comprising at least one amino acid modification relative to a second wild-type feline IgG Fc polypeptide, wherein:

a) the first variant canine IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 138 of SEQ ID NO: 1, position 137 of SEQ ID NO: 2, position 137 of SEQ ID NO: 3, or position 138 of SEQ ID NO: 4;

b) the second variant canine IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 138, position 140, and/or position 181 of SEQ ID NO: 1, position 137, position 139, and/or position 180 of SEQ ID NO: 2, position 137, position 139, and/or position 180 of SEQ ID NO: 3, or position 138, position 140, and/or position 181 of SEQ ID NO: 4;

c) the first variant feline IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 154 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118; and/or

d) the second variant feline IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 154, position 156, and/or position 197 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

Embodiment 64. The heterodimeric protein of embodiment 63, wherein the first wild-type canine IgG Fc polypeptide and the second wild-type canine IgG Fc polypeptide are from the same IgG subtype and/or the first wild-type feline IgG Fc polypeptide and the second wild-type feline IgG Fc polypeptide are from the same IgG subtype.

Embodiment 65. The heterodimeric protein of embodiment 63, wherein the first wild-type canine IgG Fc polypeptide and the second wild-type canine IgG Fc polypeptide are from a different IgG subtype and/or the first wild-type feline IgG Fc polypeptide and the second wild-type feline IgG Fc polypeptide are from the same IgG subtype.

Embodiment 66. The heterodimeric protein of any one of embodiments 63 to 65, wherein:

a) the first variant canine IgG Fc polypeptide comprises a tyrosine or tryptophan at a position corresponding to position 138 of SEQ ID NO: 1, position 137 of SEQ ID NO: 2, position 137 of SEQ ID NO: 3, or position 138 of SEQ ID NO: 4; and/or

b) the first variant feline IgG Fc polypeptide comprises a tryptophan at a position corresponding to position 154 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

Embodiment 67. The heterodimeric protein of any one of embodiments 63 to 66, wherein:

a) the second variant canine IgG Fc polypeptide comprises a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 1, a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 2, a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 3, and/or a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 4; and/or

b) the second variant feline IgG Fc polypeptide comprises a serine at a position corresponding to position 154, an alanine at a position corresponding to position 156, and/or a threonine at a position corresponding to position 197 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

Embodiment 68. The heterodimeric protein of any one of embodiments 63 to 67, wherein:

a) the first variant canine IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, or SEQ ID NO: 115; and/or

b) the first variant feline IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

Embodiment 69. The heterodimeric protein of any one of embodiments 63 to 68, wherein:

a) the second variant canine IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, or SEQ ID NO: 116; and/or

b) the second variant feline IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 123.

Embodiment 70. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 69, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type IgG Fc polypeptide and has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.

Embodiment 71. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 70, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 205 of SEQ ID NO: 1, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 1;

b) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 24 of SEQ ID NO: 3;
or

c) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 4, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 4.

Embodiment 72. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 71, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) an amino acid substitution at position 21 of SEQ ID NO: 1, an amino acid substitution at position 23 of SEQ ID NO: 1, an amino acid substitution at position 25 of SEQ ID NO: 1, an amino acid substitution at position 80 of SEQ ID NO: 1, an amino acid substitution at position 205 of SEQ ID NO: 1, and/or an amino acid substitution at position 207 of SEQ ID NO: 1;

b) an amino acid substitution at position 21 of SEQ ID NO: 3, an amino acid substitution at position 23 of SEQ ID NO: 3, and/or an amino acid substitution at position 24 of SEQ ID NO: 3; or

c) an amino acid substitution at position 21 of SEQ ID NO: 4, an amino acid substitution at position 23 of SEQ ID NO: 4, an amino acid substitution at position 25 of SEQ ID NO: 4, an amino acid substitution at position 80 of SEQ ID NO: 4, and/or an amino acid substitution at position 207 of SEQ ID NO: 4.

Embodiment 73. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 72, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) a threonine at a position corresponding to position 21 of SEQ ID NO: 1, a leucine at a position corresponding to position 23 of SEQ ID NO: 1, an alanine at a position corresponding to position 25 of SEQ ID NO: 1, a glycine at a position corresponding to position 80 of SEQ ID NO: 1, an alanine at a position corresponding to position 205 of SEQ ID NO: 1, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 1;

b) a threonine at a position corresponding to position 21 of SEQ ID NO: 3, a leucine at a position corresponding to position 23 of SEQ ID NO: 3, and/or an isoleucine at a position corresponding to position 24 of SEQ ID NO: 3; or

c) a threonine at a position corresponding to position 21 of SEQ ID NO: 4, a leucine at a position corresponding to position 23 of SEQ ID NO: 4, an alanine at a position corresponding to position 25 of SEQ ID NO: 4, a glycine at a position corresponding to position 80 of SEQ ID NO: 4, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 4.

Embodiment 74. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 73, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) a threonine at position 21 of SEQ ID NO: 1, a leucine at position 23 of SEQ ID NO: 1, an alanine at position 25 of SEQ ID NO: 1, a glycine at position 80 of SEQ ID NO: 1, an alanine at position 205 of SEQ ID NO: 1, and/or a histidine at position 207 of SEQ ID NO: 1;

b) a threonine at position 21 of SEQ ID NO: 3, a leucine at position 23 of SEQ ID NO: 3, and/or an isoleucine at position 24 of SEQ ID NO: 3; or

c) a threonine at position 21 of SEQ ID NO: 4, a leucine at position 23 of SEQ ID NO: 4, an alanine at position 25 of SEQ ID NO: 4, a glycine at position 80 of SEQ ID NO: 4, and/or a histidine at position 207 of SEQ ID NO: 4.

Embodiment 75. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 74, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type IgG Fc polypeptide and has decreased binding affinity to CD16 relative to the wild-type IgG Fc polypeptide.

Embodiment 76. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 75, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 2, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 2; or

b) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 3.

Embodiment 77. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 76, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) an amino acid substitution at position 5 of SEQ ID NO: 2, an amino acid substitution at position 38 of SEQ ID NO: 2, an amino acid substitution at position 39 of SEQ ID NO: 2, an amino acid substitution at position 97 of SEQ ID NO: 2, and/or an amino acid substitution at position 98 of SEQ ID NO: 2; or

b) an amino acid substitution at position 5 of SEQ ID NO: 3, an amino acid substitution at position 38 of SEQ ID NO: 3, an amino acid substitution at position 39 of SEQ ID NO: 3, an amino acid substitution at position 97 of SEQ ID NO: 3, and/or an amino acid substitution at position 98 of SEQ ID NO: 3.

Embodiment 78. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 77, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) a proline at a position corresponding to position 5 of SEQ ID NO: 2, a glycine at a position corresponding to position 38 of SEQ ID NO: 2, an arginine at a position

corresponding to position 39 of SEQ ID NO: 2, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 2, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 2; or

b) a proline at a position corresponding to position 5 of SEQ ID NO: 3, a glycine at a position corresponding to position 38 of SEQ ID NO: 3, an arginine at a position corresponding to position 39 of SEQ ID NO: 3, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 3, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 3.

Embodiment 79. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 78, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

a) a proline at position 5 of SEQ ID NO: 2, a glycine at position 38 of SEQ ID NO: 2, an arginine at position 39 of SEQ ID NO: 2, an isoleucine at position 97 of SEQ ID NO: 2, and/or a glycine at position 98 of SEQ ID NO: 2; or

b) a proline at position 5 of SEQ ID NO: 3, a glycine at position 38 of SEQ ID NO: 3, an arginine at position 39 of SEQ ID NO: 3, an isoleucine at position 97 of SEQ ID NO: 3, and/or a glycine at position 98 of SEQ ID NO: 3.

Embodiment 80. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 79, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type canine IgG Fc polypeptide and has decreased binding affinity to C1q relative to the wild-type canine IgG Fc polypeptide.

Embodiment 81. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 80, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 2, or an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 3.

Embodiment 82. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 81, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an amino acid substitution at position 93 of SEQ ID NO: 2, or an amino acid substitution at position 93 of SEQ ID NO: 3.

Embodiment 83. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 82, wherein the variant IgG Fc polypeptide, the first

variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an arginine at a position corresponding to position 93 of SEQ ID NO: 2, or an arginine at a position corresponding to position 93 of SEQ ID NO: 3.

Embodiment 84. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 42 to 83, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an arginine at position 93 of SEQ ID NO: 2, or an arginine at position 93 of SEQ ID NO: 3.

Embodiment 85. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 1 to 84, wherein the polypeptide is an antibody, an antibody fusion, or a fusion polypeptide.

Embodiment 86. A contiguous polypeptide comprising:

- a) a first glucagon-like peptide-1 (GLP1) polypeptide (GLP1A);
- b) a first linker (L1);
- c) an Fc polypeptide (Fc) of a companion animal species;
- d) optionally, a second linker (L2); and
- e) optionally, a second GLP1 polypeptide (GLP1B).

Embodiment 87. The contiguous polypeptide of embodiment 65 comprising:

formula (I): GLP1A—L1—Fc; or

formula (II): Fc—L1—GLP1A.

Embodiment 88. The contiguous polypeptide of embodiment 65 comprising:

formula (III): GLP1A—L1—Fc—L2—GLP1B.

Embodiment 89. The contiguous polypeptide of any one of embodiments 86 to 88, wherein GLP1B, if present, comprises the same amino acid sequence as GLP1A.

Embodiment 90. A contiguous polypeptide comprising:

- a) a glucagon-like peptide-1 (GLP1) polypeptide;
- b) a first linker (L1);
- c) an Fc polypeptide (Fc);
- d) a second linker (L2); and
- e) a glucagon polypeptide (Gluc).

Embodiment 91. The contiguous polypeptide of embodiment 90 comprising:

Formula (IV): GLP1—L1—Fc—L2—Gluc; or

Formula (V): Gluc—L1—Fc—L2—GLP1.

Embodiment 92. The contiguous polypeptide of any one of embodiments 86 to 91, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises a wild-type GLP1 polypeptide.

Embodiment 93. The contiguous polypeptide of any one of embodiments 86 to 92, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises a variant GLP1 polypeptide.

Embodiment 94. The contiguous polypeptide of any one of embodiments 86 to 93, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises an amino acid sequence of SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 98, or SEQ ID NO: 99.

Embodiment 95. The contiguous polypeptide of any one of embodiments 86 to 94, wherein the glucagon polypeptide comprises a wild-type glucagon polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 21.

Embodiment 96. The contiguous polypeptide of any one of embodiments 86 to 95, wherein the glucagon polypeptide is a variant glucagon polypeptide.

Embodiment 97. The contiguous polypeptide of any one of embodiments 86 to 96, wherein the Fc polypeptide is a human IgG Fc.

Embodiment 98. The contiguous polypeptide of any one of embodiments 86 to 97, wherein the Fc polypeptide is a human IgG1 Fc, IgG2 Fc, IgG3 Fc, or IgG4 Fc.

Embodiment 99. The contiguous polypeptide of any one of embodiments 86 to 98, wherein the Fc polypeptide is an Fc of a companion animal species.

Embodiment 100. The contiguous polypeptide of any one of embodiments 86 to 97 or 99, wherein the Fc polypeptide comprises:

- a) a canine IgG-A Fc, IgG-B Fc, IgG-C Fc, or IgG-D Fc;
- b) an equine IgG1 Fc, IgG2 Fc, IgG3 Fc, IgG4 Fc, IgG5 Fc, IgG6 Fc, or IgG7 Fc; or
- c) a feline IgG1a Fc, IgG1b Fc, or IgG2 Fc.

Embodiment 101. The contiguous polypeptide of any one of embodiments 86 to 100, wherein the Fc polypeptide is a wild-type IgG Fc polypeptide.

Embodiment 102. The contiguous polypeptide of any one of embodiments 86 to 100, wherein the Fc polypeptide is a variant IgG Fc polypeptide.

Embodiment 103. The contiguous polypeptide of any one of embodiments 86 to 102, wherein the Fc polypeptide comprises the polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of embodiments 1 to 84.

Embodiment 104. The contiguous polypeptide of any one of embodiments 85 to 102, wherein the contiguous polypeptide has a longer serum half-life than a wild-type GLP1 polypeptide.

Embodiment 105. The contiguous polypeptide of any one of embodiments 86 to 104, wherein L1 and L2, if present, each independently is a flexible linker.

Embodiment 106. The contiguous polypeptide of any one of embodiments 86 to 105, wherein the amino acid sequence of L1 and L2, if present, each independently comprises 100%, at least 95%, at least 90%, at least 85% serine and/or glycine amino acid residues.

Embodiment 107. The contiguous polypeptide of any one of embodiments 86 to 106, wherein the contiguous polypeptide comprises an extension at its C-terminus.

Embodiment 108. The contiguous polypeptide of any one of embodiments 86 to 107, wherein the contiguous polypeptide comprises a glycine residue, two glycine residues, three glycine residues, four glycine residues, five glycine residues, six glycine residues, seven glycine residues, eight glycine residues, or greater than eight glycine residues at its C-terminus.

Embodiment 109. The contiguous polypeptide of any one of embodiments 86 to 108, wherein the contiguous polypeptide comprises an amino acid sequence of SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, or SEQ ID NO: 95 at its C-terminus.

Embodiment 110. The contiguous polypeptide of any one of embodiments 86 to 109, wherein the contiguous polypeptide comprises:

a) the amino acid sequence of SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29; SEQ ID NO: 30; SEQ ID NO: 31; SEQ ID NO: 32; SEQ ID NO: 33; SEQ ID NO: 34; SEQ ID NO: 35; SEQ ID NO: 36; SEQ ID NO: 37; SEQ ID NO: 38; SEQ ID NO: 39; SEQ ID NO: 40; SEQ ID NO: 41; SEQ ID NO: 42; SEQ ID NO: 43; SEQ ID NO: 44; SEQ ID NO: 45; SEQ ID NO: 46; SEQ ID NO: 47, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, or SEQ ID NO: 106; or

b) the amino acid sequence of SEQ ID NO: 52; SEQ ID NO: 53; SEQ ID NO: 54; SEQ ID NO: 55; SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; or SEQ ID NO: 59.

Embodiment 111. A polypeptide comprising an amino acid sequence of SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29; SEQ ID NO: 30; SEQ ID NO: 31; SEQ ID NO: 32; SEQ ID NO: 33; SEQ ID NO: 34; SEQ ID NO: 35; SEQ ID NO: 36; SEQ ID NO: 37; SEQ ID NO: 38; SEQ ID NO: 39; SEQ ID NO: 40; SEQ ID NO: 41; SEQ ID NO: 42; SEQ ID NO: 43; SEQ ID NO: 44; SEQ ID NO: 45; SEQ ID NO: 46; SEQ ID NO: 47, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 52; SEQ ID NO: 53; SEQ ID NO: 54; SEQ ID NO: 55; SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 103; SEQ ID NO: 104, SEQ ID NO: 105, or SEQ ID NO: 106.

Embodiment 112. The polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of the preceding embodiments, wherein the at least one amino acid modification or substitution comprises an amino acid substitution with an amino acid derivative.

Embodiment 113. An isolated nucleic acid encoding the polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of the preceding embodiments.

Embodiment 114. A host cell comprising the nucleic acid of embodiment 113.

Embodiment 115. A method of producing a polypeptide comprising culturing the host cell of embodiment 114 and isolating the polypeptide.

Embodiment 116. A pharmaceutical composition comprising the polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of embodiments 1 to 112, and a pharmaceutically acceptable carrier.

Embodiment 117. A method of increasing production of cAMP in a cell, the method comprising exposing the cell to the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of embodiments 1 to 112 or 116 under conditions permissive for binding of the polypeptide, heterodimeric protein, or contiguous polypeptide to GLP1R.

Embodiment 118. The method of embodiment 117, wherein the cell is exposed to the polypeptide, heterodimeric protein, contiguous polypeptide, or the pharmaceutical composition *ex vivo*.

Embodiment 119. The method of embodiment 117, wherein the cell is exposed to the polypeptide, heterodimeric protein, contiguous polypeptide, or the pharmaceutical composition *in vivo*.

Embodiment 120. The method of any one of embodiments 118 to 119, wherein the cell is a human cell, a canine cell, a feline cell, or an equine cell.

Embodiment 121. A method of delivering a polypeptide to a subject comprising administering the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of embodiments 1 to 112 or 116 parenterally.

Embodiment 122. A method of delivering a polypeptide to a subject comprising administering the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of embodiments 1 to 112 or 116 by an intramuscular route, an intraperitoneal route, an intracerebrospinal route, a subcutaneous route, an intra-arterial route, an intrasynovial route, an intrathecal route, or an inhalation route.

Embodiment 123. A method of treating a subject having diabetes or obesity, the method comprising administering to the subject a therapeutically effective amount of the

polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of embodiments 1 to 112 or 116.

Embodiment 124. The method of embodiment 123, comprising administering insulin, a DPP4 inhibitor, a SGLT2 inhibitor, a biguanides sulfonylureas meglitinide derivative, an alpha-glucosidase inhibitor, a thiazolidinedion (TZD), an amylinomimetic, a bile acid sequestrant, a dopamine agonist.

Embodiment 125. The method of any one of embodiments 121 to 124, wherein the subject is a human subject.

Embodiment 126. The method of any one of embodiments 121 to 124, wherein the subject is a companion animal species.

Embodiment 127. The method of embodiment 126, wherein the companion animal species is canine, equine, or feline.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] Figure 1 shows an alignment of canine IgG-A, B, C, and D Fc sequences. The boxes indicate the regions likely in contact with Protein A.

[0007] Figure 2A shows an SDS-PAGE analysis of GLP1-G8/GLP-2G_III_WTfeIgG2 (SEQ ID NO: 23; “GLP1 A variant” in this figure) and GLP1-G8_I_WTfeIgG2 (SEQ ID NO: 24; “GLP1 B variant” in this figure) having wild-type feline IgG2 hinge with one disulfide bond in the absence and presence of reducing agent (DTT).

[0008] Figure 2B shows an SDS-PAGE analysis of GLP1-G8/GLP-2G_III_VARfeIgG2 (SEQ ID NO: 25; “GLP1 MA variant” in this figure) of GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26; “GLP1 MB variant” in this figure) having variant feline IgG2 hinge with two disulfide bonds in the absence and presence of reducing agent (DTT).

[0009] Figure 3 shows a cAMP CHO-K1 GLP1R Bioassay to evaluate activity of GLP1-G8/GLP1-2G_III_VARfeIgG2 (SEQ ID NO: 25) and GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) compared to controls (GLP1 (7-37) and Extendin-4).

[0010] Figure 4 shows a cell-based bioassay to evaluate activity of GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) (“GLP1-B” in this figure) after 1 year of storage with CHOK1-GLP1R cells and cAMP-glo (n=2).

[0011] Figure 5 shows a Western Blot analysis of GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) (“GLP1B” in this figure) after incubation in serum for 24 hours at 37°C (lane 1), in PBS for 24 hours at 37°C (lane 2), in PBS for 24 hours at 4°C (lane 9). A mouse anti-GLP1 antibody was used.

[0012] Figure 6 is a plot of GLP1-G8_I_VARfIgG2 (SEQ ID NO:26) concentration in the serum over time after subcutaneous administration to 5 cats, as measured by quantitative ELISA.

[0013] Figure 7 shows a plot of GLP1-G8_I_VARfIgG2 (SEQ ID NO:26) concentration in the serum over time after subcutaneous administration to 5 cats, as measured by cell-based activity assay. The mean AUC from 0 to 168 hours was about 840 $\mu\text{g(h)}/\text{mL}$ and the mean $t_{1/2}$ was 36 hours.

DESCRIPTION OF THE SEQUENCES

[0014] Table 1 provides a listing of exemplary sequences referenced herein.

Table 1: Description of the Sequences		
SEQ ID NO:	SEQUENCE	DESCRIPTION
1	PVPEPLGGPSVLIFFPKPKDILRITRTPVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE QQFNGTYRVVSVLPPIHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNQQE PERKHRMTPPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSSLHSPGK	Exemplary wild-type canine IgG-A Fc Protein A – C1q – CD16 –
2	PAPEMPLGGPSVFIFFPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPPIHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary wild-type canine IgG-B Fc Protein A + C1q + CD16 +
107	PKRENGRVPRPPDCPKCPAPEMPLGGPSVFIFFP PKPDITLLIARTPEVTCVVVDLDPEDPEVQISW FVDGKQMOTAKTQPREEQFNGTYRVVSVLPPIG HQDWLKGKQFTCKVNNKALPSPIERTISKARG QAHQPSVYVLPSPREELSKNTVSLTCLIKDFF PPDIDVEWQSNQQEPESKYRTTPPQLDEDGS YFLYSKLSVDKSRWQRGDTFICAVMHEALHNH YTQESLSHSPGK	Exemplary wild-type canine IgG-B Fc with hinge Protein A + C1q + CD16 +
3	PGCGLLGGPSVFIFFPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPPIHQDWLSGKQFKCKVNN KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary wild-type canine IgG-C Fc Protein A – C1q + CD16 +
108	AKECECKCNCNNPCPGCGLLGGPSVFIFFPK PKDILVTARTPTVTCVVVDLDPENPEVQISWF VDSKQVQTANTQPREEQSNGTYRVVSVLPPIG QDWLSGKQFKCKVNNKALPSPIEEIISKTPGQ AHQPNVYVLPSPRDEMKNVTTLTCLVKDFFP	Exemplary wild-type canine IgG-C Fc with hinge Protein A – C1q +

	PEIDVEWQSNGQQEPESKYRMTTPQLDEDGSY FLYSKLSVDKSRWQRGDTFICAVMHEALHNHY TQISLSHSPGK	CD16 +
4	PVPESLGGPSVFIFPPKPKDILRITRTPEITC VVLDLGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLP ^{IEHQDWLTGKEFKCRVNH} IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFPPEIDVEWQSNGQPE PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDL ^{SLSHSPGK}	Exemplary wild-type canine IgG-D Fc Protein A – C1q – CD16 –
5	PVPEPLGGPSVLIFFPPKPKD ^{TLLI} ARTPEVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE QQFNSTYRVVSVLP ^{IGHQDWLTGKEFKCRVNH} IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNGQQE PERKHRMTTPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHE ^{ALHN} HYTDL ^{SLSHSPGK}	Exemplary variant canine IgG-A Fc C1q – Protein A + I(21)T R(23)L T(25)A E(80)G T(205)A Q(207)H
6	PGCGLLGGPSVFIFPPKPKD ^{TLLI} ARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLP ^{IGHQDWLSGKQFKCKVNN} KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTTLTCLVKDFFPPEIDVEWQSNGQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc C1q + Protein A + I(21)T V(23)L T(24)I
7	PVPESLGGPSVFIFPPKPKD ^{TLLI} ARTPEITC VVLDLGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLP ^{IGHQDWLTGKEFKCRVNH} IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFPPEIDVEWQSNGQPE PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEAL ^{HN} HYTDL ^{SLSHSPGK}	Exemplary variant canine IgG-D Fc C1q – Protein A + I(21)T R(23)L T(25)A E(80)G Q(207)H
8	PVPEPLGGPSVLIFFPPKPKDILRITRTPEVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE QQFNSTYRVVSVLP ^{IEHQDWLTGKEFKCRVNH} IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSI ^Y CLIKDFYPPDIDVEWQSNGQQE PERKHRMTTPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDL ^{SLSHSPGK}	Exemplary variant canine IgG-A Fc Heterodimer chain 1 T(138)Y
9	PVPEPLGGPSVLIFFPPKPKDILRITRTPEVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE QQFNSTYRVVSVLP ^{IEHQDWLTGKEFKCRVNH} IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNGQQE PERKHRMTTPQLDEDGSYFL ^T SKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDL ^{SLSHSPGK}	Exemplary variant canine IgG-A Fc Heterodimer chain 2 Y(181)T

10	PAP EMLGGPSVFIFPPKPKD TLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMQTAKTQPRE EQFNGTYRVVSVLP IGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSL <u>Y</u> CLIKDFFPPDIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Heterodimer chain 1 T(137)Y
11	PAP EMLGGPSVFIFPPKPKD TLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMQTAKTQPRE EQFNGTYRVVSVLP IGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFL <u>T</u> SKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Heterodimer chain 2 Y(180)T
12	PGCGLLGGPSVFIFPPKPKD ILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLP IGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLY <u>Y</u> CLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Heterodimer chain 1 T(137)Y
13	PGCGLLGGPSVFIFPPKPKD ILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLP IGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTTLTCLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPPQLDEDGSYFL <u>T</u> SKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Heterodimer chain 2 Y(180)T
14	PVPESLGGPSVFIFPPKPKD ILRITRTPEITC VVLDLGGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLP IGHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTL <u>Y</u> CLIKDFFPPEIDVEWQSNQQEP PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary variant canine IgG-D Fc Heterodimer chain 1 T(138)Y
15	PVPESLGGPSVFIFPPKPKD ILRITRTPEITC VVLDLGGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLP IGHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFFPPEIDVEWQSNQQEP PESKYHTTAPQLDEDGSYFL <u>T</u> SKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary variant canine IgG-D Fc Heterodimer chain 2 Y(181)T
109	PVPEPLGGPSVLIFFPPKPKD ILRITRTPEVTC VVLDLGGREDPEVQISWFVDGKEVHTAKTQSRE QQFNGTYRVVSVLP IGHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSI <u>W</u> CLIKDFYPPDIDVEWQSNQQEP PERKHRMTTPPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSLSHSPGK	Exemplary variant canine IgG-A Fc Heterodimer chain 3 T(138)W
110	PVPEPLGGPSVLIFFPPKPKD ILRITRTPEVTC VVLDLGGREDPEVQISWFVDGKEVHTAKTQSRE QQFNGTYRVVSVLP IGHQDWLTGKEFKCRVNH	Exemplary variant canine IgG-A Fc

	IDLPSPIERTISKARGRAHKPSVYVLPPSPKE LSSSDTVSI <u>SCA</u> IKDFYPPDIDVEWQSNQQE PERKHRMTPPQLDEDGSYFL <u>T</u> SKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSLSHSPGK	Heterodimer chain 4 T(138)S L(140)A Y(181)T
111	PAPEMPLGGPSVFIFPPKPKDILLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMQTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSL <u>W</u> CLIKDFFPPDIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Heterodimer chain 3 T(137)W
112	PAPEMPLGGPSVFIFPPKPKDILLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMQTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSL <u>SCA</u> IKDFFPPDIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFL <u>T</u> SKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Heterodimer chain 4 T(137)S L(139)A Y(180)T
113	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEIISKTPGQAHQPNVYVLPPSRDE MSKNTVT <u>LW</u> CLVKDFFPPEIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Heterodimer chain 3 T(137)W
114	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEIISKTPGQAHQPNVYVLPPSRDE MSKNTVT <u>LSCA</u> VKDFFPPEIDVEWQSNQQEP ESKYRTTPPQLDEDGSYFL <u>T</u> SKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Heterodimer chain 4 T(137)S L(139)A Y(180)T
115	PVPESLGGPSVFIFPPKPKDILRITRTPETC VVLDLGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLPIDHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPPSPKE LSSSDTVTL <u>W</u> CLIKDFFPPEIDVEWQSNQQEP PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary variant canine IgG-D Fc Heterodimer chain 3 T(138)W
116	PVPESLGGPSVFIFPPKPKDILRITRTPETC VVLDLGREDPEVQISWFVDGKEVHTAKTQPRE QQFNSTYRVVSVLPIDHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPPSPKE LSSSDTVTL <u>SCA</u> IKDFFPPEIDVEWQSNQQEP PESKYHTTAPQLDEDGSYFL <u>T</u> SKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary variant canine IgG-D Fc Heterodimer chain 4 T(138)S L(140)A Y(181)T
16	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVSVTCLIKGF	Exemplary wild-type feline IgG2 Fc Protein A + C1q –

	HPPDIAVEWEITGQPEPENNYQTTPPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	
117	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary wild-type feline IgG1a Fc Protein A + C1q +
118	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary wild-type feline IgG1b Fc Protein A + C1q +
119	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVS W CLIKGF HPPDIAVEWEITGQPEPENNYQTTPPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG2 Fc Heterodimer chain 1 T(154)W
120	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVS S <u>CA</u> IKGF HPPDIAVEWEITGQPEPENNYQTTPPQLDSDG TYFL T SRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG2 Fc Heterodimer chain 2 T(154)S L(156)A Y(197)T
121	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVS W CLIKSF HPPDIAVEWEITGQPEPENNYRTTPPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1a Fc Heterodimer chain 1 T(154)W
122	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVS S <u>CA</u> IKSF HPPDIAVEWEITGQPEPENNYRTTPPQLDSDG TYFV T SKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1a Fc Heterodimer chain 2 T(154)S L(156)A Y(197)T

123	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPAPAEELSENKVS W CLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1b Fc Heterodimer chain 1 T(154)W
124	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPAPAEELSENKVS SCA IEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFL T SRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1b Fc Heterodimer chain 2 T(154)S L(156)A Y(197)T
17	PKTASTIESKTGE C PKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG2 Fc Hinge Cys G(14)C
125	<i>RKTDHPPGPKPCDCPKCPPPEMLGGPSVFIFP</i> PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG2 Fc with feline IgG1 hinge
126	PKTASTIESKTGEG P CPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKVSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG2 Fc with modified hinge K(16)P
127	RKTDHPPGPKPCDC P CPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1a Fc with modified hinge K(16)P
128	RKTDHPPGPKPCDC P CPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK	Exemplary variant feline IgG1b Fc with modified hinge

	GQPHEPQVYVLPAPAEELSENKVSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	K(16)P
18	<u>DMSKCPKCPAPELL</u> GGPSVFI FPPNPKDALMI SRTFVVTCTVVNLSDQYPDVQFSWYVDNTEVH SAITKQREAFNSTYRVVSVLP IQH QDWLSGK EFKCSVTNVGVPQPISR AISRGKGPSRVPQVY VLPPHPDELAKSKVSVTCLVKDFYPPDISVEW QSNRWPELEGKYSTTPAQLDGDGSYFLYSKLS LETSRWQQVESFTCAVMHEALHNHFTKTDISE SLGK	Exemplary variant equine Fc IgG2 (with equine IgG1 hinge) Protein A – C1q –
19	<u>DMSKCPKCPAPELL</u> GGPSVFI FPPNPKD <u>TL</u> MI SRTFVVTCTVVNLSDQYPDVQFSWYVDNTEVH SAITKQREAFNSTYRVVSVLP IQH QDWLSGK EFKCSVTNVGVPQPISR AISRGKGPSRVPQVY VLPPHPDELAKSKVSVTCLVKDFYPPDISVEW QSNRWPELEGKYSTTPAQLDGDGSYFLYSKLS LETSRWQQVESFTCAVMHEALHNH <u>Y</u> TKTDISE SLGK	Exemplary variant equine IgG2 Fc (with equine IgG1 hinge) C1q – Protein A + A(29)T F(217)Y
20	H <u>X</u> EGTFTSDVSSYLEGQAAKEFIAWL VKG	Exemplary variant GLP1 (7- 35) X8 may be G or S
21	HSQGTFTSDYSKYLD SRR AQDFVQWLMNT	Glucagon (Gluc)
22	HGEFTFTSDLSKQMEEEAVRLFIEWLKNGGPS SGAPPPS	Extendin-4
23	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWL VKG GGG SGGGSGGGSGGGSPKTA TIESKTGEGPK CPVPEIPGAPSVFI FPPKPKDTLSISRTPEVT CLVVDLGPDDSNVQITWFVDNTEMHTAKTRPR EEQFNSTYRVVSVLPILHQDWLKGKEFKCKVN SKSLPSAMERTISKAKGQPHEPQVYVLPPTQE ELSENKVSVTCLIKGFHPPDIAVEWEITGQPE PENNYQTTPQLDSDGTYFLYSRLSVDRSHWQ RGNTYTCSVSHEALHSHTQKSLTQSPGK GGG GSGGGGHAEGTFTSDVSSYLEGQAAKEFIAWL VKGGG	GLP1-G8/GLP-2G_III_ WTfeIgG2
24	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWL VKG GGG SGGGSGGGSGGGSPKTA TIESKTGEGPK CPVPEIPGAPSVFI FPPKPKDTLSISRTPEVT CLVVDLGPDDSNVQITWFVDNTEMHTAKTRPR EEQFNSTYRVVSVLPILHQDWLKGKEFKCKVN SKSLPSAMERTISKAKGQPHEPQVYVLPPTQE ELSENKVSVTCLIKGFHPPDIAVEWEITGQPE PENNYQTTPQLDSDGTYFLYSRLSVDRSHWQ RGNTYTCSVSHEALHSHTQKSLTQSPGK	GLP1-G8_I_WTfeIgG2
25	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWL VKG GGG SGGGSGGGSGGGSPKTA TIESKTGE <u>CP</u> K CPVPEIPGAPSVFI FPPKPKDTLSISRTPEVT CLVVDLGPDDSNVQITWFVDNTEMHTAKTRPR	GLP1-G8/GLP1-2G_III_ VARfeIgG2

	EEQFNSTYRVVSVLPILHQDWLKGKEFKCKVN SKSLPSAMERTISKAKGQPHEPQVYVLPPTQE ELSENKVSVTCLIKGFHPPDIAVEWEITGQPE PENNYQTTPPQLDSDGTYFLYSRLSVDRSHWQ RGNTYTCSVSHEALHSHHTQKSLTQSPGKGGG GSGGGGHAEGTFTSDVSSYLEGQAAKEFIAWL VKGGG	
26	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGG SGGGSGGGSGGGSGGGSPKTASTIESKTGE <u>C</u> PK CPVPEIPGAPSVFIFPPKPKDTLSISRTPEVT CLVVDLGPDDSNVQITWFVDNTEMHTAKTRPR EEQFNSTYRVVSVLPILHQDWLKGKEFKCKVN SKSLPSAMERTISKAKGQPHEPQVYVLPPTQE ELSENKVSVTCLIKGFHPPDIAVEWEITGQPE PENNYQTTPPQLDSDGTYFLYSRLSVDRSHWQ RGNTYTCSVSHEALHSHHTQKSLTQSPGK	GLP1-G8_I_VARfeIgG2
27	H <u>S</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSPKTASTIESKTGEGP KCPVPEIPGAPSVFIFPPKPKDTLSISRTPEV TCLVVDLGPDDSNVQITWFVDNTEMHTAKTRP REEQFNSTYRVVSVLPILHQDWLKGKEFKCKV NSKSLPSAMERTISKAKGQPHEPQVYVLPPTQ EELSENKVSVTCLIKGFHPPDIAVEWEITGQP EPENNYQTTPPQLDSDGTYFLYSRLSVDRSHW QRGNTYTCSVSHEALHSHHTQKSLTQSPGKGG GGSGGGGHAEGTFTSDVSSYLEGQAAKEFIAW LVKGGG	GLP1-S8/GLP1-3G_III_ WTfeIgG2
28	H <u>S</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSPKTASTIESKTGEGP KCPVPEIPGAPSVFIFPPKPKDTLSISRTPEV TCLVVDLGPDDSNVQITWFVDNTEMHTAKTRP REEQFNSTYRVVSVLPILHQDWLKGKEFKCKV NSKSLPSAMERTISKAKGQPHEPQVYVLPPTQ EELSENKVSVTCLIKGFHPPDIAVEWEITGQP EPENNYQTTPPQLDSDGTYFLYSRLSVDRSHW QRGNTYTCSVSHEALHSHHTQKSLTQSPGK	GLP1-S8_I_WTfeIgG2
29	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSPKESTSKCISPCVP ESLGGPSVFIFPPKPKD <u>TLLI</u> ARTPEITCVVL DLGREDPEVQISWFVDGKEVHTAKTQPREQQF NSTYRVVSVLP <u>I</u> <u>G</u> HQDWLTGKEFKCRVNHIGL PSPIERTISKARGQAHQPSVYVLPSPKELSS SDTVTLTCLIKDFPPEIDVEWQSNQPEPES KYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGD TFTCAVMHEAL <u>H</u> NHYTDLSSLHSPGKGGGGSG GGGHAEGTFTSDVSSYLEGQAAKEFIAWLVKG GGG	GLP1-G8/GLP1-3G_III_ VARcalgGD
30	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSPKESTCKCISPCVP ESLGGPSVFIFPPKPKD <u>TLLI</u> ARTPEITCVVL DLGREDPEVQISWFVDGKEVHTAKTQPREQQF NSTYRVVSVLP <u>I</u> <u>G</u> HQDWLTGKEFKCRVNHIGL	GLP1-G8_I_VARcalgGD

	PSPIERTISKARGQAHQPSVYVLPSPKELSS SDTVTLTCLIKDFFPPEIDVEWQSNQPEPES KYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGD TFTCAVMHEALHNHYTDLSLSHSPGK	
31	HSEGTFTSDVSSYLEGQAAKEFIAWLKGGAG GGGGSGGGSGGGSGGGSPKESTSKCISPCVP ESLGGPSVFI FPPKPKD TLLIA RTPEITCVVL DLGREDPEVQISWFVDGKEVHTAKTQPREQQF NSTYRVSVLPI GH QDWLTGKEFKCRVNHIGL PSPIERTISKARGQAHQPSVYVLPSPKELSS SDTVTLTCLIKDFFPPEIDVEWQSNQPEPES KYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGD TFTCAVMHEALHNHYTDLSLSHSPGKGGGGSG GGGHAEGTFTSDVSSYLEGQAAKEFIAWLKGG GGG	GLP1-S8/GLP1-3G_III_ VARcalgGD
32	HSEGTFTSDVSSYLEGQAAKEFIAWLKGGAG GGGGSGGGSGGGSGGGSPKESTCKCISPCVP ESLGGPSVFI FPPKPKD TLLIA RTPEITCVVL DLGREDPEVQISWFVDGKEVHTAKTQPREQQF NSTYRVSVLPI GH QDWLTGKEFKCRVNHIGL PSPIERTISKARGQAHQPSVYVLPSPKELSS SDTVTLTCLIKDFFPPEIDVEWQSNQPEPES KYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGD TFTCAVMHEALHNHYTDLSLSHSPGK	GLP1-S8_I_VARcalgGD
33	HGEFTFTSDVSSYLEGQAAKEFIAWLKGGAG GGGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFI FPPNPKD TL MISRTPVVTCTVVNLSD QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLPIQHQDWLSGKEFKCSVTNVGVPQPI SRAISRKGKPSRVPQVYVLPHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLETSRWQQVESFTCA VMHEALHNHYTKTDISESLGKGGGGSGGGGHA EGTFTSDVSSYLEGQAAKEFIAWLKGGGG	GLP1-G8/GLPL1-3G_III_ VAReqIgG2
34	HGEFTFTSDVSSYLEGQAAKEFIAWLKGGAG GGGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFI FPPNPKD TL MISRTPVVTCTVVNLSD QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLPIQHQDWLSGKEFKCSVTNVGVPQPI SRAISRKGKPSRVPQVYVLPHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLETSRWQQVESFTCA VMHEALHNHYTKTDISESLGK	GLP1-G8_I_VAReqIgG2
35	HSEGTFTSDVSSYLEGQAAKEFIAWLKGGAG GGGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFI FPPNPKD TL MISRTPVVTCTVVNLSD QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLPIQHQDWLSGKEFKCSVTNVGVPQPI SRAISRKGKPSRVPQVYVLPHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLETSRWQQVESFTCA VMHEALHNHYTKTDISESLGKGGGGSGGGGHA	GLP1-S8/GLP1-3G_III_ VAReqIgG2

	EGTFTSDVSSYLEGQAAKEFIAWLVKGGG	
36	HSEGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFIFPPNPKDTLMISRTFVVTCTVVNLSD QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLPPIQHQDWLSGKEFKCSVTNVGVPQPI SRAISRKGKPSRVPQVYVLPHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLETSRWQQVESFTCA VMHEALHNHYTKTDISESLGK	GLP1-S8_I_VAREqIgG2
37	MAVLGLLFLCLVTFPSCVLSHSEGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGGG GGSPKTAETIESKTGEGPKCPVPEIPGAPSV FIFPPKPKDTLSISRTPEVTCLVVDLGPDDSN VQITWFVDNTEMHAKTRPREEQFNSTYRVVS VLPILHQDWLKGKEFKCKVNSKSLPSAMERTI SKAKGQPHEPQVYVLPPTQEELSENKVSVTCL IKGFHPPDIAVEWEITGQPEPENNYQTTPQL DSDGTYFLYSRLSVDRSHWQRGNTYTCSVSHE ALHSHHTQKSLTQSPGKGGGGSGGGGHAEGTF TSDVSSYLEGQAAKEFIAWLVKGGG	ssGLP1-S8/GLP1-3G_III_ WTfIgG2
38	MAVLGLLFLCLVTFPSCVLSHSEGTFTSDVSSY LEGQAAKEFIAWLVKGGGGSGGGSGGGSGG GGSPKTAETIESKTGECPKCPVPEIPGAPSVF IFPPKPKDTLSISRTPEVTCLVVDLGPDDSNV QITWFVDNTEMHAKTRPREEQFNSTYRVVSV LPILHQDWLKGKEFKCKVNSKSLPSAMERTIS KAKGQPHEPQVYVLPPTQEELSENKVSVTCLI KGFHPPDIAVEWEITGQPEPENNYQTTPQLD SDGTYFLYSRLSVDRSHWQRGNTYTCSVSHEA LHSHHTQKSLTQSPGKGGGGSGGGGHAEGTFT SDVSSYLEGQAAKEFIAWLVKGGG	ssGLP1-G8/GLP1-2G_III_ VARfIgG2
39	MAVLGLLFLCLVTFPSCVLSHSEGTFTSDVSSY LEGQAAKEFIAWLVKGGGGSGGGSGGGSGG GGSPKTAETIESKTGECPKCPVPEIPGAPSVF IFPPKPKDTLSISRTPEVTCLVVDLGPDDSNV QITWFVDNTEMHAKTRPREEQFNSTYRVVSV LPILHQDWLKGKEFKCKVNSKSLPSAMERTIS KAKGQPHEPQVYVLPPTQEELSENKVSVTCLI KGFHPPDIAVEWEITGQPEPENNYQTTPQLD SDGTYFLYSRLSVDRSHWQRGNTYTCSVSHEA LHSHHTQKSLTQSPGK	ssGLP1-G8_I_VARfIgG2
40	MAVLGLLFLCLVTFPSCVLSHSEGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGGG GGSPKTAETIESKTGEGPKCPVPEIPGAPSV FIFPPKPKDTLSISRTPEVTCLVVDLGPDDSN VQITWFVDNTEMHAKTRPREEQFNSTYRVVS VLPILHQDWLKGKEFKCKVNSKSLPSAMERTI SKAKGQPHEPQVYVLPPTQEELSENKVSVTCL IKGFHPPDIAVEWEITGQPEPENNYQTTPQL DSDGTYFLYSRLSVDRSHWQRGNTYTCSVSHE ALHSHHTQKSLTQSPGK	ssGLP1-S8_I_WTfIgG2

41	MAVLGLLLFCLVTFPSCVLSHGEGTFTSDVSSY LEGQAAKEFIAWLVKGGGSGGGSGGGSGGG GGSPKESTCKCISPCVPESLGGPSVFIFPPK PKDTLLIARTPEITCVVLDLGREDPEVQISWF VDGKEVHTAKTQPREQQFNSTYRVVSVLPIGH QDWLTGKEFKCRVNHIGLPSPIERTISKARGQ AHQPSVYVLPSPKELSSSDTVTLTCLIKDFF PPEIDVEWQSNQPEPESEKYHTTAPQLDEDGS YFLYSKLSVDKSRWQQGDTFTCAVMHEALHNH YTDLSLSHSPGKGGGSGGGGHAEGTFTSDVS SYLEGQAAKEFIAWLVKGGG	ssGLP1-G8/GLP1-2G_III_ VARcIgGD
42	MAVLGLLLFCLVTFPSCVLSHGEGTFTSDVSSY LEGQAAKEFIAWLVKGGGSGGGSGGGSGGG GGSPKESTSKCISPCVPESLGGPSVFIFPPK PKDTLLIARTPEITCVVLDLGREDPEVQISWF VDGKEVHTAKTQPREQQFNSTYRVVSVLPIGH QDWLTGKEFKCRVNHIGLPSPIERTISKARGQ AHQPSVYVLPSPKELSSSDTVTLTCLIKDFF PPEIDVEWQSNQPEPESEKYHTTAPQLDEDGS YFLYSKLSVDKSRWQQGDTFTCAVMHEALHNH YTDLSLSHSPGKGGGSGGGGHAEGTFTSDVS SYLEGQAAKEFIAWLVKGGG	ssGLP1-G8/GLP1-2G_III_ VARcIgGD
43	MAVLGLLLFCLVTFPSCVLSHSEGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGG GGGSPKESTSKCISPCVPESLGGPSVFIFPP KPKDTLLIARTPEITCVVLDLGREDPEVQISW FVDGKEVHTAKTQPREQQFNSTYRVVSVLPIGH HQDWLTGKEFKCRVNHIGLPSPIERTISKARG QAHQPSVYVLPSPKELSSSDTVTLTCLIKDF FPPEIDVEWQSNQPEPESEKYHTTAPQLDEDG SYFLYSKLSVDKSRWQQGDTFTCAVMHEALHN HYTDLSLSHSPGKGGGSGGGGHAEGTFTSDV SSYLEGQAAKEFIAWLVKGGG	ssGLP1-S8/GLP1-3G_III_ VARcIgGD
44	MAVLGLLLFCLVTFPSCVLSHGEGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGG GGGSDMSKCPKCPAPELLGGPSVFIFPPNPKD TLMISRTPVVTCTVVNLSQYPDVQFSWYVDN TEVHSAITKQREAQFNSTYRVVSVLPIQHQDW LSGKEFKCSVTNVGVPQPISRASRGKGPSRV PQVYVLPHPDELAKSKVSVTCLVKDFYPPDI SVEWQSNRWPELEGKYSTTPAQLDGDGSYFLY SKLSLETSRWQQVESFTCAVMHEALHNHYTKT DISESLGKGGGSGGGGHAEGTFTSDVSSYLE GQAAKEFIAWLVKGGG	ssGLP1-G8/GLP1-3G_III_ VAReqlgG2
45	MAVLGLLLFCLVTFPSCVLSHGEGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGG GGGSSVPKPQCPPYTHSKFLGGPSVFIFPPNP KDTLMISRTPVVTCTVVNLSQYPDVQFSWYV DNTEVHSAITKQREAQFNSTYRVVSVLPIQH DWLSGKEFKCSVTNVGVPQPISRASRGKGPS RVPQVYVLPHPDELAKSKVSVTCLVKDFYPP DISVEWQSNRWPELEGKYSTTPAQLDGDGSYF	ssGLP1-G8_I_VAReqlgG2

	LYSKLSLETSRWQQVESFTCAVMHEALHNH <u>Y</u> T KTDISESLGK	
46	MAVLGLLFCLVTFPSCVL <u>S</u> EGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGGG GGGSDMSKCPKCPAPELLGGPSVFIFPPNPKD <u>T</u> LMISRTPVVTCTVVNLSDQYPDVQFSWYVDN TEVHSAITKQREAFNSTYRVVSVLP IQHQDW LSGKEFKCSVTNVGVPQPI SRAISRKGPSRV PQVYVLP PHPDELAKSKVSVTCLVKDFYPPDI SVEWQSNRWPELEGKYSTTPAQLDGDGSYFLY SKLSLETSRWQQVESFTCAVMHEALHNH <u>Y</u> TKT DISESLGKGGGGSGGGGHAEGTFTSDVSSYLE GQAAKEFIAWLVKGGG	ssGLP1-S8/GLP1-3G_III_ VAReqIgG2
47	MAVLGLLFCLVTFPSCVL <u>S</u> EGTFTSDVSSY LEGQAAKEFIAWLVKGGAGGGGGSGGGSGGGG GGGSSVPKPQCPPYTHSKFLGGPSVFIFPPNP KD <u>T</u> LMISRTPVVTCTVVNLSDQYPDVQFSWYV DNTEVHSAITKQREAFNSTYRVVSVLP IQHQ DWLSGKEFKCSVTNVGVPQPI SRAISRKGPS RVPQVYVLP PHPDELAKSKVSVTCLVKDFYPP DISVEWQSNRWPELEGKYSTTPAQLDGDGSYF LYSKLSLETSRWQQVESFTCAVMHEALHNH <u>Y</u> T KTDISESLGK	ssGLP1-S8_I_VAREqIgG2
48	MGLVAPVVLLHQDDEEHGQDEGPEDGSGYLLG TLTRFSSDFDSAPEVILAPDDQLQLPHSSRE NFWARTGLCAESFLLRPVGPVGPVMGWSEGFH KRNSRQEFLLRRRLFAGGLCAASTQESRNRCS RGCKSSPADCPELDRTQHLGNSVGPIQAAHQE LALGAGGPGDECQCCSVNSLFIPEPQSTCPY NGYTSWPLEGNLRVACAPPPPPPARTLFGGSR RGAVDKKAGGGRSPGGGAGTGEFGAPGAGGG LGRRPEVGAWTAAEGTNPADLASSPPPPSTRP PAAPRPPCADFCAASPQTTFPTSPRRPLPAS <u>GGATVSLSETVQKWREYRHQCQRFLTEAPPPA</u> <u>TGLFCNRTFDEYACWPDGLPGSFVNVSCPWYL</u> <u>PWASSVLQGHVYRFCTAEGWLRLQDNSSLPWR</u> <u>NLSECEESKRGRSSPEEQLLSFS</u> IIYTVGYT LSFSALVIASAILLSFRHLHCTRNYIHLNLFA SFILRALSVFIRDAVLKWMYSTAPQQHQWDGL LSYQDSLGCRLVFLMQYCVAANYWLLVEGV YLYTLLAFSVFSEQRIFRLYLSIGWGVPLLFV IWGIVKLYEDEGCWTRNSNMNYWLIIRLPIL FAIGVNFLIFVRVICIVVSKLKANLMCKTDIK CRLAKSTLTLLIPLLGTHEVVFAFVMDEHARGT LRFIKLFTELSFTSFQGLMVAILYCFVNNEVQ MEFRRSWERWRLKHLHIQRDSSMKPLKCPTSS LTSGGTVGSSVYAASCQASCS	Feline glucagon-like peptide 1 receptor (GLP1R)
49	RPLPASGGATVSLSETVQKWREYRHQCQRFLT EAPPPATGLFCNRTFDEYACWPDGLPGSFVNV SCPWYLPWASSVLQGHVYRFCTAEGWLRLQDN SSLPWRNLSECEESKRGRSSPEEQLLSFS	Mature feline glucagon-like peptide 1 receptor-N-terminal domain (GLP1R-N)

50	<i>METDTLLLWVLLLWVPGSTGRPLPASGGATVSLSETVQKWREYRHQCQRFLTEAPPPATGLFCNRTFDEYACWPDGLPGSFVNVSCPWYLPWASSVLQGHVYRFCTAEGWLWRQDNSSLPWRNLSECEESKRGRSSPEEQLLSFSGSENLYFQGPBKCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMSRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVVFSCSVMHEALHNHYTQKSLSLSPGKHHHHHH</i>	ssFeGLP1R-N_huFc_PolyHis
51	<i>METDTLLLWVLLLWVPGSTGRPLPASGGATVSLSETVQKWREYRHQCQRFLTEAPPPATGLFCNRTFDEYACWPDGLPGSFVNVSCPWYLPWASSVLQGHVYRFCTAEGWLWRQDNSSLPWRNLSECEESKRGRSSPEEQLLSFSGGGSHHHHHH</i>	ssFeGLP1R-N_PolyHis
52	<i>HGEFTFTSDVSSYLEGQAAKEFIAWLVKGGGGSGGGGSGGGGSGGGGSPKTASTIESKTGEGPKCPVPEIPGAPSVFIFPPKPKDTLSISRTPEVTCVVVDLGPDDSNVQITWFDNTEMHTAKTRPREEQFNSTYRVVSVLPILHQDWLKGKEFKCKVNSKSLPSAMERTISKAKGQPHEPQVYVLPPTQEEELSENKVSVTCLIKGFHPPDIAVEWEITGQPEPENNYQTTPQLDSDGTYFLYSRLSVD RSHWQRGNTYTCSVSHEALHSHHTQKSLTQSPGKGGGSGGGGHSQGTFTSDYSKYLDSRRAQDFVQWLMNTGGG</i>	GLP1-G8/Gluc-3G_IV_WTfeIgG2
53	<i>HSQGTFTSDYSKYLDSRRAQDFVQWLMNTGGGSGGGGSGGGGSGGGGSPKTASTIESKTGEGPKCPVPEIPGAPSVFIFPPKPKDTLSISRTPEVTCLVVDLGPDDSNVQITWFDNTEMHTAKTRPREEQFNSTYRVVSVLPILHQDWLKGKEFKCKVNSKSLPSAMERTISKAKGQPHEPQVYVLPPTQEEELSENKVSVTCLIKGFHPPDIAVEWEITGQPEPENNYQTTPQLDSDGTYFLYSRLSVD RSHWQRGNTYTCSVSHEALHSHHTQKSLTQSPGKGGGSGGGGHAEGTFTSDVSSYLEGQAAKEFIAWLVKGGG</i>	Gluc/GLP1-2G_V_WTfeIgG2
54	<i>HGEFTFTSDVSSYLEGQAAKEFIAWLVKGGAGGGGGSGGGGSGGGGSGGGSPKESTSKCISPCVPESLGGPSVFI FPPKPKDTLLIARTPEITCVVLDLGREDEPVQISWFVDGKEVHTAKTQPREQQFNSTYRVVSVLPIGHQDWLTGKEFKCRVNHIGLPSPIERTISKARGQAHQPSVYVLPSPKELSSDVTVTLTCLIKDFPPEIDVEWQSNQPEPESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGDTFTCAVMHEALHNHYTDLSLSHSPGKGGGGSGGGGHSQGTFTSDYSKYLDSRRAQDFVQWLMNTGGG</i>	GLP1-G8/Glu-4G_IV_VARcalgGD

55	HSQGTFTSDYSKYLDSRRAQDFVQWLMNTGAG GGGSGGGSGGGSGGGSPKESTSKCISPCVP ESLGGPSVFI FPPKPKDTLLIARTPEITCVVL DLGREDPEVQISWFVDGKEVHTAKTQPREQQF NSTYRVVSVLPIGHQDWLTGKEFKCRVNHIGL PSPIERTISKARGQAHQPSVYVLPSPKELSS SDTVTLTCLIKDFFPPEIDVEWQSNQPEPES KYHTTAPQLDEDGSYFLYSKLSVDKSRWQQGD TFTCAVMHEALHNHYTDLSSLHSPGKGGGSG GGGHAEGTFTSDVSSYLEGQAAKEFIAWLVKG GGG	Gluc/GLP1-3G_V_ VARcaIgGD
56	HGEFTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFI FPPNPKDTLMISRTPVVTCVNVNLS QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLP IQH QDWLSGKEFKCSVTNVGVPQPI SRAISRKGPSRVPQVYVLP PHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLET SRWQQVESFTCA VMHEALHNHYTKTDISESLGKGGGSGGGGHS QGTFTSDYSKYLDSRRAQDFVQWLMNTGGGG	GLP1-G8/Gluc-4G_IV_ VAReqIgGD
57	HSQGTFTSDYSKYLDSRRAQDFVQWLMNTGAG GGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFI FPPNPKDTLMISRTPVVTCVNVNLS QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLP IQH QDWLSGKEFKCSVTNVGVPQPI SRAISRKGPSRVPQVYVLP PHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLET SRWQQVESFTCA VMHEALHNHYTKTDISESLGKGGGSGGGGHA EGTFTSDVSSYLEGQAAKEFIAWLVKGGGG	Gluc/GLP1-3G_V_ VAReqIgG2
58	HGEFTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGSGGGSGGGSGGGSSSESKYGPPCPPCPAP EFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQF NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGL PSSIEKTISKAKGQPREPQVYTLPPSQEEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSRLTVDKSRWQEGNVFS CSVMHEALHNHYTQKSLSLSLGKGGGSGGGG HSQGTFTSDYSKYLDSRRAQDFVQWLMNTGGG G	GLP1-G8/Glu-4G_IV_ huIgG4
59	HSQGTFTSDYSKYLDSRRAQDFVQWLMNTGGG GGSGGGSGGGSGGGSSSESKYGPPCPPCPAPEF LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV SQEDPEVQFNWYVDGVEVHNAKTKPREEQFNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPS SIEKTISKAKGQPREPQVYTLPPSQEEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCS VMHEALHNHYTQKSLSLSLGKGGGSGGGGHA	Gluc/GLP1-3G_V_huIgG4

	EGTFTSDVSSYLEGQAAKEFIAWLKGGAGGG G	
60	PVPEPLGGPSVLIFFPPKPKD T LRITRTPEVTC VVLDLGGREDPEVQISWFDVGKEVHTAKTQSRE QQFNGTYRVVSVLP I EHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNQQE PERKHRMTPPQLDEDEGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETL H NHYTDLSLSHSPGK	Exemplary variant canine IgG-A Fc C1q – Protein A + I(21)T Q(207)H
61	PGCGLLGGPSVFIFFPPKPKD T LVTARTPTVTC VVVDLDPENPEVQISWFDVSKQVQTANTQPRE EQSNGTYRVVSVLP I GHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPPQLDEDEGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc C1q + Protein A + I(21)T
62	PVPESLGGPSVFIFFPPKPKD T LRITRTPEITC VVLDLGGREDPEVQISWFDVGKEVHTAKTQPRE QQFNSTYRVVSVLP I EHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFFPPEIDVEWQSNQQEP PESKYHTTAPQLDEDEGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEAL H NHYTDLSLSHSPGK	Exemplary variant canine IgG-D Fc C1q – Protein A + I(21)T Q(207)H
63	GGPSVFLFPPNPKDTLMITRTPEVTCVVVDVS QENPDVKFNWYMDGVEVRTATTTRPKEEQFNST YRVVSVLRIQHQDWLSGKEFKCKVNNQALPQP IERTITKTGRSQEPQVYVLAPHPDESKKSKV SVTCLVKDFYPPPEINIEWQSNQQPELETKYST TQAQQSDGSYFLYSKLSVDRNRWQQGTTFTC GVMHEALHNHYTQKNVSKNPGK	Exemplary wild-type equine IgG1 Fc Protein A + C1q +
64	GGPSVFIFFPPNPKDALMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFNST YRVVSVLPIQHQDWLSGKEFKCSVTNVGVPQP ISRAISRKGPSRVPQVYVLPHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSYFLYSKLSLETSRWQQVESFTC AVMHEALHNHFTKTDISESLGK	Exemplary wild-type equine IgG2 Fc Protein A – C1q –
65	GGPSVFIFFPPKPKDVLMITRMPEVTCLVVDVS HDSSDVLFTWYVDGTEVKTAKTMPNEEQNNST YRVVSVLRIQHQDWLNGKKFKCKVNNQALPAP VERTISKATGQTRVPQVYVLAPHPDELAKSKV SVTCLVKDFYPPDITVEWQSNHPEPEGKYRT TEAQKSDGSYFLYSKLTVEKDRWQQGTTFTC VVMHEALHNHVMQKNISKNPGK	Exemplary wild-type equine IgG3 Fc Protein A + C1q+
66	VGPSVFIFFPPKPKDVLMISRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHTATTEPKQEAFNST YRVVSVLPIQHKDWLSGKEFKCKVNNKALPAP VERTISAPTGPQPREPQVYVLAPHRDELAKSKV SVTCLVKDFYPPDIDIEWKSNQQPEPETKYST TPAQLSDGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary wild-type equine IgG4 Fc Protein A + C1q +

67	GGPSVFIFPPKPKDVLMI SRKPEVTCVVVDLG HDDPDVQFTWFVDGVETHTATTEPKKEEQFNST YRVVSVLPPIQH QDWLSGKEFKCSVTSKALPAP VERTISKAKGQLRVPQVYVLAPHPDELAKNTV SVTCLVKDFYPPEIDVEWQSNEHPEPEGKYST TPAQLNSDGSYFLY SKLSVETSRWKQGESFTC GVMHEAVENHYTQKNVSHSPGK	Exemplary wild-type equine IgG5 Fc Protein A – C1q –
68	GRPSVFIFPPNPKDTLMISRTPEVTCVVVDVS QENPDVKFNWYVDGVEAHTATTKAKEKQDNST YRVVSVLPPIQH QDWRRGKEFKCKVNNRALPAP VERTITKAKGELQDPQVY ILAPHPDEVTKNTV SVTCLVKDFYPPDINVEWQSNEEPEPEVKYST TPAQLDGDGSYFLY SKLTVETDRWEQGESFTC VVMHEAIRHTYRQKSITNFPKG	Exemplary wild-type equine IgG6 Fc Protein A – C1q –
69	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHTATTEPKQEQQNST YRVVSI LAIQHKDWLSGKEFKCKVNNQALPAP VQKTISKPTGQPREPQVYVLAPHPDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLDGDGSYFLY SKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary wild-type equine IgG7 Fc Protein A + C1q +
70	GGPSVFLFPPNPKDTLMITRTPEVTCVVVDVS QENPDVKFNWYMDGVEVRTATTRPKKEEQFNST YRVVSVLR IQH QDWLSGKEFKC <u>S</u> VNNQALPQP IERTITKTGRSQEPQVYVLAPHPDESKKSKV SVTCLVKDFYPPDINIEWQSNQPELETKYST TQAQQSDGSYFLY SKLSVDRNRWQQGTTFTC GVMHEALHNHYTQKNVSKNPGK	Exemplary variant equine IgG1 Fc Protein A + C1q – K(87)S
71	GGPSVFIFPPNPKDALMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFNST YRVVSVLPPIQH QDWLSGKEFKCSVTNVGVPQP ISRAISRKGKPSRVPQVYVLPPHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSYFLY SKLSLET SRWQQGESFTC AVMHEALHNH <u>Y</u> TKTDISESLGK	Exemplary variant equine IgG2 Fc C1q – Protein A + F(203)Y
72	GGPSVFIFPPNPKD <u>T</u> LMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFNST YRVVSVLPPIQH QDWLSGKEFKCSVTNVGVPQP ISRAISRKGKPSRVPQVYVLPPHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSYFLY SKLSLET SRWQQVESFTC AVMHEALHNH <u>Y</u> TKTDISESLGK	Exemplary variant equine IgG2 Fc C1q – Protein A + A(15)T F(203)Y
129	PPCVLSAEGVPIPSVPKPQCPPYTHSKFLGG PSVFIFPPNPKDALMISRTPVVTCVVVNLS DQ YPDVQFSWYVDNTEVHSAITKQREAFNSTYR VVSVPPIQH QDWLSGKEFKCSVTNVGVPQPIS RAISRKGKPSRVPQVYVLPPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLY SKLSLET SRWQQVESFTCAV MHEALHNHFTKTDISESLGK	Exemplary wild-type equine IgG2 Fc with hinge Protein A – C1q –

130	PPCVLSAEGVIPIPSVPKP P CPPYTHSKFLGG PSVFI FPPNPKDALMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNHFTKTDISESLGK	Exemplary variant equine IgG2 Fc with modified hinge Protein A – C1q – Q(20)P
131	PP S VLSAEGVIPIPSVPKPQCPPYTHSKFLGG PSVFI FPPNPKDALMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNHFTKTDISESLGK	Exemplary variant equine IgG2 Fc with modified hinge Protein A – C1q – C(3)S
132	PP S VLSAEGVIPIPSVPKP P CPPYTHSKFLGG PSVFI FPPNPKDALMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNHFTKTDISESLGK	Exemplary variant equine IgG2 Fc with modified hinge Protein A – C1q – C(3)S Q(20)P
133	PPCVLSAEGVIPIPSVPKPQCPPYTHSKFLGG PSVFI FPPNPKD T LMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNH Y TKTDISESLGK	Exemplary variant equine IgG2 Fc with hinge Protein A + C1q – A(45)T F(233)Y
134	PPCVLSAEGVIPIPSVPKP P CPPYTHSKFLGG PSVFI FPPNPKD T LMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNH Y TKTDISESLGK	Exemplary variant equine IgG2 Fc with modified hinge Protein A + C1q – Q(20)P A(45)T F(233)Y
135	PP S VLSAEGVIPIPSVPKP P CPPYTHSKFLGG PSVFI FPPNPKD T LMISRTPVVTCVVVNLSDQ YPDVQFSWYVDNTEVHSAITKQREAQFNSTYR VVSVLPIQHQQDWLSGKEFKCSVTNVGVPQPIS RAISRGKGPSRVPQVYVLPHPDELAKSKVSV TCLVKDFYPPDISVEWQSNRWPELEGKYSTTP AQLDGDGSYFLYSKLSLETSRWQQVESFTCAV MHEALHNH Y TKTDISESLGK	Exemplary variant equine IgG2 Fc with modified hinge Protein A + C1q – C(3)S Q(20)P A(45)T F(233)Y
73	GGPSVFI FPPKPKDVLMITRMPEVTCLVVDVS HDSSDVLFTWYVDGTEVKTAKTMPNEEQNNST	Exemplary variant equine IgG3 Fc

	YRVVSVLRIQHQDWLNGKKFKC <u>S</u> VNNQALPAP VERTISKATGQTRVPQVYVLAPHPDELSKNKV SVTCLVKDFYPPDITVEWQSNEHPEPEGKYRT TEAQKSDSGSYFLYSKLTVEKDRWQQGTTFTC VVMHEALHNHVMQKNISKNPGR	Protein A + C1q – K(87)S
74	VGPSVFIFFPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHTATTEPKQE QFNST YRVVSVLP IQHKDWLSGKEFKC <u>S</u> VNNKALPAP VERTISAPTGPQPREPQVYVLAPHRDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLDSDSGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary variant equine IgG4 Fc Protein A + C1q – K(87)S
75	GGPSVFIFFPKPKDVLMI SRKPEVTCVVVDLG HDDPDVQFTWFVDGVETHTATTEPKEE QFNST YRVVSVLP IQHKDWLSGKEFKCSVT SKALPAP VERTISKAKGQLRVPQVYVLAPHPDELA KNTV SVTCLVKDFYPP EIDVEWQSNEHPEPEGKYST TPAQLNSDGSYFLYSKLSVETSRWKQGESFTC GVMHEAL <u>LHN</u> HYTQKNVSHSPGK	Exemplary variant equine IgG5 Fc C1q – Protein A + V(199)L E(200)H
76	GRPSVFIFFPNPKDTLMI SRTPEVTCVVVDVS QENPDVKFNWYVDGVEAHTATT KAKEKQDNST YRVVSVLP IQHKDWRRGKEFKCKVNNRALPAP VERTITKAKGELQDPQVY ILAPHPDEVTKNTV SVTCLVKDFYPP DINVEWQSNEEPEPEVKYST TPAQLDGDGSYFLYSKLTVETDRWEQGESFTC VVMHEAL <u>LHN</u> HYRQKSITNFPGR	Exemplary variant equine IgG6 Fc C1q – Protein A + I(199)L R(200)H H(201)N T(202)H
77	VGPSVFIFFPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHTATTEPKQE QNNST YRVVSVLP IQHKDWLSGKEFKC <u>S</u> VNNQALPAP VQKTISKPTGPQPREPQVYVLAPHPDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLDGDGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary variant equine IgG7 Fc Protein A + C1q – K(87)S
78	PAP EMLGGPSVFIFFPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQM QTAKTQPRE EQFNGTYRVVSVLP IGHQDWLKGKQFTC <u>R</u> VNN KALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFPPDIDVEWQSNGQQEP ESKYRTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q – K(93)R
79	PGCGLLGGPSVFIFFPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLP IGHQDWLSGKQFKC <u>R</u> VNN KALPSPIEEEIISKTPGQAHQPNVYVLPPSRDE MSKNTVTLTCLVKDFFPEIDVEWQSNGQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A – C1q – K(93)R
80	RKTDHPPGPKTGEGPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTC LVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP I	Exemplary wild-type feline IgG1a Fc

	LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Protein A + C1q +
81	RKTDHPPGPKTGEGPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPAPAEELSENKVSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary wild-type feline IgG1b Fc Protein A + C1q +
136	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPS <u>P</u> PIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1a Fc Protein A + C1q – P(198)A
82	RKTDHPPGPKTGEGPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPS <u>P</u> PIERTISKAK GQPHEPQVYVLPAPAEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1a Fc Protein A + C1q – P(198)A
137	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPS <u>P</u> PIERTISKDK GQPHEPQVYVLPAPAEELSENKVSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1b Fc Protein A + C1q – P(198)A
83	RKTDHPPGPKTGEGPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNSTYRVVSVLP LHQDWLKGKEFKCKVNSKSLPS <u>P</u> PIERTISKDK GQPHEPQVYVLPAPAEELSENKVSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary variant feline IgG1b Fc Protein A + C1q – P(198)A
84	PGCGLLGGPSVFIFPPKPKD <u>TL</u> <u>LI</u> ARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKC <u>R</u> VNN KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRMTTPQLDEGSGYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc C1q – K(93)R Protein A + I(21)T

		V(23)L T(24)I
85	HAEGTFTSDVSSYLEGQAAKEFIAWLVKGAG	Wild-type GLP1 (7-37)
86	H <u>S</u> EGTFTSDVSSYLEGQAAKEFIAWLVKG	GLP1-S8 (7-35)
87	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKG	GLP1-G8 (7-35)
88	G	1G extension
89	GG	2G extension
90	GGG	3G extension
91	GGGG	4G extension
92	GGGGG	5G extension
93	GGGGGG	6G extension
94	GGGGGGG	7G extension
95	GGGGGGGG	8G extension
96	MAVLGLLFCLVTFPSCVL <u>S</u> H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAGGGGSGGGSGGGSGGGSPKTASTIESKTGEGPKCPVPEIPGAPSVFIFPPKPKDTLSISRTPEVTCLVVDLGPDDSNVQITWFVDNTEMHTAKTRPREEQFNSTYRVVSVLPILHQDWLKGKEFKCKVNSKSLPSAMERTISKAKGQPHEPQVYVLPPTQEELSENKVSVTCLIKGFHPPDIAVEWEITGQPEPENNYQTTPPQLDSDGTYFLYSRLSVDRSHWQRGNTYTCSVSHEALHSHHTQKSLTQSPGK	ssGLP1-G8_I_WTfeIgG2
97	MAVLGLLFCLVTFPSCVL <u>S</u> H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAGGGGSGGGSGGGSGGGSPKTASTIESKTGEGPKCPVPEIPGAPSVFIFPPKPKDTLSISRTPEVTCLVVDLGPDDSNVQITWFVDNTEMHTAKTRPREEQFNSTYRVVSVLPILHQDWLKGKEFKCKVNSKSLPSAMERTISKAKGQPHEPQVYVLPPTQEELSENKVSVTCLIKGFHPPDIAVEWEITGQPEPENNYQTTPPQLDSDGTYFLYSRLSVDRSHWQRGNTYTCSVSHEALHSHHTQKSLTQSPGKGGGGSGGGGHAEGTFTSDVSSYLEGQAAKEFIAWLVKGGGG	ssGLP1-G8/GLP1-3G_III_WTfeIgG2
98	HAEGTFTSDVSSYLEGQAAKEFIAWLVKGA	Variant GLP1 (7-36)
99	HAEGTFTSDVSSYLEGQAAKEFIAWLVKG	Variant GLP1 (7-35)
100	VPKPQCPYTHSKFLGGPSVFIFPPNPKDALMISRTPVVTCTVVNLSQYPDVQFSWYVDNTEVHSAITKQREAQFNSTYRVVSVLPILHQDWLSGKEFKCSVTNVGVPQPISRISRKGKPSRVPQVYVLPHPDELAKSKSVTCLVKDFYPPDISVEWQSNRWPELEGKYSTTPAQLDGDGSYFLYSKLSLETSRWQQVESFTCAVMHEALHNHFTKTDISESLGK	Exemplary wild-type equine Fc IgG2 (including equine IgG2 hinge) Protein A – C1q –

101	DMSKCPKCPAPELL	Exemplary wild-type equine IgG1 hinge
102	VPKPQCPPYTHSKFL	Exemplary wild-type equine IgG2 hinge
138	<u>PPCVLSAEGVIPIPSV</u> PKPQCPPYTHSKFL	Exemplary wild-type equine IgG2 hinge
103	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSDMSKCPKCPAPELLG GPSVFIFPPNPKD <u>T</u> LMISRTPVVTCTVVNLSD QYPDVQFSWYVDNTEVHSAITKQREAFNSTY RVVSVLPPIQHQDWLSGKEFKCSVTNVGVPQPI SRAISRKGKPSRVPQVYVLPHPDELAKSKVS VTCLVKDFYPPDISVEWQSNRWPELEGKYSTT PAQLDGDGSYFLYSKLSLETSRWQQVESFTCA VMHEALHNH <u>Y</u> TKTDISESLGKGGGGSGGGGHA EGTFTSDVSSYLEGQAAKEFIAWLVKGGGG	GLP1-G8/GLP1-3G_III_ VAReqIgG2
104	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGAG GGGGSGGGSGGGSGGGSSVPKPQCPPYTHSKF LGGPSVFIFPPNPKD <u>T</u> LMISRTPVVTCTVVNL SDQYPDVQFSWYVDNTEVHSAITKQREAFNS TYRVVSVLPPIQHQDWLSGKEFKCSVTNVGVPQ PISRAISRKGKPSRVPQVYVLPHPDELAKSK VSVTCLVKDFYPPDISVEWQSNRWPELEGKYS TTPAQLDGDGSYFLYSKLSLETSRWQQVESFT CAVMHEALHNH <u>Y</u> TKTDISESLGK	GLP1-G8_I_VAReqIgG2
105	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGGG SGGGSGGGSGGGSGGGSPKESTCKCISPCPVPE SLGGPSVFIFPPKPKD <u>TLLIART</u> PEITCVVLD LGREDPEVQISWFVDGKEVHTAKTQPREQQFN STYRVVSVLPPI <u>G</u> HQDWLTGKEFKCRVNHIGLP SPIERTISKARGQAHQPSVYVLPSPKELSSS DTVTLTCLIKDFFPPEIDVEWQSNQPEPESEK YHTTAPQLDEDGSYFLYSKLSVDKSRWQQGDT FTCAVMHEAL <u>H</u> NHYTDLSLSHSPGKGGGGSGG GGHAEGTFTSDVSSYLEGQAAKEFIAWLVKGG G	GLP1-G8/GLP1-2G_III_ VARcalIgGD
106	H <u>G</u> EGTFTSDVSSYLEGQAAKEFIAWLVKGGGG SGGGSGGGSGGGSGGGSPKESTSKCISPCPVPE SLGGPSVFIFPPKPKD <u>TLLIART</u> PEITCVVLD LGREDPEVQISWFVDGKEVHTAKTQPREQQFN STYRVVSVLPPI <u>G</u> HQDWLTGKEFKCRVNHIGLP SPIERTISKARGQAHQPSVYVLPSPKELSSS DTVTLTCLIKDFFPPEIDVEWQSNQPEPESEK YHTTAPQLDEDGSYFLYSKLSVDKSRWQQGDT FTCAVMHEAL <u>H</u> NHYTDLSLSHSPGKGGGGSGG GGHAEGTFTSDVSSYLEGQAAKEFIAWLVKGG G	GLP1-G8/GLP1-2G_III_ VARcalIgGD
139	PAPE <u>P</u> LGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMQTAKTQPRE EQFNGTYRVVSVLPPIQHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP	Exemplary variant canine IgG-B Fc Protein A + C1q +

	ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	CD16 – M(5)P
140	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLDR E DPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q + CD16 – P(39)R
141	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLGPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q + CD16 – D(38)G
142	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN IALPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q + CD16 – K(97)I
143	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KGLPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q + CD16 – A(98)G
144	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLGPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN IGLPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q + CD16 – D(38)G K(97)I A(98)G
145	PAP E MLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLGPEDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTCRVNN IGLPSPIERTISKARGQAHQPSVYVLPPSREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q – CD16 – D(38)G K(93)R K(97)I A(98)G
146	PAP E PLGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLDR E DPEVQISWFVDGKQMOTAKTQPRE	Exemplary variant canine IgG-B Fc

	EQFNGTYRVVSVLPIGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Protein A + C1q + CD16 – M(5)P P(39)R
147	PAPE <u>P</u> LGGPSVFIFPPKPKDTLLIARTPEVTC VVVDLD <u>R</u> EDPEVQISWFVDGKQMOTAKTQPRE EQFNGTYRVVSVLPIGHQDWLKGKQFTC <u>R</u> VNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary variant canine IgG-B Fc Protein A + C1q – CD16 – M(5)P P(39)R K(93)R
148	PGCG <u>P</u> LGGPSVFIFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – L(5)P
149	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLD <u>R</u> ENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – P(39)R
150	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDL <u>G</u> PENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – D(38)G
151	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN <u>I</u> ALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – K(97)I
152	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLD <u>P</u> ENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN <u>K</u> GLPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQOQEP ESKYRTTPPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – A(98)G

153	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKC <u>R</u> VNN KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q – CD16 + K(93)R
154	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDL <u>G</u> PENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN <u>I</u> GLPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – D(38)G K(97)I A(98)G
155	PGCGLLGGPSVFIFPPKPKDILVTARTPTVTC VVVDL <u>G</u> PENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKC <u>R</u> VNN <u>I</u> GLPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q – CD16 – D(38)G K(93)R K(97)I A(98)G
156	PGCG <u>P</u> LGGPSVFIFPPKPKDILVTARTPTVTC VVVDLD <u>R</u> ENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKCKVNN KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q + CD16 – L(5)P P(39)R
157	PGCG <u>P</u> LGGPSVFIFPPKPKDILVTARTPTVTC VVVDLD <u>R</u> ENPEVQISWFVDSKQVQTANTQPRE EQSNGTYRVVSVLPIGHQDWLSGKQFKC <u>R</u> VNN KALPSPIEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary variant canine IgG-C Fc Protein A + C1q – CD16 – M(5)P P(39)R K(93)R
158	PVPEPLGGPSVLIFFPPKPKDILRITRTPEVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE QQF <u>X</u> ₁ GTYRVVSVLP ₁ IEHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNQQQEP PERKHRMTTPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSLSHSPGK	Exemplary aglycosyl variant canine IgG-A Fc N(68)X ₁ X ₁ = any amino acid except N
159	PVPEPLGGPSVLIFFPPKPKDILRITRTPEVTC VVLDLGREDPEVQISWFVDGKEVHTAKTQSRE	Exemplary aglycosyl variant canine IgG-A Fc

	QQFN <u>P</u> TYRVVSVLP ₁ IEHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNQQE PERKHRMTTPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSLHSPGK	G(69)P
160	PVPEPLGGPSVLIFFPPKPKDILRITRTPEVTC VVLDLGGREDPEVQISWFVDGKEVHTAKTQSRE QQFNG <u>X</u> ₂ YRVVSVLP ₁ IEHQDWLTGKEFKCRVNH IDLPSPIERTISKARGRAHKPSVYVLPSPKE LSSSDTVSITCLIKDFYPPDIDVEWQSNQQE PERKHRMTTPQLDEDGSYFLYSKLSVDKSRWQ QGDPFTCAVMHETLQNHYTDLSLHSPGK	Exemplary aglycosyl variant canine IgG-A Fc T(70)X ₂ X ₂ = any amino acid except T or S
161	PAPFMLGGPSVFIFFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQF <u>X</u> ₁ GTYRVVSVLP ₁ IGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP ESKYRTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary aglycosyl variant canine IgG-B Fc N(68)X ₁ X ₁ = any amino acid except N
162	PAPFMLGGPSVFIFFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQFN <u>P</u> TYRVVSVLP ₁ IGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP ESKYRTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary aglycosyl variant canine IgG-B Fc G(69)P
163	PAPFMLGGPSVFIFFPPKPKDTLLIARTPEVTC VVVDLDPEDPEVQISWFVDGKQMOTAKTQPRE EQFNG <u>X</u> ₂ YRVVSVLP ₁ IGHQDWLKGKQFTCKVNN KALPSPIERTISKARGQAHQPSVYVLPSPREE LSKNTVSLTCLIKDFFPPDIDVEWQSNQQEP ESKYRTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQESLSHSPGK	Exemplary aglycosyl variant canine IgG-B Fc T(70)X ₂ X ₂ = any amino acid except T or S
164	PGCGLLGGPSVFIFFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQS <u>X</u> ₁ GTYRVVSVLP ₁ IGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary aglycosyl variant canine IgG-C Fc N(68)X ₁ X ₁ = any amino acid except N
165	PGCGLLGGPSVFIFFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSN <u>P</u> TYRVVSVLP ₁ IGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQEP ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFICAVMHEALHNHYTQISLSHSPGK	Exemplary aglycosyl variant canine IgG-C Fc G(69)P
166	PGCGLLGGPSVFIFFPPKPKDILVTARTPTVTC VVVDLDPENPEVQISWFVDSKQVQTANTQPRE EQSNG <u>X</u> ₂ YRVVSVLP ₁ IGHQDWLSGKQFKCKVNN KALPSPIEEEIISKTPGQAHQPNVYVLPSPRDE MSKNTVTLTCLVKDFFPPEIDVEWQSNQQEP	Exemplary aglycosyl variant canine IgG-C Fc T(70)X ₂

	ESKYRMTTPQLDEDGSYFLYSKLSVDKSRWQR GDTFTCAVMHEALHNHYTQISLSHSPGK	X ₂ = any amino acid except T or S
167	PVPESLGGPSVFIFPPKPKDILRITRTPETC VVLDLGGREDPEVQISWFVDGKEVHTAKTQPRE QQF X ₁ STYRVVSVLPIEHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFPPEIDVEWQSNQPE PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary aglycosyl variant canine IgG-D Fc N(68)X ₁ X ₁ = any amino acid except N
168	PVPESLGGPSVFIFPPKPKDILRITRTPETC VVLDLGGREDPEVQISWFVDGKEVHTAKTQPRE QQFN P TYRVVSVLPIEHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFPPEIDVEWQSNQPE PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary aglycosyl variant canine IgG-D Fc S(69)P
169	PVPESLGGPSVFIFPPKPKDILRITRTPETC VVLDLGGREDPEVQISWFVDGKEVHTAKTQPRE QQFNS X ₂ YRVVSVLPIEHQDWLTGKEFKCRVNH IGLPSPIERTISKARGQAHQPSVYVLPSPKE LSSSDTVTLTCLIKDFPPEIDVEWQSNQPE PESKYHTTAPQLDEDGSYFLYSKLSVDKSRWQ QGDTFTCAVMHEALQNHYTDLSLSHSPGK	Exemplary aglycosyl variant canine IgG-D Fc T(70)X ₂ X ₂ = any amino acid except T or S
170	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQF X ₁ STYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPPEEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG1a Fc N(85)X ₁ X ₁ = any amino acid except N
171	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFN P TYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPPEEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG1a Fc S(86)P
172	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFNS X ₂ YRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKAK GQPHEPQVYVLPPEEELSENKVSVTCLIKSF HPPDIAVEWEITGQPEPENNYRTTPQLDSDG TYFVYSKLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG1a Fc T(87)X ₂ X ₂ = any amino acid except T or S
173	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQF X ₁ STYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPPEEELSENKVSVTCLIEGF	Exemplary aglycosyl variant feline IgG1b Fc N(85)X ₁ X ₁ = any amino acid except N

	YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	
174	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFN <u>P</u> TYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPAPAQEELSENKSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG1b Fc S(86)P
175	RKTDHPPGPKPCDCPKCPPPEMLGGPSIFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSDVQIT WFVDNTQVYTAKTSPREEQFN <u>S</u> ₂ YRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSPIERTISKDK GQPHEPQVYVLPAPAQEELSENKSVTCLIEGF YPSDIAVEWEITGQPEPENNYRTTPQLDSDG TYFLYSRLSVDRSRWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG1b Fc T(87)X ₂ X ₂ = any amino acid except T or S
176	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFN <u>X</u> ₁ STYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG2 Fc N(85)X ₁ X ₁ = any amino acid except N
177	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFN <u>P</u> TYRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG2 Fc S(86)P
178	PKTASTIESKTGEGPKCPVPEIPGAPSVFIFP PKPKDTLSISRTPEVTCLVVDLGPDDSNVQIT WFVDNTEMHTAKTRPREEQFN <u>S</u> ₂ YRVVSVLPI LHQDWLKGKEFKCKVNSKSLPSAMERTISKAK GQPHEPQVYVLPPTQEELSENKSVTCLIKGF HPPDIAVEWEITGQPEPENNYQTTPQLDSDG TYFLYSRLSVDRSHWQRGNTYTCSVSHEALHS HHTQKSLTQSPGK	Exemplary aglycosyl variant feline IgG2 Fc T(87)X ₂ X ₂ = any amino acid except T or S
179	GGPSVFLFPPNPKDTLMITRTPEVTCVVVDVS QENPDVKFNWYMDGVEVRTATTTRPKEEQFN <u>X</u> ₁ ST YRVVSVLRIQHGDWLSGKEFKCKVNNQALPQP IERTITKTGKRSQEPQVYVLAPHPDESKKSKV SVTCLVKDFYPPEINIEWQSNQPELETKYST TQAQQSDSGSYFLYSKLSVDRNRWQQGTTFTC GVMHEALHNHYTQKNVSKNPGK	Exemplary aglycosyl variant equine IgG1 Fc N(62)X ₁ X ₁ = any amino acid except N
180	GGPSVFLFPPNPKDTLMITRTPEVTCVVVDVS QENPDVKFNWYMDGVEVRTATTTRPKEEQFN <u>P</u> T	Exemplary aglycosyl variant equine IgG1 Fc

	YRVVSVLRIQHQQDWLSGKEFKCKVNNQALPQP IERTITKTKGRSQEPQVYVLAPHPDESKKSKV SVTCLVKDFYPPEINIEWQSNQPELETKYST TQAQQDSGSGSYFLYSKLSVDRNRWQQGTTFTC GVMHEALHNHYTQKNVSKNPGK	S(63)P
181	GGPSVFLFPPNPKDTLMITRTPVTCVVVDVS QENPDVKFNWYMDGVEVRTATTRPKEEQFNSX ₂ YRVVSVLRIQHQQDWLSGKEFKCKVNNQALPQP IERTITKTKGRSQEPQVYVLAPHPDESKKSKV SVTCLVKDFYPPEINIEWQSNQPELETKYST TQAQQDSGSGSYFLYSKLSVDRNRWQQGTTFTC GVMHEALHNHYTQKNVSKNPGK	Exemplary aglycosyl variant equine IgG1 Fc T(64)X ₂ X ₂ = any amino acid except T or S
182	GGPSVFI FPPNPKDALMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFX ₁ ST YRVVSVLP IQHQQDWLSGKEFKCSVTNVGVPQP ISRAISRKGKPSRVPQVYVLP PHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSGSYFLYSKLSLET SRWQQVESFTC AVMHEALHNHFTKTDISESLGK	Exemplary aglycosyl variant equine IgG2 Fc N(62)X ₁ X ₁ = any amino acid except N
183	GGPSVFI FPPNPKDALMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFNPT YRVVSVLP IQHQQDWLSGKEFKCSVTNVGVPQP ISRAISRKGKPSRVPQVYVLP PHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSGSYFLYSKLSLET SRWQQVESFTC AVMHEALHNHFTKTDISESLGK	Exemplary aglycosyl variant equine IgG2 Fc S(63)P
184	GGPSVFI FPPNPKDALMISRTPVVTCVVVNLS DQYPDVQFSWYVDNTEVHSAITKQREAFNSX ₂ YRVVSVLP IQHQQDWLSGKEFKCSVTNVGVPQP ISRAISRKGKPSRVPQVYVLP PHPDELAKSKV SVTCLVKDFYPPDISVEWQSNRWPELEGKYST TPAQLDGDGSGSYFLYSKLSLET SRWQQVESFTC AVMHEALHNHFTKTDISESLGK	Exemplary aglycosyl variant equine IgG2 Fc T(64)X ₂ X ₂ = any amino acid except T or S
185	GGPSVFI FPPKPKDVLMITRMPVTCVVVDVS HDSSDVLFTWYVDGTEVKTAKTMPNEEQNX ₁ ST YRVVSVLRIQHQQDWLNGKKFKCKVNNQALPAP VERTISKATGQTRVPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDITVEWQSNEHPEPEGKYRT TEAQKDSGSGSYFLYSKLTVEKDRWQQGTTFTC VVMHEALHNHVMQKNISKNPGK	Exemplary aglycosyl variant equine IgG3 Fc N(62)X ₁ X ₁ = any amino acid except N
186	GGPSVFI FPPKPKDVLMITRMPVTCVVVDVS HDSSDVLFTWYVDGTEVKTAKTMPNEEQNNPT YRVVSVLRIQHQQDWLNGKKFKCKVNNQALPAP VERTISKATGQTRVPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDITVEWQSNEHPEPEGKYRT TEAQKDSGSGSYFLYSKLTVEKDRWQQGTTFTC VVMHEALHNHVMQKNISKNPGK	Exemplary aglycosyl variant equine IgG3 Fc S(63)P
187	GGPSVFI FPPKPKDVLMITRMPVTCVVVDVS HDSSDVLFTWYVDGTEVKTAKTMPNEEQNNSX ₂ YRVVSVLRIQHQQDWLNGKKFKCKVNNQALPAP VERTISKATGQTRVPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDITVEWQSNEHPEPEGKYRT	Exemplary aglycosyl variant equine IgG3 Fc T(64)X ₂

	TEAQKDSGSGSYFLYSKLTVEKDRWQQGTTFTC VVMHEALHNHVMQKNI SKNPGK	X ₂ = any amino acid except T or S
188	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHATTEPKQE Q F N X ₁ ST YRVVSVLP IQHKDWLSGKEFKCKVNNKALPAP VERTISAPTGPQPREPQVYVLAPHRDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLSDGSGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary aglycosyl variant equine IgG4 Fc N(62)X ₁ X ₁ = any amino acid except N
189	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHATTEPKQE Q F N P T YRVVSVLP IQHKDWLSGKEFKCKVNNKALPAP VERTISAPTGPQPREPQVYVLAPHRDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLSDGSGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary aglycosyl variant equine IgG4 Fc S(63)P
190	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETHATTEPKQE Q F N S X ₂ YRVVSVLP IQHKDWLSGKEFKCKVNNKALPAP VERTISAPTGPQPREPQVYVLAPHRDELSKNKV SVTCLVKDFYPPDIDIEWKSNGQPEPETKYST TPAQLSDGSGSYFLYSKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSPGK	Exemplary aglycosyl variant equine IgG4 Fc T(64)X ₂ X ₂ = any amino acid except T or S
191	GGPSVFIFPPKPKDVLMI SRKPEVTCVVVDLG HDDPDVQFTWFVDGVETHATTEPKEE Q F N X ₁ PT YRVVSVLP IQHQDWLSGKEFKCSVT SKALPAP VERTISKAKGQLRVPQVYVLAPHPDELA KNTV SVTCLVKDFYPPDIDIEWQSNHPEPEGEKYST TPAQLNSDGSYFLYSKLSVETSRWKQGESFTC GVMHEAVENHYTQKNVSHSPGK	Exemplary aglycosyl variant equine IgG5 Fc N(62)X ₁ X ₁ = any amino acid except N
192	GGPSVFIFPPKPKDVLMI SRKPEVTCVVVDLG HDDPDVQFTWFVDGVETHATTEPKEE Q F N P T YRVVSVLP IQHQDWLSGKEFKCSVT SKALPAP VERTISKAKGQLRVPQVYVLAPHPDELA KNTV SVTCLVKDFYPPDIDIEWQSNHPEPEGEKYST TPAQLNSDGSYFLYSKLSVETSRWKQGESFTC GVMHEAVENHYTQKNVSHSPGK	Exemplary aglycosyl variant equine IgG5 Fc S(63)P
193	GGPSVFIFPPKPKDVLMI SRKPEVTCVVVDLG HDDPDVQFTWFVDGVETHATTEPKEE Q F N S X ₂ YRVVSVLP IQHQDWLSGKEFKCSVT SKALPAP VERTISKAKGQLRVPQVYVLAPHPDELA KNTV SVTCLVKDFYPPDIDIEWQSNHPEPEGEKYST TPAQLNSDGSYFLYSKLSVETSRWKQGESFTC GVMHEAVENHYTQKNVSHSPGK	Exemplary aglycosyl variant equine IgG5 Fc T(64)X ₂ X ₂ = any amino acid except T or S
194	GRPSVFIFPPNPKDTLMI SRTPEVTCVVVDVS QENPDVKFNWYVDGVEAHTATT KAKEKQD N X ₁ ST YRVVSVLP IQHQDWRRGKEFKCKVNNRALPAP VERTITKAKGELQDPQVY ILAPHPDEVTKNTV SVTCLVKDFYPPDINVEWQSNEEPEPEVKYST TPAQLDGDGSYFLYSKLTVETDRWEQGESFTC VVMHEAIRHTYRQKSITNFP GK	Exemplary aglycosyl variant equine IgG6 Fc N(62)X ₁ X ₁ = any amino acid except N

195	GRPSVFIFPPNPKDTLMISRTPEVTCVVVDVS QENPDVKFNWYVDGVEAHTATTKAKEKQDN <u>P</u> T YRVVSVLP IQHQDWRRGKEFKCKVNNRALPAP VERTITKAKGELQDPQVY ILAPHPDEVTKNTV SVTCLVKDFYPPDINVEWQSNEEPEPEVKYST TPAQLDGDGSYFLY SKLTVETDRWEQGESFTC VVMHEAIRHTYRQKSITNFP GK	Exemplary aglycosyl variant equine IgG6 Fc S(63)P
196	GRPSVFIFPPNPKDTLMISRTPEVTCVVVDVS QENPDVKFNWYVDGVEAHTATTKAKEKQDNS <u>X</u> ₂ YRVVSVLP IQHQDWRRGKEFKCKVNNRALPAP VERTITKAKGELQDPQVY ILAPHPDEVTKNTV SVTCLVKDFYPPDINVEWQSNEEPEPEVKYST TPAQLDGDGSYFLY SKLTVETDRWEQGESFTC VVMHEAIRHTYRQKSITNFP GK	Exemplary aglycosyl variant equine IgG6 Fc T(64)X ₂ X ₂ = any amino acid except T or S
197	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETH TATTEPKQE QN <u>X</u> ₁ ST YRVVSILAIQHKDWLSGKEFKCKVNNQALPAP VQKTISKPTGQPREPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDIDIEWK SNGQPEPETKYST TPAQLDGDGSYFLY SKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSP GK	Exemplary aglycosyl variant equine IgG7 Fc N(62)X ₁ X ₁ = any amino acid except N
198	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETH TATTEPKQE QNN <u>P</u> T YRVVSILAIQHKDWLSGKEFKCKVNNQALPAP VQKTISKPTGQPREPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDIDIEWK SNGQPEPETKYST TPAQLDGDGSYFLY SKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSP GK	Exemplary aglycosyl variant equine IgG7 Fc S(63)P
199	VGPSVFIFPPKPKDVLMI SRTPTVTCVVVDVG HDFPDVQFNWYVDGVETH TATTEPKQE QNN <u>S</u> X ₂ YRVVSILAIQHKDWLSGKEFKCKVNNQALPAP VQKTISKPTGQPREPQVYVLAPHPDEL SKNKV SVTCLVKDFYPPDIDIEWK SNGQPEPETKYST TPAQLDGDGSYFLY SKLTVETNRWQQGTTFTC AVMHEALHNHYTEKSVSKSP GK	Exemplary aglycosyl variant equine IgG7 Fc T(64)X ₂ X ₂ = any amino acid except T or S

DESCRIPTION OF THE EMBODIMENTS

[0015] Variant IgG Fc polypeptides from companion animals, such as canine, equine, and feline, are described. In some embodiments, the variant igG Fc polypeptides have increased binding to Protein A, decreased binding to C1q, decreased binding to CD16, increased stability, increased recombinant production, increased hinge disulfide formation, and/or form heterodimeric polypeptides. In some embodiments, antibodies, antibody fragments, or fusion proteins comprise a variant IgG Fc polypeptide. Methods of producing or purifying variant IgG Fc polypeptides and methods of administering variant IgG Fc polypeptides to companion animals are also provided assay.

[0016] Also provided are various embodiments relating to contiguous polypeptides and heterodimeric polypeptides comprising one or more variant GLP1 polypeptide(s) having improved serum half-life. In some embodiments, the contiguous polypeptides or heterodimeric polypeptides comprise a GLP1 polypeptide and a glucagon polypeptide as a dual GLP1 receptor and glucagon receptor agonist. In some embodiments, such polypeptides may be used to treat, for example, diabetes, obesity, or related indications, in companion animals, such as canines, felines, and equines.

[0017] For the convenience of the reader, the following definitions of terms used herein are provided.

[0018] As used herein, numerical terms such as K_D are calculated based upon scientific measurements and, thus, are subject to appropriate measurement error. In some instances, a numerical term may include numerical values that are rounded to the nearest significant figure.

[0019] As used herein, “a” or “an” means “at least one” or “one or more” unless otherwise specified. As used herein, the term “or” means “and/or” unless specified otherwise. In the context of a multiple dependent claim, the use of “or” when referring back to other claims refers to those claims in the alternative only.

Exemplary Variant IgG Fc Polypeptides

[0020] Novel variant IgG Fc polypeptides are provided, for example, variant IgG Fc polypeptides for increased binding to Protein A, for decreased binding to C1q, for decreased binding to CD16, for increased stability, for increased recombinant production, for increased hinge disulfide formation, and/or for forming heterodimeric proteins assay.

[0021] “Amino acid sequence,” means a sequence of amino acid residues in a peptide or protein. The terms “polypeptide” and “protein” are used interchangeably to refer to a polymer of amino acid residues, and are not limited to a minimum length. Such polymers of amino acid residues may contain natural or unnatural amino acid residues, and include, but are not limited to, peptides, oligopeptides, dimers, trimers, and multimers of amino acid residues. Both full-length proteins and fragments thereof are encompassed by the definition. The terms also include post-expression modifications of the polypeptide, for example, glycosylation, sialylation, acetylation, phosphorylation, and the like. Furthermore, for purposes of the present disclosure, a “polypeptide” refers to a protein which includes modifications, such as deletions, additions, and substitutions (generally conservative in nature), to the native sequence, as long as the protein maintains the desired activity. These modifications may be deliberate, as through site-directed mutagenesis, or may be accidental, such as through mutations of hosts which produce the proteins or errors due to PCR amplification.

[0022] A “fragment crystallizable polypeptide” or “Fc polypeptide” is the portion of an antibody molecule that interacts with effector molecules and cells. It comprises the C-terminal portions of the immunoglobulin heavy chains. As used herein, an Fc polypeptide includes fragments of the Fc domain having one or more biological activities of an entire Fc polypeptide. In some embodiments, a biological activity of an Fc polypeptide is the ability to bind FcRn. In some embodiments, a biological activity of an Fc polypeptide is the ability to bind C1q. In some embodiments, a biological activity of an Fc polypeptide is the ability to bind CD16. In some embodiments, a biological activity of an Fc polypeptide is the ability to bind protein A. An “effector function” of the Fc polypeptide is an action or activity performed in whole or in part by any antibody in response to a stimulus and may include complement fixation and/or ADCC (antibody-dependent cellular cytotoxicity) induction.

[0023] “IgX Fc” refers to an Fc polypeptide derived from a particular antibody isotype (e.g., IgG, IgA, IgD, IgE, IgM, etc.), where “X” denotes the antibody isotype. Thus, “IgG Fc” denotes that the Fc polypeptide is derived from a γ chain, “IgA Fc” denotes that the Fc polypeptide is derived from an α chain, “IgD Fc” denotes that the Fc polypeptide is derived from a δ chain, “IgE Fc” denotes that the Fc polypeptide is derived from a ϵ chain, “IgM Fc” denotes that the Fc polypeptide is derived from a μ chain, etc. In some embodiments, the IgG Fc polypeptide comprises the hinge, CH2, and CH3, but does not comprise CH1 or CL. In some embodiments, the IgG Fc polypeptide comprises CH2 and CH3, but does not comprise CH1, the hinge, or CL. In some embodiments, the IgG Fc polypeptide comprises CH1, hinge, CH2, CH3, with or without CL. “IgX-N Fc” or “IgGXN Fc” denotes that the Fc polypeptide is derived from a particular subclass of antibody isotype (such as canine IgG subclass IgG-A, IgG-B, IgG-C, or IgG-D; feline IgG subclass IgG1a, IgG1b, or IgG2; or equine IgG subclass IgG1, IgG2, IgG3, IgG4, IgG5, IgG6, or IgG7, etc.), where “N” denotes the subclass.

[0024] “Hinge” refers to any portion of an Fc polypeptide or variant Fc polypeptide that is proline-rich and comprises at least one cysteine residue located between CH1 and CH2 of a full-length heavy chain constant region.

[0025] In some embodiments, a hinge is capable of forming a disulfide linkage within the same hinge region, within the same Fc polypeptide, with a hinge region of a separate Fc polypeptide, or with a separate Fc polypeptide. In some embodiments, a hinge comprises at least one, at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, or at least ten proline residues.

[0026] The term “companion animal species” refers to an animal suitable to be a companion to humans. In some embodiments, a companion animal species is a canine (or dog), a

feline (or cat), or an equine (or horse). In some embodiments, a companion animal species is a small mammal, such as a canine, feline, dog, cat, rabbit, ferret, guinea pig, rodent, etc. In some embodiments, a companion animal species is a farm animal, such as a horse, cow, pig, etc.

[0027] In some embodiments, an IgX Fc polypeptide or an IgX-N Fc polypeptide is derived from a companion animal, such as a dog, a cat, or a horse. In some embodiments, IgG Fc polypeptides are isolated from canine γ heavy chains, such as IgG-A, IgG-B, IgG-C, or IgG-D. In some instances, IgG Fc polypeptides are isolated from feline γ heavy chains, such as IgG1a, IgG1b, or IgG2. In other instances, IgG Fc polypeptides are isolated from equine γ heavy chains, such as IgG1, IgG2, IgG3, IgG4, IgG5, IgG6, or IgG7.

[0028] The terms “IgX Fc” and “IgX Fc polypeptide” include wild-type IgX Fc polypeptides and variant IgX Fc polypeptides, unless indicated otherwise.

[0029] “Wild-type” refers to a non-mutated version of a polypeptide that occurs in nature, or a fragment thereof. A wild-type polypeptide may be produced recombinantly.

[0030] In some embodiments, a wild-type IgG Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 16, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 100, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 117, SEQ ID NO: 118.

[0031] A “variant” is a polypeptide that differs from a reference polypeptide by single or multiple non-native amino acid substitutions, deletions, and/or additions. In some embodiments, a variant retains at least one biological activity of the reference polypeptide. In some embodiments, a variant (e.g., a variant canine IgG-A Fc, a variant canine IgG-C Fc, a variant canine IgG-D Fc, variant equine IgG2 Fc, variant equine IgG5 Fc, or variant equine IgG6 Fc) has an activity that the reference polypeptide substantially lacks. For example, in some embodiments, a variant canine IgG-A Fc, a variant canine IgG-C Fc, a variant canine IgG-D Fc, variant equine IgG2 Fc, variant equine IgG5 Fc, or variant equine IgG6 Fc binds Protein A.

[0032] As used herein, “percent (%) amino acid sequence identity” and “homology” with respect to a nucleic acid molecule or polypeptide sequence are defined as the percentage of nucleotide or amino acid residues in a reference sequence that are identical with the nucleotide or amino acid residues in the specific nucleic acid molecule or polypeptide sequence, after aligning the sequences and introducing gaps, if necessary to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as

BLAST, BLAST-2, ALIGN, or MEGALINE™ (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of sequences being compared.

[0033] In some embodiments, a variant has at least about 50% sequence identity with the reference nucleic acid molecule or polypeptide after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Such variants include, for instance, polypeptides wherein one or more amino acid residues are added, deleted, at the N- or C-terminus of the polypeptide. In some embodiments, a variant has at least about 50% sequence identity, at least about 60% sequence identity, at least about 65% sequence identity, at least about 70% sequence identity, at least about 75% sequence identity, at least about 80% sequence identity, at least about 85% sequence identity, at least about 90% sequence identity, at least about 95% sequence identity, at least about 97% sequence identity, at least about 98% sequence identity, or at least about 99% sequence identity with the sequence of the reference nucleic acid or polypeptide.

[0034] A “point mutation” is a mutation that involves a single amino acid residue. The mutation may be the loss of an amino acid, substitution of one amino acid residue for another, or the insertion of an additional amino acid residue.

[0035] An “amino acid substitution” refers to the replacement of one amino acid in a polypeptide with another amino acid. In some embodiments, an amino acid substitution is a conservative substitution. Nonlimiting exemplary conservative amino acid substitutions are shown in Table 2. Amino acid substitutions may be introduced into a molecule of interest and the products screened for a desired activity, for example, retained/improved antigen binding, decreased immunogenicity, or improved ADCC or CDC or enhanced pharmacokinetics.

[0036] Table 2.

Original Residue	Exemplary Substitutions
Ala (A)	Val; Leu; Ile
Arg (R)	Lys; Gln; Asn
Asn (N)	Gln; His; Asp; Lys; Arg
Asp (D)	Glu; Asn
Cys (C)	Ser; Ala
Gln (Q)	Asn; Glu
Glu (E)	Asp; Gln

Gly (G)	Ala
His (H)	Asn; Gln; Lys; Arg
Ile (I)	Leu; Val; Met; Ala; Phe; Norleucine
Leu (L)	Norleucine; Ile; Val; Met; Ala; Phe
Lys (K)	Arg; Gln; Asn
Met (M)	Leu; Phe; Ile
Phe (F)	Trp; Leu; Val; Ile; Ala; Tyr
Pro (P)	Ala
Ser (S)	Thr
Thr (T)	Val; Ser
Trp (W)	Tyr; Phe
Tyr (Y)	Trp; Phe; Thr; Ser
Val (V)	Ile; Leu; Met; Phe; Ala; Norleucine

[0037] Amino acids may be grouped according to common side-chain properties:

- (1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;
- (2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
- (3) acidic: Asp, Glu;
- (4) basic: His, Lys, Arg;
- (5) residues that influence chain orientation: Gly, Pro;
- (6) aromatic: Trp, Tyr, Phe.

[0038] Non-conservative substitutions entail exchanging a member of one of these classes with another class.

[0039] A “variant IgG Fc” as used herein is an IgG Fc polypeptide that differs from a reference IgG Fc polypeptide by single or multiple amino acid substitutions, deletions, and/or additions and substantially retains at least one biological activity of the reference IgG Fc polypeptide.

[0040] An “amino acid derivative,” as used herein, refers to any amino acid, modified amino acid, and/or amino acid analogue, that is not one of the 20 common natural amino acids found in humans. Exemplary amino acid derivatives include natural amino acids not found in humans (e.g., seleno cysteine and pyrrolysine, which may be found in some microorganisms) and

unnatural amino acids. Exemplary amino acid derivatives, include, but are not limited to, amino acid derivatives commercially available through chemical product manufacturers (e.g., [sigmaaldrich.com/chemistry/chemistry-products.html?TablePage=16274965](https://www.sigmaaldrich.com/chemistry/chemistry-products.html?TablePage=16274965), accessed on May 6, 2017, which is incorporated herein by reference). One or more amino acid derivatives may be incorporated into a polypeptide at a specific location using a translation system that utilizes host cells, orthogonal aminoacyl-tRNA synthetases derived from eubacterial synthetases, orthogonal tRNAs, and an amino acid derivative. For further descriptions, see, e.g., U.S. Patent No. 9,624,485.

[0041] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution with an amino acid derivative. In some embodiments, the amino acid derivative is an alanine derivative, a cysteine derivative, an aspartic acid derivative, a glutamic acid derivative, a phenylalanine derivative, a glycine derivative, a histidine derivative, an isoleucine derivative, a lysine derivative, a leucine derivative, a methionine derivative, an asparagine derivative, a proline derivative, a glutamine derivative, an arginine derivative, a serine derivative, a threonine derivative, a valine derivative, a tryptophan derivative, or a tyrosine derivative.

[0042] In some embodiments, a variant IgG Fc polypeptide comprises a variant IgG Fc polypeptide of a companion animal species. In some embodiments, a variant IgG Fc polypeptide comprises a variant canine IgG Fc polypeptide, a variant equine IgG Fc polypeptide, or a feline IgG Fc polypeptide.

Exemplary Variant IgG Fc Polypeptides with Modified Protein A Binding

[0043] In some embodiments, a variant IgG Fc polypeptide has modified Protein A binding affinity. In some embodiments, a variant IgG Fc polypeptide has increased binding affinity to Protein A. In some embodiments, a variant IgG Fc polypeptide may be purified using Protein A column chromatography.

[0044] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 21, position 23, position 25, position 80, position 205, and/or position 207 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 21, position 23, and/or position 24 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 21, position 23, position 25, position 80, and/or position 207 of SEQ ID NO: 4.

[0045] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 15, and/or position 203 of SEQ ID NO: 64. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a

position corresponding to position 199 and/or position 200 of SEQ ID NO: 67. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 199, position 200, position 201, and/or 202 of SEQ ID NO: 68.

[0046] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 21, position 23, position 25, position 80, position 205, and/or position 207 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 21, position 23, and/or position 24 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 21, position 23, position 25, position 80, and/or position 207 of SEQ ID NO: 3.

[0047] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 15 and/or position 203 of SEQ ID NO: 64. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 199 and/or position 200 of SEQ ID NO: 67. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 199, position 200, position 201, and/or position 202 of SEQ ID NO: 68.

[0048] In some embodiments, a variant IgG Fc polypeptide comprises a threonine at a position corresponding to position 21 of SEQ ID NO: 1, a leucine at a position corresponding to position 23 of SEQ ID NO: 1, an alanine at a position corresponding to position 25 of SEQ ID NO: 1, a glycine at a position corresponding to position 80 of SEQ ID NO: 1, an alanine at a position corresponding to position 205 of SEQ ID NO: 1, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises a threonine at a position corresponding to position 21 of SEQ ID NO: 3, a leucine at a position corresponding to position 23 of SEQ ID NO: 3, and/or an isoleucine at a position corresponding to position 24 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a threonine at a position corresponding to position 21 of SEQ ID NO: 4, a leucine at a position corresponding to position 23 of SEQ ID NO: 4, an alanine at a position corresponding to position 25 of SEQ ID NO: 4, a glycine at a position corresponding to position 80 of SEQ ID NO: 3, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 4.

[0049] In some embodiments, a variant IgG Fc polypeptide comprises a threonine or a valine at a position corresponding to position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at a position corresponding to position 203 of SEQ ID NO: 64. In some embodiments, a variant IgG Fc polypeptide comprises a leucine at a position corresponding to position 199 of SEQ ID NO: 67, and/or a histidine at a position corresponding to position 200 of SEQ ID NO: 67. In some embodiments, a variant IgG Fc polypeptide comprises an isoleucine at a position corresponding

to position 199 of SEQ ID NO: 68, a histidine at a position corresponding to position 200 of SEQ ID NO: 68, an asparagine at a position corresponding to position 201 of SEQ ID NO: 68, and/or a histidine at a position corresponding to position 202 of SEQ ID NO: 68.

[0050] In some embodiments, a variant IgG Fc polypeptide comprises a threonine at position 21 of SEQ ID NO: 1, a leucine at position 23 of SEQ ID NO: 1, an alanine at position 25 of SEQ ID NO: 1, a glycine at position 80 of SEQ ID NO: 1, an alanine at position 205 of SEQ ID NO: 1, and/or a histidine at position 207 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises a threonine at position 21 of SEQ ID NO: 3, a leucine at position 23 of SEQ ID NO: 3, and/or an isoleucine at position 24 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprise a threonine at a position 21 of SEQ ID NO: 4, a leucine at position 23 of SEQ ID NO: 4, an alanine at position 25 of SEQ ID NO: 4, a glycine at position 80 of SEQ ID NO: 4, and/or a histidine at position 207 of SEQ ID NO: 4.

[0051] In some embodiments, a variant IgG Fc polypeptide comprises a threonine or a valine at position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at position 203 of SEQ ID NO: 64. In some embodiments, a variant IgG Fc polypeptide comprises a leucine at position 199 of SEQ ID NO: 67, and/or a histidine at position 200 of SEQ ID NO: 67. In some embodiments, a variant IgG Fc polypeptide comprises an isoleucine at position 199 of SEQ ID NO: 68, a histidine at position 200 of SEQ ID NO: 68, an asparagine at position 201 of SEQ ID NO: 68, and/or a histidine at position 202 of SEQ ID NO: 68.

[0052] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 84. In some embodiments, a variant IgG Fc polypeptide comprises SEQ ID NO: 19, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 75, or SEQ ID NO: 76.

Exemplary Variant IgG Fc Polypeptides with Modified CD16 Binding

[0053] In some embodiments, a variant IgG Fc polypeptide has modified CD16 binding affinity. In some embodiments, a variant IgG Fc polypeptide has decreased binding affinity to CD16.. In some embodiments, a vaiant IgG Fc may have a reduced ADCC immune response.

[0054] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 5, position 38, position 39, position 97, and/or position 98 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 5, position 38, position 39, position 97, and/or position 98 of SEQ ID NO: 3.

[0055] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 5, position 38, position 39, position 97, and/or position 98 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 5, position 38, position 39, position 97, and/or position 98 of SEQ ID NO: 3.

[0056] In some embodiments, a variant IgG Fc polypeptide comprises a proline at a position corresponding to position 5, a glycine at a position corresponding to position 38, an arginine at a position corresponding to position 39, a isoleucine at a position corresponding to position 97, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a proline at a position corresponding to position 5, a glycine at a position corresponding to position 38, an arginine at a position corresponding to position 39, a isoleucine at a position corresponding to position 97, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 3.

[0057] In some embodiments, a variant IgG Fc polypeptide comprises a proline at position 5, a glycine at position 38, an arginine at position 39, a isoleucine at position 97, and/or a glycine at position 98 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a proline at position 5, a glycine at position 38, an arginine at position 39, a isoleucine at position 97, and/or a glycine at position 98 of SEQ ID NO: 3.

[0058] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

Exemplary Variant IgG Fc Polypeptides with Modified C1q Binding

[0059] In some embodiments, a variant IgG Fc polypeptide has modified C1q binding affinity. In some embodiments, a variant IgG Fc polypeptide has reduced binding affinity to C1q. In some embodiments, a variant IgG Fc polypeptide may have reduced complement fixation. In some embodiments, a variant IgG Fc may have a reduced complement-mediated immune response.

[0060] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 63. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 65. In some embodiments, a variant IgG Fc

polypeptide comprises an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 66. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 80. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 81.

[0061] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 93 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 93 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 87 of SEQ ID NO: 63. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 87 of SEQ ID NO: 65. In some embodiments, a variant IgG Fc polypeptide comprises or an amino acid substitution at position 87 of SEQ ID NO: 66. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 198 of SEQ ID NO: 80. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 198 of SEQ ID NO: 81.

[0062] In some embodiments, a variant IgG Fc polypeptide comprises an arginine at a position corresponding to position 93 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an arginine at a position corresponding to position 93 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 87 of SEQ ID NO: 63. In some embodiments, a variant IgG Fc polypeptide comprises a serine substitution at a position corresponding to position 87 of SEQ ID NO: 65. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 87 of SEQ ID NO: 66. In some embodiments, a variant IgG Fc polypeptide comprises an alanine at a position corresponding to position 198 of SEQ ID NO: 80. In some embodiments, a variant IgG Fc polypeptide comprises an alanine at a position corresponding to position 198 of SEQ ID NO: 81.

[0063] In some embodiments, a variant IgG Fc polypeptide comprises an arginine at position 93 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 93 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 87 of SEQ ID NO: 63. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 87 of SEQ ID NO: 65. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 87 of SEQ ID NO: 66. In some embodiments, a variant IgG Fc polypeptide comprises an alanine at position 198 of SEQ ID

NO: 80. In some embodiments, a variant IgG Fc polypeptide comprises an alanine at position 198 of SEQ ID NO: 81.

[0064] In some embodiments, a variant IgG Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 78, SEQ ID NO: 79, or SEQ ID NO: 84. In some embodiments, a variant IgG Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, or SEQ ID NO: 77. In some embodiments, a variant IgG Fc polypeptide comprises the amino acid sequence of SEQ ID NO: 82 or SEQ ID NO: 83.

Exemplary Variant IgG Fc Polypeptides with a Modified Inter-Chain Disulfide Linkage

[0065] In some embodiments, a variant feline IgG Fc polypeptide has at least one additional inter-chain disulfide linkage relative to the wild-type feline IgG Fc polypeptide. In some embodiments, a variant feline IgG Fc polypeptide has at least one additional inter-chain disulfide linkage in the hinge region. In some embodiments, a variant feline IgG2 Fc polypeptide with at least one additional inter-chain disulfide linkage has increased inter-chain stability relative to the wild-type feline IgG Fc polypeptide. In some embodiments, a variant IgG polypeptide has at least one amino acid modification to a hinge region relative to a wild-type IgG Fc polypeptide. In some embodiments, the wild-type IgG Fc polypeptide is a wild-type feline or equine IgG Fc polypeptide. In some embodiments, the variant IgG Fc polypeptide comprises a hinge region or a portion of a hinge region from an IgG Fc polypeptide of a different isotype. In some embodiments, the variant IgG Fc polypeptide comprises a hinge region from a wild-type feline IgG-1a Fc polypeptide, from a wild-type feline IgG-1b Fc polypeptide, or from a wild-type equine IgG1 Fc polypeptide. In some embodiments, a variant IgG2 Fc polypeptide has increased recombinant production and/or increased hinge disulfide formation relative to the wild-type IgG Fc polypeptide. In some embodiments, the increased recombinant production and/or increased hinge disulfide formation can be determined by SDS-PAGE analysis under reducing and/or non-reducing conditions.

[0066] In some embodiments, a variant IgG Fc polypeptide comprises a cysteine at a position corresponding to position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, or position 16 of SEQ ID NO: 16. In some embodiments, a variant IgG Fc polypeptide comprises a cysteine at position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, or position 16 of SEQ ID NO: 16. In some embodiments, a variant IgG Fc polypeptide comprises SEQ ID NO: 17.

[0067] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118. In some embodiments, a variant IgG Fc

polypeptide comprises an amino acid substitution at a position corresponding to position 3 and/or at a position corresponding to position 20 of SEQ ID NO: 129.

[0068] In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118. In some embodiments, a variant IgG Fc polypeptide comprises an amino acid substitution at position 3 and/or at a position corresponding to position 20 of SEQ ID NO: 129.

[0069] In some embodiments, a variant IgG Fc polypeptide comprises a proline at a position corresponding to position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 3 and/or a proline at a position corresponding to position 20 of SEQ ID NO: 129.

[0070] In some embodiments, a variant IgG Fc polypeptide comprises a proline at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 3 and/or a proline at position 20 of SEQ ID NO: 129.

[0071] In some embodiments, the variant IgG Fc polypeptide comprises SEQ ID NO: 19, SEQ ID NO: 125 or SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135.

Exemplary Variant IgG Fc Polypeptides for Heterodimeric Polypeptides

[0072] In certain embodiments, a heterodimeric polypeptide provided herein is a bispecific antibody. A bispecific antibody has a binding specificity for two different epitopes or target molecules. In some embodiments, a bispecific antibody binds to two different epitopes of the same target molecule. Bispecific antibodies may be full length antibodies or antibody fragments.

[0073] In some embodiments, the heterodimeric polypeptide comprises a first variant IgG Fc polypeptide comprising a “knob” mutation and a second variant IgG Fc polypeptide comprising a “hole” mutation. Nonlimiting exemplary knob and hole mutations are described, for example, in Merchant, A. M. *et al.* An efficient route to human bispecific IgG. *Nat Biotechnol*, 16(7):677-81 (1998).

[0074] In some embodiments, a variant canine or variant feline IgG Fc polypeptide comprises a knob mutation. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 1. In some

embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 4. In some embodiments, a variant IgG Fc polypeptide comprises a tryptophan at a position corresponding to position 154 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118.

[0075] In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at position 138 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at position 137 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at position 137 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a tyrosine or a tryptophan at position 138 of SEQ ID NO: 4. In some embodiments, a variant IgG Fc polypeptide comprises a tryptophan at position 154 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118.

[0076] In some embodiments, a variant IgG Fc polypeptide comprising a knob mutation comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

[0077] In some embodiments, a variant canine or a variant feline IgG Fc polypeptide comprises a hole mutation. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 4. In some embodiments, a variant IgG Fc polypeptide comprises a serine at a position corresponding to position 154, an alanine at a position corresponding to position 156, and/or a threonine at a

position corresponding to position 197 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118.

[0078] In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 138, an alanine at position 140, and/or a threonine at position 181 of SEQ ID NO: 1. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 137, an alanine at position 139, and/or a threonine at position 181 of SEQ ID NO: 2. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 137, an alanine at position 139, and/or a threonine at position 181 of SEQ ID NO: 3. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 138, an alanine at position 140, and/or a threonine at position 181 of SEQ ID NO: 4. In some embodiments, a variant IgG Fc polypeptide comprises a serine at position 154, an alanine at position 156, and/or a threonine at position 197 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118.

[0079] In some embodiments, a variant IgG Fc polypeptide comprising a hole mutation comprises an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 124.

[0080] In some embodiments, a contiguous polypeptide comprises a GLP1 polypeptide and a variant canine or feline IgG Fc polypeptide comprising a knob mutation. In some embodiments, a contiguous polypeptide comprises a glucagon polypeptide and a variant canine or feline IgG Fc polypeptide comprising a knob mutation. In some embodiments, a contiguous polypeptide comprises a GLP1 polypeptide and a variant canine or feline IgG Fc polypeptide comprising a hole mutation. In some embodiments, a contiguous polypeptide comprises a glucagon polypeptide and a variant canine or feline IgG Fc polypeptide comprising a hole mutation.

[0081] In some embodiments, the heterodimeric polypeptide comprises a first contiguous polypeptide comprises a GLP1 polypeptide and a variant canine or feline IgG Fc polypeptide comprising a knob mutation, and a second contiguous polypeptide comprises a glucagon polypeptide and a variant canine or feline IgG Fc polypeptide comprising a hole mutation. In some embodiments, the heterodimeric polypeptide comprises a first contiguous polypeptide comprises a glucagon polypeptide and a variant canine or feline IgG Fc polypeptide comprising a knob mutation, and a second contiguous polypeptide comprises a GLP1 polypeptide and a variant canine or feline IgG Fc polypeptide comprising a hole mutation.

Exemplary GLP1 Polypeptides and Glucagon Polypeptides

[0082] “GLP1” or a “GLP1 polypeptide,” as used herein, is a polypeptide comprising the entirety or a fragment of glucagon-like peptide-1 that binds to a glucagon-like peptide 1 receptor (GLP1R).

[0083] For example, “GLP1” refers to a GLP1 polypeptide from any vertebrate source, including mammals such as primates (e.g., humans and cynomolgus monkeys), rodents (e.g., mice and rats), and companion animals (e.g., dogs, cats, and equine), unless otherwise indicated. In some embodiments, a GLP1 polypeptide is a wild-type GLP1 polypeptide, such as GLP1 (7-37) (SEQ ID N: 85). In some embodiments, a GLP1 polypeptide is a variant GLP1 polypeptide, such as GLP1 (7-36) (SEQ ID NO: 98), GLP1 (7-35) (SEQ ID NO: 99), GLP1-S8 (7-35) (SEQ ID NO: 86), or GLP1-G8 (7-35) (SEQ ID NO: 87). In some embodiments, GLP1 comprises the amino acid sequence of SEQ ID NO: 20.

[0084] “GLP1R,” as used herein, is a polypeptide comprising the entirety or a fragment of a glucagon-like peptide 1 receptor that is capable of binding to a wild-type GLP1.

[0085] For example, “GLP1R” refers to a GLP1R polypeptide from any vertebrate source, including mammals such as primates (e.g., humans and cynomolgus monkeys), rodents (e.g., mice and rats), and companion animals (e.g., dogs, cats, and equine), unless otherwise indicated. In some embodiments, GLP1R is an extracellular domain fragment that binds a wild-type GLP1 polypeptide. In some embodiments, a feline GLP1R comprises the amino acid sequence of SEQ ID NO: 49. In some embodiments, a feline GLP1R comprises the amino acid sequence of SEQ ID NO: 48.

[0086] An “extracellular domain” (“ECD”) is the portion of a polypeptide that extends beyond the transmembrane domain into the extracellular space. The term “extracellular domain,” as used herein, may comprise a complete extracellular domain or may comprise a truncated extracellular domain missing one or more amino acids, that binds to its ligand. The composition of the extracellular domain may depend on the algorithm used to determine which amino acids are in the membrane. Different algorithms may predict, and different systems may express, different extracellular domains for a given protein.

[0087] “Glucagon” or a “glucagon polypeptide,” as used herein, is a polypeptide comprising the entirety or a fragment of glucagon that binds to a glucagon receptor.

[0088] For example, “glucagon” refers to a glucagon polypeptide from any vertebrate source, including mammals such as primates (e.g., humans and cynomolgus monkeys), rodents (e.g., mice and rats), and companion animals (e.g., dogs, cats, and equine), unless otherwise

indicated. In some embodiments, a glucagon polypeptide is a wild-type glucagon polypeptide, such as SEQ ID NO: 21.

Exemplary Variant IgG Fc Polypeptides and Fusion Molecules

[0089] Polypeptides and other molecules may comprise a variant IgG Fc polypeptide. In some embodiments, a fusion molecule comprises a variant IgG Fc polypeptide, such as the variant IgG Fc polypeptides described herein. In some embodiments, an antibody or an antibody fragment comprises a variant IgG Fc polypeptide, such as the variant IgG Fc polypeptides described herein.

[0090] A “fusion molecule,” as used herein, refers to a molecule comprising one or more “fusion partners.” In some embodiments, the fusion partners are covalently linked (“fused”). If two fusion partners are both polypeptides, the fusion partner polypeptides may be part of a contiguous amino acid sequence (i.e., a contiguous polypeptide). A first fusion partner polypeptide may be linked to either the N-terminus or the C-terminus of a second fusion partner. In some embodiments, the fusion partners are translated as a single polypeptide from a coding sequence that encodes both fusion partners. Fusion partners may be covalently linked through other means, such as, for example, a chemical linkage other than a peptide bond. Many known methods of covalently linking polypeptides to other molecules (for example, fusion partners) may be used. In other embodiments, the fusion partners are fused through a “linker,” which is comprised of at least one amino acid or chemical moiety. In some embodiments, fusion partners are noncovalently linked. In some such embodiments, they may be linked, for example, using binding pairs. Exemplary binding pairs include, but are not limited to, biotin and avidin or streptavidin, an antibody and its antigen, etc.

[0091] In some embodiments, the fusion partners include an IgG Fc polypeptide and at least one GLP1 polypeptide. In some embodiments, the fusion partners include an IgG Fc polypeptide, a GLP1 polypeptide, and a glucagon polypeptide. In some embodiments, a GLP1 polypeptide may be linked to either the N-terminus or the C-terminus of an IgG Fc polypeptide. In some embodiments, a glucagon polypeptide may be linked to either the N-terminus or the C terminus of an IgG Fc polypeptide.

[0092] The term “contiguous polypeptide” herein is used to mean an uninterrupted sequence of amino acids. A contiguous polypeptide is typically translated from a single continuous DNA sequence. It can be made by genetic engineering, for example, by removing the stop codon from the DNA sequence of the first protein, then appending the DNA sequence of the second protein in frame, so that the DNA sequence is expressed as a single protein. Typically, this is accomplished by cloning a cDNA into an expression vector in frame with an existing gene.

[0093] A “linker” refers to one or more amino acid residues that connects a first polypeptide with a second polypeptide.

[0094] In some embodiments, the linker is a flexible, non-structural linker. In some embodiments, the linker is a glycine-rich, serine-rich, or glycine- and serine-rich linker. In some embodiments, a linker comprises 100%, at least 95%, at least 90%, or at least 85% serine and/or glycine amino acid residues.

[0095] An “extension,” as used herein, refers to one or more amino acid residues that are connected to a polypeptide at its C-terminus or at its N-terminus.

[0096] In some embodiments, an extension is flexible. In some embodiments, the extension adds flexibility to the polypeptide without interfering with the biological activity of the polypeptide. In some embodiments, the extension increases solubility of the polypeptide. In some embodiments, the extension comprises one or more glycine residues. In some embodiments, the extension comprises a glycine residue (SEQ ID NO: 88), two glycine residues (SEQ ID NO: 89), a three glycine residues (SEQ ID NO: 90), four glycine residues (SEQ ID NO: 91), five glycine residues (SEQ ID NO: 92), six glycine residues (SEQ ID NO: 93), seven glycine residues (SEQ ID NO: 94), eight glycine residues (SEQ ID NO: 95), or more glycine residues.

[0097] In some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a GLP1 polypeptide comprising an amino acid sequence of SEQ ID NO: 85. In some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a GLP1 polypeptide comprising an amino acid sequence of SEQ ID NO: 86. In

some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a GLP1 polypeptide comprising an amino acid sequence of SEQ ID NO: 87. In some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a GLP1 polypeptide comprising an amino acid sequence of SEQ ID NO: 98. In some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175, 176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a GLP1 polypeptide comprising an amino acid sequence of SEQ ID NO: 99.

[0098] In some embodiments, the contiguous polypeptide comprises an IgG Fc polypeptide comprising an amino acid sequence of any one of SEQ ID NOs: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 100, 107, 108, 109, 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122, 123, 124, 125, 126, 127, 128, 129, 130, 131, 132, 133, 134, 135, 136, 137, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 167, 158, 159, 160, 161, 162, 163, 164, 165, 166, 167, 168, 169, 170, 171, 172, 173, 174, 175,

176, 177, 178, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, or 199 and a glucagon polypeptide comprising an amino acid sequence of SEQ ID NO: 21.

[0099] In some embodiments, a contiguous polypeptide comprises a first GLP1 polypeptide (GLP1A), a first linker (L1), an Fc polypeptide of a companion animal species, optionally a second linker (L2), and optionally a second GLP1 polypeptide (GLP1B). In some embodiments, the contiguous polypeptide comprises:

Formula (I): GLP1A—L1—Fc;

Formula (II): Fc—L1—GLP1A; or

Formula (III): GLP1A—L1—Fc—L2—GLP1B.

[0100] In some embodiments, a contiguous polypeptide comprises a GLP1 polypeptide, a first linker (L1), an Fc polypeptide, a second linker (L2), and a glucagon polypeptide (Gluc). In some embodiments, the contiguous polypeptide comprises:

Formula (IV): GLP1—L1—Fc—L2—Gluc; or

Formula (V): Gluc—L1—Fc—L2—GLP1.

[0101] In some embodiments, the GLP1 fusion molecule has an increased serum half-life compared to a wild-type GLP1 polypeptide. The increased half-life of the GLP1 fusion molecules described herein may require lower doses and less-frequent dosing regimen than wild-type GLP1 polypeptides.

[0102] In some embodiments, GLP1B, if present, comprises the same amino acid sequence as GLP1A.

[0103] In some embodiments, GLP1, GLP1A, or GLP1B, if present, comprises a wild-type GLP1 polypeptide. In some embodiments, GLP1, GLP1A, or GLP1B, if present, comprises a variant GLP1 polypeptide. In some embodiments, GLP1, GLP1A, or GLP1B, if present, comprises an amino acid sequence of SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 98, or SEQ ID NO: 99.

[0104] In some embodiments, the glucagon polypeptide comprises a wild-type glucagon polypeptide. In some embodiments, the glucagon polypeptide comprises an amino acid sequence of SEQ ID NO: 21. In some embodiments, the glucagon polypeptide comprises a variant glucagon polypeptide.

[0105] In some embodiments, the Fc polypeptide is a human IgG Fc. In some embodiments, the Fc polypeptide is a human IgG1 Fc, a human IgG2 Fc, a human IgG3 Fc, or a human IgG4 Fc. In some embodiments, the Fc polypeptide is a variant human IgG Fc.

[00106] In some embodiments, the Fc polypeptide is an IgG Fc from a companion animal. In some embodiments, the Fc polypeptide is a canine IgG-A Fc, a canine IgG-B Fc, a canine IgG-C Fc, a canine IgG-D Fc. In some embodiments, the Fc is an equine IgG1 Fc, an equine IgG2 Fc, an equine IgG3 Fc, an equine IgG4 Fc, an equine IgG5 Fc, an equine IgG6 Fc, or an equine IgG7 Fc. In some embodiments, the Fc is a feline IgG1a Fc, a feline IgG1b Fc, or a feline IgG2 Fc.

[00107] In some embodiments, the Fc polypeptide is a variant IgG Fc. In some embodiments, the Fc polypeptide is a variant canine IgG-A Fc, a variant canine IgG-B Fc, a variant canine IgG-C Fc, a variant canine IgG-D Fc. In some embodiments, the Fc is a variant equine IgG1 Fc, a variant equine IgG2 Fc, a variant equine IgG3 Fc, a variant equine IgG4 Fc, a variant equine IgG5 Fc, a variant equine IgG6 Fc, or a variant equine IgG7 Fc. In some embodiments, the Fc is a variant feline IgG1a Fc, a variant feline IgG1b Fc, or a variant feline IgG2 Fc.

[00108] In some embodiments, L1 and L2, if present, each independently is a flexible linker. In some embodiments, the amino acid sequence of L1 and L2, if present, each independently comprises 100%, at least 95%, at least 90%, at least 85% serine and/or glycine amino acid residues.

[00109] In some embodiments, the contiguous polypeptide comprises an extension at its C-terminus. In some embodiments, the contiguous polypeptide comprises a glycine residue, two glycine residues, three glycine residues, four glycine residues, five glycine residues, six glycine residues, seven glycine residues, eight glycine residues, or greater than eight glycine residues at its C-terminus. In some embodiments, the contiguous polypeptide comprises an amino acid sequence of SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, or SEQ ID NO: 95 at its C-terminus.

[00110] In some embodiments, the contiguous polypeptide comprises the amino acid sequence of SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29; SEQ ID NO: 30; SEQ ID NO: 31; SEQ ID NO: 32; SEQ ID NO: 33; SEQ ID NO: 34; SEQ ID NO: 35; SEQ ID NO: 36; SEQ ID NO: 37; SEQ ID NO: 38; SEQ ID NO: 39; SEQ ID NO: 40; SEQ ID NO: 41; SEQ ID NO: 42; SEQ ID NO: 43; SEQ ID NO: 44; SEQ ID NO: 45; SEQ ID NO: 46; SEQ ID NO: 47, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 52; SEQ ID NO: 53; SEQ ID NO: 54; SEQ ID NO: 55; SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 103; SEQ ID NO: 104; SEQ ID NO: 105; or SEQ ID NO: 106.

[00111] A nucleotide sequence encoding a polypeptide of interest, such as a variant IgG Fc polypeptide or other polypeptide described herein, can be inserted into an expression vector

suitable for expression in a selected host cell. A variant IgG Fc polypeptide or other polypeptide described herein may be expressed by culturing a host cell transfected with an expression vector comprising the nucleotide sequence.

[00112] A “vector” is a plasmid that can be used to transfer DNA sequences from one organism to another or to express a gene of interest. A vector typically includes an origin of replication and regulatory sequences which regulate the expression of the gene of interest, and may or may not carry a selective marker gene, such as an antibiotic resistance gene. A vector is suitable for the host cell in which it is to be expressed. A vector may be termed a “recombinant vector” when the gene of interest is present in the vector.

[00113] A “host cell” refers to a cell that may be or has been a recipient of a vector or isolated polynucleotide. Host cells may be prokaryotic cells or eukaryotic cells. Exemplary eukaryotic cells include mammalian cells, such as primate or non-primate animal cells; fungal cells, such as yeast; plant cells; and insect cells. Nonlimiting exemplary mammalian cells include, but are not limited to, NS0 cells, PER.C6® cells (Crucell), 293 cells, and CHO cells, and their derivatives, such as 293-6E, DG44, CHO-S, and CHO-K cells. Host cells include progeny of a single host cell, and the progeny may not necessarily be completely identical (in morphology or in genomic DNA complement) to the original parent cell due to natural, accidental, or deliberate mutation. A host cell includes cells transfected in vivo with a polynucleotide(s) encoding an amino acid sequence(s) provided herein.

[00114] The term “isolated” as used herein refers to a molecule that has been separated from at least some of the components with which it is typically found in nature or produced. For example, a polypeptide is referred to as “isolated” when it is separated from at least some of the components of the cell in which it was produced. Where a polypeptide is secreted by a cell after expression, physically separating the supernatant containing the polypeptide from the cell that produced it is considered to be “isolating” the polypeptide. Similarly, a polynucleotide is referred to as “isolated” when it is not part of the larger polynucleotide (such as, for example, genomic DNA or mitochondrial DNA, in the case of a DNA polynucleotide) in which it is typically found in nature, or is separated from at least some of the components of the cell in which it was produced, for example, in the case of an RNA polynucleotide. Thus, a DNA polynucleotide that is contained in a vector inside a host cell may be referred to as “isolated.”

[00115] A “signal sequence” refers to a sequence of amino acid residues or polynucleotides encoding such, which facilitates secretion of a polypeptide of interest and is typically cleaved upon export of the polypeptide to the outside of the cell surface membrane.

[00116] In some embodiments, a variant IgG Fc polypeptide or a contiguous polypeptide comprising a variant Fc polypeptide is isolated using chromatography, such as size exclusion chromatography, ion exchange chromatography, protein A column chromatography, hydrophobic interaction chromatography, and CHT chromatography.

[00117] A label can be attached to a variant IgG Fc polypeptides or a contiguous polypeptide comprising a variant Fc polypeptide. A “label” means a moiety attached to a molecule to render it detectable. In some embodiments, a variant IgG Fc polypeptide or a contiguous polypeptide comprising a variant Fc polypeptide is labeled with a detectable moiety including but not limited to radioisotopes, fluorescent labels, and various enzyme-substrate labels known in the art. In some embodiments, the label is a detectable marker that can produce a signal that is detectable by visual or instrumental means, for example, incorporation of a radiolabeled amino acid or attachment to a polypeptide of biotinyl moieties that can be detected by marked avidin (for example, streptavidin containing a fluorescent marker or enzymatic activity that can be detected by optical or colorimetric methods). Examples of labels for polypeptides include, but are not limited to, the following: radioisotopes or radionuclides (for example, ^3H , ^{14}C , ^{35}S , ^{90}Y , ^{99}Tc , ^{111}In , ^{125}I , ^{131}I , ^{177}Lu , ^{166}Ho , or ^{153}Sm); chromogens, fluorescent labels (for example, FITC, rhodamine, lanthanide phosphors), enzymatic labels (for example, p-galactosidase, horseradish peroxidase, luciferase, alkaline phosphatase); chemiluminescent markers; biotinyl groups; predetermined polypeptide epitopes recognized by a secondary reporter (for example, leucine zipper pair sequences, binding sites for secondary antibodies, metal binding domains, epitope tags); and magnetic agents, such as gadolinium chelates. Representative examples of labels commonly employed for immunoassays include moieties that produce light, for example, acridinium compounds, and moieties that produce fluorescence, for example, fluorescein. In this regard, the moiety itself may not be detectably labeled but may become detectable upon reaction with yet another moiety. General techniques to be used in performing the various immunoassays noted above are known to those of ordinary skill in the art.

Exemplary Variant IgG Fc Polypeptide Affinity to Protein A and/or C1q and/or CD16

[00118] The variant IgG Fc polypeptides described herein may have altered binding affinity to Protein A and/or C1q and/or CD16. In some embodiments, a variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide. Such variant IgG Fc polypeptides may be purified by Protein A column chromatography. In some embodiments, a variant IgG Fc polypeptide has reduced binding affinity to C1q relative to the wild-type IgG Fc polypeptide. Such variant IgG Fc polypeptides may have reduced complement-mediated immune responses. In some embodiments, a variant IgG Fc polypeptide has reduced

binding affinity to CD16 relative to the wild-type IgG Fc polypeptide. Such variant IgG Fc polypeptides may have reduced ADCC immune responses. In some embodiments, a variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide and/or has reduced binding affinity to C1q relative to the wild-type IgG Fc polypeptide and/or has reduced binding affinity to CD16 relative to the wild-type IgG Fc polypeptide.

[00119] “Protein A,” as used herein, is a polypeptide comprising the entirety or a portion of Protein A that is capable of binding a wild-type canine IgG-B Fc, a wild-type equine IgG1 Fc, a wild-type equine IgG3 Fc, a wild-type equine IgG4 Fc, a wild-type equine IgG7 Fc, a wild-type feline IgG1a Fc, a wild-type feline IgG1b Fc, or a wild-type feline IgG2 Fc.

[00120] “C1q” or “C1q complex” is used interchangeably to refer to a protein complex involved in the complement system, or a portion thereof, that can bind a wild-type canine IgG-B Fc, a wild-type canine IgG-C Fc, a wild-type equine IgG1 Fc, a wild-type equine IgG3 Fc, a wild-type equine IgG4 Fc, a wild-type equine IgG7 Fc, a wild-type feline IgG1a Fc, or a wild-type feline IgG1b Fc.

[00121] “CD16,” as used herein, is a polypeptide comprising the entirety or a portion of CD16 that is capable of binding a wild-type canine IgG-A Fc or a wild-type canine IgG-D Fc. The term “binds” to a substance is a term that is well understood in the art, and methods to determine such binding are also well known in the art. A molecule is said to exhibit “binding” if it reacts, associates with, or has affinity for a particular cell or substance and the reaction, association, or affinity is detectable by one or more methods known in the art, such as, for example, immunoblot, ELISA, KinEx A, biolayer interferometry (BLI), surface plasmon resonance devices, or etc.

[00122] “Protein A +,” as used herein, means that the Fc polypeptide has Protein A binding affinity. In some embodiments, a Protein A+ Fc polypeptide comprises at least one amino acid modification that increases Protein A binding affinity.

[00123] “Protein A −,” as used herein, means that the Fc polypeptide has low or no Protein A binding affinity.

[00124] “C1q +,” as used herein, means that the Fc polypeptide has C1q binding affinity.

[00125] “C1q −,” as used herein, means that the Fc polypeptide has low or no C1q binding affinity. In some embodiments, a C1q− Fc polypeptide has at least one amino acid modification that reduces C1q binding affinity.

[00126] “CD16 +,” as used herein, means that the Fc polypeptide has CD16 binding affinity.

[00127] “CD16 –,” as used herein, means that the Fc polypeptide has low or no CD16 binding affinity. In some embodiments, a CD16– Fc polypeptide has at least one amino acid modification that reduces CD16 binding affinity.

[00128] The term “affinity” means the strength of the sum total of noncovalent interactions between a single binding site of a molecule (for example, a receptor) and its binding partner (for example, a ligand). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_D). Affinity can be measured by common methods known in the art, such as, for example, immunoblot, ELISA, KinEx A, biolayer interferometry (BLI), or surface plasmon resonance devices.

[00129] “Surface plasmon resonance” denotes an optical phenomenon that allows for the analysis of real-time biospecific interactions by detection of alterations in protein concentrations within a biosensor matrix, for example using the BIAcore™ system (BIAcore International AB, a GE Healthcare company, Uppsala, Sweden and Piscataway, N.J.). For further descriptions, see Jonsson et al. (1993) *Ann. Biol. Clin.* 51: 19-26.

[00130] “Biolayer interferometry” refers to an optical analytical technique that analyzes the interference pattern of light reflected from a layer of immobilized protein on a biosensor tip and an internal reference layer. Changes in the number of molecules bound to the biosensor tip cause shifts in the interference pattern that can be measured in real-time. A nonlimiting exemplary device for biolayer interferometry is an Octet® system (Pall ForteBio LLC). See, e.g., Abdiche et al., 2008, *Anal. Biochem.* 377: 209-277.

[00131] The terms “ K_D ,” “ K_d ,” “ K_d ” or “ K_d value” as used interchangeably to refer to the equilibrium dissociation constant of a receptor - ligand interaction or antibody-antigen interaction.

[00132] In some embodiments, a variant IgG Fc polypeptide binds to Protein A with a dissociation constant (K_D) of less than 5×10^{-6} M, less than 1×10^{-6} M, less than 5×10^{-7} M, less than 1×10^{-7} M, less than 5×10^{-8} M, less than 1×10^{-8} M, less than 5×10^{-9} M, less than 1×10^{-9} M, less than 5×10^{-10} M, less than 1×10^{-10} M, less than 5×10^{-11} M, less than 1×10^{-11} M, less than 5×10^{-12} M, or less than 1×10^{-12} M, as measured by biolayer interferometry.

[00133] In some embodiments, a variant IgG Fc polypeptide binds to C1q or CD16 with a dissociation constant (K_D) of greater than 5×10^{-6} M, greater than 1×10^{-5} M, greater than 5×10^{-5} M, greater than 1×10^{-4} M, greater than 5×10^{-4} M, or greater than 1×10^{-3} M, as measured by biolayer interferometry.

[00134] In some embodiments, the K_D of an IgG Fc polypeptide, such as a variant IgG Fc polypeptide, to Protein A or to C1q or to CD16 is measured by using biolayer interferometry assays using a biosensor, such as an Octet® System (Pall ForteBio LLC, Fremont, CA) according

to the supplier's instructions. In brief, biotinylated Protein A or C1q or CD16 is bound to the sensor tip and the association of IgG Fc polypeptide is monitored for a specified time or until steady state is reached. Dissociation may be monitored for a specified time or until steady state is reached. A buffer only blank curve is subtracted to correct for any drift. The data are fit to a 2:1 binding model using ForteBio data analysis software to determine association rate constant (k_{on}), dissociation rate constant (k_{off}), and the K_d . The equilibrium dissociation constant (K_D) is calculated as the ratio of k_{off}/k_{on} . The term " k_{on} " refers to the rate constant for association of a molecule X to its partner Y and the term " k_{off} " refers to the rate constant for dissociation of a molecule X or partner Y from the molecule X / partner Y complex.

[00135] To "increase" or "stimulate" means to increase, improve, or augment an activity, function, or amount as compared to a reference. In some embodiments, by "increase" or "stimulate" is meant the ability to cause an overall increase of about 5% or greater, of about 10% or greater, of about 20% or greater, of about 30% or greater, of about 40% or greater, of about 50% or greater, of about 60% or greater, of about 70% or greater, of about 80% or greater, of about 90% or greater, of about 100% or greater, of about 125% or greater, of about 200% or greater relative to a reference value. In some embodiments, by "increase" or "stimulate" is meant the ability to cause an overall increase of about 5% to about 50%, of about 10% to about 20%, of about 50% to about 100%, of about 25% to about 70% relative to a reference value. In some embodiments, by "increase" or "stimulate" is meant the ability to cause an overall increase of 50% or greater. In some embodiments, by "increase" or "stimulate" is meant the ability to cause an overall increase of 75%, 85%, 90%, 95%, or greater. In some embodiments, the amount noted above is stimulated or increased over a period of time, relative to a control dose (such as a placebo) over the same period of time.

[00136] In some embodiments, a variant IgG Fc polypeptide is capable of binding to Protein A with an increased affinity of about 5% or greater, of about 10% or greater, of about 20% or greater, of about 30% or greater, of about 40% or greater, of about 50% or greater, of about 60% or greater, of about 70% or greater, of about 80% or greater, of about 90% or greater, of about 100% or greater, of about 125% or greater, of about 150% or greater, of about 200% or greater relative to a reference IgG Fc polypeptide. In some embodiments, a variant IgG Fc polypeptide is capable of binding to Protein A with an increased affinity of about 5% to about 50%, of about 10% to about 20%, of about 50% to about 100%, of about 25% to about 70% relative to a reference IgG Fc polypeptide. In some embodiments, the reference IgG Fc polypeptide is a wild-type IgG Fc polypeptide. In some embodiments, the reference IgG Fc polypeptide is a different variant IgG Fc polypeptide.

[00137] To “reduce” or “inhibit” means to decrease, reduce, or arrest an activity, function, or amount as compared to a reference. In some embodiments, by “reduce” or “inhibit” is meant the ability to cause an overall decrease of about 5% or greater, of about 10% or greater, of about 20% or greater, of about 30% or greater, of about 40% or greater, of about 50% or greater, of about 60% or greater, of about 70% or greater, of about 80% or greater, or of about 90% or greater relative to a reference IgG Fc polypeptide. In some embodiments, by “reduce” or “inhibit” is meant the ability to cause an overall decrease of about 5% to about 50%, of about 10% to about 20%, of about 50% to about 100%, of about 25% to about 70% relative to a reference value. In some embodiments, by “reduce” or “inhibit” is meant the ability to cause an overall decrease of 50% or greater. In some embodiments, by “reduce” or “inhibit” is meant the ability to cause an overall decrease of 75%, 85%, 90%, 95%, or greater. In some embodiments, the amount noted above is inhibited or decreased over a period of time, relative to a control dose (such as a placebo) over the same period of time.

[00138] In some embodiments, a variant IgG Fc polypeptide is capable of binding to C1q or CD16 with a decreased affinity of about 5% or greater, of about 10% or greater, of about 20% or greater, of about 30% or greater, of about 40% or greater, of about 50% or greater, of about 60% or greater, of about 70% or greater, of about 80% or greater, of about 90% or greater relative to a reference IgG Fc polypeptide. In some embodiments, a variant IgG Fc polypeptide is capable of binding to C1q or CD16 with a decreased affinity of about 5% to about 50%, of about 10% to about 20%, of about 50% to about 100%, of about 25% to about 70% relative to a reference IgG Fc polypeptide. In some embodiments, the reference IgG Fc polypeptide is a wild-type IgG Fc polypeptide. In some embodiments, the reference IgG Fc polypeptide is a different variant IgG Fc polypeptide.

[00139] A “reference” as used herein, refers to any sample, standard, or level that is used for comparison purposes. A reference may be a wild-type reference or a variant reference. A reference may be obtained from a healthy or non-diseased sample. In some examples, a reference is obtained from a non-diseased or non-treated sample of a companion animal. In some examples, a reference is obtained from one or more healthy animals of a particular species, which are not the animal being tested or treated.

Exemplary Biological Activity of Variant GLP1 Fusion Molecules

[00140] In some embodiments, a GLP1 fusion molecule binds to GLP1R and activates cAMP production. In some embodiments, a GLP1 fusion polypeptide increases production of cAMP in a cell by at least 10%, at least 15%, at least 20%, at least 25%, at least 30%, at least

35%, at least 40%, at least 45%, at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, or 100% compared to signaling function in the absence of the GLP1 fusion polypeptide.

Exemplary Pharmaceutical Compositions

[00141] The terms “pharmaceutical formulation” and “pharmaceutical composition” refer to a preparation which is in such form as to permit the biological activity of the active ingredient(s) to be effective, and which contains no additional components that are unacceptably toxic to a subject to which the formulation would be administered.

[00142] A “pharmaceutically acceptable carrier” refers to a non-toxic solid, semisolid, or liquid filler, diluent, encapsulating material, formulation auxiliary, or carrier conventional in the art for use with a therapeutic agent that together comprise a “pharmaceutical composition” for administration to a subject. A pharmaceutically acceptable carrier is non-toxic to recipients at the dosages and concentrations employed and is compatible with other ingredients of the formulation. The pharmaceutically acceptable carrier is appropriate for the formulation employed. Examples of pharmaceutically acceptable carriers include alumina; aluminum stearate; lecithin; serum proteins, such as human serum albumin, canine or other animal albumin; buffers such as phosphate, citrate, tromethamine or HEPES buffers; glycine; sorbic acid; potassium sorbate; partial glyceride mixtures of saturated vegetable fatty acids; water; salts or electrolytes, such as protamine sulfate, disodium hydrogen phosphate, potassium hydrogen phosphate, sodium chloride, zinc salts, colloidal silica, or magnesium trisilicate; polyvinyl pyrrolidone, cellulose-based substances; polyethylene glycol; sucrose; mannitol; or amino acids including, but not limited to, arginine.

[00143] The pharmaceutical composition can be stored in lyophilized form. Thus, in some embodiments, the preparation process includes a lyophilization step. The lyophilized composition may then be reformulated, typically as an aqueous composition suitable for parenteral administration, prior to administration to the dog, cat, or horse. In other embodiments, particularly where a variant IgG Fc polypeptide or other polypeptide described herein is highly stable to thermal and oxidative denaturation, the pharmaceutical composition can be stored as a liquid, i.e., as an aqueous composition, which may be administered directly, or with appropriate dilution, to the dog, cat, or horse. A lyophilized composition can be reconstituted with sterile Water for Injection (WFI). Bacteriostatic reagents, such as benzyl alcohol, may be included. Thus, the invention provides pharmaceutical compositions in solid or liquid form.

[00144] The pH of the pharmaceutical compositions may be in the range of from about pH 5 to about pH 8, when administered. The compositions of the invention are sterile if they are to be used for therapeutic purposes. Sterility can be achieved by any of several means known in the

art, including by filtration through sterile filtration membranes (e.g., 0.2 micron membranes). Sterility may be maintained with or without anti-bacterial agents.

Certain Uses of Fc Polypeptides and Pharmaceutical Compositions

[00145] A polypeptide comprising a variant Fc polypeptide, such as a variant IgG Fc polypeptide, of the invention or pharmaceutical compositions comprising a variant Fc polypeptide of the invention may be useful for extending product half-life *in vivo* in a companion animal, including, but not limited to, canine, feline, or equine.

[00146] As used herein, “treatment” is an approach for obtaining beneficial or desired clinical results. “Treatment” as used herein, covers any administration or application of a therapeutic for disease in a mammal, including a companion animal. For purposes of this disclosure, beneficial or desired clinical results include, but are not limited to, any one or more of: alleviation of one or more symptoms, diminishment of extent of disease, preventing or delaying spread of disease, preventing or delaying recurrence of disease, delay or slowing of disease progression, amelioration of the disease state, inhibiting the disease or progression of the disease, inhibiting or slowing the disease or its progression, arresting its development, and remission (whether partial or total). Also encompassed by “treatment” is a reduction of pathological consequence of a proliferative disease. The methods provided herein contemplate any one or more of these aspects of treatment. In-line with the above, the term treatment does not require one-hundred percent removal of all aspects of the disorder.

[00147] A “therapeutically effective amount” of a substance/molecule, agonist or antagonist may vary according to factors such as the type of disease to be treated, the disease state, the severity and course of the disease, the type of therapeutic purpose, any previous therapy, the clinical history, the response to prior treatment, the discretion of the attending veterinarian, age, sex, and weight of the animal, and the ability of the substance/molecule, agonist or antagonist to elicit a desired response in the animal. A therapeutically effective amount is also one in which any toxic or detrimental effects of the substance/molecule, agonist or antagonist are outweighed by the therapeutically beneficial effects. A therapeutically effective amount may be delivered in one or more administrations. A therapeutically effective amount refers to an amount effective, at dosages and for periods of time necessary, to achieve the desired therapeutic or prophylactic result.

[00148] In some embodiments, a variant IgG Fc polypeptide or other polypeptide described herein, or a pharmaceutical composition comprising such is administered parenterally, by subcutaneous administration, intravenous infusion, or intramuscular injection. In some embodiments, a variant IgG Fc polypeptide or other polypeptide described herein, or a pharmaceutical composition comprising such is administered as a bolus injection or by continuous

infusion over a period of time. In some embodiments, a variant IgG Fc polypeptide or other polypeptide described herein, or a pharmaceutical composition comprising such is administered by an intramuscular, an intraperitoneal, an intracerebrospinal, a subcutaneous, an intra-arterial, an intrasynovial, an intrathecal, or an inhalation route.

[00149] In some embodiments, a GLP1 fusion polypeptide or pharmaceutical compositions comprising it can be utilized in accordance with the methods herein to treat high blood glucose-related conditions. In some embodiments, an GLP1 fusion polypeptide or pharmaceutical compositions is administered to a companion animal, such as a canine, a feline, or equine, to treat high blood glucose-related condition.

[00150] In some embodiments, a variant IgG Fc polypeptide or other polypeptide described herein, or a pharmaceutical composition comprising such is administered in an amount in the range of 0.0001 mg/kg body weight to 100 mg/kg body weight per dose. In some embodiments, GLP1 analog may be administered in an amount in the range of 0.005 mg/kg body weight to 20 mg/kg body weight per dose. In some embodiments, GLP1 analog may be administered in an amount in the range of 1 mg/kg body weight to 10 mg/kg body weight per dose. In some embodiments, GLP1 analog may be administered in an amount in the range of 0.5 mg/kg body weight to 100 mg/kg body weight, in the range of 1 mg/kg body weight to 100 mg/kg body weight, in the range of 5 mg/kg body weight to 100 mg/kg body weight, in the range of 10 mg/kg body weight to 100 mg/kg body weight, in the range of 20 mg/kg body weight to 100 mg/kg body weight, in the range of 50 mg/kg body weight to 100 mg/kg body weight, in the range of 1 mg/kg body weight to 10 mg/kg body weight, in the range of 5 mg/kg body weight to 10 mg/kg body weight, in the range of 0.5 mg/kg body weight to 10 mg/kg body weight, or in the range of 5 mg/kg body weight to 50 mg/kg body weight.

[00151] In some embodiments, a variant IgG Fc polypeptide or other polypeptide described herein, or a pharmaceutical composition comprising such is administered to a companion animal at one time or over a series of treatments. In some embodiments, the dose is administered once per week for at least two or three consecutive weeks, and in some embodiments, this cycle of treatment is repeated two or more times, optionally interspersed with one or more weeks of no treatment. In other embodiments, the therapeutically effective dose is administered once per day for two to five consecutive days, and in some embodiments, this cycle of treatment is repeated two or more times, optionally interspersed with one or more days or weeks of no treatment.

[00152] Administration “in combination with” one or more further therapeutic agents includes simultaneous (concurrent) and consecutive or sequential administration in any order. The term “concurrently” is used herein to refer to administration of two or more therapeutic agents,

where at least part of the administration overlaps in time or where the administration of one therapeutic agent falls within a short period of time relative to administration of the other therapeutic agent. For example, the two or more therapeutic agents are administered with a time separation of no more than about a specified number of minutes. The term “sequentially” is used herein to refer to administration of two or more therapeutic agents where the administration of one or more agent(s) continues after discontinuing the administration of one or more other agent(s), or wherein administration of one or more agent(s) begins before the administration of one or more other agent(s). For example, administration of the two or more therapeutic agents are administered with a time separation of more than about a specified number of minutes. As used herein, “in conjunction with” refers to administration of one treatment modality in addition to another treatment modality. As such, “in conjunction with” refers to administration of one treatment modality before, during or after administration of the other treatment modality to the animal.

[00153] In some embodiments, the dose is administered once per week for at least two or three consecutive weeks, and in some embodiments, this cycle of treatment is repeated two or more times, optionally interspersed with one or more weeks of no treatment. In other embodiments, the therapeutically effective dose is administered once per day for two to five consecutive days, and in some embodiments, this cycle of treatment is repeated two or more times, optionally interspersed with one or more days or weeks of no treatment.

[00154] Administration “in combination with” one or more further therapeutic agents includes simultaneous (concurrent) and consecutive or sequential administration in any order. The term “concurrently” is used herein to refer to administration of two or more therapeutic agents, where at least part of the administration overlaps in time or where the administration of one therapeutic agent falls within a short period of time relative to administration of the other therapeutic agent. For example, the two or more therapeutic agents are administered with a time separation of no more than about a specified number of minutes. The term “sequentially” is used herein to refer to administration of two or more therapeutic agents where the administration of one or more agent(s) continues after discontinuing the administration of one or more other agent(s), or wherein administration of one or more agent(s) begins before the administration of one or more other agent(s). For example, administration of the two or more therapeutic agents are administered with a time separation of more than about a specified number of minutes. As used herein, “in conjunction with” refers to administration of one treatment modality in addition to another treatment modality. As such, “in conjunction with” refers to administration of one

treatment modality before, during or after administration of the other treatment modality to the animal.

[00155] In some embodiments, the method comprises administering in combination with a GLP1 fusion polypeptide insulin, a DPP4 inhibitor, a SGLT2 inhibitor, a biguanides sulfonylurea, a meglitinide derivative, an alpha-glucosidase inhibitor, a thiazolidinedione (TZD), an amylinomimetic, a bile acid sequestrant, a dopamine agonist.

[00156] The following examples illustrate particular aspects of the disclosure and are not intended in any way to limit the disclosure.

EXAMPLES

Example 1

Variant canine IgG Fc polypeptides for increased Protein A binding
and/or decreased complement binding and/or decreased CD16 binding

[00157] Purification of antibodies using Protein A affinity is a well-developed process. However, among four subtypes of canine IgG, only IgG-B Fc (e.g., SEQ ID NO: 2 or SEQ ID NO: 107) has Protein A binding affinity. Canine IgG-A Fc (e.g., SEQ ID NO: 1), IgG-C Fc (e.g., SEQ ID NO: 3 or SEQ ID NO: 108), and IgG-D Fc (e.g., SEQ ID NO: 4) have weak or no measurable Protein A binding affinity. Variant canine IgG-A Fc, IgG-C Fc, and IgG-D Fc polypeptides were designed for altered Protein A binding.

[00158] In addition, canine IgG-B Fc and IgG-C Fc have complement activity and bind to C1q, while canine IgG-A Fc and IgG-D Fc have weak or no measurable binding affinity to C1q. To potentially reduce the C1q binding and/or potentially reduce complement-mediated immune responses, variant canine IgG-B Fc and IgG-C Fc polypeptides were designed.

[00159] Furthermore, canine IgG-B Fc and IgG-C Fc have CD16 binding activity. To potentially reduce the binding of CD16 to IgG-B Fc and IgG-C Fc, and/or potentially reduce ADCC, variant canine IgG-B Fc and IgG-C Fc polypeptides were designed.

[00160] Table 3, below summarizes the Protein A and C1q binding characteristics of canine IgG Fc subtypes. Notably, none of the wild-type canine IgG Fc subtypes lacks C1q binding and binds Protein A.

[00161] Table 3.

Wild-type Canine IgG Fc	Protein A Binding	C1q Binding	CD16 Binding
IgG-A Fc	–	–	–
IgG-B Fc	+	+	+

IgG-C Fc	–	+	+
IgG-D Fc	–	–	–

(–) denotes low or no measurable binding activity.

[00162] Using three-dimensional protein modeling and protein sequence analysis, the sequences of canine IgG-B Fc that are likely in contact with Protein A were identified. Figure 1 shows an alignment of canine IgG-A, B, C, and D Fc sequences. The boxes indicate the regions likely in contact with Protein A.

[00163] Two approaches were used to design variant canine IgG-A, IgG-C, and IgG-D Fc polypeptides for increased Protein A binding. For the first approach, variant canine IgG-A, IgG-C, and IgG-D Fc polypeptides were designed to have the same Protein A binding motif sequences as canine IgG-B Fc (e.g., SEQ ID NO: 5, SEQ ID NO: 6, and SEQ ID NO: 7, respectively). For the second approach, variant canine IgG-A Fc I(21)T/Q(207)H (SEQ ID NO: 60), variant canine IgG-C Fc I(21)T (SEQ ID NO: 61), and variant canine IgG-D Fc I(21)T/Q(207)H (SEQ ID NO: 62) were designed with one or two amino acid substitutions in the Protein A binding region to correspond with the canine IgG-B Fc sequence.

[00164] In addition, variant canine IgG-A Fc, IgG-C Fc, and IgG-D Fc polypeptides with increased Protein A binding may be prepared having one or more of the amino acid substitutions listed in Table 4.

[00165] Table 4.

Variant Canine IgG Fc Amino Acid Substitutions* (Protein A +)		
Canine IgG-A Fc (SEQ ID NO: 1)	Canine IgG-C Fc (SEQ ID NO: 3)	Canine IgG-D Fc (SEQ ID NO: 4)
Ile (21) Thr	Ile (21) Thr	Ile (23) Thr
Arg (23) Leu	Val (23) Leu	Arg (23) Leu
Thr (25) Ala	Thr (24) Ile	Thr (25) Ala
Glu (80) Gly		Glu (80) Gly
Thr (205) Ala		Gln (207) His
Gln (207) His		

* The amino acid positions listed are relative to the SEQ ID NO. indicated.

[00166] To potentially reduce the binding of C1q to canine IgG-B Fc and IgG-C Fc, and/or potentially reduce complement-mediated immune responses, variant canine IgG-B Fc and IgG-C Fc polypeptides may be prepared having an amino acid substitution of Lys with any amino acid except Lys at an amino acid position corresponding to position 93 of SEQ ID NO: 2 or of SEQ ID NO: 3, respectively. These amino acid substitutions were identified after analysis of the protein sequence and 3-D structure modeling of canine IgG-B Fc and IgG-C Fc compared to canine IgG-

A Fc and IgG-D Fc, which are understood to not exhibit complement activity. For example, variant canine IgG-B Fc K(93)R (SEQ ID NO: 78) and variant canine IgG-C Fc K(93)R (SEQ ID NO: 79) may be prepared. Reduced binding between human C1q and a fusion protein comprising variant canine IgG-B Fc K(93)R was observed when compared to a fusion protein comprising wild-type canine IgG-B Fc.

[00167] To potentially reduce the binding of CD16 to IgG-B Fc and IgG-C Fc, and/or potentially reduce ADCC, variant canine IgG-B Fc and IgG-C Fc polypeptides may be prepared having one or more of the amino acid substitutions listed in Table 5. The amino acid substitution(s) were identified after analysis of the protein sequence and 3-D structure modeling of canine IgG-B and IgG-C compared to IgG-A and IgG-D, which are understood to not exhibit ADCC activity.

[00168] Table 5.

Original residue position*		Substitution(s)
Canine IgG-B Fc (SEQ ID NO: 2)	Canine IgG-C Fc (SEQ ID NO: 3)	
Met (5)	Leu (5)	Any amino acid except original residue, such as Pro
Asp (38)	Asp (38)	Any amino acid except original residue, such as Gly
Pro (39)	Pro (39)	Any amino acid except original residue, such as Arg
Lys (97)	Lys (97)	Any amino acid except original residue, such as Ile
Ala (98)	Ala (98)	Any amino acid except original residue, such as Gly

* The amino acid positions listed are relative to the SEQ ID NO. indicated.

[00169] Since wild-type canine IgG-C Fc lacks Protein A binding and has C1q binding, a double variant canine IgG-C Fc that binds Protein A and has reduced binding to C1q may be prepared by combining one or more of the amino acid substitutions listed in Table 4 with a K(93)R substitution or K(93)X substitution, wherein X is any amino acid except Lys. A double variant canine IgG-B Fc or double variant canine IgG-C Fc with reduced binding to C1q and reduced binding to CD16 may be prepared by combining one or more of the amino acid substitutions listed in Table 5 with a K(93)R substitution or K(93)X substitution, wherein X is any amino acid except

Lys. A triple variant canine-IgG-C Fc that binds Protein A and has reduced binding to C1q and CD16 may be prepared by combining one or more of the amino acid substitutions listed in Table 4 and one or more of the amino acid substitutions listed in Table 5 with a K(93)R substitution or K(93)X substitution, wherein X is any amino acid except Lys.

[00170] The binding of any variant canine IgG Fc to Protein A, CD16, and/or C1q may be determined and compared to the binding of another IgG Fc to Protein A, CD16, and/or C1q (e.g., the corresponding wild-type canine IgG Fc, another wild-type or variant canine IgG Fc, or a wild-type or variant IgG Fc of another companion animal, etc.).

[00171] Binding analysis may be performed using an Octet biosensor. Briefly, the target molecule (e.g., Protein A, C1q, CD16, etc.) may be biotinylated and free unreacted biotin removed (e.g., by dialysis). The biotinylated target molecule is captured on streptavidin sensor tips. Association of the target molecule with various concentrations (e.g., 10 µg/mL) of IgG Fc polypeptide is monitored for a specified time or until steady state is reached. Dissociation is monitored for a specified time or until steady state is reached. A buffer only blank curve may be subtracted to correct for any drift. The data are fit to a 1:1 binding model using ForteBio™ data analysis software to determine the k_{on} , k_{off} , and the K_d .

Example 2

Variant equine IgG Fc polypeptides for increased Protein A binding and/or decreased complement binding

[00172] Of the seven subtypes of equine IgG, IgG1 Fc (e.g., SEQ ID NO: 63), IgG3 Fc (e.g., SEQ ID NO: 65), IgG4 Fc (e.g., SEQ ID NO: 66), IgG7 Fc (e.g., SEQ ID NO: 69) have Protein A binding affinity. Equine IgG2 Fc (e.g., SEQ ID NO: 18, SEQ ID NO: 64), IgG5 Fc (e.g., SEQ ID NO: 67), and IgG6 Fc (e.g., SEQ ID NO: 68) have weak or no measurable Protein A binding affinity. Variant equine IgG2 Fc, IgG5 Fc, and IgG6 Fc polypeptides were designed for altered Protein A binding.

[00173] In addition, equine IgG2 Fc, IgG5 Fc, and IgG6 Fc have weak or no measurable binding affinity to C1q, while equine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc bind to C1q. To potentially reduce the C1q binding and/or potentially reduce complement-mediated immune responses, variant equine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc polypeptides were designed.

[00174] Table 6, below summarizes the Protein A and C1q binding characteristics of equine IgG Fc subtypes. Notably, none of the wild-type equine IgG Fc subtypes lacks C1q binding and binds Protein A.

[00175] Table 6.

Wild-type Equine IgG Fc	Protein A Binding	C1q Binding
IgG1 Fc	+	+
IgG2 Fc	–	–
IgG3 Fc	+	+
IgG4 Fc	+	+
IgG5 Fc	–	–
IgG6 Fc	–	–
IgG7 Fc	+	+

(–) denotes low or no measurable binding activity.

[00176] Using three-dimensional protein modeling and protein sequence analysis, the sequences of equine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc that are likely in contact with Protein A were identified. Variant equine IgG2 Fc, IgG5 Fc, and IgG6 Fc polypeptides with increased Protein A binding may be prepared having one or more of the amino acid substitutions listed in Table 7.

[00177] Table 7.

Variant Equine IgG Fc Amino Acid Substitutions* (Protein A +)		
Equine IgG2 Fc (SEQ ID NO: 64)	Equine IgG5 Fc (SEQ ID NO: 67)	Equine IgG6 Fc (SEQ ID NO: 68)
Ala (15) Thr	Val (199) Leu	Ile (199) Leu
Phe (203) Tyr	Glu (200) Tyr	Arg (200) His
		His (201) Asn
		Thr (202) His

* The amino acid positions listed are relative to the SEQ ID NO. indicated

[00178] For example, variant equine IgG2 Fc, IgG5 Fc, and IgG6 Fc polypeptides were designed with one or multiple amino acid substitutions in the Protein A binding region to correspond with the sequence of wild-type equine IgG Fc, which does bind Protein A. Variant equine IgG2 Fc F(203)Y (SEQ ID NO: 71); variant equine IgG2 Fc A(15)T/F(203)Y (SEQ ID NO: 72); variant equine IgG5 Fc V(199)L/E(200)Y (SEQ ID NO: 75); and variant equine IgG6 Fc I(199)L/R(200)H/H(201)N/T(202)H (SEQ ID NO: 76) with increased Protein A binding may be prepared.

[00179] To potentially reduce the binding of C1q to equine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc, and/or potentially reduce complement-mediated immune responses, variant canine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc polypeptides may be prepared having an amino acid substitution of Lys with any amino acid except Lys at an amino acid position corresponding to

position 87 of SEQ ID NO: 63, of SEQ ID NO: 65, of SEQ ID NO: 66, of SEQ ID NO: 69, respectively. These amino acid substitutions were identified after analysis of the protein sequence and 3-D structure modeling of equine IgG1 Fc, IgG3 Fc, IgG4 Fc, and IgG7 Fc compared to equine IgG2 Fc, IgG5 Fc, and IgG6 Fc, which are understood to not exhibit complement activity. For example, variant equine IgG1 Fc K(87)S (SEQ ID NO: 70), variant equine IgG 3 Fc K(87)S (SEQ ID NO: 73), variant equine IgG4 Fc K(87)S (SEQ ID NO: 74), and variant equine IgG7 Fc K(87)S (SEQ ID NO: 77) may be prepared.

[00180] The binding of any variant equine IgG Fc to Protein A and/or C1q may be determined and compared to the binding of another IgG Fc to Protein A and/or C1q (e.g., the corresponding wild-type equine IgG Fc, another wild-type or variant equine IgG Fc, or a wild-type or variant IgG Fc of another companion animal, etc.). The binding assay described in Example 1 may be used.

Example 3

Variant feline IgG Fc polypeptides for decreased complement binding

[00181] Each of the three subtypes of feline IgG, IgG1a Fc (SEQ ID NO: 80 or SEQ ID NO: 117), IgG1b Fc (SEQ ID NO: 81 or SEQ ID NO: 118), and IgG2 Fc (SEQ ID NO: 16) have Protein A binding affinity. However, only feline IgG2 Fc has weak or no measurable binding affinity to C1q, while feline IgG1a Fc, IgG1b Fc bind to C1q. To potentially reduce the C1q binding and/or potentially reduce complement-mediated immune responses, variant feline IgG1a Fc and IgG1b Fc polypeptides were designed.

[00182] Table 8, below summarizes the Protein A and C1q binding characteristics of feline IgG Fc subtypes. Notably, none of the wild-type equine IgG Fc subtypes lacks C1q binding and binds Protein A.

[00183] Table 8.

Wild-type Feline IgG Fc	Protein A Binding	C1q Binding
IgG1a Fc	+	+
IgG1b Fc	+	+
IgG2 Fc	+	–

(–) denotes low or no measurable binding activity.

[00184] To potentially reduce the binding of C1q to feline IgG1a Fc and IgG1b Fc, and/or potentially reduce complement-mediated immune responses, variant feline IgG1a Fc and IgG1b Fc polypeptides may be prepared having an amino acid substitution of Pro with any amino acid except Pro at an amino acid position corresponding to position 198 of SEQ ID NO: 80 or of SEQ

ID NO: 81, respectively. These amino acid substitutions were identified after analysis of the protein sequence and 3-D structure modeling of feline IgG1a Fc and IgG1b Fc compared to feline IgG2 Fc, which is understood to not exhibit complement activity. For example, variant feline IgG1a Fc P(198)A (SEQ ID NO: 82) and variant feline IgG1b Fc P(198)A (SEQ ID NO: 83) may be prepared.

[00185] The binding of any variant feline IgG Fc to C1q may be determined and compared to the binding of another IgG Fc to C1q (e.g., the corresponding wild-type feline IgG Fc, another wild-type or variant feline IgG Fc, or a wild-type or variant IgG Fc of another companion animal, etc.). The binding assay described in Example 1 may be used.

Example 4

Variant canine and feline IgG Fc polypeptides for heterodimeric proteins

[00186] To enable the preparation of a bispecific canine or feline antibody or a bifunctional canine or feline Fc fusion protein using a knob-in-hole heterodimerization approach, pairing of variant canine IgG Fc polypeptides and variant feline IgG Fc polypeptides was investigated.

[00187] An amino acid substitution of threonine at a position corresponding to position 138 of canine IgG-A (SEQ ID NO: 1), at a position corresponding to position 137 of canine IgG-B Fc (SEQ ID NO: 2), at a position corresponding to position 137 of canine IgG-C Fc (SEQ ID NO: 3), or at a position corresponding to position 138 of canine IgG-D Fc (SEQ ID NO: 4) to tyrosine (T138Y or T137Y) can be introduced to one Fc chain (heterodimer chain 1). Examples of amino acid sequences of variant canine IgG-A Fc, IgG-B Fc, IgG-C Fc, and IgG-D Fc heterodimer chain 1 are SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, and SEQ ID NO: 14, respectively.

[00188] An amino acid substitution of tyrosine at a position corresponding to position 181 of canine IgG-A (SEQ ID NO: 1), at a position corresponding to position 180 of canine IgG-B Fc (SEQ ID NO: 2), at a position corresponding to position 180 of canine IgG-C Fc (SEQ ID NO: 3), or at a position corresponding to position 181 of canine IgG-D Fc (SEQ ID NO: 4) to threonine (Y181T or Y180T) can be introduced to a second Fc chain (heterodimer chain 2). Examples of amino acid sequences of variant canine IgG-A Fc, IgG-B Fc, IgG-C Fc, and IgG-D Fc heterodimer chain 2 are SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, and SEQ ID NO: 15, respectively.

[00189] A second pairing of variant canine IgG Fc heterodimer chains 3 and 4 was also investigated. An amino acid substitution of threonine to tryptophan at a position corresponding to position 138 of canine IgG-A (SEQ ID NO: 1) or of canine IgG-D (SEQ ID NO: 4) (T138W), or at a position corresponding to position 137 of canine IgG-B Fc (SEQ ID NO: 2) or of canine IgG-C Fc (SEQ ID NO: 3) (T137W) can be introduced to one Fc chain (heterodimer chain 3).

Examples of amino acid sequences of variant canine IgG-A Fc, IgG-B Fc, IgG-C Fc, and IgG-D Fc heterodimer chain 3 are SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, and SEQ ID NO: 115.

[00190] An amino acid substitution of threonine to serine at a position corresponding to position 138, of leucine to alanine at a position corresponding to position 140, and of tyrosine to threonine at a position corresponding to position 181 of canine IgG-A (SEQ ID NO: 1) or of IgG-D (SEQ ID NO: 4) (T138S, L140A, Y181T), or of threonine to serine at a position corresponding to position 137, of leucine to alanine at a position corresponding to position 139, and of tyrosine to threonine at a position corresponding to position 180 of canine IgG-B Fc (SEQ ID NO: 2) or of IgG-C (SEQ ID NO: 3) (T137S, L139A, Y180T) can be introduced to a second Fc chain (heterodimer chain 4). Examples of amino acid sequences of variant canine IgG-A Fc, IgG-B Fc, IgG-C Fc, and IgG-D Fc heterodimer chain 4 are SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, and SEQ ID NO: 116.

[00191] An amino acid substitution of threonine to tryptophan at a position corresponding to position 154 of feline IgG2 (SEQ ID NO: 16), of feline IgG1a Fc (SEQ ID NO: 80 or SEQ ID NO: 117), or of feline IgG1b Fc (SEQ ID NO: 81 or SEQ ID NO: 118) (T154W) can be introduced to one Fc chain (heterodimer chain 1). Examples of amino acid sequences of variant feline IgG2 Fc, IgG1a Fc, and IgG1b Fc heterodimer chain 1 are SEQ ID NO: 119, SEQ ID NO: 121, and SEQ ID NO: 123, respectively.

[00192] An amino acid substitution of threonine to serine at a position corresponding to position 154, of leucine to alanine at a position corresponding to position 156, and of tyrosine to threonine at a position corresponding to position 197 of feline IgG2 Fc (SEQ ID NO: 16), of IgG-1a (SEQ ID NO: 80 or SEQ ID NO: 117), or of IgG-1b Fc (SEQ ID NO: 81 or SEQ ID NO: 118) (T154S, L156A, Y197T) can be introduced to a second Fc chain (heterodimer chain 4). Examples of amino acid sequences of variant feline IgG2 Fc, IgG1a Fc, and IgG1b Fc heterodimer chain 4 are SEQ ID NO: 120, SEQ ID NO: 122, and SEQ ID NO: 124.

[00193] The pairing of variant canine IgG Fc heterodimer chains 1 and 2, the pairing of variant canine IgG Fc heterodimer chains 3 and 4, or the pairing of variant feline IgG Fc heterodimer chains 1 and 2 may allow for Fc heterodimerization and prevent or reduce Fc homodimerization. A heterodimer chain 1 of one canine IgG subtype may be combined with a heterodimer chain 2 of the same or a different canine IgG subtype. A heterodimer chain 3 of one canine IgG subtype may be combined with a heterodimer chain 4 of the same or a different canine IgG subtype. A heterodimer chain 1 of one feline IgG subtype may be combined with a heterodimer chain 2 of the same or a different feline IgG subtype. The design can enable

dimerization of bispecific canine or feline antibodies. In addition, two different peptides or proteins or a combination of different proteins can be fused to the heterodimeric Fc chains. For example, a dual GLP1 and glucagon molecule can be created using variant canine IgG Fc heterodimer chains or variant feline IgG Fc heterodimer chains, such as a GLP1 polypeptide (e.g., SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, or SEQ ID NO: 91) fused to a variant canine IgG-D Fc heterodimer chain 1 (e.g., SEQ ID NO: 14) and a glucagon polypeptide (e.g., SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, or SEQ ID NO: 95) fused to a variant canine IgG-D Fc heterodimer chain 2 (e.g., SEQ ID NO: 15).

Example 5

GLP1 fusion proteins

[00194] The amino acid sequence of GLP1 is conserved among human, feline, canine, and equine, among other species. GLP1 proteolytic products (e.g., GLP1 (amino acids 7-37) (SEQ ID NO: 85) are rapidly degraded by dipeptidyl peptidase-4 (DPP-4) and are understood to have a short serum half-life of a couple minutes.

[00195] The design of contiguous polypeptides comprising at least one GLP1 polypeptide and feline, canine, or equine IgG Fc polypeptides was investigated to generate long-acting GLP1 fusion proteins. The following constructs were designed:

Formula (I): GLP1A—L1—Fc;

Formula (II): Fc—L1—GLP1A; or

Formula (III): GLP1A—L1—Fc—L2—GLP1B.

wherein GLP1A is a first GLP1 polypeptide, GLP1B is a second GLP1 polypeptide, L1 and L2 are linkers; and Fc is an IgG Fc polypeptide of a companion animal species.

[00196] GLP1 was modified to be DPP-4 resistant by replacing alanine with either glycine or serine at a position corresponding to position 8 of wild-type GLP1 (7-37) (SEQ ID NO: 85). A minimal sequence of wild-type GLP1 (7-37) (SEQ ID NO: 87) for binding to the N-terminal domain of mature feline GLP1R (SEQ ID NO: 49) was analyzed by three-dimensional protein modeling of the complex. Based on this modeling, the two C-terminal amino acids were removed from the DPP-4 resistant GLP1 to generate GLP1-S8 (7-35) (SEQ ID NO: 86) and GLP1-G8 (7-35) (SEQ ID NO: 87) polypeptides.

[00197] GLP1 polypeptides when positioned at the C-terminus of a construct, such as in formulas II and III, are not susceptible to DPP-4 degradation. Therefore, the alanine to glycine or serine substitution is not necessary for GLP1 polypeptides positioned at the C-terminus. Accordingly, wild-type GLP1 (7-37) (SEQ ID NO: 85) may be used at the C-terminus.

[00198] The linker may be a flexible, non-structural linker, such as a glycine- and serine-rich linker. A flexible extension may be added to the C-terminus of the contiguous polypeptide. The extension may comprise a glycine residue (SEQ ID NO: 88), two glycine residues (SEQ ID NO: 89), a three glycine residues (SEQ ID NO: 90), four glycine residues (SEQ ID NO: 91), five glycine residues (SEQ ID NO: 92), six glycine residues (SEQ ID NO: 93), seven glycine residues (SEQ ID NO: 94), eight glycine residues (SEQ ID NO: 95), or more glycine residues.

Example 6

GLP1 and feline IgG Fc fusion proteins

[00199] Nucleotide sequences encoding (1) a contiguous polypeptide of Formula I having a signal sequence, GLP1-G8 (7-35) (SEQ ID NO: 87), a flexible linker, and wildtype feline IgG2 Fc (ssGLP1-G8_I_WTfIgG2; SEQ ID NO: 96); and (2) a contiguous polypeptide of Formula III having a signal sequence, GLP1-G8 (7-35) (SEQ ID NO: 87), GLP1 (7-35) (SEQ ID NO: 89), two flexible linkers, a 2G C-terminal extension, and wildtype feline IgG2 Fc (ssGLP1-G8/GLP1-2G_III_WTfIgG2; SEQ ID NO: 97) were synthesized and cloned into separate mammalian expression vectors. Wild-type feline IgG2 Fc (SEQ ID NO: 16) was chosen based on its low or no C1Q binding for reduced complement activity and Protein A binding for ease of purification.

[00200] The resulting vectors were separately transfected to CHO cells. The supernatant containing the contiguous polypeptides without the signal peptide (SEQ ID NOs: 24 and 23) was collected and filtered. Both proteins were affinity purified using a Protein A column (CaptivA[®] Protein A Affinity Resin, Repligen). The proteins were determined to be monomeric as assessed by HPLC gel filtration. However, the SDS-PAGE analysis showed that a percentage of both continuous polypeptides migrated to the same position in the gel in the absence and presence of reducing agent (DTT) (Figure 2A). This result suggests that the hinge of wild-type feline IgG2 Fc, which has only one pair of cysteine residues, may not be enough to form an effective disulfide linkage.

[00201] Three-dimensional protein modeling analysis of several ortholog hinge structures was used to determine the approximate locations for modifying the feline IgG2 hinge to increase disulfide formation. To increase disulfide formation at the feline IgG2 hinge, the hinge sequence may be modified by substituting an amino acid with cysteine. For example, a variant feline IgG2 Fc (SEQ ID NO: 17) having a modified hinge was prepared by substituting Gly with Cys at an amino acid position corresponding to position 14 of SEQ ID NO: 16. The corresponding contiguous polypeptides ssGLP1-G8_I_VARfIgG2 (SEQ ID NO: 39) and ssGLP1-G8/GLP1-2G_III_WTfIgG2 (SEQ ID NO: 38) comprising variant feline IgG Fc of SEQ ID NO: 17 were

designed, expressed in CHO cells, and purified by Protein A chromatography. The amino acid sequences of the secreted proteins after cleavage of the signal sequence are SEQ ID NOs 26 and 25, respectively. The SDS-PAGE analysis of the variant feline IgG2 constructs showed a decrease in the amount of protein in the lower molecular weight band in absence of reducing agent compared to the wild-type feline IgG2 constructs (compare Figure 2 B to Figure 2A). These results suggest that the Fc covalent pairing was improved for both variant feline IgG2 constructs.

[00202] Furthermore, differential scanning fluorimetry was used to assess the stability of the contiguous polypeptides at various pH, as reflected by mean melting point temperature (n=3) (Table 9, below). The increased stability of the variant feline IgG2 hinge is most evident at pH 6. For example, the constructs having variant feline IgG2 (SEQ ID NOs: 25 and 26) exhibited a higher T_m at pH 6 (56.9 and 59.7 °C) than the corresponding constructs having wild-type feline IgG2 (SEQ ID NOs: 23 and 24), which had a T_m of 55.2 and 56.9 °C, respectively.

[00203] Table 9.

Construct (10 µg)	Mean Melting Point Temperature (T _m °C) (n=3)					
	pH 3	pH 4	pH 5	pH 6	pH 7	pH 8
GLP1-G8/GLP1-2G_III_WTfIgG2 (SEQ ID NO:23)	NC	NC	NC	55.2	55.7	54.2
GLP1-G8_I_WTfIgG2 (SEQ ID NO:24)	NC	NC	48.5	56.9	59.9	59
GLP1-G8/GLP1-2G_III_WTfIgG2 (SEQ ID NO:25)	NC	NC	NC	56.9	55	52.5
GLP1-G8_I_VARfIgG2 (SEQ ID NO:26)	NC	NC	53.1	59.7	59.9	58.2

NC = no curve because no distinct transition point was observed.

[00204] Contiguous polypeptides of Formulas I, II, and III comprising GLP1-S8 (7-35) (SEQ ID NO: 86) instead of GLP1-G8 (7-35) (SEQ ID NO: 87) may be similarly designed and prepared. For example, ssGLP1-S8_I_WTfIgG2 (SEQ ID NO: 40), GLP1-S8_I_WTfIgG2 (SEQ ID NO: 28), ssGLP1-S8/GLP1-3G_III_WTfIgG2 (SEQ ID NO: 37), and GLP1-S8/GLP1-3G_III_WTfIgG2 (SEQ ID NO: 27) may be prepared. Similar constructs having variant instead of wild-type feline IgG Fc, such as GLP1-S8_I_VARfIgG2, GLP1-S8_I_VARfIgG2, GLP1-S8/GLP1-2G_III_VARfIgG2, and GLP1-S8/GLP1-3G_III_VARfIgG2, may also be prepared.

[00205] While feline IgG2 Fc was used in this example, contiguous polypeptides of Formulas I, II, and III comprising feline IgG1a Fc or IgG1b Fc instead of IgG2 may be designed and prepared. For example, similar contiguous polypeptides having wild-type feline IgG1a Fc, wild-type feline IgG1b Fc, variant feline IgG1a Fc, or variant feline IgG1b Fc (SEQ ID NOs: 80 to 83, respectively), may be designed and prepared.

Example 7

GLP1 and canine IgG Fc fusion proteins

[00206] Various Formula I, II, and III contiguous polypeptides comprising a variant GLP1 and a canine IgG Fc may be designed and prepared. For example, a variant canine IgGD Fc (e.g., SEQ ID NO: 7 or SEQ ID NO: 62) may be chosen based on its low or no C1q binding for reduced complement activity and Protein A binding for ease of purification. In addition, a flexible, non-structural linker, such as a glycine- and/or serine-rich linker, may be used.

[00207] GLP1-G8_I_VARcaIgGD (SEQ ID NO: 30) and GLP1-S8_I_VARcaIgGD (SEQ ID NO: 32) are examples of Formula I contiguous polypeptides comprising (1) either GLP1-G8 (7-35) or GLP1-S8 (7-35), (2) a flexible linker, and (3) a variant canine IgGD Fc (e.g., SEQ ID NO: 7). GLP1-G8/GLP1-3G_III_VARcaIgGD (SEQ ID NO: 29) and GLP1-S8/GLP1-3G_III_VARcaIgGD (SEQ ID NO: 31) are examples of Formula III contiguous polypeptides comprising (1) either GLP1-G8 (SEQ ID NO: 87) or GLP1-S8 (SEQ ID NO: 86), (2) GLP1 (7-35) (SEQ ID NO: 61), (3) two flexible linkers, (4) a 3G C-terminal extension, and (5) a variant canine IgGD Fc.

[00208] The contiguous polypeptides may be designed with a signal sequence, a different GLP1 polypeptide (e.g., SEQ ID NO: 85, 86, 87, 98, or 99), or different modifications to the canine IgG Fc. Examples with such variations include ssGLP1-S8/GLP1-2G_III_VARcaIgGD (SEQ ID NO: 41), ssGLP1-G8/GLP1-2G_III_VARcaIgGD (SEQ ID NO: 42), ssGLP1-S8/GLP1-3G_III_VARcaIgGD (SEQ ID NO: 43), GLP1-S8/GLP1-2G_III_VARcaIgGD (SEQ ID NO: 105), and GLP1-G8/GLP1-2G_III_VARcaIgGD (SEQ ID NO: 106).

[00209] Furthermore, contiguous polypeptides of Formulas I, II, and III may comprise a wild-type canine IgGD, or a wild-type or variant canine IgGA, IgGB, or IgGC, instead of a variant canine IgGD. For example, similar contiguous polypeptides may be designed and prepared having a wild-type canine IgGA Fc, IgGB Fc, IgGC Fc, or IgGD Fc (e.g., SEQ ID NO: 1, 2, 3, or 4, respectively). Additional examples include contiguous polypeptides comprising a variant canine IgGA Fc (e.g., SEQ ID NO: 5 or 60), a variant canine IgGB Fc (e.g., SEQ ID NO: 78), or a variant canine IgGC Fc (e.g., SEQ ID NO: 6, 61, 79, or 84).

[00210] GLP1-G8/GLP1-3G_III_VARcaIgGD (SEQ ID NO: 29) and GLP1-G8_I_VARcaIgGD (SEQ ID NO: 30) were expressed separately in CHO cells and the supernatants containing the proteins collected and filtered. Both contiguous polypeptides were affinity purified by Protein A chromatography. The SDS-PAGE profiles of the two contiguous polypeptides in the absence and presence of reducing agent (DTT) were compared and the results suggested that the Fc disulfide bond was effectively formed for both polypeptides (data not shown).

Example 8

GLP1 and equine IgG Fc fusion proteins

[00211] Various Formula I, II, and III contiguous polypeptides comprising a variant GLP1 and an equine IgG Fc may be designed and prepared. For example, a variant canine IgG2 Fc (e.g., SEQ ID NO: 19, 71, or 72) may be chosen based on its low or no C1q binding for reduced complement activity and Protein A binding for ease of purification. In addition, a flexible, non-structural linker, such as a glycine- and/or serine-rich linker, may be used.

[00212] GLP1-G8_I_VAREqIgG2 (SEQ ID NO: 34) and GLP1-S8_I_VAREqIgG2 (SEQ ID NO: 36) are examples of Formula I contiguous polypeptides comprising (1) either GLP1-G8 or GLP1-S8, (2) a flexible linker, and (3) a variant equine IgG2 Fc (e.g., SEQ ID NO: 19). GLP1-G8/GLP1-3G_III_VAREqIgG2 (SEQ ID NO: 33) and GLP1-S8/GLP1-3G_III_VAREqIgG2 (SEQ ID NO: 35) are examples of Formula III contiguous polypeptides comprising (1) either GLP1-G8 (7-35) (SEQ ID NO: 87) or GLP1-S8 (7-35) (SEQ ID NO: 86), (2) GLP1 (7-35) (SEQ ID NO: 61), (3) two flexible linkers, (4) a 3G C-terminal extension, and (5) a variant equine IgG2 Fc.

[00213] The contiguous polypeptides may be designed with a signal sequence, a different GLP1 analog (e.g., SEQ ID NO: 86, 87, 98, or 99), a glycine extension (e.g., SEQ ID NO: 88 to 95) or additional modifications to the equine IgG Fc. Examples with such variations include ssGLP1-G8/GLP1-3G_III_VAREqIgG2 (SEQ ID NO: 44), ssGLP1-G8_I_VAREqIgG2 (SEQ ID NO: 45), ssGLP1-S8/GLP1-3G_III_VAREqIgG2 (SEQ ID NO: 46), and ssGLP1-S8_I_VAREqIgG2 (SEQ ID NO: 47).

[00214] Furthermore, contiguous polypeptides of Formulas I, II, and III may comprise a wild-type equine IgG2, or a wild-type or variant equine IgG1, IgG3, IgG4, IgG5, IgG6, IgG7, instead of a variant equine IgG2. For example, similar contiguous polypeptides may be designed and prepared having a wild-type equine IgG1 Fc (e.g., SEQ ID NO: 63), IgG2 Fc (e.g., SEQ ID NO: 18 or 64), IgG3 Fc (e.g., SEQ ID NO: 65), IgG4 Fc (e.g., SEQ ID NO: 66), IgG5 Fc (e.g., SEQ ID NO: 67), IgG6 Fc (e.g., SEQ ID NO: 68), or IgG7 Fc (e.g., SEQ ID NO: 69). Additional examples include contiguous polypeptides comprising a variant equine IgG1Fc (e.g., SEQ ID NO: 70), a variant equine IgG3 Fc (e.g., SEQ ID NO: 73), a variant equine IgG4 Fc (e.g., SEQ ID NO: 74), a variant equine IgG5 Fc (e.g., SEQ ID NO: 75), a variant equine IgG6 Fc (e.g., SEQ ID NO: 76), or a variant equine IgG7 Fc (e.g., SEQ ID NO: 77).

[00215] The nucleotide sequences encoding ssGLP1-G8/GLP1-3G_III_VAREqIgG2 (SEQ ID NO: 44) and ssGLP1-G8_I_VAREqIgG2 (SEQ ID NO: 45) were synthesized and cloned into separate mammalian expression vectors. The resulting vectors were separately transfected to CHO

cells. The supernatant containing the contiguous polypeptides following cleavage of the signal peptide (SEQ ID NOs: 103 and 104) was collected and filtered. Both proteins were affinity purified using a Protein A column (CaptivA[®] Protein A Affinity Resin, Repligen). were expressed separately in CHO cells and the supernatants containing the proteins collected and filtered. Both contiguous polypeptides were affinity purified by Protein A chromatography. The SDS-PAGE profiles of the two contiguous polypeptides in the absence and presence of reducing agent (DTT) were compared and the results suggested that the Fc disulfide bond was effectively formed for both polypeptides (data not shown).

Example 9

Expression and purification of feline GLP1R N-terminal soluble domain

[00216] The N-terminal domain of mature feline GLP1R (SEQ ID NO: 49) responsible for binding GLP1 to GLP1R was identified from the full-length feline GLP1R amino acid sequence (SEQ ID NO: 48). Nucleotide sequences encoding (1) a signal sequence, feline N-terminal GLP1R, human Fc, and a poly-His tag (ssFeGLP1R-N-huFc_PolyHis; SEQ ID NO: 50) and (2) a signal sequence, feline N-terminal GLP1R, and a poly-His tag (ssFeGLP1R-N_polyHis; SEQ ID NO: 51) were synthesized and cloned into separate mammalian expression vectors. The resulting vectors were separately transfected to CHO cells. The supernatant containing the polypeptides was collected and filtered. The proteins were affinity purified using a Ni-Sepharose column or Protein A column (CaptivA[®] Protein A Affinity Resin, Repligen) for the huFc construct. Both proteins were used for GLP1 functional binding and ELISAs.

Example 10

GLP1 fusion protein binding kinetics

[00217] The binding affinity of GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) to FeGLP1R-N-huFc_PolyHis was assessed using biolayer interferometry (Octet). Briefly, FeGLP1R-N-huFc_PolyHis was biotinylated, the free unreacted biotin was removed, and the biotinylated protein was captured to streptavidin sensor tips. The association of different concentrations GLP1-G8_I_VARfeIgG2 was monitored for ninety seconds. Dissociation was monitored for 600 seconds. A buffer only blank curve was subtracted to correct for any drift. The data were fit to a 1:1 binding model using ForteBio[™] data analysis software to determine the k_{on} , k_{off} , and the K_d . The buffer for dilutions and all binding steps was: 20 mM phosphate, 150 mM NaCl, pH 7.2. The K_d between Feline GLP1R N-terminal domain and GLP1-G8_I_VARfeIgG2 was between 8.0×10^{-9} and 16×10^{-9} M.

Example 11

GLP1 fusion protein bioactivity in a cell-based assay

[00218] CHOK-1-GL1R cell line (Discoverx, cat# 95-0062C2), a hamster ovarian cell line which overexpresses Gs-coupled human glucagon ligand peptide-1 receptors (GLP1R) on the cell surface, was used to measure GLP1 cellular activity with a cAMP Hunter Bioassay kit (Discoverx, Cat# 95-0062Y2). Cells were plated in a 96-well plate and incubated at 37°C, 5% CO₂ for 24 hours. Cells were then treated with a control agonist—either GLP1 human (37 a.a.) (Prospec, Cat# HOR-236) or Extendin-4 (Discoverx, Cat# 92-1115)—or a contiguous polypeptide comprising a variant GLP1 at a series of 3-fold dilutions followed by incubation at 37°C for 30 min. The contiguous polypeptides tested were GLP1-G8/GLP1-2G_III_VARfIgG2 (SEQ ID NO: 25) and GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26).

[00219] Upon GLP1 binding to the Gs-coupled GLP1R receptor, Gs stimulates adenylate cyclase to generate cAMP. At the end of incubation, cAMP Antibody Reagent and cAMP Working Detection Solution, which contains lysis buffer, β -galactosidase (β -gal) small fragment conjugated cAMPs, and substrates, were added to the cells. The cells were incubated in the dark for 1 hour at room temperature to allow the immunocompetition reaction to occur between endogenously generated cAMPs and β -gal small fragment conjugated cAMPs for cAMP antibody binding.

[00220] At the end of the 1 hour incubation, cAMP Solution A containing β -gal large fragments, which can complement with the free (non-antibody binding) β -gal small fragment-cAMPs to form functional enzymes, were added to the cell lysate. The lysate was incubated for 3 to 6 hours in the dark at room temperature to allow the β -gal to hydrolyze the substrate and generate luminescent signals.

[00221] The more unbound free β -gal small fragment-cAMPs that remain, the more functional β -gal enzymes form. Therefore, the amount of signal produced is directly proportional to the amount of cAMP in the cell lysate. At the end of incubation, luminescence was read on a Synergy HT microplate reader (Biotek, Winooski, VT). The EC₅₀s were calculated with a software GraphPad Prism (GraphPad Software, Inc. La Jolla, USA).

[00222] Figure 3 shows a plot of the relative light units (RLU) versus concentration for each sample tested. The EC₅₀s are listed in Table 10, below. Both GLP1-G8/GLP1-2G_III_VARfIgG2 (SEQ ID NO: 25) and GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26) are more active than GLP1 (7-37) and Extendin-4. GLP1-G8/GLP1-2G_III_VARfIgG2 (SEQ ID NO: 25) is more potent than GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26), suggesting that the C-terminal GLP1 may contribute additional activity.

[00223] Table 10.

Sample	EC 50 (nM)
GLP1 (7-37)	0.1449
Extendin-4	0.4596
GLP1-G8/GLP1-2G_III_VARfIgG2 (SEQ ID NO: 25)	0.01751
GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26)	0.02806

Example 12

GLP1 fusion protein long-term stability

[00224] GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26) was stored in PBS, pH7.2 at a concentration of 1.3 mg/mL, placed in 1.5 mL Eppendorf tube, and stored at 2-8 °C for one year (Lot 2-29-2016). GLP1-G8_I_VARfIgG2 (SEQ ID NO: 26) was also stored in PBS, pH7.2 at a concentration of 10 mg/mL, placed in 1.5 mL Eppendorf tube, and stored at 2-8 °C for one day (Lot 2-2-2017). To evaluate stability, the stored sample were analyzed by cell-based assay using the same CHOK-1-GL1R cell line (Discoverx, cat # 95-0062C2) described in Example 11, but cellular activity was assessed using a cAMP-Glo™ Max Assay (Promega, Cat# PAV1682).

[00225] CHOK-1-GL1R cells were plated in a 96-well plate (Corning, Cat# 3610) at a density of 20,000 cells per well in F-12K Medium (ATCC, Cat# ATCC® 30-2004) supplemented with 10% Fetal Bovine Serum, heat inactivated (Sigma, Cat#2868) and incubated at 37°C, 5% CO2 for 24 hours. Cells were then stimulated with a control agonist GLP1 human (37 a.a.) (Prospec, Cat# HOR-236), Lot 2-20-2016, or Lot 2-2-2017 at a series of 3-fold dilutions with serum-free medium followed by addition of Complete Induction Buffer which contains MgCl₂ to a final concentration 20 mM, isobutyl-1-methylxanthine (IBMX) (Sigma-Aldrich Cat.# I7018) to a final concentration 500 µM and Ro 20-1724 [4-(3-butoxy-4-methoxy-benzyl) imidazolidone] (Sigma Aldrich, Cat.# B8279) to a final concentration 100 µM.

[00226] The cells were incubated at room temperature for 30 minutes. In this process, upon GLP1 binding to the Gs-coupled GLP1R receptor, Gs stimulates adenylate cyclase to generate cAMP. At the end of incubation, cAMP Detection Solution, which contains an inactive protein kinase A holoenzyme, protein kinase A substrate, and lysis buffer, was added to the cells. The plates placed on an orbital shaker for 1–2 minutes and then incubated at room temperature (23°C) for 20 minutes. Cellular cAMP will activate protein kinase A by binding its regulatory-inhibitory subunits and releasing the catalytic subunits. The free catalytic subunits catalyze the transfer of the terminal phosphate of ATP to the protein kinase A substrate, consuming cellular ATP in the process. At the end of incubation, a luciferase-based Kinase-Glo® Reagent was added to the cell

lysates and the plates were shaken on an orbital shaker for 2 min followed by incubation in the dark at room temperature for 10 min.

[00227] Mono-oxygenation of luciferin was catalyzed by luciferase in the presence of Mg^{2+} and ATP that presented in the cell lysate, resulting in a luminescent signal proportional to the amount of ATP in the cells. At the end of 10 min incubation, the plate was read on a Synergy HT microplate reader (Biotek, Winooski, VT). Luminescence is proportional to ATP levels but inversely proportional to cAMP levels. Thus, as cAMP concentration increases, luminescence decreases.

[00228] Figure 4 shows the results of the cell-based assay as a plot of luminescence versus concentration for Lot 2-29-2016 compared to Lot 2-2-2017 and GLP1 (31 a.a.). The GLP1-G8_I_VARfeIgG2 sample maintained cellular activity after storage in PBS at 2-8 °C for one year.

Example 13

GLP1 fusion protein serum stability

[00229] GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) was stored in PBS, pH7.2 with feline serum at 37 °C for 24 hours to test in vitro serum stability. The cell-based assay was performed as described in Example 12 and results suggested that the activity was maintained (data not shown). In addition, no visible degradations were observed by Western blot analysis (Figure 5).

Example 14

GLP1 fusion protein *in vivo* pharmacokinetics

[00230] GLP1-G8_I_VARfeIgG2 (SEQ ID NO: 26) was administered as a single dose (2 mg/kg) by subcutaneous injection to 5 cats. Serum samples were taken before dosing (time 0) and at 4 hours, 8 hours, 12 hours, 24 hours, 48 hours, 72 hours, and 168 hours. The concentration of GLP1-G8_I_VARfeIgG2 in the serum samples was measured by quantitative ELISA. GLP1-G8_I_VARfeIgG2 polypeptide with a detection limit of 4 ng/mL was used as a reference. The serum concentration of GLP1-G8_I_VARfeIgG2 was plotted against time (Figure 6). The mean serum half-life ($t_{1/2}$) of GLP1-G8_I_VARfeIgG2 was 39 hours. The average T_{max} was 22 hours, the average C_{max} was 12 $\mu g/mL$, and the mean area under the curve (AUC) was about 950 $\mu g(h)/mL$.

[00231] The quantitative ELISA used an anti-GLP1 antibody (4F3, Novus Biologicals, Catalog No. NBP1-97413) and a goat anti-cat IgG-Fc, HRP conjugated antibody (Bethyl Laboratories, Inc., Catalog No. A20-117P) for quantification of GLP1-G8_I_VARfeIgG2 in feline serum samples from the *in vivo* pharmacokinetics study. A 96-well plate was coated with anti-GLP1 antibody (5 $\mu g/mL$ in coating buffer, 100 $\mu l/well$). The plate was sealed and incubated

overnight at 4°C. The plate was washed in triplicate with 1X TBST (10X TBST, Teknova, Catalog No. T9511) and blocking buffer was added. After removing the blocking buffer, serial dilutions of reference standard and samples in blocking buffer were added (100 µl/well) and the plate was incubated for 2 hours at room temperature. The plate was washed in triplicate with 1X TBST and goat anti-cat IgG Fc antibody was added (0.1 µg/mL in blocking buffer, 100 µl/well). After incubation for 1 hour at room temperature, the plate was washed 5 times with 1X TBST. TMB substrate (ScyTek, Catalog No. TM1999) was added (100 µl/well) and allowed to incubate at room temperature for 1 minute. The reaction was stopped by the addition of 2M H₂SO₄ (50 µl/well). Absorbance at 450 nm was measured and the concentration of GLP1-G8_I_VARfeIgG2 in the serum samples calculated.

[00232] Furthermore, GLP1-G8_I_VARfeIgG2 concentration in the same serum samples (no DPP-4 inhibitor added) was assessed using a cell-based activity assay. The same CHOK-1-GL1R cell line (Discoverx, cat # 95-0062C2) and cAMP-Glo™ Max Assay (Promega, Cat# PAV1682) described in Example 12 was used. In this Example, however, the cells were stimulated with a control agonist GLP1 human (37 a.a.) (Prospec, Cat# HOR-236) or samples of cat serum taken before dosing (time 0) and at 4 hours, 8 hours, 12 hours, 24 hours, 48 hours, 72 hours, and 168 hours diluted in serum-free medium (5%, 0.5%, and 0.05% dilutions). The concentration of GLP1-G8_I_VARfeIgG2 in each sample was calculated using SoftMax pro 7 (Molecular Devices, Sunnyvale, CA). The mean concentration of GLP1-G8_I_VARfeIgG2 for the 5 cats was plotted against time (Figure 7). The mean AUC was about 840 µg(h)/mL and the mean t_{1/2} was 36 hours. The concentrations calculated from the cell-based activity assay are consistent with the concentrations obtained from the ELISA, which suggests that the variant GLP1 detected by ELISA is biologically active.

Example 15

GLP1, glucagon, and IgG Fc fusion proteins

[00233] To investigate a long acting GLP1 receptor and Glucagon receptor dual agonist, contiguous polypeptides comprising a GLP1 polypeptide, a glucagon polypeptide, and an IgG Fc polypeptide having the following constructs were designed:

Formula (IV): GLP1—L1—Fc—L2—Gluc; and

Formula (V): Gluc—L1—Fc—L2—GLP1,

wherein GLP1 is a GLP1 polypeptide, Gluc is a glucagon polypeptide, L1 and L2 are linkers, and Fc is an Fc polypeptide.

[00234] As discussed above, GLP1 was modified to be DPP-4 resistant by replacing alanine with either glycine or serine at a position corresponding to position 8 of wild-type GLP1 (7-37) (SEQ ID NO: 85). In addition, the DPP-4 resistant GLP1 was further modified by removing the two C-terminal amino acids to generate variant GLP1-S8 (7-35) (SEQ ID NO: 86) and variant GLP1-G8 (7-35) (SEQ ID NO: 87) polypeptides.

[00235] GLP1 polypeptides when positioned at the C-terminus of a construct, such as in Formula (V), are not susceptible to DPP-4 degradation. Therefore, the alanine to glycine or serine substitution is not necessary for GLP1 polypeptides positioned at the C-terminus. Accordingly, wild-type GLP1 (7-37) (SEQ ID NO: 85) may be used at the C-terminus.

[00236] The linker may be a flexible, non-structural linker, such as a glycine- and serine-rich linker. A flexible extension may be added to the C-terminus of the contiguous polypeptide. The extension may comprise a glycine residue (SEQ ID NO: 88), two glycine residues (SEQ ID NO: 89), a three glycine residues (SEQ ID NO: 90), four glycine residues (SEQ ID NO: 91), five glycine residues (SEQ ID NO: 92), six glycine residues (SEQ ID NO: 93), seven glycine residues (SEQ ID NO: 94), eight glycine residues (SEQ ID NO: 95), or more glycine residues.

[00237] The contiguous polypeptide may comprise a wildtype glucagon polypeptide (e.g., SEQ ID NO: 21) or a variant glucagon polypeptide.

[00238] The contiguous polypeptide may comprise a human IgG Fc or an IgG Fc of a companion animal species, such as canine, feline, or equine. The subtype of IgG Fc used may be based on having low or no C1q binding activity and/or having Protein A binding capacity. For example, a wild-type or variant human, canine, equine, or feline IgG Fc having low or no C1q binding and/or having Protein A binding capacity may be used (e.g., SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, or 84).

[00239] Exemplary contiguous polypeptides comprising a GLP1 polypeptide, a Glucagon polypeptide, and a feline IgG Fc polypeptide include GLP1-G8/Gluc-3G_IV_WTfIgG2 (SEQ ID NO: 52) and Gluc/GLP1-2G_V_WTfIgG2 (SEQ ID NO: 53).

[00240] Exemplary contiguous polypeptides comprising a GLP1 polypeptide, a Glucagon polypeptide, and a canine IgG Fc polypeptide include GLP1-G8/Gluc-4G_IV_VARcaIgGD (SEQ ID NO: 54) and Gluc/GLP1-3G_V_VARcaIgGD (SEQ ID NO: 55).

[00241] Exemplary contiguous polypeptides comprising a GLP1 polypeptide, a Glucagon polypeptide, and an equine IgG Fc polypeptide include GLP1-G8/Gluc-4G_IV_VAREqIgGD (SEQ ID NO: 56) and Gluc/GLP1-3G_V_VAREqIgG2 (SEQ ID NO: 57).

[00242] Exemplary contiguous polypeptides comprising a GLP1 polypeptide, a Glucagon polypeptide, and a human IgG Fc polypeptide include GLP1-G8/Gluc-4G_IV_huIgG4 (SEQ ID NO: 8) and Gluc/GLP1-3G_V_huIgG4 (SEQ ID NO: 59).

Example 16

Variant IgG Fc polypeptides for enhanced hinge disulfide formation

[00243] Additional three-dimensional protein modeling analysis of several ortholog hinge structures was used to modify feline and equine IgG hinges to enhance disulfide formation. To enhance disulfide formation at the feline IgG hinge, the hinge sequence may be modified by substituting lysine with proline at a position corresponding to position 16 of feline IgG2 (SEQ ID NO: 16), of feline IgG1a (SEQ ID NO: 80 or SEQ ID NO: 117), or of feline IgG1b (SEQ ID NO: 81 or SEQ ID NO: 118) (e.g., K16P). Examples of amino acid sequences of variant feline IgG polypeptides having a modified hinge include SEQ ID NO: 125, SEQ ID NO: 126, and SEQ ID NO: 127.

[00244] To enhance disulfide formation at the equine IgG hinge, the hinge sequence may be modified by substitution cysteine with serine at a position corresponding to position 3 of an equine IgG (e.g., IgG2 Fc (SEQ ID NO: 129)) and/or substituting glutamine with proline at a position corresponding to position 20 of an equine IgG (e.g., IgG2 Fc (SEQ ID NO: 129) (e.g., C3S, Q20P). Examples of amino acid sequences of variant equine IgG polypeptides having a modified hinge include SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 134, and SEQ ID NO: 135.

Example 17

Variant IgG Fc polypeptides for enhanced recombinant production and/or enhanced hinge disulfide formation

[00245] Three-dimensional protein modeling was used to design feline and equine variant IgG Fc polypeptides comprising sequences from the hinge region from a different IgG isotype for enhanced recombinant production and improved hinge disulfide formation. Variant feline IgG2 Fc polypeptides may be prepared that comprise sequences from the hinge region of feline IgG1a or IgG1b (e.g., SEQ ID NO: 125). In addition, variant equine IgG2 Fc polypeptides may be prepared that comprise sequences from the hinge region of equine IgG1 (e.g., SEQ ID NO: 19).

[00246] Levels of recombinant production of variant IgG Fc polypeptides and/or levels of hinge disulfide formation may be determined and compared to that of another IgG Fc by SDS-PAGE analysis under reducing and non-reducing conditions (e.g., the corresponding wild-type

IgG Fc of the same or different isotype, or a wild-type or variant IgG Fc of another companion animal, etc.).

CLAIMS

1. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification relative to a wild-type IgG Fc polypeptide of a companion animal species, wherein the variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.
2. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification relative to a wild-type IgG Fc polypeptide of a companion animal species, wherein the variant IgG Fc polypeptide has reduced binding affinity to C1q and/or CD16 relative to the wild-type IgG Fc polypeptide.
3. The polypeptide of claim 1 or claim 2, wherein the variant IgG Fc polypeptide binds to C1q and/or CD16 with a dissociation constant (K_d) of greater than 5×10^{-6} M, greater than 1×10^{-5} M, greater than 5×10^{-5} M, greater than 1×10^{-4} M, greater than 5×10^{-4} M, or greater than 1×10^{-3} M, as measured by biolayer interferometry.
4. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.
5. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide binds to Protein A with a dissociation constant (K_d) of less than 5×10^{-6} M, less than 1×10^{-6} M, less than 5×10^{-7} M, less than 1×10^{-7} M, less than 5×10^{-8} M, less than 1×10^{-8} M, less than 5×10^{-9} M, less than 1×10^{-9} M, less than 5×10^{-10} M, less than 1×10^{-10} M, less than 5×10^{-11} M, less than 1×10^{-11} M, less than 5×10^{-12} M, or less than 1×10^{-12} M, as measured by biolayer interferometry.
6. The polypeptide of any one of the preceding claims, wherein the companion animal species is canine, feline, or equine.
7. The polypeptide of any one of the preceding claims, wherein the wild-type IgG Fc polypeptide is
 - a) a canine IgG-A Fc, IgG-B Fc, IgG-C Fc, or IgG-D Fc;
 - b) an equine IgG1 Fc, IgG2 Fc, IgG3 Fc, IgG4 Fc, IgG5 Fc, IgG6 Fc, or IgG7 Fc; or
 - c) a feline IgG1a Fc, IgG1b Fc, or IgG2 Fc.

8. A polypeptide comprising a variant IgG Fc polypeptide comprising at least one amino acid modification to a hinge region relative to a wild-type feline or equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide has increased recombinant production and/or increased hinge disulfide formation relative to the wild-type IgG Fc polypeptide, as determined by SDS-PAGE analysis under reducing and/or nonreducing conditions.
9. The polypeptide of any one the preceding claims, wherein the variant IgG Fc polypeptide comprises:
- a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;
 - b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 3 of SEQ ID NO: 129; and/or
 - c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 20 of SEQ ID NO: 129.
10. The polypeptide of any one the preceding claims, wherein the variant IgG Fc polypeptide comprises:
- a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;
 - b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 3 of SEQ ID NO: 129; and/or
 - c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises an amino acid substitution at position 20 of SEQ ID NO: 129.
11. The polypeptide of any one the preceding claims, wherein the variant IgG Fc polypeptide comprises:
- a) at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a proline at a position corresponding to

position 16 or at position 16 of SEQ ID NO: 16, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 117, or SEQ ID NO: 118;

b) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a serine at a position corresponding to position 3 or at position 3 of SEQ ID NO: 129; and/or

c) at least one amino acid substitution relative to a wild-type equine IgG Fc polypeptide, wherein the variant IgG Fc polypeptide comprises a proline at a position corresponding to position 20 or at position 20 of SEQ ID NO: 129.

12. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises a hinge region or a portion of a hinge region from an IgG Fc polypeptide of a different isotype.

13. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises a hinge region or a portion of a hinge region from a wild-type feline IgG-1a Fc polypeptide, from a wild-type feline IgG-1b Fc polypeptide, or from a wild-type equine IgG1 Fc polypeptide.

14. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises SEQ ID NO: 19, SEQ ID NO: 125 or SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135.

15. A polypeptide comprising an amino acid sequence of SEQ ID NO: 19, SEQ ID NO: 125 or SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135.

16. A polypeptide comprising a variant IgG2 Fc polypeptide comprising at least one amino acid substitution relative to a wild-type feline IgG2 Fc polypeptide, wherein the at least one amino acid substitution is a cysteine, and wherein the variant IgG2 Fc polypeptide is capable of forming at least one additional inter-chain disulfide linkage relative to the wild-type feline IgG2 Fc polypeptide.

17. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises at least one amino acid substitution relative to a wild-type feline IgG Fc polypeptide, wherein the at least one amino acid substitution is a cysteine, and wherein the variant IgG Fc

polypeptide is capable of forming at least one additional inter-chain disulfide linkage relative to the wild-type feline IgG Fc polypeptide.

18. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises a cysteine at a position corresponding to position 8, position 9, position 10, position 11, position 12, position 13, position 14, position 15, or position 16 of SEQ ID NO: 16.

19. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises a cysteine at a position corresponding to position 14 of SEQ ID NO: 16.

20. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises a cysteine at position 14 of SEQ ID NO: 16.

21. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide is at least 90% identical, at least 95% identical, at least 97% identical, or at least 99% identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, SEQ ID NO: 11, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80, SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, SEQ ID NO: 100, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 114, SEQ ID NO: 115, SEQ ID NO: 116, SEQ ID NO: 117, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 120, SEQ ID NO: 121, SEQ ID NO: 122, SEQ ID NO: 123, SEQ ID NO: 124, SEQ ID NO: 125, SEQ ID NO: 126, SEQ ID NO: 127, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 130, SEQ ID NO: 131, SEQ ID NO: 132, SEQ ID NO: 133, SEQ ID NO: 134, SEQ ID NO: 135, SEQ ID NO: 136, SEQ ID NO: 137, SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 153, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

22. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises SEQ ID NO: 17.

23. A polypeptide comprising an amino acid sequence of SEQ ID NO: 17.

24. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 205 of SEQ ID NO: 1, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 1;
- b) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 24 of SEQ ID NO: 3;
- c) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 4, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 4;
- d) an amino acid substitution at a position corresponding to position 15 of SEQ ID NO: 64, and/or an amino acid substitution at a position corresponding to position 203 of SEQ ID NO: 64;
- e) an amino acid substitution at a position corresponding to position 199 of SEQ ID NO: 67, and/or an amino acid substitution at a position corresponding to position 200 of SEQ ID NO: 67; and/or
- f) an amino acid substitution at a position corresponding to position 199 of SEQ ID NO: 68, an amino acid substitution at a position corresponding to position 200 of SEQ ID NO: 68, an amino acid substitution at a position corresponding to position 201 of SEQ ID NO: 68, and/or an amino acid substitution at a position corresponding to position 202 of SEQ ID NO: 68.

25. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 21 of SEQ ID NO: 1, an amino acid substitution at position 23 of SEQ ID NO: 1, an amino acid substitution at position 25 of SEQ ID NO: 1, an amino acid substitution at position 80 of SEQ ID NO: 1, an amino acid substitution at position 205 of SEQ ID NO: 1, and/or an amino acid substitution at position 207 of SEQ ID NO: 1;
- b) an amino acid substitution at position 21 of SEQ ID NO: 3, an amino acid substitution at position 23 of SEQ ID NO: 3, and/or an amino acid substitution at position 24 of SEQ ID NO: 3;
- c) an amino acid substitution at position 21 of SEQ ID NO: 4, an amino acid substitution at position 23 of SEQ ID NO: 4, an amino acid substitution at position 25 of SEQ ID NO: 4, an amino acid substitution at position 80 of SEQ ID NO: 4, and/or an amino acid substitution at position 207 of SEQ ID NO: 4;
- d) an amino acid substitution at position 15 of SEQ ID NO: 64, and/or an amino acid substitution at position 203 of SEQ ID NO: 64;
- e) an amino acid substitution at position 199 of SEQ ID NO: 67, and/or an amino acid substitution at position 200 of SEQ ID NO: 67; and/or
- f) an amino acid substitution at position 199 of SEQ ID NO: 68, an amino acid substitution at position 200 of SEQ ID NO: 68, an amino acid substitution at position 201 of SEQ ID NO: 68, and/or an amino acid substitution at position 202 of SEQ ID NO: 68.

26. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) a threonine at a position corresponding to position 21 of SEQ ID NO: 1, a leucine at a position corresponding to position 23 of SEQ ID NO: 1, an alanine at a position corresponding to position 25 of SEQ ID NO: 1, a glycine at a position corresponding to position 80 of SEQ ID NO: 1, an alanine at a position corresponding to position 205 of SEQ ID NO: 1, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 1;
- b) a threonine at a position corresponding to position 21 of SEQ ID NO: 3, a leucine at a position corresponding to position 23 of SEQ ID NO: 3, and/or an isoleucine at a position corresponding to position 24 of SEQ ID NO: 3;

- c) a threonine at a position corresponding to position 21 of SEQ ID NO: 4, a leucine at a position corresponding to position 23 of SEQ ID NO: 4, an alanine at a position corresponding to position 25 of SEQ ID NO: 4, a glycine at a position corresponding to position 80 of SEQ ID NO: 4, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 4;
- d) a threonine or a valine at a position corresponding to position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at a position corresponding to position 203 of SEQ ID NO: 64;
- e) a leucine at a position corresponding to position 199 of SEQ ID NO: 67, and/or a histidine at a position corresponding to position 200 of SEQ ID NO: 67; and/or
- f) a leucine at a position corresponding to position 199 of SEQ ID NO: 68, a histidine at a position corresponding to position 200 of SEQ ID NO: 68, an asparagine at a position corresponding to position 201 of SEQ ID NO: 68, and/or a histidine at a position corresponding to position 202 of SEQ ID NO: 68.

27. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) a threonine at position 21 of SEQ ID NO: 1, a leucine at position 23 of SEQ ID NO: 1, an alanine at position 25 of SEQ ID NO: 1, a glycine at position 80 of SEQ ID NO: 1, an alanine at position 205 of SEQ ID NO: 1, and/or a histidine at position 207 of SEQ ID NO: 1;
- b) a threonine at position 21 of SEQ ID NO: 3, a leucine at position 23 of SEQ ID NO: 3, and/or an isoleucine at position 24 of SEQ ID NO: 3;
- c) a threonine at a position 21 of SEQ ID NO: 4, a leucine at position 23 of SEQ ID NO: 4, an alanine at position 25 of SEQ ID NO: 4, a glycine at position 80 of SEQ ID NO: 4, and/or a histidine at position 207 of SEQ ID NO: 4;
- d) a threonine or a valine at position 15 of SEQ ID NO: 64, and/or a tyrosine or a valine at position 203 of SEQ ID NO: 64;
- e) a leucine at position 199 of SEQ ID NO: 67, and/or a histidine at position 200 of SEQ ID NO: 67; and/or
- f) a leucine at position 199 of SEQ ID NO: 68, a histidine at position 200 of SEQ ID NO: 68, an asparagine at position 201 of SEQ ID NO: 68, and/or a histidine at position 202 of SEQ ID NO: 68.

28. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of:

- a) SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, or SEQ ID NO: 84; or
- b) SEQ ID NO: 19, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 75, or SEQ ID NO: 76.

29. A polypeptide comprising an amino sequence of SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 84, SEQ ID NO: 19, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 75, or SEQ ID NO: 76.

30. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 2, or an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 3;
- b) an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 63, an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 65, an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 66, or an amino acid substitution at a position corresponding to position 87 of SEQ ID NO: 69; or
- c) an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 80, or an amino acid substitution at a position corresponding to position 198 of SEQ ID NO: 81.

31. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 93 of SEQ ID NO: 2, or an amino acid substitution at position 93 of SEQ ID NO: 3;
- b) an amino acid substitution at position 87 of SEQ ID NO: 63, an amino acid substitution at position 87 of SEQ ID NO: 65, an amino acid substitution at position 87 of SEQ ID NO: 66, or an amino acid substitution at position 87 of SEQ ID NO: 69; or
- c) an amino acid substitution at position 198 of SEQ ID NO: 80, or an amino acid substitution at position 198 of SEQ ID NO: 81.

32. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an arginine at a position corresponding to position 93 of SEQ ID NO: 2, or an arginine at a position corresponding to position 93 of SEQ ID NO: 3;
- b) a serine at a position corresponding to position 87 of SEQ ID NO: 63, a serine substitution at a position corresponding to position 87 of SEQ ID NO: 65, a serine at a position corresponding to position 87 of SEQ ID NO: 66, or a serine at a position corresponding to position 87 of SEQ ID NO: 69; or
- c) an alanine at a position corresponding to position 198 of SEQ ID NO: 80, or an alanine at a position corresponding to position 198 of SEQ ID NO: 81.

33. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an arginine at position 93 of SEQ ID NO: 2, or an arginine at position 93 of SEQ ID NO: 3;
- b) a serine at position 87 of SEQ ID NO: 63, a serine at position 87 of SEQ ID NO: 65, a serine at position 87 of SEQ ID NO: 66, or a serine at position 87 of SEQ ID NO: 69; or
- c) an alanine at position 198 of SEQ ID NO: 80, or alanine at position 198 of SEQ ID NO: 81.

34. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises the amino acid sequence of:

- a) SEQ ID NO: 78, SEQ ID NO: 79, or SEQ ID NO: 84; or
- b) SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, or SEQ ID NO: 77; or
- c) SEQ ID NO: 82 or SEQ ID NO: 83.

35. A polypeptide comprising an amino sequence of SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 84, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77, SEQ ID NO: 82, or SEQ ID NO: 83.

36. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 2, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 2; or

- b) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 3.

37. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 5 of SEQ ID NO: 2, an amino acid substitution at position 38 of SEQ ID NO: 2, an amino acid substitution at position 39 of SEQ ID NO: 2, an amino acid substitution at position 97 of SEQ ID NO: 2, and/or an amino acid substitution at position 98 of SEQ ID NO: 2; or
- b) an amino acid substitution at position 5 of SEQ ID NO: 3, an amino acid substitution at position 38 of SEQ ID NO: 3, an amino acid substitution at position 39 of SEQ ID NO: 3, an amino acid substitution at position 97 of SEQ ID NO: 3, and/or an amino acid substitution at position 98 of SEQ ID NO: 3.

38. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) a proline at a position corresponding to position 5 of SEQ ID NO: 2, a glycine at a position corresponding to position 38 of SEQ ID NO: 2, an arginine at a position corresponding to position 39 of SEQ ID NO: 2, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 2, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 2; or
- b) a proline at a position corresponding to position 5 of SEQ ID NO: 3, a glycine at a position corresponding to position 38 of SEQ ID NO: 3, an arginine at a position corresponding to position 39 of SEQ ID NO: 3, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 3, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 3.

39. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

- a) a proline at position 5 of SEQ ID NO: 2, a glycine at position 38 of SEQ ID NO: 2, an arginine at position 39 of SEQ ID NO: 2, an isoleucine at position 97 of SEQ ID NO: 2, and/or a glycine at position 98 of SEQ ID NO: 2; or
- b) a proline at position 5 of SEQ ID NO: 3, a glycine at position 38 of SEQ ID NO: 3, an arginine at position 39 of SEQ ID NO: 3, an isoleucine at position 97 of SEQ ID NO: 3, and/or a glycine at position 98 of SEQ ID NO: 3.

40. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of:

- a) SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, or SEQ ID NO: 147; or
- b) SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

41. A polypeptide comprising an amino sequence of SEQ ID NO: 139, SEQ ID NO: 140, SEQ ID NO: 141, SEQ ID NO: 142, SEQ ID NO: 143, SEQ ID NO: 144, SEQ ID NO: 145, SEQ ID NO: 146, SEQ ID NO: 147, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 150, SEQ ID NO: 151, SEQ ID NO: 152, SEQ ID NO: 154, SEQ ID NO: 155, SEQ ID NO: 156, or SEQ ID NO: 157.

42. A polypeptide comprising a variant IgG Fc polypeptide comprising:

- a) a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 1, a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 2, a tyrosine or a tryptophan at a position corresponding to position 137 of SEQ ID NO: 3, or a tyrosine or a tryptophan at a position corresponding to position 138 of SEQ ID NO: 4; or
- b) a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 16, a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118.

43. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

a) a tyrosine or a tryptophan at position 138 of SEQ ID NO: 1, a tyrosine or a tryptophan at position 137 of SEQ ID NO: 2, a tyrosine or a tryptophan at position 137 of SEQ ID NO: 3, or a tyrosine or a tryptophan at position 138 of SEQ ID NO: 4; or

b) a tyrosine or a tryptophan at position 154 of SEQ ID NO: 16, a tyrosine or a tryptophan at position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a tyrosine or a tryptophan at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118.

44. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

45. A polypeptide comprising an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, SEQ ID NO: 115, SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

46. A contiguous polypeptide comprising the polypeptide of any one of the preceding claims and a glucagon-like peptide-1 (GLP1) polypeptide.

47. A contiguous polypeptide comprising the polypeptide of any one of the preceding claims and a glucagon polypeptide.

48. A polypeptide comprising a variant IgG Fc polypeptide comprising:

a) a serine at a position corresponding to position 138 of SEQ ID NO: 1, a serine at a position corresponding to position 137 of SEQ ID NO: 2, a serine at a position corresponding to position 137 of SEQ ID NO: 3, a serine at a position corresponding to position 138 of SEQ ID NO: 4, a serine at a position corresponding to position 154 of SEQ ID NO: 16, a serine at a position corresponding to position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a serine at a position corresponding to position 154 of SEQ ID NO: 81 or SEQ ID NO: 118;

b) an alanine at a position corresponding to position 140 of SEQ ID NO: 1, an alanine at a position corresponding to position 139 of SEQ ID NO: 2, an alanine at a position corresponding to position 139 of SEQ ID NO: 3, an alanine at a position corresponding to position 140 of SEQ ID NO: 4, an alanine at a position corresponding to position 156 of SEQ ID NO: 16, an alanine at a position corresponding to position 156 of SEQ ID NO: 80 or SEQ ID NO: 117, or an alanine at a position corresponding to position 156 of SEQ ID NO: 81 or SEQ ID NO: 118; and/or

c) a threonine at a position corresponding to position 181 of SEQ ID NO: 1, a threonine at a position corresponding to position 180 of SEQ ID NO: 2, a threonine at a position corresponding to position 180 of SEQ ID NO: 3, a threonine at a position corresponding to position 181 of SEQ ID NO: 4, a threonine at a position corresponding to position 197 of SEQ ID NO: 16, a threonine at a position corresponding to position 197 of SEQ ID NO: 80 or SEQ ID NO: 117, or a threonine at a position corresponding to position 197 of SEQ ID NO: 81 or SEQ ID NO: 118.

49. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises:

a) a serine at position 138 of SEQ ID NO: 1, a serine at position 137 of SEQ ID NO: 2, a serine at position 137 of SEQ ID NO: 3, a serine at position 138 of SEQ ID NO: 4, a serine at position 154 of SEQ ID NO: 16, a serine at position 154 of SEQ ID NO: 80 or SEQ ID NO: 117, or a serine at position 154 of SEQ ID NO: 81 or SEQ ID NO: 118;

b) an alanine at position 140 of SEQ ID NO: 1, an alanine at position 139 of SEQ ID NO: 2, an alanine at position 139 of SEQ ID NO: 3, an alanine at position 140 of SEQ ID NO: 4, an alanine at position 156 of SEQ ID NO: 16, an alanine at position 156 of SEQ ID NO: 80 or SEQ ID NO: 117, or an alanine at position 156 of SEQ ID NO: 81 or SEQ ID NO: 118; and/or;

c) a threonine at position 181 of SEQ ID NO: 1, a threonine at position 181 of SEQ ID NO: 2, a threonine at position 181 of SEQ ID NO: 3, a threonine at position 181 of SEQ ID NO: 4, a threonine at position 197 of SEQ ID NO: 16, a threonine at position 197 of SEQ ID NO: 80 or SEQ ID NO: 117, or a threonine at position 197 of SEQ ID NO: 81 or SEQ ID NO: 118.

50. The polypeptide of any one of the preceding claims, wherein the variant IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 124.

51. A polypeptide comprising an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, SEQ ID NO: 116, SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 124.

52. The polypeptide of any one of the preceding claims, wherein the polypeptide is glycosylated.

53. The polypeptide of any one of claims 1 to 51, wherein the polypeptide is aglycosylated.

54. A contiguous polypeptide comprising the polypeptide of any one of claims 48 to 53 and a glucagon-like peptide-1 (GLP1) polypeptide.
55. A contiguous polypeptide comprising the polypeptide of any one of claims 48 to 53 and a glucagon polypeptide.
56. A heterodimeric protein comprising the contiguous polypeptide of claim 46 and the contiguous polypeptide of claim 54.
57. A heterodimeric protein comprising the contiguous polypeptide of claim 47 and the contiguous polypeptide of claim 55.
58. The contiguous polypeptide or heterodimeric protein of any one of claims 46, 47, or 54 to 57, wherein the GLP1 polypeptide is a wild-type GLP1 polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 85.
59. The contiguous polypeptide or heterodimeric protein of any one of claims 46, 47, or 54 to 58, wherein the GLP1 polypeptide is a variant GLP1 polypeptide.
60. The contiguous polypeptide or heterodimeric protein of any one of claims 46, 47, or 54 to 59, wherein the GLP1 polypeptide comprises the amino acid sequence of SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 98, or SEQ ID NO: 99.
61. The contiguous polypeptide or heterodimeric protein of any one of claims 46, 47, or 54 to 60, wherein the glucagon polypeptide is a wild-type glucagon polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 21.
62. The contiguous polypeptide or heterodimeric protein of any one of claims 46, 47, or 54 to 61, wherein the glucagon polypeptide is a variant glucagon polypeptide.
63. A heterodimeric protein comprising:
- i) a first variant canine IgG Fc polypeptide comprising at least one amino acid modification relative to a first wild-type canine IgG Fc polypeptide and a second variant canine IgG Fc polypeptide comprising at least one amino acid modification relative to a second wild-type canine IgG Fc polypeptide; or
 - ii) a first variant feline IgG Fc polypeptide comprising at least one amino acid modification relative to a first wild-type feline IgG Fc polypeptide and a second variant feline IgG Fc

polypeptide comprising at least one amino acid modification relative to a second wild-type feline IgG Fc polypeptide, wherein:

- a) the first variant canine IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 138 of SEQ ID NO: 1, position 137 of SEQ ID NO: 2, position 137 of SEQ ID NO: 3, or position 138 of SEQ ID NO: 4;
- b) the second variant canine IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 138, position 140, and/or position 181 of SEQ ID NO: 1, position 137, position 139, and/or position 180 of SEQ ID NO: 2, position 137, position 139, and/or position 180 of SEQ ID NO: 3, or position 138, position 140, and/or position 181 of SEQ ID NO: 4;
- c) the first variant feline IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 154 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118; and/or
- d) the second variant feline IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 154, position 156, and/or position 197 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

64. The heterodimeric protein of claim 63, wherein the first wild-type canine IgG Fc polypeptide and the second wild-type canine IgG Fc polypeptide are from the same IgG subtype and/or the first wild-type feline IgG Fc polypeptide and the second wild-type feline IgG Fc polypeptide are from the same IgG subtype.

65. The heterodimeric protein of claim 63, wherein the first wild-type canine IgG Fc polypeptide and the second wild-type canine IgG Fc polypeptide are from a different IgG subtype and/or the first wild-type feline IgG Fc polypeptide and the second wild-type feline IgG Fc polypeptide are from the same IgG subtype.

66. The heterodimeric protein of any one of claims 63 to 65, wherein:

- a) the first variant canine IgG Fc polypeptide comprises a tyrosine or tryptophan at a position corresponding to position 138 of SEQ ID NO: 1, position 137 of SEQ ID NO: 2, position 137 of SEQ ID NO: 3, or position 138 of SEQ ID NO: 4; and/or
- b) the first variant feline IgG Fc polypeptide comprises a tryptophan at a position corresponding to position 154 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

67. The heterodimeric protein of any one of claims 63 to 66, wherein:

- a) the second variant canine IgG Fc polypeptide comprises a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 1, a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 2, a serine at a position corresponding to position 137, an alanine at a position corresponding to position 139, and/or a threonine at a position corresponding to position 180 of SEQ ID NO: 3, and/or a serine at a position corresponding to position 138, an alanine at a position corresponding to position 140, and/or a threonine at a position corresponding to position 181 of SEQ ID NO: 4; and/or
- b) the second variant feline IgG Fc polypeptide comprises a serine at a position corresponding to position 154, an alanine at a position corresponding to position 156, and/or a threonine at a position corresponding to position 197 of SEQ ID NO: 6, of SEQ ID NO: 80, of SEQ ID NO: 81, of SEQ ID NO: 117, or of SEQ ID NO: 118.

68. The heterodimeric protein of any one of claims 63 to 67, wherein:

- a) the first variant canine IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, SEQ ID NO: 109, SEQ ID NO: 111, SEQ ID NO: 113, or SEQ ID NO: 115; and/or
- b) the first variant feline IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 119, SEQ ID NO: 121, or SEQ ID NO: 123.

69. The heterodimeric protein of any one of claims 63 to 68, wherein:

- a) the second variant canine IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 9, SEQ ID NO: 11, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 110, SEQ ID NO: 112, SEQ ID NO: 114, or SEQ ID NO: 116; and/or
- b) the second variant feline IgG Fc polypeptide comprises an amino acid sequence of SEQ ID NO: 120, SEQ ID NO: 122, or SEQ ID NO: 123.

70. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 69, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type IgG Fc polypeptide and has increased binding affinity to Protein A relative to the wild-type IgG Fc polypeptide.

71. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 70, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 1, an amino acid substitution at a position corresponding to position 205 of SEQ ID NO: 1, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 1;
- b) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 24 of SEQ ID NO: 3; or
- c) an amino acid substitution at a position corresponding to position 21 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 23 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 25 of SEQ ID NO: 4, an amino acid substitution at a position corresponding to position 80 of SEQ ID NO: 4, and/or an amino acid substitution at a position corresponding to position 207 of SEQ ID NO: 4.

72. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 71, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 21 of SEQ ID NO: 1, an amino acid substitution at position 23 of SEQ ID NO: 1, an amino acid substitution at position 25 of SEQ ID NO: 1, an amino acid substitution at position 80 of SEQ ID NO: 1, an amino acid substitution at position 205 of SEQ ID NO: 1, and/or an amino acid substitution at position 207 of SEQ ID NO: 1;
- b) an amino acid substitution at position 21 of SEQ ID NO: 3, an amino acid substitution at position 23 of SEQ ID NO: 3, and/or an amino acid substitution at position 24 of SEQ ID NO: 3; or
- c) an amino acid substitution at position 21 of SEQ ID NO: 4, an amino acid substitution at position 23 of SEQ ID NO: 4, an amino acid substitution at position 25 of SEQ ID NO: 4, an amino acid substitution at position 80 of SEQ ID NO: 4, and/or an amino acid substitution at position 207 of SEQ ID NO: 4.

NO: 4, an amino acid substitution at position 80 of SEQ ID NO: 4, and/or an amino acid substitution at position 207 of SEQ ID NO: 4.

73. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 72, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) a threonine at a position corresponding to position 21 of SEQ ID NO: 1, a leucine at a position corresponding to position 23 of SEQ ID NO: 1, an alanine at a position corresponding to position 25 of SEQ ID NO: 1, a glycine at a position corresponding to position 80 of SEQ ID NO: 1, an alanine at a position corresponding to position 205 of SEQ ID NO: 1, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 1;
- b) a threonine at a position corresponding to position 21 of SEQ ID NO: 3, a leucine at a position corresponding to position 23 of SEQ ID NO: 3, and/or an isoleucine at a position corresponding to position 24 of SEQ ID NO: 3; or
- c) a threonine at a position corresponding to position 21 of SEQ ID NO: 4, a leucine at a position corresponding to position 23 of SEQ ID NO: 4, an alanine at a position corresponding to position 25 of SEQ ID NO: 4, a glycine at a position corresponding to position 80 of SEQ ID NO: 4, and/or a histidine at a position corresponding to position 207 of SEQ ID NO: 4.

74. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 73, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) a threonine at position 21 of SEQ ID NO: 1, a leucine at position 23 of SEQ ID NO: 1, an alanine at position 25 of SEQ ID NO: 1, a glycine at position 80 of SEQ ID NO: 1, an alanine at position 205 of SEQ ID NO: 1, and/or a histidine at position 207 of SEQ ID NO: 1;
- b) a threonine at position 21 of SEQ ID NO: 3, a leucine at position 23 of SEQ ID NO: 3, and/or an isoleucine at position 24 of SEQ ID NO: 3; or
- c) a threonine at position 21 of SEQ ID NO: 4, a leucine at position 23 of SEQ ID NO: 4, an alanine at position 25 of SEQ ID NO: 4, a glycine at position 80 of SEQ ID NO: 4, and/or a histidine at position 207 of SEQ ID NO: 4.

75. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 74, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide,

and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type IgG Fc polypeptide and has decreased binding affinity to CD16 relative to the wild-type IgG Fc polypeptide.

76. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 75, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 2, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 2, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 2; or
- b) an amino acid substitution at a position corresponding to position 5 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 38 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 39 of SEQ ID NO: 3, an amino acid substitution at a position corresponding to position 97 of SEQ ID NO: 3, and/or an amino acid substitution at a position corresponding to position 98 of SEQ ID NO: 3.

77. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 76, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) an amino acid substitution at position 5 of SEQ ID NO: 2, an amino acid substitution at position 38 of SEQ ID NO: 2, an amino acid substitution at position 39 of SEQ ID NO: 2, an amino acid substitution at position 97 of SEQ ID NO: 2, and/or an amino acid substitution at position 98 of SEQ ID NO: 2; or
- b) an amino acid substitution at position 5 of SEQ ID NO: 3, an amino acid substitution at position 38 of SEQ ID NO: 3, an amino acid substitution at position 39 of SEQ ID NO: 3, an amino acid substitution at position 97 of SEQ ID NO: 3, and/or an amino acid substitution at position 98 of SEQ ID NO: 3.

78. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 77, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) a proline at a position corresponding to position 5 of SEQ ID NO: 2, a glycine at a position corresponding to position 38 of SEQ ID NO: 2, an arginine at a position corresponding to position 39 of SEQ ID NO: 2, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 2, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 2; or
- b) a proline at a position corresponding to position 5 of SEQ ID NO: 3, a glycine at a position corresponding to position 38 of SEQ ID NO: 3, an arginine at a position corresponding to position 39 of SEQ ID NO: 3, an isoleucine at a position corresponding to position 97 of SEQ ID NO: 3, and/or a glycine at a position corresponding to position 98 of SEQ ID NO: 3.

79. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 78, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises:

- a) a proline at position 5 of SEQ ID NO: 2, a glycine at position 38 of SEQ ID NO: 2, an arginine at position 39 of SEQ ID NO: 2, an isoleucine at position 97 of SEQ ID NO: 2, and/or a glycine at position 98 of SEQ ID NO: 2; or
- b) a proline at position 5 of SEQ ID NO: 3, a glycine at position 38 of SEQ ID NO: 3, an arginine at position 39 of SEQ ID NO: 3, an isoleucine at position 97 of SEQ ID NO: 3, and/or a glycine at position 98 of SEQ ID NO: 3.

80. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 79, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises at least one additional amino acid modification relative to a wild-type canine IgG Fc polypeptide and has decreased binding affinity to C1q relative to the wild-type canine IgG Fc polypeptide.

81. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 80, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 2, or an amino acid substitution at a position corresponding to position 93 of SEQ ID NO: 3.

82. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 81, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide,

and/or the second variant IgG Fc polypeptide comprises an amino acid substitution at position 93 of SEQ ID NO: 2, or an amino acid substitution at position 93 of SEQ ID NO: 3.

83. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 82, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an arginine at a position corresponding to position 93 of SEQ ID NO: 2, or an arginine at a position corresponding to position 93 of SEQ ID NO: 3.

84. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 42 to 83, wherein the variant IgG Fc polypeptide, the first variant IgG Fc polypeptide, and/or the second variant IgG Fc polypeptide comprises an arginine at position 93 of SEQ ID NO: 2, or an arginine at position 93 of SEQ ID NO: 3.

85. The polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 1 to 84, wherein the polypeptide is an antibody, an antibody fusion, or a fusion polypeptide.

86. A contiguous polypeptide comprising:

- a) a first glucagon-like peptide-1 (GLP1) polypeptide (GLP1A);
- b) a first linker (L1);
- c) an Fc polypeptide (Fc) of a companion animal species;
- d) optionally, a second linker (L2); and
- e) optionally, a second GLP1 polypeptide (GLP1B).

87. The contiguous polypeptide of claim 65 comprising:

formula (I): GLP1A—L1—Fc; or

formula (II): Fc—L1—GLP1A.

88. The contiguous polypeptide of claim 65 comprising:

formula (III): GLP1A—L1—Fc—L2—GLP1B.

89. The contiguous polypeptide of any one of claims 86 to 88, wherein GLP1B, if present, comprises the same amino acid sequence as GLP1A.

90. A contiguous polypeptide comprising:

- a) a glucagon-like peptide-1 (GLP1) polypeptide;
- b) a first linker (L1);

- c) an Fc polypeptide (Fc);
- d) a second linker (L2); and
- e) a glucagon polypeptide (Gluc).

91. The contiguous polypeptide of claim 90 comprising:

Formula (IV): GLP1—L1—Fc—L2—Gluc; or

Formula (V): Gluc—L1—Fc—L2—GLP1.

92. The contiguous polypeptide of any one of claims 86 to 91, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises a wild-type GLP1 polypeptide.

93. The contiguous polypeptide of any one of claims 86 to 92, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises a variant GLP1 polypeptide.

94. The contiguous polypeptide of any one of claims 86 to 93, wherein GLP1A, GLP1, and/or GLP1B, if present, comprises an amino acid sequence of SEQ ID NO: 85, SEQ ID NO: 86, SEQ ID NO: 87, SEQ ID NO: 98, or SEQ ID NO: 99.

95. The contiguous polypeptide of any one of claims 86 to 94, wherein the glucagon polypeptide comprises a wild-type glucagon polypeptide, optionally comprising the amino acid sequence of SEQ ID NO: 21.

96. The contiguous polypeptide of any one of claims 86 to 95, wherein the glucagon polypeptide is a variant glucagon polypeptide.

97. The contiguous polypeptide of any one of claims 86 to 96, wherein the Fc polypeptide is a human IgG Fc.

98. The contiguous polypeptide of any one of claims 86 to 97, wherein the Fc polypeptide is a human IgG1 Fc, IgG2 Fc, IgG3 Fc, or IgG4 Fc.

99. The contiguous polypeptide of any one of claims 86 to 98, wherein the Fc polypeptide is an Fc of a companion animal species.

100. The contiguous polypeptide of any one of claims 86 to 97 or 99, wherein the Fc polypeptide comprises:

- a) a canine IgG-A Fc, IgG-B Fc, IgG-C Fc, or IgG-D Fc;
- b) an equine IgG1 Fc, IgG2 Fc, IgG3 Fc, IgG4 Fc, IgG5 Fc, IgG6 Fc, or IgG7 Fc; or

c) a feline IgG1a Fc, IgG1b Fc, or IgG2 Fc.

101. The contiguous polypeptide of any one of claims 86 to 100, wherein the Fc polypeptide is a wild-type IgG Fc polypeptide.

102. The contiguous polypeptide of any one of claims 86 to 100, wherein the Fc polypeptide is a variant IgG Fc polypeptide.

103. The contiguous polypeptide of any one of claims 86 to 102, wherein the Fc polypeptide comprises the polypeptide, the contiguous polypeptide, or the heterodimeric protein of any one of claims 1 to 84.

104. The contiguous polypeptide of any one of claims 85 to 102, wherein the contiguous polypeptide has a longer serum half-life than a wild-type GLP1 polypeptide.

105. The contiguous polypeptide of any one of claims 86 to 104, wherein L1 and L2, if present, each independently is a flexible linker.

106. The contiguous polypeptide of any one of claims 86 to 105, wherein the amino acid sequence of L1 and L2, if present, each independently comprises 100%, at least 95%, at least 90%, at least 85% serine and/or glycine amino acid residues.

107. The contiguous polypeptide of any one of claims 86 to 106, wherein the contiguous polypeptide comprises an extension at its C-terminus.

108. The contiguous polypeptide of any one of claims 86 to 107, wherein the contiguous polypeptide comprises a glycine residue, two glycine residues, three glycine residues, four glycine residues, five glycine residues, six glycine residues, seven glycine residues, eight glycine residues, or greater than eight glycine residues at its C-terminus.

109. The contiguous polypeptide of any one of claims 86 to 108, wherein the contiguous polypeptide comprises an amino acid sequence of SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 90, SEQ ID NO: 91, SEQ ID NO: 92, SEQ ID NO: 93, SEQ ID NO: 94, or SEQ ID NO: 95 at its C-terminus.

110. The contiguous polypeptide of any one of claims 86 to 109, wherein the contiguous polypeptide comprises:

a) the amino acid sequence of SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29; SEQ ID NO: 30; SEQ ID NO: 31; SEQ ID NO: 32; SEQ ID NO: 33; SEQ ID NO: 34; SEQ ID NO: 35; SEQ ID NO: 36; SEQ ID NO: 37; SEQ ID NO: 38; SEQ ID NO: 39; SEQ ID NO: 40; SEQ ID NO: 41; SEQ ID NO: 42; SEQ ID NO: 43; SEQ ID NO: 44; SEQ ID NO: 45; SEQ ID NO: 46; SEQ ID NO: 47; SEQ ID NO: 96; SEQ ID NO: 97; SEQ ID NO: 103; SEQ ID NO: 104; SEQ ID NO: 105, or SEQ ID NO: 106; or

b) the amino acid sequence of SEQ ID NO: 52; SEQ ID NO: 53; SEQ ID NO: 54; SEQ ID NO: 55; SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; or SEQ ID NO: 59.

111. A polypeptide comprising an amino acid sequence of SEQ ID NO: 23; SEQ ID NO: 24; SEQ ID NO: 25; SEQ ID NO: 26; SEQ ID NO: 27; SEQ ID NO: 28; SEQ ID NO: 29; SEQ ID NO: 30; SEQ ID NO: 31; SEQ ID NO: 32; SEQ ID NO: 33; SEQ ID NO: 34; SEQ ID NO: 35; SEQ ID NO: 36; SEQ ID NO: 37; SEQ ID NO: 38; SEQ ID NO: 39; SEQ ID NO: 40; SEQ ID NO: 41; SEQ ID NO: 42; SEQ ID NO: 43; SEQ ID NO: 44; SEQ ID NO: 45; SEQ ID NO: 46; SEQ ID NO: 47; SEQ ID NO: 96; SEQ ID NO: 97; SEQ ID NO: 52; SEQ ID NO: 53; SEQ ID NO: 54; SEQ ID NO: 55; SEQ ID NO: 56; SEQ ID NO: 57; SEQ ID NO: 58; SEQ ID NO: 59; SEQ ID NO: 103; SEQ ID NO: 104; SEQ ID NO: 105, or SEQ ID NO: 106.

112. The polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of the preceding claims, wherein the at least one amino acid modification or substitution comprises an amino acid substitution with an amino acid derivative.

113. An isolated nucleic acid encoding the polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of the preceding claims.

114. A host cell comprising the nucleic acid of claim 113.

115. A method of producing a polypeptide comprising culturing the host cell of claim 114 and isolating the polypeptide.

116. A pharmaceutical composition comprising the polypeptide, the heterodimeric protein, or the contiguous polypeptide of any one of claims 1 to 112, and a pharmaceutically acceptable carrier.

117. A method of increasing production of cAMP in a cell, the method comprising exposing the cell to the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the

pharmaceutical composition of any one of claims 1 to 112 or 116 under conditions permissive for binding of the polypeptide, heterodimeric protein, or contiguous polypeptide to GLP1R.

118. The method of claim 117, wherein the cell is exposed to the polypeptide, heterodimeric protein, contiguous polypeptide, or the pharmaceutical composition *ex vivo*.

119. The method of claim 117, wherein the cell is exposed to the polypeptide, heterodimeric protein, contiguous polypeptide, or the pharmaceutical composition *in vivo*.

120. The method of any one of claims 118 to 119, wherein the cell is a human cell, a canine cell, a feline cell, or an equine cell.

121. A method of delivering a polypeptide to a subject comprising administering the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of claims 1 to 112 or 116 parenterally.

122. A method of delivering a polypeptide to a subject comprising administering the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of claims 1 to 112 or 116 by an intramuscular route, an intraperitoneal route, an intracerebrospinal route, a subcutaneous route, an intra-arterial route, an intrasynovial route, an intrathecal route, or an inhalation route.

123. A method of treating a subject having diabetes or obesity, the method comprising administering to the subject a therapeutically effective amount of the polypeptide, the heterodimeric protein, the contiguous polypeptide, or the pharmaceutical composition of any one of claims 1 to 112 or 116.

124. The method of claim 123, comprising administering insulin, a DPP4 inhibitor, a SGLT2 inhibitor, a biguanides sulfonylureas meglitinide derivative, an alpha-glucosidase inhibitor, a thiazolidinedione (TZD), an amylinomimetic, a bile acid sequestrant, a dopamine agonist.

125. The method of any one of claims 121 to 124, wherein the subject is a human subject.

126. The method of any one of claims 121 to 124, wherein the subject is a companion animal species.

127. The method of claim 126, wherein the companion animal species is canine, equine, or feline.

IgG-A	PVPEPLGGPSVLIFFPKPKKDILIRITRTEVTCTVVLDLGRDPEVQISWFVDGKEVHTAKT
IgG-D	PVPESLGGPSVFIFFPKPKDILIRITRTEITCVVLDLGRDPEVQISWFVDGKEVHTAKT
IgG-B	PAPEMLGGPSVFIFFPKPKDITLLIARTPEVTCVVVDLDPEDPEVQISWFVDGKQMQTAKT
IgG-C	PGCGLLGGPSVFIFFPKPKDILVTRTPTVTTCVVVDLDPENPEVQISWFVDSKQVQTANT
	* ****;**** * :***;*** **;*****.***;***;****
IgG-A	QSQEQFNGTYRVVSVLP IEHQDWL TGKEFKRCRVNHIDLPSPERTISKARGRAHKPSVY
IgG-D	QPREQQFNSTYRVVSVLP IEHQDWL TGKEFKRCRVNHIGLPSPIERTISKARGQAHQPSVY
IgG-B	QPREEQFNGTYRVVSVLP IGHQDWL KGKQFTCKVNNKALPSPIERTISKARGQAHQPSVY
IgG-C	QPREEQSNGTYRVVSVLP IGHQDWL SGKQFKCKVNNKALPSPIEEIISKTPGQAHQPNVY
	* **;* ****;**** * **;***;**** ***** ***; **;***;****
IgG-A	VLPPSPKELSSDTSITCLIKDFYPPDIDVEWQSNQEQEPERKHRMTTPQLDEDEGSYFL
IgG-D	VLPPSPKELSSDTSITCLIKDFFPPEIDVEWQSNQEQEPESKYHTTAPQLDEDEGSYFL
IgG-B	VLPPSREELS-KNTVSLTCLIKDFFPDDIDVEWQSNQEQEPESKYRTTPQLDEDEGSYFL
IgG-C	VLPPSRDEMS-KNTVTTLTCLVKDFFPPEIDVEWQSNQEQEPESKYRMTTPQLDEDEGSYFL
	***** *.* :***;****;***;***** ***** *** *; * *****
IgG-A	YSKLSVDKSRWQQGDPFTCAVM MHETLQNH YTDLSLSHSPGK
IgG-D	YSKLSVDKSRWQQGDTFTCAVM MHEALQNH YTDLSLSHSPGK
IgG-B	YSKLSVDKSRWQRGDTFICAVM MHEALHNHY TQESLSHSPGK
IgG-C	YSKLSVDKSRWQRGDTFICAVM MHEALHNHY TQISLSHSPGK
	*****;*** * ****;***;****;***** *****
IgG-A	SEQ ID NO: 1
IgG-D	SEQ ID NO: 4
IgG-B	SEQ ID NO: 2
IgG-C	SEQ ID NO: 3

Fig. 1

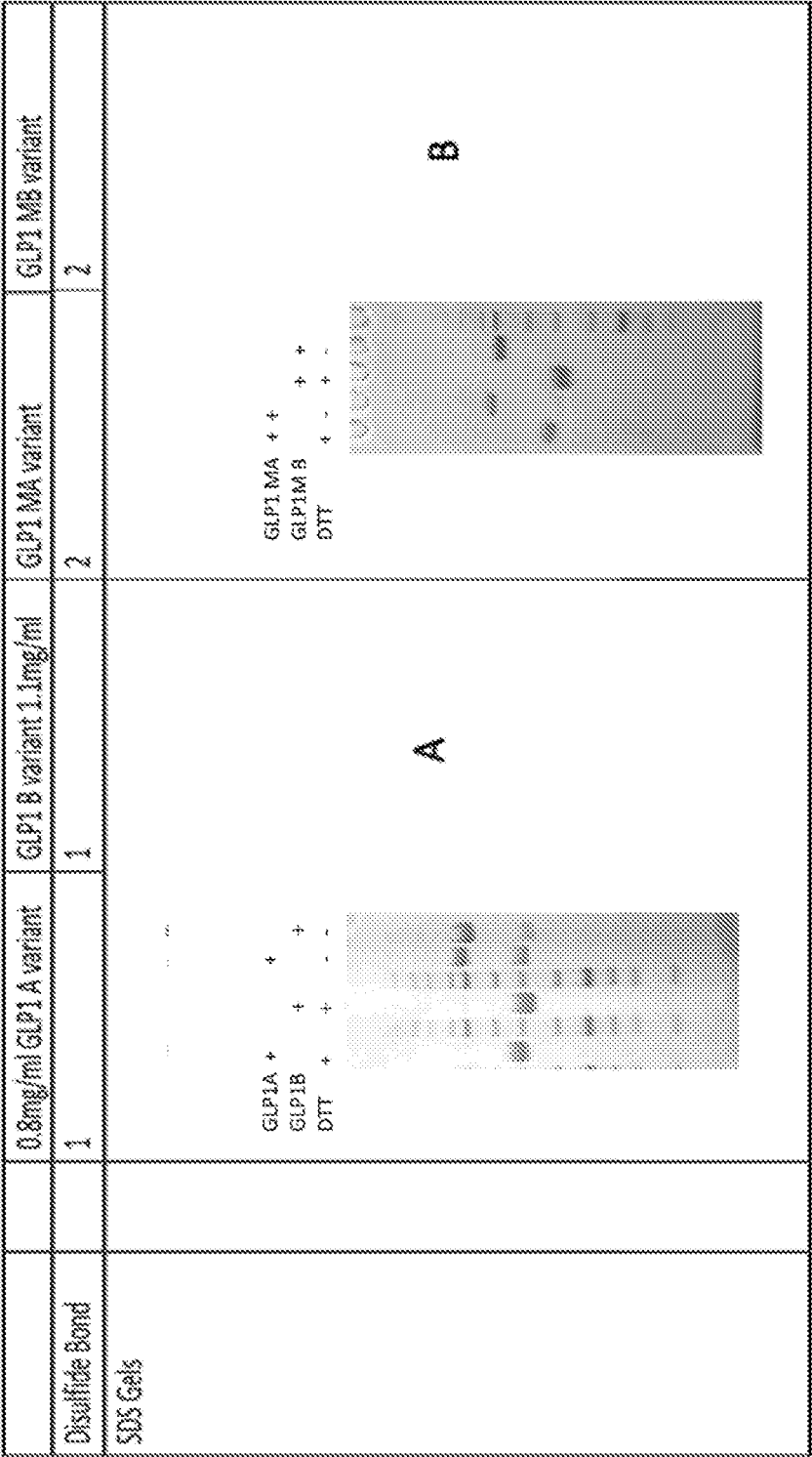


Fig. 2

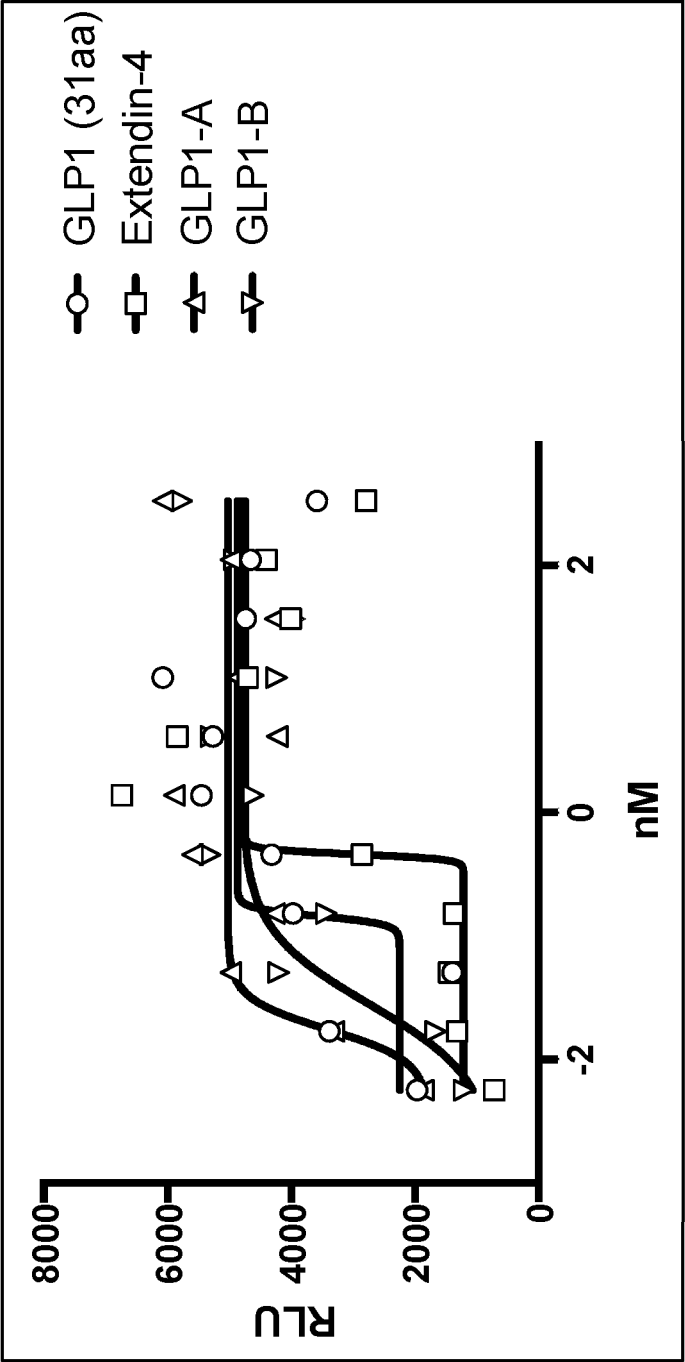
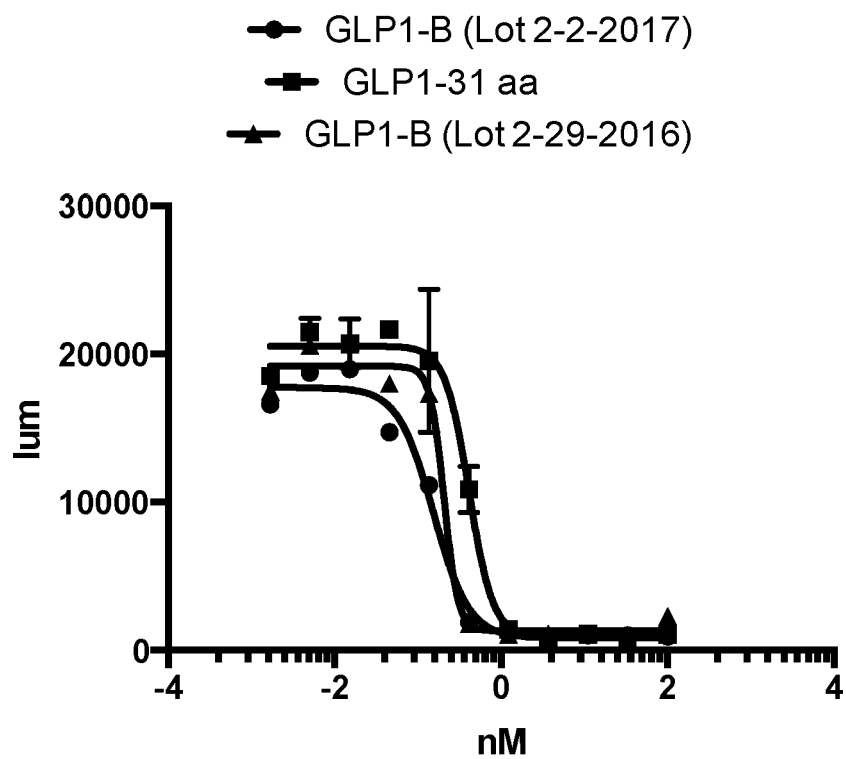
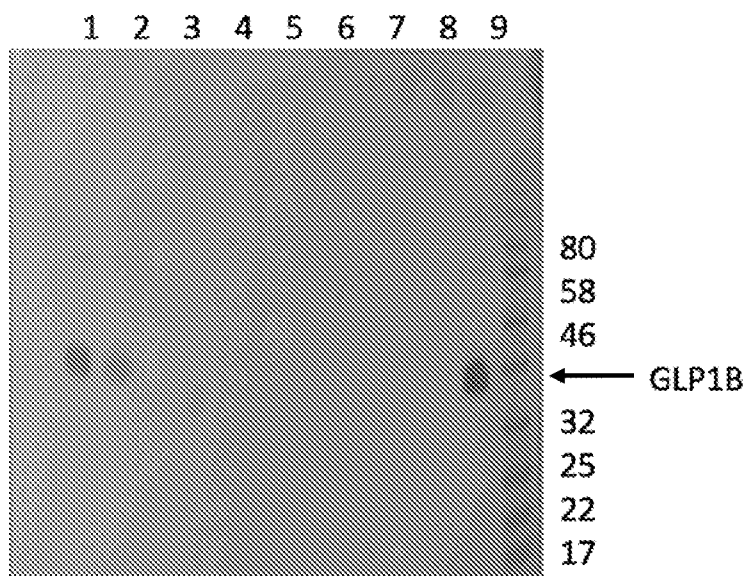


Fig. 3

*Fig. 4**Fig. 5*

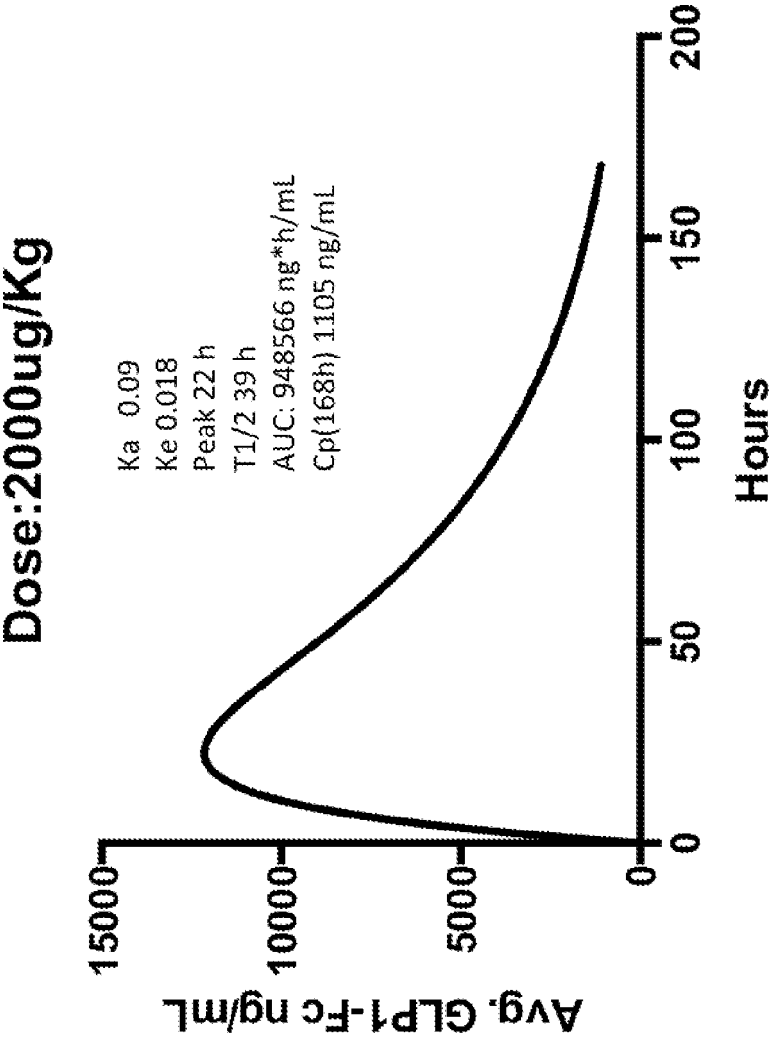


Fig. 6

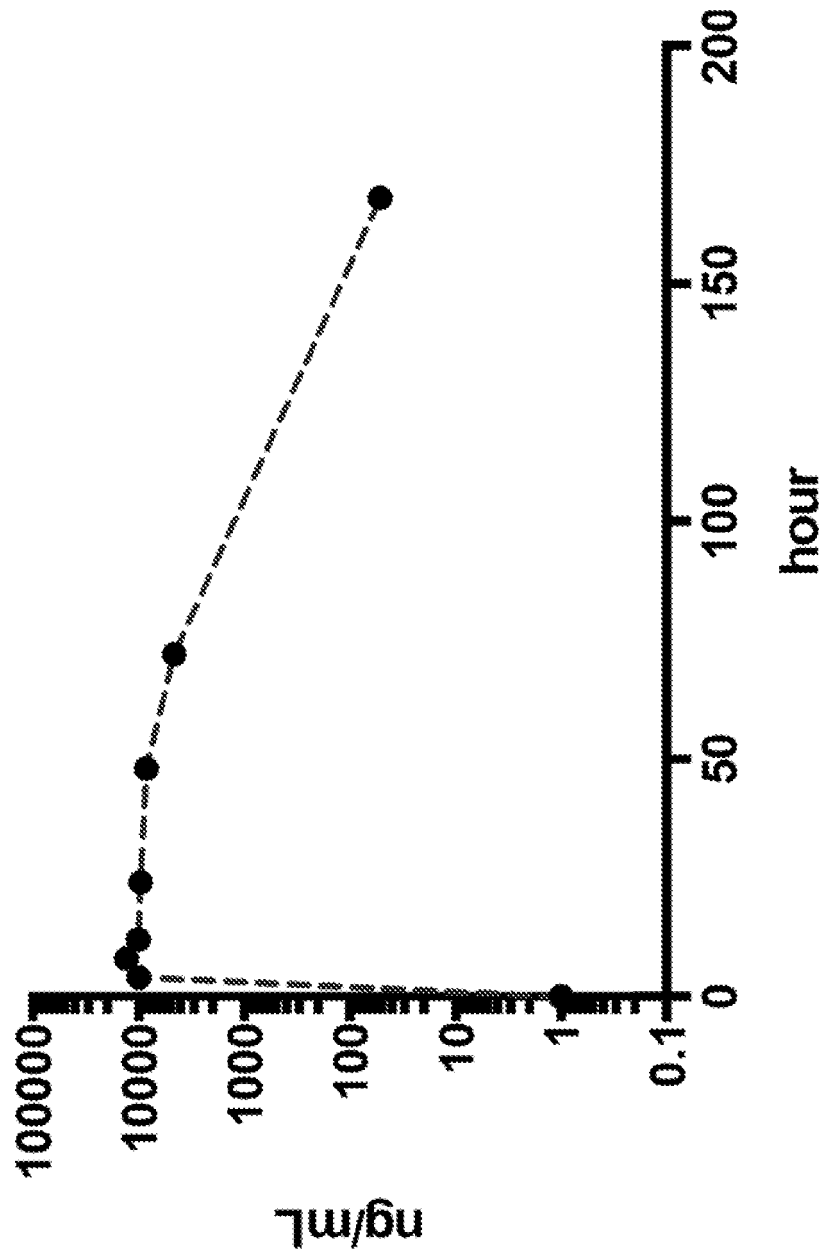


Fig. 7

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<150> US 62/545,858
<151> 2017-08-15
<160> 199
<170> PatentIn version 3.5
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Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
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Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

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Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

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<220>
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<400> 2

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys

20

25

30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
 130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys

210

215

220

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<211> 220

<212> PRT

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<220>

<223> Wild-type canine IgG-C Fc , Protein A - , C1q +, CD16 +

<400> 3

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 4
<211> 221
<212> PRT
<213> Unknown

<220>
<223> Wild-type canine IgG-D Fc , Protein A -, C1q -, CD16

<400> 4

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu

65

70

75

80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
 130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
 145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

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 R(23)L, T(25)A, E(80)G, T(205)A, Q(207)H

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Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
 50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
 130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
 145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

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 V(23)L, T(24)I

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 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

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Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
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Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
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Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
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 R(23)L, T(25)A, E(80)G, Q(207)H

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Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys
 20 25 30

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Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn
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His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
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20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Tyr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
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Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

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 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
 50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
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His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

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Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Tyr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
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Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

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Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

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1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Tyr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
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1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

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Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
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Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
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<213> Artificial Sequence

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<400> 14

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1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Tyr Cys Leu Ile Lys Asp Phe
 130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
 145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 15

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-D Fc , Heterodimer chain 2, Y(181)T

<400> 15

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
 20 25 30

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Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 16
 <211> 237
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type feline IgG2 Fc, Protein A +, C1q -
 <400> 16

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
 1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 17
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: Variant feline IgG2 Fc , Hinge Cys, G(14)C

<400> 17

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Cys Pro Lys
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

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Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 18
<211> 228
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine Fc IgG2 (with equine IgG1 hinge),
Protein A - , C1q -

<400> 18

Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly Gly
1 5 10 15

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met Ile
20 25 30

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
35 40 45

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
50 55 60

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
65 70 75 80

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
85 90 95

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
100 105 110

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
115 120 125

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
130 135 140

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
145 150 155 160

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro

165

170

175

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
 180 185 190

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
 195 200 205

Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser Glu
 210 215 220

Ser Leu Gly Lys
 225

<210> 19
 <211> 228
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: Variant equine IgG2 Fc (with equine IgG1 hinge), C1q
 -, Protein A +, A(29)T, F(217)Y

<400> 19

Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly Gly
 1 5 10 15

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met Ile
 20 25 30

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
 35 40 45

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
 50 55 60

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
 65 70 75 80

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
85 90 95

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
100 105 110

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
115 120 125

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
130 135 140

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
145 150 155 160

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
165 170 175

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
180 185 190

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
195 200 205

Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser Glu
210 215 220

Ser Leu Gly Lys
225

<210> 20
<211> 29
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic: Variant GLP1 (7-35)

<220>

<221> misc_feature

<222> (2)..(2)

<223> X may be G or S

<400> 20

His	Xaa	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
1				5				10					15		

Gln	Ala	Ala	Lys	Glu	Phe	Ile	Ala	Trp	Leu	Val	Lys	Gly
			20				25					

<210> 21

<211> 29

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Glucagon (Gluc)

<400> 21

His	Ser	Gln	Gly	Thr	Phe	Thr	Ser	Asp	Tyr	Ser	Lys	Tyr	Leu	Asp	Ser
1				5				10					15		

Arg	Arg	Ala	Gln	Asp	Phe	Val	Gln	Trp	Leu	Met	Asn	Thr
			20				25					

<210> 22

<211> 39

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Extendin-4

<400> 22

His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu
1				5				10					15		

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
 20 25 30

Ser Gly Ala Pro Pro Pro Ser
 35

<210> 23
 <211> 325
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: GLP1-G8/GLP-2G_III_ WTfeIgG2

<400> 23

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
 20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 35 40 45

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
 50 55 60

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 65 70 75 80

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 85 90 95

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 100 105 110

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Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
115 120 125

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
130 135 140

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
145 150 155 160

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
165 170 175

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
180 185 190

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
195 200 205

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
210 215 220

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
225 230 235 240

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
245 250 255

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
260 265 270

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys Gly Gly Gly
275 280 285

Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val
290 295 300

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Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu
305 310 315 320

Val Lys Gly Gly Gly
325

<210> 24
<211> 285
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8_I_WTfeIgG2

<400> 24

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
35 40 45

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
50 55 60

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
65 70 75 80

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
85 90 95

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
100 105 110

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
115 120 125

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 130 135 140

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 145 150 155 160

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 165 170 175

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 180 185 190

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
 195 200 205

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 210 215 220

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 225 230 235 240

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
 245 250 255

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 260 265 270

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 275 280 285

<210> 25
 <211> 325
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8/GLP1-2G_III_ VARfeIgG2

<400> 25

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
 20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 35 40 45

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Cys Pro Lys
 50 55 60

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 65 70 75 80

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 85 90 95

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 100 105 110

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 115 120 125

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 130 135 140

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 145 150 155 160

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 165 170 175

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Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
180 185 190

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
195 200 205

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
210 215 220

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
225 230 235 240

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
245 250 255

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
260 265 270

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys Gly Gly Gly
275 280 285

Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val
290 295 300

Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu
305 310 315 320

Val Lys Gly Gly Gly
325

<210> 26

<211> 285

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8_I_VARfeIgG2

<400> 26

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
 20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 35 40 45

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Cys Pro Lys
 50 55 60

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 65 70 75 80

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 85 90 95

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 100 105 110

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 115 120 125

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 130 135 140

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 145 150 155 160

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 165 170 175

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 180 185 190

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
 195 200 205

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 210 215 220

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 225 230 235 240

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
 245 250 255

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 260 265 270

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 275 280 285

<210> 27
 <211> 327
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: GLP1-S8/GLP1-3G_III_ WTfeIgG2

<400> 27

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

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Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro
50 55 60

Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe
65 70 75 80

Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val
85 90 95

Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile
100 105 110

Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro
115 120 125

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro
130 135 140

Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val
145 150 155 160

Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala
165 170 175

Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln
180 185 190

Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly
195 200 205

Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro
210 215 220

Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp
225 230 235 240

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Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp
 245 250 255

Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His
 260 265 270

Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys Gly Gly
 275 280 285

Gly Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp
 290 295 300

Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp
 305 310 315 320

Leu Val Lys Gly Gly Gly Gly
 325

<210> 28

<211> 286

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-S8_I_WTfeIgG2

<400> 28

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro
 50 55 60

Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe
65 70 75 80

Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val
85 90 95

Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile
100 105 110

Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro
115 120 125

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro
130 135 140

Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val
145 150 155 160

Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala
165 170 175

Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln
180 185 190

Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly
195 200 205

Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro
210 215 220

Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp
225 230 235 240

Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp
245 250 255

Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His
 260 265 270

Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 275 280 285

<210> 29
 <211> 323
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: GLP1-G8/GLP1-3G_III_ VARcaIgGD

<400> 29

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro Val Pro
 50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
 85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
 100 105 110

01157011-seql-000001.txt

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
 115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
 130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
 145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
 165 170 175

Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
 180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
 195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
 210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe
 225 230 235 240

Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
 245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
 260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
 275 280 285

Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
 290 295 300

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Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
305 310 315 320

Gly Gly Gly

<210> 30
<211> 282
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8_I_VARcaIgGD

<400> 30

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Pro Lys Glu Ser Thr Cys Lys Cys Ile Ser Pro Cys Pro Val Pro
50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
100 105 110

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
 130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
 145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
 165 170 175

Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
 180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
 195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
 210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe
 225 230 235 240

Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
 245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
 260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 275 280

<210> 31
 <211> 323
 <212> PRT
 <213> Artificial Sequence

<220>

<223> Synthetic: GLP1-S8/GLP1-3G_III_ VARcaIgGD

<400> 31

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro Val Pro
 50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
 85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
 100 105 110

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
 115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
 130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
 145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
 165 170 175

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Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe
225 230 235 240

Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
275 280 285

Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
290 295 300

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
305 310 315 320

Gly Gly Gly

<210> 32

<211> 282

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-S8_I_VARcaIgGD

<400> 32

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Ser Pro Lys Glu Ser Thr Cys Lys Cys Ile Ser Pro Cys Pro Val Pro
 50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
 85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
 100 105 110

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
 115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
 130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
 145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
 165 170 175

Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
 180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe
225 230 235 240

Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys
275 280

<210> 33
<211> 318
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8/GLPL1-3G_III_ VAREqIgG2

<400> 33

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

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Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly
50 55 60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
65 70 75 80

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
225 230 235 240

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Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
260 265 270

Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala
275 280 285

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
290 295 300

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
305 310 315

<210> 34
<211> 277
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8_I_VAREqIgG2

<400> 34

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly
50 55 60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
65 70 75 80

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
260 265 270

Glu Ser Leu Gly Lys
275

<210> 35
<211> 318
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-S8/GLP1-3G_III_ VAREqIgG2

<400> 35

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly
50 55 60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
65 70 75 80

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
115 120 125

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Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
260 265 270

Glu Ser Leu Gly Lys Gly Gly Gly Ser Gly Gly Gly Gly His Ala
275 280 285

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
290 295 300

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
305 310 315

<210> 36

<211> 277

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-S8_I_VAREqIgG2

<400> 36

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly
50 55 60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
65 70 75 80

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
 165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
 180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
 195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
 210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
 225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
 245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
 260 265 270

Glu Ser Leu Gly Lys
 275

<210> 37
 <211> 346
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: ssGLP1-S8/GLP1-3G_III_ WTfeIgG2

<400> 37

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
 1 5 10 15

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Val Leu Ser His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly
65 70 75 80

Glu Gly Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val
85 90 95

Phe Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr
100 105 110

Pro Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn
115 120 125

Val Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys
130 135 140

Thr Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
145 150 155 160

Val Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys
165 170 175

Cys Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile
180 185 190

Ser Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro
195 200 205

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Pro Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu
210 215 220

Ile Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr
225 230 235 240

Gly Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu
245 250 255

Asp Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg
260 265 270

Ser His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu
275 280 285

Ala Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly
290 295 300

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe
305 310 315 320

Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe
325 330 335

Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
340 345

<210> 38

<211> 344

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: ssGLP1-G8/GLP1-2G_III_ VARfeIgG2

<400> 38

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
50 55 60

Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu
65 70 75 80

Cys Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe
85 90 95

Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro
100 105 110

Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val
115 120 125

Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr
130 135 140

Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val
145 150 155 160

Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys
165 170 175

Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser
180 185 190

Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro
195 200 205

Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile
 210 215 220

Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly
 225 230 235 240

Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp
 245 250 255

Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser
 260 265 270

His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala
 275 280 285

Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 290 295 300

Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr
 305 310 315 320

Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile
 325 330 335

Ala Trp Leu Val Lys Gly Gly Gly
 340

<210> 39
 <211> 304
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: ssGLP1-G8_I_VARfeIgG2

<400> 39

01157011-seql-000001.txt

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
50 55 60

Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu
65 70 75 80

Cys Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe
85 90 95

Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro
100 105 110

Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val
115 120 125

Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr
130 135 140

Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val
145 150 155 160

Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys
165 170 175

Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser
180 185 190

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Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro
195 200 205

Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile
210 215 220

Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly
225 230 235 240

Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp
245 250 255

Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser
260 265 270

His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala
275 280 285

Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
290 295 300

<210> 40
<211> 305
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssGLP1-S8_I_WTfeIgG2

<400> 40

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly
65 70 75 80

Glu Gly Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val
85 90 95

Phe Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr
100 105 110

Pro Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn
115 120 125

Val Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys
130 135 140

Thr Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
145 150 155 160

Val Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys
165 170 175

Cys Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile
180 185 190

Ser Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro
195 200 205

Pro Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu
210 215 220

Ile Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr
225 230 235 240

Gly Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu
245 250 255

Asp Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg
260 265 270

Ser His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu
275 280 285

Ala Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly
290 295 300

Lys
305

<210>	41
<211>	340
<212>	PRT
<213>	Artificial Sequence

<220>
<223> Synthetic: ssGLP1-G8/GLP1-2G_III_ VARcaIgGD

<400> 41

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
50 55 60

01157011-seq1-000001.txt

Gly Gly Ser Pro Lys Glu Ser Thr Cys Lys Cys Ile Ser Pro Cys Pro
65 70 75 80

Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys
85 90 95

Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val
100 105 110

Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe
115 120 125

Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln
130 135 140

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His
145 150 155 160

Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile
165 170 175

Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln
180 185 190

Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu
195 200 205

Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe
210 215 220

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro
225 230 235 240

Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser
245 250 255

01157011-seql-000001.txt

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln
260 265 270

Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His
275 280 285

Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly
290 295 300

Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser
305 310 315 320

Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
325 330 335

Lys Gly Gly Gly
340

<210> 42

<211> 340

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: ssGLP1-G8/GLP1-2G_III_ VARcaIgGD

<400> 42

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
50 55 60

Gly Gly Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro
65 70 75 80

Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys
85 90 95

Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val
100 105 110

Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe
115 120 125

Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln
130 135 140

Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His
145 150 155 160

Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile
165 170 175

Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln
180 185 190

Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu
195 200 205

Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe
210 215 220

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro
225 230 235 240

Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser
245 250 255

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln
 260 265 270

Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His
 275 280 285

Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly
 290 295 300

Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser
 305 310 315 320

Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
 325 330 335

Lys Gly Gly Gly
 340

<210> 43

<211> 342

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: ssGLP1-S8/GLP1-3G_III_ VARcaIgGD

<400> 43

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
 1 5 10 15

Val Leu Ser His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
 20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 35 40 45

01157011-seq1-000001.txt

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys
65 70 75 80

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
85 90 95

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys
100 105 110

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
115 120 125

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
130 135 140

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
145 150 155 160

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
165 170 175

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
180 185 190

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
195 200 205

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
210 215 220

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
225 230 235 240

01157011-seq1-000001.txt

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
245 250 255

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
260 265 270

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn
275 280 285

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly
290 295 300

Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val
305 310 315 320

Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu
325 330 335

Val Lys Gly Gly Gly Gly
340

<210> 44
<211> 337
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssGLP1-G8/GLP1-3G_III_ VAREqIgG2

<400> 44

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu
65 70 75 80

Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp
85 90 95

Thr Leu Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn
100 105 110

Leu Ser Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn
115 120 125

Thr Glu Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn
130 135 140

Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp
145 150 155 160

Leu Ser Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro
165 170 175

Gln Pro Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val
180 185 190

Pro Gln Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser
195 200 205

Lys Val Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile
210 215 220

Ser Val Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr
225 230 235 240

Ser Thr Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr
245 250 255

Ser Lys Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe
260 265 270

Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr
275 280 285

Asp Ile Ser Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly
290 295 300

Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
305 310 315 320

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly
325 330 335

Gly

<210> 45
<211> 298
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssGLP1-G8_I_VAREqIgG2

<400> 45

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

01157011-seq1-000001.txt

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
 50 55 60

Gly Gly Gly Ser Ser Val Pro Lys Pro Gln Cys Pro Pro Tyr Thr His
 65 70 75 80

Ser Lys Phe Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro
 85 90 95

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val
 100 105 110

Val Asn Leu Ser Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val
 115 120 125

Asp Asn Thr Glu Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln
 130 135 140

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln
 145 150 155 160

Asp Trp Leu Ser Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly
 165 170 175

Val Pro Gln Pro Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser
 180 185 190

Arg Val Pro Gln Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala
 195 200 205

Lys Ser Lys Val Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro
 210 215 220

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Asp Ile Ser Val Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly
225 230 235 240

Lys Tyr Ser Thr Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe
245 250 255

Leu Tyr Ser Lys Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu
260 265 270

Ser Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
275 280 285

Lys Thr Asp Ile Ser Glu Ser Leu Gly Lys
290 295

<210> 46
<211> 337
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssGLP1-S8/GLP1-3G_III_ VAREqIgG2

<400> 46

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu
65 70 75 80

Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp
85 90 95

Thr Leu Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn
100 105 110

Leu Ser Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn
115 120 125

Thr Glu Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn
130 135 140

Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp
145 150 155 160

Leu Ser Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro
165 170 175

Gln Pro Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val
180 185 190

Pro Gln Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser
195 200 205

Lys Val Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile
210 215 220

Ser Val Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr
225 230 235 240

Ser Thr Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr
245 250 255

Ser Lys Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe
260 265 270

Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr
 275 280 285

Asp Ile Ser Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly
 290 295 300

Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu
 305 310 315 320

Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly
 325 330 335

Gly

<210> 47
 <211> 298
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: ssGLP1-S8_I_VAREqIgG2

<400> 47

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
 1 5 10 15

Val Leu Ser His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
 20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
 50 55 60

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Gly Gly Gly Ser Ser Val Pro Lys Pro Gln Cys Pro Pro Tyr Thr His
65 70 75 80

Ser Lys Phe Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro
85 90 95

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val
100 105 110

Val Asn Leu Ser Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val
115 120 125

Asp Asn Thr Glu Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln
130 135 140

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln
145 150 155 160

Asp Trp Leu Ser Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly
165 170 175

Val Pro Gln Pro Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser
180 185 190

Arg Val Pro Gln Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala
195 200 205

Lys Ser Lys Val Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro
210 215 220

Asp Ile Ser Val Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly
225 230 235 240

Lys Tyr Ser Thr Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe
245 250 255

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Leu Tyr Ser Lys Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu
260 265 270

Ser Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
275 280 285

Lys Thr Asp Ile Ser Glu Ser Leu Gly Lys
290 295

<210> 48

<211> 757

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Feline glucagon-like peptide 1 receptor (GLP1R)

<400> 48

Met Gly Leu Val Ala Pro Val Val Leu Leu His Gln Asp Asp Glu Glu
1 5 10 15

His Gly Gln Asp Glu Gly Pro Glu Asp Gly Ser Gly Tyr Leu Leu Gly
20 25 30

Thr Leu Thr Arg Phe Ser Ser Asp Phe Asp Ser Ala Pro Glu Val Ile
35 40 45

Leu Ala Pro Asp Asp Gln Leu Gln Leu Pro His Pro Ser Ser Arg Glu
50 55 60

Asn Phe Trp Ala Arg Thr Gly Leu Cys Ala Glu Ser Phe Leu Leu Arg
65 70 75 80

Pro Val Gly Pro Val Gly Pro Val Met Gly Trp Ser Glu Gly Phe His
85 90 95

Lys Arg Asn Ser Arg Gln Glu Phe Leu Arg Arg Arg Leu Phe Ala Gly
100 105 110

Gly Leu Cys Ala Ala Ser Thr Gln Glu Ser Arg Asn Arg Cys Ser Ser
115 120 125

Arg Gly Cys Lys Ser Ser Pro Ala Asp Cys Pro Glu Leu Asp Arg Thr
130 135 140

Gln His Leu Gly Asn Ser Val Gly Pro Ile Gln Ala Ala His Gln Glu
145 150 155 160

Leu Ala Leu Gly Ala Gly Gly Pro Gly Asp Glu Cys Gln Cys Cys Ser
165 170 175

Val Ser Asn Ser Leu Phe Ile Pro Glu Pro Gln Ser Thr Cys Pro Tyr
180 185 190

Asn Gly Tyr Thr Ser Trp Pro Leu Glu Gly Asn Leu Arg Val Ala Cys
195 200 205

Ala Pro Pro Pro Pro Pro Pro Ala Arg Thr Leu Phe Gly Gly Ser Arg
210 215 220

Arg Gly Ala Val Asp Lys Lys Ala Gly Gly Gly Asn Arg Ser Pro Gly
225 230 235 240

Gly Gly Ala Gly Thr Gly Glu Phe Gly Ala Pro Gly Ala Gly Gly Gly
245 250 255

Leu Gly Arg Arg Pro Glu Val Gly Ala Trp Thr Ala Ala Glu Gly Thr
260 265 270

Asn Pro Ala Asp Leu Ala Ser Ser Pro Pro Pro Pro Ser Thr Arg Pro
275 280 285

Pro Ala Ala Pro Arg Pro Pro Cys Ala Asp Phe Cys Ala Ala Ser Pro
290 295 300

Gln Thr Thr Phe Pro Thr Pro Ser Pro Arg Arg Pro Leu Pro Ala Ser
305 310 315 320

Gly Gly Ala Thr Val Ser Leu Ser Glu Thr Val Gln Lys Trp Arg Glu
325 330 335

Tyr Arg His Gln Cys Gln Arg Phe Leu Thr Glu Ala Pro Pro Pro Ala
340 345 350

Thr Gly Leu Phe Cys Asn Arg Thr Phe Asp Glu Tyr Ala Cys Trp Pro
355 360 365

Asp Gly Leu Pro Gly Ser Phe Val Asn Val Ser Cys Pro Trp Tyr Leu
370 375 380

Pro Trp Ala Ser Ser Val Leu Gln Gly His Val Tyr Arg Phe Cys Thr
385 390 395 400

Ala Glu Gly Leu Trp Leu Arg Gln Asp Asn Ser Ser Leu Pro Trp Arg
405 410 415

Asn Leu Ser Glu Cys Glu Glu Ser Lys Arg Gly Glu Arg Ser Ser Pro
420 425 430

Glu Glu Gln Leu Leu Ser Phe Ser Ile Ile Tyr Thr Val Gly Tyr Thr
435 440 445

Leu Ser Phe Ser Ala Leu Val Ile Ala Ser Ala Ile Leu Leu Ser Phe
450 455 460

Arg His Leu His Cys Thr Arg Asn Tyr Ile His Leu Asn Leu Phe Ala
465 470 475 480

Ser Phe Ile Leu Arg Ala Leu Ser Val Phe Ile Arg Asp Ala Val Leu
485 490 495

Lys Trp Met Tyr Ser Thr Ala Pro Gln Gln His Gln Trp Asp Gly Leu
500 505 510

Leu Ser Tyr Gln Asp Ser Leu Gly Cys Arg Leu Val Phe Leu Leu Met
515 520 525

Gln Tyr Cys Val Ala Ala Asn Tyr Tyr Trp Leu Leu Val Glu Gly Val
530 535 540

Tyr Leu Tyr Thr Leu Leu Ala Phe Ser Val Phe Ser Glu Gln Arg Ile
545 550 555 560

Phe Arg Leu Tyr Leu Ser Ile Gly Trp Gly Val Pro Leu Leu Phe Val
565 570 575

Ile Trp Gly Ile Val Lys Tyr Leu Tyr Glu Asp Glu Gly Cys Trp Thr
580 585 590

Arg Asn Ser Asn Met Asn Tyr Trp Leu Ile Ile Arg Leu Pro Ile Leu
595 600 605

Phe Ala Ile Gly Val Asn Phe Leu Ile Phe Val Arg Val Ile Cys Ile
610 615 620

Val Val Ser Lys Leu Lys Ala Asn Leu Met Cys Lys Thr Asp Ile Lys
625 630 635 640

Cys Arg Leu Ala Lys Ser Thr Leu Thr Leu Ile Pro Leu Leu Gly Thr
645 650 655

His Glu Val Val Phe Ala Phe Val Met Asp Glu His Ala Arg Gly Thr
660 665 670

Leu Arg Phe Ile Lys Leu Phe Thr Glu Leu Ser Phe Thr Ser Phe Gln
675 680 685

Gly Leu Met Val Ala Ile Leu Tyr Cys Phe Val Asn Asn Glu Val Gln
690 695 700

Met Glu Phe Arg Arg Ser Trp Glu Arg Trp Arg Leu Lys His Leu His
705 710 715 720

Ile Gln Arg Asp Ser Ser Met Lys Pro Leu Lys Cys Pro Thr Ser Ser
725 730 735

Leu Thr Ser Gly Gly Thr Val Gly Ser Ser Val Tyr Ala Ala Ser Cys
740 745 750

Gln Ala Ser Cys Ser
755

<210> 49
<211> 126
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: Mature feline glucagon-like peptide 1
receptor-N-terminal domain (GLP1R-N)

<400> 49

Arg Pro Leu Pro Ala Ser Gly Gly Ala Thr Val Ser Leu Ser Glu Thr
1 5 10 15

Val Gln Lys Trp Arg Glu Tyr Arg His Gln Cys Gln Arg Phe Leu Thr
20 25 30

Glu Ala Pro Pro Pro Ala Thr Gly Leu Phe Cys Asn Arg Thr Phe Asp
35 40 45

Glu Tyr Ala Cys Trp Pro Asp Gly Leu Pro Gly Ser Phe Val Asn Val
50 55 60

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Ser Cys Pro Trp Tyr Leu Pro Trp Ala Ser Ser Val Leu Gln Gly His
65 70 75 80

Val Tyr Arg Phe Cys Thr Ala Glu Gly Leu Trp Leu Arg Gln Asp Asn
85 90 95

Ser Ser Leu Pro Trp Arg Asn Leu Ser Glu Cys Glu Glu Ser Lys Arg
100 105 110

Gly Glu Arg Ser Ser Pro Glu Glu Gln Leu Leu Ser Phe Ser
115 120 125

<210> 50
<211> 392
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssFeGLP1R-N_huFc_ PolyHis

<400> 50

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
1 5 10 15

Gly Ser Thr Gly Arg Pro Leu Pro Ala Ser Gly Gly Ala Thr Val Ser
20 25 30

Leu Ser Glu Thr Val Gln Lys Trp Arg Glu Tyr Arg His Gln Cys Gln
35 40 45

Arg Phe Leu Thr Glu Ala Pro Pro Pro Ala Thr Gly Leu Phe Cys Asn
50 55 60

Arg Thr Phe Asp Glu Tyr Ala Cys Trp Pro Asp Gly Leu Pro Gly Ser
65 70 75 80

Phe Val Asn Val Ser Cys Pro Trp Tyr Leu Pro Trp Ala Ser Ser Val

85

90

95

Leu Gln Gly His Val Tyr Arg Phe Cys Thr Ala Glu Gly Leu Trp Leu
 100 105 110

Arg Gln Asp Asn Ser Ser Leu Pro Trp Arg Asn Leu Ser Glu Cys Glu
 115 120 125

Glu Ser Lys Arg Gly Glu Arg Ser Ser Pro Glu Glu Gln Leu Leu Ser
 130 135 140

Phe Ser Gly Ser Glu Asn Leu Tyr Phe Gln Gly Pro Lys Ser Cys Asp
 145 150 155 160

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly
 165 170 175

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile
 180 185 190

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu
 195 200 205

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His
 210 215 220

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg
 225 230 235 240

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys
 245 250 255

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu
 260 265 270

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr

275

280

285

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu
 290 295 300

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp
 305 310 315 320

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val
 325 330 335

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp
 340 345 350

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His
 355 360 365

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro
 370 375 380

Gly Lys His His His His His His
 385 390

<210> 51

<211> 156

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: ssFeGLP1R-N_PolyHis

<400> 51

Met Glu Thr Asp Thr Leu Leu Leu Trp Val Leu Leu Leu Trp Val Pro
 1 5 10 15

Gly Ser Thr Gly Arg Pro Leu Pro Ala Ser Gly Gly Ala Thr Val Ser
 20 25 30

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Leu Ser Glu Thr Val Gln Lys Trp Arg Glu Tyr Arg His Gln Cys Gln
35 40 45

Arg Phe Leu Thr Glu Ala Pro Pro Pro Ala Thr Gly Leu Phe Cys Asn
50 55 60

Arg Thr Phe Asp Glu Tyr Ala Cys Trp Pro Asp Gly Leu Pro Gly Ser
65 70 75 80

Phe Val Asn Val Ser Cys Pro Trp Tyr Leu Pro Trp Ala Ser Ser Val
85 90 95

Leu Gln Gly His Val Tyr Arg Phe Cys Thr Ala Glu Gly Leu Trp Leu
100 105 110

Arg Gln Asp Asn Ser Ser Leu Pro Trp Arg Asn Leu Ser Glu Cys Glu
115 120 125

Glu Ser Lys Arg Gly Glu Arg Ser Ser Pro Glu Glu Gln Leu Leu Ser
130 135 140

Phe Ser Gly Gly Gly Ser His His His His His His
145 150 155

<210> 52
<211> 326
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8/Gluc-3G_IV_ WTfeIgG2

<400> 52

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly

20

25

30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 35 40 45

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
 50 55 60

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 65 70 75 80

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 85 90 95

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 100 105 110

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 115 120 125

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 130 135 140

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 145 150 155 160

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 165 170 175

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 180 185 190

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
 195 200 205

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu

210

215

220

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 225 230 235 240

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
 245 250 255

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 260 265 270

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys Gly Gly Gly
 275 280 285

Gly Ser Gly Gly Gly Gly His Ser Gln Gly Thr Phe Thr Ser Asp Tyr
 290 295 300

Ser Lys Tyr Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu
 305 310 315 320

Met Asn Thr Gly Gly Gly
 325

<210> 53

<211> 326

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Gluc/GLP1-2G_V_ WTfeIgG2

<400> 53

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
 1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Gly Gly
 20 25 30

Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly
35 40 45

Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro
50 55 60

Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe
65 70 75 80

Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val
85 90 95

Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile
100 105 110

Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro
115 120 125

Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro
130 135 140

Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val
145 150 155 160

Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala
165 170 175

Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln
180 185 190

Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly
195 200 205

Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro
210 215 220

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Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp
225 230 235 240

Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp
245 250 255

Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His
260 265 270

Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys Gly Gly
275 280 285

Gly Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp
290 295 300

Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp
305 310 315 320

Leu Val Lys Gly Gly Gly
325

<210> 54
<211> 324
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8/Glu-4G_IV_ VARcaIgGD

<400> 54

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly

35

40

45

Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro Val Pro
 50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
 65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
 85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
 100 105 110

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
 115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
 130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
 145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
 165 170 175

Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
 180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
 195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
 210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe

225 230 235 240

Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
 245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
 260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
 275 280 285

Gly Gly Gly His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr
 290 295 300

Leu Asp Ser Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr
305 310 315 320

Gly Gly Gly Gly

<210> 55

<211> 323

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Gluc/GLP1-3G_V_ VARcaIgGD

<400> 55

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

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Ser Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro Val Pro
50 55 60

Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys
65 70 75 80

Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu
85 90 95

Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp
100 105 110

Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe
115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp
130 135 140

Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu
145 150 155 160

Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His
165 170 175

Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser
180 185 190

Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro
195 200 205

Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser
210 215 220

Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe
225 230 235 240

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Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp
245 250 255

Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr
260 265 270

Asp Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly
275 280 285

Gly Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
290 295 300

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
305 310 315 320

Gly Gly Gly

<210> 56
<211> 319
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8/Gluc-4G_IV_ VAREqIgGD

<400> 56

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly

50

55

60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
 65 70 75 80

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
 85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
 100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
 115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
 130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
 145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
 165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
 180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
 195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
 210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
 225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala

245

250

255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
 260 265 270

Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ser
 275 280 285

Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser Arg Arg
 290 295 300

Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Gly Gly Gly
 305 310 315

<210> 57

<211> 318

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Gluc/GLP1-3G_V_ VAREqIgG2

<400> 57

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
 1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Ala Gly
 20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
 35 40 45

Ser Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu Gly
 50 55 60

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met
 65 70 75 80

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Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
85 90 95

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
100 105 110

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
260 265 270

Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala
275 280 285

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
290 295 300

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
305 310 315

<210> 58

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8/Glu-4G_IV_ huIgG4

<400> 58

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Ser Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro
50 55 60

Glu Phe Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys
65 70 75 80

Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val
85 90 95

Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp

100

105

110

Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe
 115 120 125

Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp
 130 135 140

Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu
 145 150 155 160

Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg
 165 170 175

Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys
 180 185 190

Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp
 195 200 205

Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys
 210 215 220

Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser
 225 230 235 240

Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser
 245 250 255

Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser
 260 265 270

Leu Ser Leu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly
 275 280 285

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser

290

295

300

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Gly Gly
 305 310 315 320

Gly

<210> 59

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Gluc/GLP1-3G_V_huIgG4

<400> 59

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser
 1 5 10 15

Arg Arg Ala Gln Asp Phe Val Gln Trp Leu Met Asn Thr Gly Gly Gly
 20 25 30

Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Ser
 35 40 45

Glu Ser Lys Tyr Gly Pro Pro Cys Pro Pro Cys Pro Ala Pro Glu Phe
 50 55 60

Leu Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr
 65 70 75 80

Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val
 85 90 95

Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val Asp Gly Val
 100 105 110

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Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Phe Asn Ser
 115 120 125

Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu
 130 135 140

Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly Leu Pro Ser
 145 150 155 160

Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro
 165 170 175

Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr Lys Asn Gln
 180 185 190

Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala
 195 200 205

Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr
 210 215 220

Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Arg Leu
 225 230 235 240

Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe Ser Cys Ser
 245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser
 260 265 270

Leu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala
 275 280 285

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
 290 295 300

Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly Gly Gly
305 310 315 320

Gly

<210> 60

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-A Fc , C1q -, Protein A +, I(21)T,
Q(207)H

<400> 60

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

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Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu His Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 61

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-C Fc , C1q +, Protein A +, I(21)T

<400> 61

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 62
<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-D Fc , C1q -, Protein A +, I(21)T,
Q(207)H

<400> 62

Pro	Val	Pro	Glu	Ser	Leu	Gly	Gly	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro
1				5				10						15	

Lys	Pro	Lys	Asp	Thr	Leu	Arg	Ile	Thr	Arg	Thr	Pro	Glu	Ile	Thr	Cys
			20				25						30		

Val	Val	Leu	Asp	Leu	Gly	Arg	Glu	Asp	Pro	Glu	Val	Gln	Ile	Ser	Trp
		35					40					45			

Phe	Val	Asp	Gly	Lys	Glu	Val	His	Thr	Ala	Lys	Thr	Gln	Pro	Arg	Glu
	50					55					60				

Gln	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Pro	Ile	Glu
65					70				75					80	

His	Gln	Asp	Trp	Leu	Thr	Gly	Lys	Glu	Phe	Lys	Cys	Arg	Val	Asn	His
			85						90					95	

Ile	Gly	Leu	Pro	Ser	Pro	Ile	Glu	Arg	Thr	Ile	Ser	Lys	Ala	Arg	Gly
		100						105					110		

Gln	Ala	His	Gln	Pro	Ser	Val	Tyr	Val	Leu	Pro	Pro	Ser	Pro	Lys	Glu
		115					120					125			

Leu	Ser	Ser	Ser	Asp	Thr	Val	Thr	Leu	Thr	Cys	Leu	Ile	Lys	Asp	Phe
	130					135					140				

Phe	Pro	Pro	Glu	Ile	Asp	Val	Glu	Trp	Gln	Ser	Asn	Gly	Gln	Pro	Glu
145					150					155					160

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Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 63

<211> 214

<212> PRT

<213> Unknown

<220>

<223> Wild-type equine IgG1 Fc , Protein A +, C1q +

<400> 63

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Asn Pro Lys Asp Thr Leu
1 5 10 15

Met Ile Thr Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Met Asp Gly Val Glu
35 40 45

Val Arg Thr Ala Thr Thr Arg Pro Lys Glu Glu Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Gln Pro

85

90

95

Ile Glu Arg Thr Ile Thr Lys Thr Lys Gly Arg Ser Gln Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Ser Lys Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asn Ile
 130 135 140

Glu Trp Gln Ser Asn Gly Gln Pro Glu Leu Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Gln Ala Gln Gln Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Asp Arg Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 64
 <211> 214
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type equine IgG2 Fc, Protein A -, C1q -

<400> 64

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu
 1 5 10 15

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Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu
35 40 45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro
85 90 95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile
195 200 205

Ser Glu Ser Leu Gly Lys
210

<210> 65
<211> 214
<212> PRT
<213> Unknown

<220>
<223> Wild-type equine IgG3 Fc, Protein A +, C1q+

<400> 65

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Thr Arg Met Pro Glu Val Thr Cys Leu Val Val Asp Val Ser
20 25 30

His Asp Ser Ser Asp Val Leu Phe Thr Trp Tyr Val Asp Gly Thr Glu
35 40 45

Val Lys Thr Ala Lys Thr Met Pro Asn Glu Glu Gln Asn Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Asn
65 70 75 80

Gly Lys Lys Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Thr Gly Gln Thr Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Thr Val

130

135

140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Arg Thr
 145 150 155 160

Thr Glu Ala Gln Lys Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Lys Asp Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Val Val Met His Glu Ala Leu His Asn His Val Met Gln Lys Asn Ile
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 66

<211> 214

<212> PRT

<213> Unknown

<220>

<223> Wild-type equine IgG4 Fc, Protein A +, C1q +

<400> 66

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
 20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Phe Asn Ser Thr
 50 55 60

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Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Ala Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Arg Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
195 200 205

Ser Lys Ser Pro Gly Lys
210

<210> 67
<211> 214
<212> PRT
<213> Unknown

<220>
<223> Wild-type equine IgG5 Fc, Protein A -, C1q -

<400> 67

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Lys Pro Glu Val Thr Cys Val Val Val Asp Leu Gly
20 25 30

His Asp Asp Pro Asp Val Gln Phe Thr Trp Phe Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Glu Glu Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Ser Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Lys Gly Gln Leu Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ala Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asp Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asn Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Val Glu Thr Ser Arg Trp Lys Gln Gly Glu Ser Phe Thr Cys

180

185

190

Gly Val Met His Glu Ala Val Glu Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser His Ser Pro Gly Lys
 210

<210> 68
 <211> 214
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type equine IgG6 Fc, Protein A -, C1q -
 <400> 68

Gly Arg Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Ala His Thr Ala Thr Thr Lys Ala Lys Glu Lys Gln Asp Asn Ser Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Arg Arg
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ala Pro
 85 90 95

Val Glu Arg Thr Ile Thr Lys Ala Lys Gly Glu Leu Gln Asp Pro Gln
 100 105 110

Val Tyr Ile Leu Ala Pro His Pro Asp Glu Val Thr Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asn Val
130 135 140

Glu Trp Gln Ser Asn Glu Glu Pro Glu Pro Glu Val Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asp Arg Trp Glu Gln Gly Glu Ser Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Ile Arg His Thr Tyr Arg Gln Lys Ser Ile
195 200 205

Thr Asn Phe Pro Gly Lys
210

<210> 69
<211> 214
<212> PRT
<213> Unknown

<220>
<223> Wild-type equine IgG7 Fc, Protein A +, C1q +

<400> 69

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu

35

40

45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Asn Asn Ser Thr
 50 55 60

Tyr Arg Val Val Ser Ile Leu Ala Ile Gln His Lys Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
 85 90 95

Val Gln Lys Thr Ile Ser Lys Pro Thr Gly Gln Pro Arg Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
 130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
 195 200 205

Ser Lys Ser Pro Gly Lys
 210

<210> 70

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG1 Fc , Protein A +, C1q - , K(87)S

<400> 70

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Asn Pro Lys Asp Thr Leu
1 5 10 15

Met Ile Thr Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Met Asp Gly Val Glu
35 40 45

Val Arg Thr Ala Thr Thr Arg Pro Lys Glu Glu Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Asn Asn Gln Ala Leu Pro Gln Pro
85 90 95

Ile Glu Arg Thr Ile Thr Lys Thr Lys Gly Arg Ser Gln Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Ser Lys Lys Ser Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asn Ile
130 135 140

Glu Trp Gln Ser Asn Gly Gln Pro Glu Leu Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Gln Ala Gln Gln Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Val Asp Arg Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
195 200 205

Ser Lys Asn Pro Gly Lys
210

<210> 71
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: Variant equine IgG2 Fc, C1q -, Protein A +, F(203)Y

<400> 71

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu
35 40 45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro

85

90

95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
 100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
 130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Gly Glu Ser Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile
 195 200 205

Ser Glu Ser Leu Gly Lys
 210

<210> 72

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG2 Fc, C1q -, Protein A +, A(15)T,
 F(203)Y

<400> 72

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu
35 40 45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro
85 90 95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile
195 200 205

Ser Glu Ser Leu Gly Lys
210

<210> 73
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: Variant equine IgG3 Fc, Protein A +, C1q - , K(87)S
<400> 73

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Thr Arg Met Pro Glu Val Thr Cys Leu Val Val Asp Val Ser
20 25 30

His Asp Ser Ser Asp Val Leu Phe Thr Trp Tyr Val Asp Gly Thr Glu
35 40 45

Val Lys Thr Ala Lys Thr Met Pro Asn Glu Glu Gln Asn Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Asn
65 70 75 80

Gly Lys Lys Phe Lys Cys Ser Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Thr Gly Gln Thr Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

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Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Thr Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Arg Thr
145 150 155 160

Thr Glu Ala Gln Lys Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Lys Asp Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Leu His Asn His Val Met Gln Lys Asn Ile
195 200 205

Ser Lys Asn Pro Gly Lys
210

<210> 74

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG4 Fc, Protein A +, C1q - , K(87)S

<400> 74

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Asn Asn Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Ala Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Arg Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
195 200 205

Ser Lys Ser Pro Gly Lys
210

<210> 75

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG5 Fc, C1q -, Protein A +, V(199)L,
E(200)H

<400> 75

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Lys Pro Glu Val Thr Cys Val Val Val Asp Leu Gly
20 25 30

His Asp Asp Pro Asp Val Gln Phe Thr Trp Phe Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Glu Glu Gln Phe Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Ser Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Lys Gly Gln Leu Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ala Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asp Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asn Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Val Glu Thr Ser Arg Trp Lys Gln Gly Glu Ser Phe Thr Cys
180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
195 200 205

Ser His Ser Pro Gly Lys
210

<210> 76

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG6 Fc, C1q -, Protein A +, I(199)L ,
R(200)H, H(201)N, T(202)H

<400> 76

Gly Arg Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Ala His Thr Ala Thr Thr Lys Ala Lys Glu Lys Gln Asp Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Arg Arg
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ala Pro
85 90 95

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Val Glu Arg Thr Ile Thr Lys Ala Lys Gly Glu Leu Gln Asp Pro Gln
100 105 110

Val Tyr Ile Leu Ala Pro His Pro Asp Glu Val Thr Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asn Val
130 135 140

Glu Trp Gln Ser Asn Glu Glu Pro Glu Pro Glu Val Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asp Arg Trp Glu Gln Gly Glu Ser Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Leu His Asn His Tyr Arg Gln Lys Ser Ile
195 200 205

Thr Asn Phe Pro Gly Lys
210

<210> 77

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant equine IgG7 Fc, Protein A +, C1q - , K(87)S

<400> 77

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Asn Asn Ser Thr
50 55 60

Tyr Arg Val Val Ser Ile Leu Ala Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Gln Lys Thr Ile Ser Lys Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
195 200 205

Ser Lys Ser Pro Gly Lys
210

<210> 78
 <211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: Variant canine IgG-B Fc, Protein A +, C1q - , K(93)R

<400> 78

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Arg Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
 130 135 140

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Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 79

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-C Fc, Protein A -, C1q - , K(93)R

<400> 79

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Arg Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 80

<211> 237

<212> PRT

<213> Unknown

<220>

<223> Alternative wild-type feline IgG1a Fc, Protein A +, C1q +

<400> 80

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Arg Lys Thr Asp His Pro Pro Gly Pro Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 81

<211> 237

<212> PRT

<213> Unknown

<220>

<223> Alternative wild-type feline IgG1b Fc, Protein A +, C1q +

<400> 81

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
 145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 225 230 235

<210> 82

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant feline IgG1a Fc, Protein A +, C1q -, P(198)A

<400> 82

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Thr Gly Glu Gly Pro Lys
 1 5 10 15

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Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

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Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 83
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: Variant feline IgG1b Fc, Protein A +, C1q -, P(198)A
<400> 83

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 84

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: Variant canine IgG-C Fc , C1q - , K(93)R , Protein A
+, I(21)T, V(23)L, T(24)I

<400> 84

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

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Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Arg Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 85
 <211> 31
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type GLP1 (7-37)

<400> 85

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Ala Gly
 20 25 30

<210> 86
 <211> 29
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: GLP1-S8 (7-35)

<400> 86

His Ser Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 20 25

<210> 87
 <211> 29
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: GLP1-G8 (7-35)

<400> 87

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly

1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
20 25

<210> 88
<211> 1
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 1G extension

<400> 88

Gly
1

<210> 89
<211> 2
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 2G extension

<400> 89

Gly Gly
1

<210> 90
<211> 3
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 3G extension

<400> 90

Gly Gly Gly
1

<210> 91
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 4G extension

<400> 91

Gly Gly Gly Gly
1

<210> 92
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 5G extension

<400> 92

Gly Gly Gly Gly Gly
1 5

<210> 93
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: 6G extension

<400> 93

Gly Gly Gly Gly Gly Gly
1 5

<210> 94
<211> 7
<212> PRT
<213> Artificial Sequence

<220>

<223> Synthetic: 7G extension

<400> 94

Gly Gly Gly Gly Gly Gly Gly
1 5

<210> 95

<211> 8

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: 8G extension

<400> 95

Gly Gly Gly Gly Gly Gly Gly Gly
1 5

<210> 96

<211> 305

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: ssGLP1-G8_I_WTfeIgG2

<400> 96

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

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Gly Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly
65 70 75 80

Glu Gly Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val
85 90 95

Phe Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr
100 105 110

Pro Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn
115 120 125

Val Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys
130 135 140

Thr Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
145 150 155 160

Val Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys
165 170 175

Cys Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile
180 185 190

Ser Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro
195 200 205

Pro Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu
210 215 220

Ile Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr
225 230 235 240

Gly Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu
245 250 255

Asp Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg
260 265 270

Ser His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu
275 280 285

Ala Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly
290 295 300

Lys
305

<210> 97
<211> 346
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: ssGLP1-G8/GLP1-3G_III_ WTfeIgG2

<400> 97

Met Ala Val Leu Gly Leu Leu Phe Cys Leu Val Thr Phe Pro Ser Cys
1 5 10 15

Val Leu Ser His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr
20 25 30

Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
35 40 45

Gly Ala Gly Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser
50 55 60

Gly Gly Gly Ser Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly
65 70 75 80

Glu Gly Pro Lys Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val

Phe Ile Phe Pro Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr
 100 105 110

Pro Glu Val Thr Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn
 115 120 125

Val Gln Ile Thr Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys
 130 135 140

Thr Arg Pro Arg Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser
 145 150 155 160

Val Leu Pro Ile Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys
 165 170 175

Cys Lys Val Asn Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile
 180 185 190

Ser Lys Ala Lys Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro
 195 200 205

Pro Thr Gln Glu Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu
 210 215 220

Ile Lys Gly Phe His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr
 225 230 235 240

Gly Gln Pro Glu Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu
 245 250 255

Asp Ser Asp Gly Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg
 260 265 270

Ser His Trp Gln Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu

275

280

285

Ala Leu His Ser His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly
 290 295 300

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala Glu Gly Thr Phe
 305 310 315 320

Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe
 325 330 335

Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
 340 345

<210> 98
 <211> 30
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: Variant GLP1 (7-36)

<400> 98

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
 1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Ala
 20 25 30

<210> 99
 <211> 29
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Synthetic: Variant GLP1 (7-35)

<400> 99

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly

1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly
 20 25

<210> 100
 <211> 229
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type equine Fc IgG2 (including equine IgG2 hinge), Protein A
 - , C1q -

<400> 100

Val Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly
 1 5 10 15

Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met
 20 25 30

Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp
 35 40 45

Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val
 50 55 60

His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
 65 70 75 80

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
 85 90 95

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
 100 105 110

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
 115 120 125

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
 130 135 140

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
 145 150 155 160

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
 165 170 175

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
 180 185 190

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
 195 200 205

Val Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser
 210 215 220

Glu Ser Leu Gly Lys
 225

<210> 101
 <211> 14
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type equine IgG1 hinge

<400> 101

Asp Met Ser Lys Cys Pro Lys Cys Pro Ala Pro Glu Leu Leu
 1 5 10

<210> 102
 <211> 15
 <212> PRT
 <213> Unknown

<220>

<223> Wild-type equine IgG2 hinge

<400> 102

Val	Pro	Lys	Pro	Gln	Cys	Pro	Pro	Tyr	Thr	His	Ser	Lys	Phe	Leu
1				5					10					15

<210> 103

<211> 318

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8/GLP1-3G_III_ VAREqIgG2

<400> 103

His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
1				5					10					15	

Gln	Ala	Ala	Lys	Glu	Phe	Ile	Ala	Trp	Leu	Val	Lys	Gly	Gly	Ala	Gly
			20					25					30		

Gly	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly	Ser	Gly	Gly	Gly
		35				40						45			

Ser	Asp	Met	Ser	Lys	Cys	Pro	Lys	Cys	Pro	Ala	Pro	Glu	Leu	Leu	Gly
	50					55					60				

Gly	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	Asn	Pro	Lys	Asp	Thr	Leu	Met
65					70					75					80

Ile	Ser	Arg	Thr	Pro	Val	Val	Thr	Cys	Val	Val	Val	Asn	Leu	Ser	Asp
				85					90					95	

Gln	Tyr	Pro	Asp	Val	Gln	Phe	Ser	Trp	Tyr	Val	Asp	Asn	Thr	Glu	Val
			100					105					110		

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His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr
 115 120 125

Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly
 130 135 140

Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile
 145 150 155 160

Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val
 165 170 175

Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser
 180 185 190

Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu
 195 200 205

Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr
 210 215 220

Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu
 225 230 235 240

Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala
 245 250 255

Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser
 260 265 270

Glu Ser Leu Gly Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly His Ala
 275 280 285

Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln Ala
 290 295 300

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Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
305 310 315

<210> 104
<211> 279
<212> PRT
<213> Artificial Sequence

<220>
<223> Synthetic: GLP1-G8_I_VAREqIgG2

<400> 104

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Ala Gly
20 25 30

Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly Ser Gly Gly Gly
35 40 45

Ser Ser Val Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe
50 55 60

Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr
65 70 75 80

Leu Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu
85 90 95

Ser Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr
100 105 110

Glu Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser
115 120 125

Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu
130 135 140

Ser Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln
145 150 155 160

Pro Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro
165 170 175

Gln Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys
180 185 190

Val Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser
195 200 205

Val Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser
210 215 220

Thr Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser
225 230 235 240

Lys Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr
245 250 255

Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp
260 265 270

Ile Ser Glu Ser Leu Gly Lys
275

<210> 105

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8/GLP1-2G_III_ VARcaIgGD

<400> 105

01157011-seq1-000001.txt

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
35 40 45

Pro Lys Glu Ser Thr Cys Lys Cys Ile Ser Pro Cys Pro Val Pro Glu
50 55 60

Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp
65 70 75 80

Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu Asp
85 90 95

Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp Gly
100 105 110

Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe Asn
115 120 125

Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp Trp
130 135 140

Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu Pro
145 150 155 160

Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His Gln
165 170 175

Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser Ser
180 185 190

01157011-seql-000001.txt

Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro Glu
195 200 205

Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser Lys
210 215 220

Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe Leu
225 230 235 240

Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp Thr
245 250 255

Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Asp
260 265 270

Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly
275 280 285

Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu
290 295 300

Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly
305 310 315 320

Gly

<210> 106

<211> 321

<212> PRT

<213> Artificial Sequence

<220>

<223> Synthetic: GLP1-G8/GLP1-2G_III_ VARcaIgGD

<400> 106

His Gly Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly Gly Gly
20 25 30

Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
35 40 45

Pro Lys Glu Ser Thr Ser Lys Cys Ile Ser Pro Cys Pro Val Pro Glu
50 55 60

Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp
65 70 75 80

Thr Leu Leu Ile Ala Arg Thr Pro Glu Ile Thr Cys Val Val Leu Asp
85 90 95

Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp Phe Val Asp Gly
100 105 110

Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu Gln Gln Phe Asn
115 120 125

Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His Gln Asp Trp
130 135 140

Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His Ile Gly Leu Pro
145 150 155 160

Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly Gln Ala His Gln
165 170 175

Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu Leu Ser Ser Ser
180 185 190

Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe Phe Pro Pro Glu
195 200 205

Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu Pro Glu Ser Lys
 210 215 220

Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly Ser Tyr Phe Leu
 225 230 235 240

Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Gln Gly Asp Thr
 245 250 255

Phe Thr Cys Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Asp
 260 265 270

Leu Ser Leu Ser His Ser Pro Gly Lys Gly Gly Gly Gly Ser Gly Gly
 275 280 285

Gly Gly His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu
 290 295 300

Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Gly
 305 310 315 320

Gly

<210> 107
 <211> 237
 <212> PRT
 <213> Unknown

<220>
 <223> Wild-type canine IgG-B Fc with hinge, Protein A +, C1q +, CD16 +

<400> 107

Pro Lys Arg Glu Asn Gly Arg Val Pro Arg Pro Pro Asp Cys Pro Lys
 1 5 10 15

01157011-seql-000001.txt

Cys Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr
35 40 45

Cys Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser
50 55 60

Trp Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Gly His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn
100 105 110

Asn Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg
115 120 125

Gly Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu
130 135 140

Glu Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe
145 150 155 160

Phe Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
165 170 175

Pro Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly
180 185 190

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
195 200 205

01157011-seql-000001.txt

Arg Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn
210 215 220

His Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
225 230 235

<210> 108
<211> 235
<212> PRT
<213> Unknown

<220>
<223> Wild-type canine IgG-C Fc with hinge, Protein A , C1q +, CD16 +
<400> 108

Ala Lys Glu Cys Glu Cys Lys Cys Asn Cys Asn Asn Cys Pro Cys Pro
1 5 10 15

Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys
20 25 30

Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys Val
35 40 45

Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp Phe
50 55 60

Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu Glu
65 70 75 80

Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly His
85 90 95

Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn Lys
100 105 110

Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly Gln
115 120 125

Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu Met
130 135 140

Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe Pro
145 150 155 160

Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro Glu
165 170 175

Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser Tyr
180 185 190

Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg Gly
195 200 205

Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His Tyr
210 215 220

Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
225 230 235

<210> 109
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant canine IgG-A Fc, Heterodimer chain 3, T(138)W

<400> 109

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
20 25 30

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Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Trp Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 110
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant canine IgG-A Fc, Heterodimer chain 4, T(138)S, L(140)A,
 Y(181)T

<400> 110

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
 50 55 60

Gln Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
 65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Ser Cys Ala Ile Lys Asp Phe
 130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu

145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 111

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Heterodimer chain 3, T(137)W

<400> 111

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

01157011-seql-000001.txt

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Trp Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 112

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Heterodimer chain 4, T(137)S, L(139)A,
Y(180)T

<400> 112

01157011-seql-000001.txt

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Ser Cys Ala Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

01157011-seql-000001.txt

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 113
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant canine IgG-C Fc, Heterodimer chain 3, T(137)W

<400> 113

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Trp Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 114
 <211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant canine IgG-C Fc, Heterodimer chain 4, T(137)S, L(139)A,
 Y(180)T

<400> 114

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

01157011-seql-000001.txt

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Ser Cys Ala Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 115
<211> 221
<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-D Fc, Heterodimer chain 3, T(138)W

<400> 115

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
 65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Trp Cys Leu Ile Lys Asp Phe
 130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
 145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly

165

170

175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 116

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-D Fc, Heterodimer chain 4, T(138)S, L(140)A,
 Y(181)T

<400> 116

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Gln Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
 65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Ser Cys Ala Ile Lys Asp Phe
130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Thr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 117
<211> 237
<212> PRT
<213> Unknown

<220>
<223> Wild-type feline IgG1a Fc, Protein A +, C1q +

<400> 117

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

01157011-seql-000001.txt

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

01157011-seql-000001.txt

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 118
<211> 237
<212> PRT
<213> Unknown

<220>
<223> Wild-type feline IgG1b Fc, Protein A +, C1q +

<400> 118

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 119
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG2 Fc, Heterodimer chain 1, T(154)W

<400> 119

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
20 25 30

01157011-seql-000001.txt

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Trp Cys Leu Ile Lys Gly Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 120
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG2 Fc, Heterodimer chain 2, T(154)S, L(156)A,
Y(197)T

<400> 120

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu

130

135

140

Glu Leu Ser Glu Asn Lys Val Ser Val Ser Cys Ala Ile Lys Gly Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Leu Thr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 225 230 235

<210> 121
 <211> 237
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant feline IgG1a Fc, Heterodimer chain 1, T(154)W

<400> 121

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
 1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

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Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Trp Cys Leu Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 122
 <211> 237
 <212> PRT
 <213> Artificial Sequence

 <220>
 <223> Variant feline IgG1a Fc, Heterodimer chain 2, T(154)S, L(156)A,
 Y(197)T

 <400> 122

 Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
 1 5 10 15

 Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
 20 25 30

 Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

 Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
 50 55 60

 Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
 65 70 75 80

 Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 85 90 95

 Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

 Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

 Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

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Glu Leu Ser Glu Asn Lys Val Ser Val Ser Cys Ala Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Thr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 123
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG1b Fc, Heterodimer chain 1, T(154)W

<400> 123

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Trp Cys Leu Ile Glu Gly Phe
145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 124

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant feline IgG1b Fc, Heterodimer chain 2, T(154)S, L(156)A, Y(197)T

<400> 124

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
 1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
 50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
 65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Ser Cys Ala Ile Glu Gly Phe
 145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Thr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 125
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG2 Fc, with feline IgG1 hinge

<400> 125

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg

65		70		75		80									
Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Pro	Ile
				85					90					95	
Leu	His	Gln	Asp	Trp	Leu	Lys	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn
			100					105					110		
Ser	Lys	Ser	Leu	Pro	Ser	Ala	Met	Glu	Arg	Thr	Ile	Ser	Lys	Ala	Lys
			115				120					125			
Gly	Gln	Pro	His	Glu	Pro	Gln	Val	Tyr	Val	Leu	Pro	Pro	Thr	Gln	Glu
		130					135					140			
Glu	Leu	Ser	Glu	Asn	Lys	Val	Ser	Val	Thr	Cys	Leu	Ile	Lys	Gly	Phe
145					150					155					160
His	Pro	Pro	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ile	Thr	Gly	Gln	Pro	Glu
				165					170					175	
Pro	Glu	Asn	Asn	Tyr	Gln	Thr	Thr	Pro	Pro	Gln	Leu	Asp	Ser	Asp	Gly
			180						185				190		
Thr	Tyr	Phe	Leu	Tyr	Ser	Arg	Leu	Ser	Val	Asp	Arg	Ser	His	Trp	Gln
		195					200					205			
Arg	Gly	Asn	Thr	Tyr	Thr	Cys	Ser	Val	Ser	His	Glu	Ala	Leu	His	Ser
	210					215					220				
His	His	Thr	Gln	Lys	Ser	Leu	Thr	Gln	Ser	Pro	Gly	Lys			
225					230					235					
<210>	126														
<211>	237														
<212>	PRT														
<213>	Artificial Sequence														

<220>

<223> Variant feline IgG2 Fc with modified hinge, K(16)P

<400> 126

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Pro
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 127
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG1a Fc with modified hinge, K(16)P

<400> 127

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Pro
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 225 230 235

<210> 128

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant feline IgG1b Fc with modified hinge, K(16)P

<400> 128

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Arg	Lys	Thr	Asp	His	Pro	Pro	Gly	Pro	Lys	Pro	Cys	Asp	Cys	Pro	Pro	1	5	10	15
Cys	Pro	Pro	Pro	Glu	Met	Leu	Gly	Gly	Pro	Ser	Ile	Phe	Ile	Phe	Pro	20	25	30	
Pro	Lys	Pro	Lys	Asp	Thr	Leu	Ser	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	35	40	45	
Cys	Leu	Val	Val	Asp	Leu	Gly	Pro	Asp	Asp	Ser	Asp	Val	Gln	Ile	Thr	50	55	60	
Trp	Phe	Val	Asp	Asn	Thr	Gln	Val	Tyr	Thr	Ala	Lys	Thr	Ser	Pro	Arg	65	70	75	80
Glu	Glu	Gln	Phe	Asn	Ser	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Pro	Ile	85	90	95	
Leu	His	Gln	Asp	Trp	Leu	Lys	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	100	105	110	
Ser	Lys	Ser	Leu	Pro	Ser	Pro	Ile	Glu	Arg	Thr	Ile	Ser	Lys	Asp	Lys	115	120	125	
Gly	Gln	Pro	His	Glu	Pro	Gln	Val	Tyr	Val	Leu	Pro	Pro	Ala	Gln	Glu	130	135	140	
Glu	Leu	Ser	Glu	Asn	Lys	Val	Ser	Val	Thr	Cys	Leu	Ile	Glu	Gly	Phe	145	150	155	160
Tyr	Pro	Ser	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ile	Thr	Gly	Gln	Pro	Glu	165	170	175	
Pro	Glu	Asn	Asn	Tyr	Arg	Thr	Thr	Pro	Pro	Gln	Leu	Asp	Ser	Asp	Gly	180	185	190	

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 129

<211> 244

<212> PRT

<213> Unknown

<220>

<223> Wild-type equine IgG2 Fc with hinge, Protein A , C1q

<400> 129

Pro Pro Cys Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met Ile
35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys

100

105

110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
 115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
 130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
 145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
 165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
 180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
 195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
 210 215 220

Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser Glu
 225 230 235 240

Ser Leu Gly Lys

<210> 130

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant equine IgG2 Fc with modified hinge, Protein A , C1q ,
 Q(20)P

<400> 130

Pro Pro Cys Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
 1 5 10 15

Pro Lys Pro Pro Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
 20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met Ile
 35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
 50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
 65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
 85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
 100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
 115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
 130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
 145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
 165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
 180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
210 215 220

Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser Glu
225 230 235 240

Ser Leu Gly Lys

<210> 131
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant equine IgG2 Fc with modified hinge, Protein A , C1q ,
C(3)S

<400> 131

Pro Pro Ser Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met Ile
35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
65 70 75 80

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Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
210 215 220

Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser Glu
225 230 235 240

Ser Leu Gly Lys

<210> 132
<211> 244
<212> PRT

<213> Artificial Sequence

<220>

<223> Variant equine IgG2 Fc with modified hinge, Protein A , C1q ,
C(3)S, Q(20)P

<400> 132

Pro Pro Ser Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Pro Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu Met Ile
35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
145 150 155 160

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Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
210 215 220

Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile Ser Glu
225 230 235 240

Ser Leu Gly Lys

<210> 133

<211> 244

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant equine IgG2 Fc with hinge, Protein A +, C1q , A(45)T,
F(233)Y

<400> 133

Pro Pro Cys Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met Ile
35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln

50

55

60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
 65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
 85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
 100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
 115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
 130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
 145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
 165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
 180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
 195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
 210 215 220

Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser Glu
 225 230 235 240

Ser Leu Gly Lys

<210> 134
 <211> 244
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant equine IgG2 Fc with modified hinge, Protein A +, C1q ,
 Q(20)P, A(45)T, F(233)Y

<400> 134

Pro Pro Cys Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
 1 5 10 15

Pro Lys Pro Pro Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
 20 25 30

Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met Ile
 35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
 50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
 65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
 85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
 100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
 115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
 130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
210 215 220

Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser Glu
225 230 235 240

Ser Leu Gly Lys

<210> 135
<211> 244
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant equine IgG2 Fc with modified hinge, Protein A +, C1q ,
C(3)S, Q(20)P, A(45)T, F(233)Y

<400> 135

Pro Pro Ser Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Pro Cys Pro Pro Tyr Thr His Ser Lys Phe Leu Gly Gly
20 25 30

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Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu Met Ile
35 40 45

Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser Asp Gln
50 55 60

Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu Val His
65 70 75 80

Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Thr Tyr Arg
85 90 95

Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser Gly Lys
100 105 110

Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro Ile Ser
115 120 125

Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln Val Tyr
130 135 140

Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val Ser Val
145 150 155 160

Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val Glu Trp
165 170 175

Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr Thr Pro
180 185 190

Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys Leu Ser
195 200 205

Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys Ala Val
210 215 220

Met His Glu Ala Leu His Asn His Tyr Thr Lys Thr Asp Ile Ser Glu
225 230 235 240

Ser Leu Gly Lys

<210> 136
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant feline IgG1a Fc, Protein A +, C1q , P(198)A

<400> 136

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys

115

120

125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 225 230 235

<210> 137
 <211> 237
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant feline IgG1b Fc, Protein A +, C1q , P(198)A

<400> 137

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
 1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
 20 25 30

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Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 138
<211> 30
<212> PRT
<213> Unknown

<220>
<223> Wild-type equine IgG2 hinge

<400> 138

Pro Pro Cys Val Leu Ser Ala Glu Gly Val Ile Pro Ile Pro Ser Val
1 5 10 15

Pro Lys Pro Gln Cys Pro Pro Tyr Thr His Ser Lys Phe Leu
20 25 30

<210> 139
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , M(5)P

<400> 139

Pro Ala Pro Glu Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

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Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 140

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , P(39)R

<400> 140

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg

180

185

190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 141

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , D(38)G

<400> 141

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Gly Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

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Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 142

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , K(97)I

<400> 142

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp

35

40

45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Ile Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
 130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 143

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , A(98)G

<400> 143

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Lys Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 144

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , D(38)G,
K(97)I, A(98)G

<400> 144

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Gly Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

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His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 145

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q , CD16 , D(38)G,
K(93)R, K(97)I, A(98)G

<400> 145

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro

1	5	10	15
Lys	Pro	Lys	Asp
	20		
Thr	Leu	Leu	Ile
			25
Ala	Arg	Thr	Pro
Glu	Val	Thr	Cys
	30		
Val	Val	Val	Asp
	35		
Leu	Gly	Pro	Glu
			40
Asp	Pro	Glu	Val
			45
Gln	Ile	Ser	Trp
Phe	Val	Asp	Gly
	50		
Lys	Gln	Met	Gln
		55	
Thr	Ala	Lys	Thr
			60
Gln	Pro	Arg	Glu
Glu	Gln	Phe	Asn
Gly	Thr	Tyr	Arg
	70		
Val	Val	Ser	Val
		75	
Leu	Pro	Ile	Gly
			80
His	Gln	Asp	Trp
Leu	Lys	Gly	Lys
	85		
Gln	Phe	Thr	Cys
			90
Arg	Val	Asn	Asn
		95	
Ile	Gly	Leu	Pro
Ser	Pro	Ile	Glu
	100		
Arg	Thr	Ile	Ser
			105
Lys	Ala	Arg	Gly
			110
Gln	Ala	His	Gln
Pro	Ser	Val	Tyr
	115		
Val	Tyr	Val	Leu
			120
Pro	Pro	Ser	Arg
			125
Glu	Glu		
Leu	Ser	Lys	Asn
	130		
Thr	Val	Ser	Leu
			135
Thr	Cys	Leu	Ile
			140
Lys	Asp	Phe	Phe
Pro	Pro	Asp	Ile
Asp	Val	Glu	Trp
	150		
Gln	Ser	Asn	Gly
		155	
Gln	Gln	Glu	Pro
			160
Glu	Ser	Lys	Tyr
Arg	Thr	Thr	Pro
	165		
Pro	Gln	Leu	Asp
			170
Glu	Asp	Gly	Ser
			175
Tyr	Phe	Leu	Tyr
Ser	Lys	Leu	Ser
	180		
Val	Asp	Lys	Ser
			185
Arg	Trp	Gln	Arg
			190
Gly	Asp	Thr	Phe
Ile	Cys	Ala	Val
Met	His	Glu	Ala
Leu	His	Asn	His

195

200

205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 146

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q +, CD16 , M(5)P, P(39)R

<400> 146

Pro Ala Pro Glu Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
 130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 147

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-B Fc, Protein A +, C1q , CD16 , M(5)P, P(39)R,
 K(93)R

<400> 147

Pro Ala Pro Glu Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

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Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Glu Gln Phe Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Arg Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 148
<211> 220
<212> PRT
<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , L(5)P

<400> 148

Pro Gly Cys Gly Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 149

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , P(39)R

<400> 149

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Arg Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

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Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 150

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , D(38)G

<400> 150

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Gly Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 151
 <211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , K(97)I

<400> 151

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
 85 90 95

Ile Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

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Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 152

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , A(98)G

<400> 152

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Gly Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 153

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q , CD16 +, K(93)R

<400> 153

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Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Arg Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

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Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 154

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , D(38)G,
K(97)I, A(98)G

<400> 154

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Gly Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu

115

120

125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 155

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q , CD16 , D(38)G,
 K(93)R, K(97)I, A(98)G

<400> 155

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Gly Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Arg Val Asn Asn
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 156

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q +, CD16 , L(5)P, P(39)R

<400> 156

Pro Gly Cys Gly Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Arg Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

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Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 157

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Variant canine IgG-C Fc, Protein A +, C1q . CD16 , M(5)P, P(39)R,
K(93)R

<400> 157

Pro Gly Cys Gly Pro Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Arg Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

Glu Gln Ser Asn Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Arg Val Asn Asn

85

90

95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 158

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant canine IgG A Fc, N(68)X

<220>

<221> MISC_FEATURE

<222> (68)..(68)

<223> X = any amino acid except N

<400> 158

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Xaa Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln

180

185

190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 159

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant canine IgG A Fc, G(69)P

<400> 159

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
 50 55 60

Gln Gln Phe Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
 65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
 85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
 130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
 145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 160
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant canine IgG A Fc, T(70)X

<220>
 <221> MISC_FEATURE
 <222> (70)..(70)
 <223> X = any amino acid except T or S

<400> 160

Pro Val Pro Glu Pro Leu Gly Gly Pro Ser Val Leu Ile Phe Pro Pro
 1 5 10 15

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Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Ser Arg Glu
50 55 60

Gln Gln Phe Asn Gly Xaa Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Asp Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Arg Ala His Lys Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Ser Ile Thr Cys Leu Ile Lys Asp Phe
130 135 140

Tyr Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu
145 150 155 160

Pro Glu Arg Lys His Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Pro Phe Thr Cys Ala Val Met His Glu Thr Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 161
 <211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant canine IgG B Fc, N(68)X

<220>
 <221> MISC_FEATURE
 <222> (68)..(68)
 <223> X = any amino acid except N

<400> 161

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Xaa Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

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Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 162
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant canine IgG B Fc, G(69)P

<400> 162

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp

35

40

45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe
 130 135 140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 163

<211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant canine IgG B Fc, T(70)X

<220>
 <221> MISC_FEATURE
 <222> (70)..(70)
 <223> X = any amino acid except T or S

<400> 163

Pro Ala Pro Glu Met Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Thr Leu Leu Ile Ala Arg Thr Pro Glu Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asp Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Gly Lys Gln Met Gln Thr Ala Lys Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Phe Asn Gly Xaa Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Lys Gly Lys Gln Phe Thr Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Arg Glu Glu
 115 120 125

Leu Ser Lys Asn Thr Val Ser Leu Thr Cys Leu Ile Lys Asp Phe Phe

130

135

140

Pro Pro Asp Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Thr Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Glu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 164

<211> 220

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant canine IgG C Fc, N(68)X

<220>

<221> MISC_FEATURE

<222> (68)..(68)

<223> X = any amino acid except N

<400> 164

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp

35

40

45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Ser Xaa Gly Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
 165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
 180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
 195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 165

<211> 220
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant canine IgG C Fc, G(69)P

<400> 165

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
 1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
 20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
 35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
 50 55 60

Glu Gln Ser Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile Gly
 65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
 85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
 100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
 115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
 130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
 145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 166
<211> 220
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant canine IgG C Fc, T(70)X

<220>
<221> MISC_FEATURE
<222> (70)..(70)
<223> X = any amino acid except T or S

<400> 166

Pro Gly Cys Gly Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Val Thr Ala Arg Thr Pro Thr Val Thr Cys
20 25 30

Val Val Val Asp Leu Asp Pro Glu Asn Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Ser Lys Gln Val Gln Thr Ala Asn Thr Gln Pro Arg Glu
50 55 60

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Glu Gln Ser Asn Gly Xaa Tyr Arg Val Val Ser Val Leu Pro Ile Gly
65 70 75 80

His Gln Asp Trp Leu Ser Gly Lys Gln Phe Lys Cys Lys Val Asn Asn
85 90 95

Lys Ala Leu Pro Ser Pro Ile Glu Glu Ile Ile Ser Lys Thr Pro Gly
100 105 110

Gln Ala His Gln Pro Asn Val Tyr Val Leu Pro Pro Ser Arg Asp Glu
115 120 125

Met Ser Lys Asn Thr Val Thr Leu Thr Cys Leu Val Lys Asp Phe Phe
130 135 140

Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Gln Glu Pro
145 150 155 160

Glu Ser Lys Tyr Arg Met Thr Pro Pro Gln Leu Asp Glu Asp Gly Ser
165 170 175

Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln Arg
180 185 190

Gly Asp Thr Phe Ile Cys Ala Val Met His Glu Ala Leu His Asn His
195 200 205

Tyr Thr Gln Ile Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 167

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant canine IgG D Fc, N(68)X

<220>

<221> MISC_FEATURE

<222> (68)..(68)

<223> X = any amino acid except N

<400> 167

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Xaa Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
210 215 220

<210> 168
<211> 221
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant canine IgG D Fc, S(69)P

<400> 168

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His

85

90

95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
 100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
 115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
 130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
 145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
 165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln
 180 185 190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 169

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant canine IgG D Fc, T(70)X

<220>

<221> MISC_FEATURE

<222> (70)..(70)

<223> X = any amino acid except T or S

<400> 169

Pro Val Pro Glu Ser Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
1 5 10 15

Lys Pro Lys Asp Ile Leu Arg Ile Thr Arg Thr Pro Glu Ile Thr Cys
20 25 30

Val Val Leu Asp Leu Gly Arg Glu Asp Pro Glu Val Gln Ile Ser Trp
35 40 45

Phe Val Asp Gly Lys Glu Val His Thr Ala Lys Thr Gln Pro Arg Glu
50 55 60

Gln Gln Phe Asn Ser Xaa Tyr Arg Val Val Ser Val Leu Pro Ile Glu
65 70 75 80

His Gln Asp Trp Leu Thr Gly Lys Glu Phe Lys Cys Arg Val Asn His
85 90 95

Ile Gly Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Arg Gly
100 105 110

Gln Ala His Gln Pro Ser Val Tyr Val Leu Pro Pro Ser Pro Lys Glu
115 120 125

Leu Ser Ser Ser Asp Thr Val Thr Leu Thr Cys Leu Ile Lys Asp Phe
130 135 140

Phe Pro Pro Glu Ile Asp Val Glu Trp Gln Ser Asn Gly Gln Pro Glu
145 150 155 160

Pro Glu Ser Lys Tyr His Thr Thr Ala Pro Gln Leu Asp Glu Asp Gly
165 170 175

Ser Tyr Phe Leu Tyr Ser Lys Leu Ser Val Asp Lys Ser Arg Trp Gln

180

185

190

Gln Gly Asp Thr Phe Thr Cys Ala Val Met His Glu Ala Leu Gln Asn
 195 200 205

His Tyr Thr Asp Leu Ser Leu Ser His Ser Pro Gly Lys
 210 215 220

<210> 170

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant feline IgG1a Fc, N(85)X

<220>

<221> MISC_FEATURE

<222> (85)..(85)

<223> X = any amino acid except N

<400> 170

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
 1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
 50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
 65 70 75 80

Glu Glu Gln Phe Xaa Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile

85

90

95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
 225 230 235

<210> 171

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant feline IgG1a Fc, S(86)P

<400> 171

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Arg	Lys	Thr	Asp	His	Pro	Pro	Gly	Pro	Lys	Pro	Cys	Asp	Cys	Pro	Lys	1	5	10	15
Cys	Pro	Pro	Pro	Glu	Met	Leu	Gly	Gly	Pro	Ser	Ile	Phe	Ile	Phe	Pro	20	25	30	
Pro	Lys	Pro	Lys	Asp	Thr	Leu	Ser	Ile	Ser	Arg	Thr	Pro	Glu	Val	Thr	35	40	45	
Cys	Leu	Val	Val	Asp	Leu	Gly	Pro	Asp	Asp	Ser	Asp	Val	Gln	Ile	Thr	50	55	60	
Trp	Phe	Val	Asp	Asn	Thr	Gln	Val	Tyr	Thr	Ala	Lys	Thr	Ser	Pro	Arg	65	70	75	80
Glu	Glu	Gln	Phe	Asn	Pro	Thr	Tyr	Arg	Val	Val	Ser	Val	Leu	Pro	Ile	85	90	95	
Leu	His	Gln	Asp	Trp	Leu	Lys	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	100	105	110	
Ser	Lys	Ser	Leu	Pro	Ser	Pro	Ile	Glu	Arg	Thr	Ile	Ser	Lys	Ala	Lys	115	120	125	
Gly	Gln	Pro	His	Glu	Pro	Gln	Val	Tyr	Val	Leu	Pro	Pro	Ala	Gln	Glu	130	135	140	
Glu	Leu	Ser	Glu	Asn	Lys	Val	Ser	Val	Thr	Cys	Leu	Ile	Lys	Ser	Phe	145	150	155	160
His	Pro	Pro	Asp	Ile	Ala	Val	Glu	Trp	Glu	Ile	Thr	Gly	Gln	Pro	Glu	165	170	175	
Pro	Glu	Asn	Asn	Tyr	Arg	Thr	Thr	Pro	Pro	Gln	Leu	Asp	Ser	Asp	Gly	180	185	190	

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 172
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant feline IgG1a Fc, T(87)X

<220>
<221> MISC_FEATURE
<222> (87)..(87)
<223> X = any amino acid except T or S

<400> 172

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

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Glu Glu Gln Phe Asn Ser Xaa Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Ser Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Val Tyr Ser Lys Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 173

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant feline IgG1b Fc, N(85)X

<220>

<221> MISC_FEATURE

<222> (85)..(85)

<223> X = any amino acid except N

<400> 173

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Xaa Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 174

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant feline IgG1b Fc, S(86)P

<400> 174

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg

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65              70              75              80

Glu Glu Gln Phe Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile
      85              90              95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
      100             105             110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
      115             120             125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
      130             135             140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe
      145             150             155             160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
      165             170             175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
      180             185             190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
      195             200             205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
      210             215             220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
      225             230             235

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<210> 175
<211> 237
<212> PRT
<213> Artificial Sequence

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<220>

<223> Aglycosyl variant feline IgG1b Fc, T(87)X

<220>

<221> MISC_FEATURE

<222> (87)..(87)

<223> X = any amino acid except T or S

<400> 175

Arg Lys Thr Asp His Pro Pro Gly Pro Lys Pro Cys Asp Cys Pro Lys
1 5 10 15

Cys Pro Pro Pro Glu Met Leu Gly Gly Pro Ser Ile Phe Ile Phe Pro
20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asp Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Gln Val Tyr Thr Ala Lys Thr Ser Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Xaa Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Pro Ile Glu Arg Thr Ile Ser Lys Asp Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Ala Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Glu Gly Phe

145 150 155 160

Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Arg Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser Arg Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 176
<211> 237
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant feline IgG2 Fc, N(85)X

<220>
<221> MISC_FEATURE
<222> (85)..(85)
<223> X= any amino acid except N

<400> 176

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr

35

40

45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 65 70 75 80

Glu Glu Gln Phe Xaa Ser Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
 145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
 165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
 180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
 195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
 210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys

225

230

235

<210> 177

<211> 237

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant feline IgG2 Fc, S(86)P

<400> 177

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
 1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
 20 25 30

Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
 35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
 50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
 65 70 75 80

Glu Glu Gln Phe Asn Pro Thr Tyr Arg Val Val Ser Val Leu Pro Ile
 85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
 100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
 115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
 130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 178
<211> 237
<212> PRT
<213> Artificial Sequence

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<220>
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<222> (87)..(87)
<223> X = any amino acid except T or S

<400> 178

Pro Lys Thr Ala Ser Thr Ile Glu Ser Lys Thr Gly Glu Gly Pro Lys
1 5 10 15

Cys Pro Val Pro Glu Ile Pro Gly Ala Pro Ser Val Phe Ile Phe Pro
20 25 30

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Pro Lys Pro Lys Asp Thr Leu Ser Ile Ser Arg Thr Pro Glu Val Thr
35 40 45

Cys Leu Val Val Asp Leu Gly Pro Asp Asp Ser Asn Val Gln Ile Thr
50 55 60

Trp Phe Val Asp Asn Thr Glu Met His Thr Ala Lys Thr Arg Pro Arg
65 70 75 80

Glu Glu Gln Phe Asn Ser Xaa Tyr Arg Val Val Ser Val Leu Pro Ile
85 90 95

Leu His Gln Asp Trp Leu Lys Gly Lys Glu Phe Lys Cys Lys Val Asn
100 105 110

Ser Lys Ser Leu Pro Ser Ala Met Glu Arg Thr Ile Ser Lys Ala Lys
115 120 125

Gly Gln Pro His Glu Pro Gln Val Tyr Val Leu Pro Pro Thr Gln Glu
130 135 140

Glu Leu Ser Glu Asn Lys Val Ser Val Thr Cys Leu Ile Lys Gly Phe
145 150 155 160

His Pro Pro Asp Ile Ala Val Glu Trp Glu Ile Thr Gly Gln Pro Glu
165 170 175

Pro Glu Asn Asn Tyr Gln Thr Thr Pro Pro Gln Leu Asp Ser Asp Gly
180 185 190

Thr Tyr Phe Leu Tyr Ser Arg Leu Ser Val Asp Arg Ser His Trp Gln
195 200 205

Arg Gly Asn Thr Tyr Thr Cys Ser Val Ser His Glu Ala Leu His Ser
210 215 220

His His Thr Gln Lys Ser Leu Thr Gln Ser Pro Gly Lys
225 230 235

<210> 179
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG1 Fc, N(62)X

<220>
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<222> (62)..(62)
<223> X = any amino acid except N

<400> 179

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Asn Pro Lys Asp Thr Leu
1 5 10 15

Met Ile Thr Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Met Asp Gly Val Glu
35 40 45

Val Arg Thr Ala Thr Thr Arg Pro Lys Glu Glu Gln Phe Xaa Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Gln Pro
85 90 95

Ile Glu Arg Thr Ile Thr Lys Thr Lys Gly Arg Ser Gln Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Ser Lys Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asn Ile
 130 135 140

Glu Trp Gln Ser Asn Gly Gln Pro Glu Leu Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Gln Ala Gln Gln Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Asp Arg Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 180
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant equine IgG1 Fc, S(63)P

<400> 180

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Thr Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Met Asp Gly Val Glu

35

40

45

Val Arg Thr Ala Thr Thr Arg Pro Lys Glu Glu Gln Phe Asn Pro Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Gln Pro
 85 90 95

Ile Glu Arg Thr Ile Thr Lys Thr Lys Gly Arg Ser Gln Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Ser Lys Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asn Ile
 130 135 140

Glu Trp Gln Ser Asn Gly Gln Pro Glu Leu Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Gln Ala Gln Gln Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Asp Arg Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 181

<211> 214
 <212> PRT
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<220>
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 <222> (64)..(64)
 <223> X = any amino acid except T or S

<400> 181

Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Thr Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Met Asp Gly Val Glu
 35 40 45

Val Arg Thr Ala Thr Thr Arg Pro Lys Glu Glu Gln Phe Asn Ser Xaa
 50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Gln Pro
 85 90 95

Ile Glu Arg Thr Ile Thr Lys Thr Lys Gly Arg Ser Gln Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Ser Lys Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asn Ile

130

135

140

Glu Trp Gln Ser Asn Gly Gln Pro Glu Leu Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Gln Ala Gln Gln Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Asp Arg Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 182

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG2 Fc, N(62)X

<220>

<221> MISC_FEATURE

<222> (62)..(62)

<223> X = any amino acid except N

<400> 182

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
 20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu

35

40

45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Xaa Ser Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro
 85 90 95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
 100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
 130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile
 195 200 205

Ser Glu Ser Leu Gly Lys
 210

<210> 183

<211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant equine IgG2 Fc, S(63)P
 <400> 183

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
 20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu
 35 40 45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Pro Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro
 85 90 95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
 100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
 130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile
195 200 205

Ser Glu Ser Leu Gly Lys
210

<210> 184
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG2 Fc, T(64)X

<220>
<221> MISC_FEATURE
<222> (64)..(64)
<223> X = any amino acid except T or S

<400> 184

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Ala Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Val Val Thr Cys Val Val Val Asn Leu Ser
20 25 30

Asp Gln Tyr Pro Asp Val Gln Phe Ser Trp Tyr Val Asp Asn Thr Glu
35 40 45

Val His Ser Ala Ile Thr Lys Gln Arg Glu Ala Gln Phe Asn Ser Xaa
50 55 60

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Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Asn Val Gly Val Pro Gln Pro
85 90 95

Ile Ser Arg Ala Ile Ser Arg Gly Lys Gly Pro Ser Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Pro Pro His Pro Asp Glu Leu Ala Lys Ser Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Ser Val
130 135 140

Glu Trp Gln Ser Asn Arg Trp Pro Glu Leu Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Leu Glu Thr Ser Arg Trp Gln Gln Val Glu Ser Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Phe Thr Lys Thr Asp Ile
195 200 205

Ser Glu Ser Leu Gly Lys
210

<210> 185

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG3 Fc, N(62)X

<220>

<221> MISC_FEATURE

<222> (62)..(62)

<223> X = any amino acid except N

<400> 185

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Thr Arg Met Pro Glu Val Thr Cys Leu Val Val Asp Val Ser
20 25 30

His Asp Ser Ser Asp Val Leu Phe Thr Trp Tyr Val Asp Gly Thr Glu
35 40 45

Val Lys Thr Ala Lys Thr Met Pro Asn Glu Glu Gln Asn Xaa Ser Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Asn
65 70 75 80

Gly Lys Lys Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Thr Gly Gln Thr Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Thr Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Arg Thr
145 150 155 160

Thr Glu Ala Gln Lys Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Lys Asp Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Leu His Asn His Val Met Gln Lys Asn Ile
195 200 205

Ser Lys Asn Pro Gly Lys
210

<210> 186
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG3 Fc, S(63)P

<400> 186

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Thr Arg Met Pro Glu Val Thr Cys Leu Val Val Asp Val Ser
20 25 30

His Asp Ser Ser Asp Val Leu Phe Thr Trp Tyr Val Asp Gly Thr Glu
35 40 45

Val Lys Thr Ala Lys Thr Met Pro Asn Glu Glu Gln Asn Asn Pro Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Asn
65 70 75 80

Gly Lys Lys Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro

Val Glu Arg Thr Ile Ser Lys Ala Thr Gly Gln Thr Arg Val Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Thr Val
 130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Arg Thr
 145 150 155 160

Thr Glu Ala Gln Lys Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Lys Asp Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Val Val Met His Glu Ala Leu His Asn His Val Met Gln Lys Asn Ile
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 187

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG3 Fc, T(64)X

<220>

<221> MISC_FEATURE

<222> (64)..(64)

<223> X = any amino acid except T or S

<400> 187

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Thr Arg Met Pro Glu Val Thr Cys Leu Val Val Asp Val Ser
20 25 30

His Asp Ser Ser Asp Val Leu Phe Thr Trp Tyr Val Asp Gly Thr Glu
35 40 45

Val Lys Thr Ala Lys Thr Met Pro Asn Glu Glu Gln Asn Asn Ser Xaa
50 55 60

Tyr Arg Val Val Ser Val Leu Arg Ile Gln His Gln Asp Trp Leu Asn
65 70 75 80

Gly Lys Lys Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Thr Gly Gln Thr Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Thr Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Arg Thr
145 150 155 160

Thr Glu Ala Gln Lys Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Lys Asp Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys

180

185

190

Val Val Met His Glu Ala Leu His Asn His Val Met Gln Lys Asn Ile
 195 200 205

Ser Lys Asn Pro Gly Lys
 210

<210> 188
 <211> 214
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 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant equine IgG4 Fc, N(62)X

<220>
 <221> MISC_FEATURE
 <222> (62)..(62)
 <223> X = any amino acid except N

<400> 188

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
 20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Phe Xaa Ser Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Lys Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu Pro Ala Pro

85

90

95

Val Glu Arg Thr Ile Ser Ala Pro Thr Gly Gln Pro Arg Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Arg Asp Glu Leu Ser Lys Asn Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
 130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
 195 200 205

Ser Lys Ser Pro Gly Lys
 210

<210> 189

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG4 Fc, S(63)P

<400> 189

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Phe Asn Pro Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Ala Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Arg Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
195 200 205

Ser Lys Ser Pro Gly Lys
210

<210> 190
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG4 Fc, T(64)X

<220>
<221> MISC_FEATURE
<222> (64)..(64)
<223> X = any amino acid except T or S

<400> 190

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Phe Asn Ser Xaa
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Ala Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Arg Asp Glu Leu Ser Lys Asn Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
 130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
 195 200 205

Ser Lys Ser Pro Gly Lys
 210

<210> 191
 <211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant equine IgG5 Fc, N(62)X

<220>
 <221> MISC_FEATURE
 <222> (62)..(62)
 <223> X = any amino acid except N

<400> 191

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

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Met Ile Ser Arg Lys Pro Glu Val Thr Cys Val Val Val Asp Leu Gly
20 25 30

His Asp Asp Pro Asp Val Gln Phe Thr Trp Phe Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Glu Glu Gln Phe Xaa Pro Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Ser Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Lys Gly Gln Leu Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ala Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asp Val
130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asn Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Ser Val Glu Thr Ser Arg Trp Lys Gln Gly Glu Ser Phe Thr Cys
180 185 190

Gly Val Met His Glu Ala Val Glu Asn His Tyr Thr Gln Lys Asn Val
195 200 205

Ser His Ser Pro Gly Lys
210

<210> 192
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG5 Fc, S(63)P

<400> 192

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Lys Pro Glu Val Thr Cys Val Val Val Asp Leu Gly
20 25 30

His Asp Asp Pro Asp Val Gln Phe Thr Trp Phe Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Glu Glu Gln Phe Asn Pro Thr
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Ser Lys Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Lys Gly Gln Leu Arg Val Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ala Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asp Val

130

135

140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asn Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Glu Thr Ser Arg Trp Lys Gln Gly Glu Ser Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Val Glu Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser His Ser Pro Gly Lys
 210

<210> 193

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG5 Fc, T(64)X

<220>

<221> MISC_FEATURE

<222> (64)..(64)

<223> X = any amino acid except T or S

<400> 193

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

Met Ile Ser Arg Lys Pro Glu Val Thr Cys Val Val Val Asp Leu Gly
 20 25 30

His Asp Asp Pro Asp Val Gln Phe Thr Trp Phe Val Asp Gly Val Glu

35

40

45

Thr His Thr Ala Thr Thr Glu Pro Lys Glu Glu Gln Phe Asn Ser Xaa
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Ser Val Thr Ser Lys Ala Leu Pro Ala Pro
 85 90 95

Val Glu Arg Thr Ile Ser Lys Ala Lys Gly Gln Leu Arg Val Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ala Lys Asn Thr Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Glu Ile Asp Val
 130 135 140

Glu Trp Gln Ser Asn Glu His Pro Glu Pro Glu Gly Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asn Ser Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Ser Val Glu Thr Ser Arg Trp Lys Gln Gly Glu Ser Phe Thr Cys
 180 185 190

Gly Val Met His Glu Ala Val Glu Asn His Tyr Thr Gln Lys Asn Val
 195 200 205

Ser His Ser Pro Gly Lys
 210

<210> 194

<211> 214
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Aglycosyl variant equine IgG6 Fc, N(62)X

<220>
 <221> MISC_FEATURE
 <222> (62)..(62)
 <223> X = any amino acid except N

<400> 194

Gly Arg Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Ala His Thr Ala Thr Thr Lys Ala Lys Glu Lys Gln Asp Xaa Ser Thr
 50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Arg Arg
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ala Pro
 85 90 95

Val Glu Arg Thr Ile Thr Lys Ala Lys Gly Glu Leu Gln Asp Pro Gln
 100 105 110

Val Tyr Ile Leu Ala Pro His Pro Asp Glu Val Thr Lys Asn Thr Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asn Val

130

135

140

Glu Trp Gln Ser Asn Glu Glu Pro Glu Pro Glu Val Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Thr Asp Arg Trp Glu Gln Gly Glu Ser Phe Thr Cys
 180 185 190

Val Val Met His Glu Ala Ile Arg His Thr Tyr Arg Gln Lys Ser Ile
 195 200 205

Thr Asn Phe Pro Gly Lys
 210

<210> 195

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG6 Fc, S(63)P

<400> 195

Gly Arg Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
 20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Ala His Thr Ala Thr Thr Lys Ala Lys Glu Lys Gln Asp Asn Pro Thr
 50 55 60

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Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Arg Arg
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Thr Lys Ala Lys Gly Glu Leu Gln Asp Pro Gln
100 105 110

Val Tyr Ile Leu Ala Pro His Pro Asp Glu Val Thr Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asn Val
130 135 140

Glu Trp Gln Ser Asn Glu Glu Pro Glu Pro Glu Val Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asp Arg Trp Glu Gln Gly Glu Ser Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Ile Arg His Thr Tyr Arg Gln Lys Ser Ile
195 200 205

Thr Asn Phe Pro Gly Lys
210

<210> 196

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG6 Fc, T(64)X

<220>

<221> MISC_FEATURE

<222> (64)..(64)

<223> X = any amino acid except T or S

<400> 196

Gly Arg Pro Ser Val Phe Ile Phe Pro Pro Asn Pro Lys Asp Thr Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
20 25 30

Gln Glu Asn Pro Asp Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Ala His Thr Ala Thr Thr Lys Ala Lys Glu Lys Gln Asp Asn Ser Xaa
50 55 60

Tyr Arg Val Val Ser Val Leu Pro Ile Gln His Gln Asp Trp Arg Arg
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Arg Ala Leu Pro Ala Pro
85 90 95

Val Glu Arg Thr Ile Thr Lys Ala Lys Gly Glu Leu Gln Asp Pro Gln
100 105 110

Val Tyr Ile Leu Ala Pro His Pro Asp Glu Val Thr Lys Asn Thr Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asn Val
130 135 140

Glu Trp Gln Ser Asn Glu Glu Pro Glu Pro Glu Val Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asp Arg Trp Glu Gln Gly Glu Ser Phe Thr Cys
180 185 190

Val Val Met His Glu Ala Ile Arg His Thr Tyr Arg Gln Lys Ser Ile
195 200 205

Thr Asn Phe Pro Gly Lys
210

<210> 197
<211> 214
<212> PRT
<213> Artificial Sequence

<220>
<223> Aglycosyl variant equine IgG7 Fc, N(62)X

<220>
<221> MISC_FEATURE
<222> (62)..(62)
<223> X = any amino acid except N

<400> 197

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Asn Xaa Ser Thr
50 55 60

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Tyr Arg Val Val Ser Ile Leu Ala Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Gln Lys Thr Ile Ser Lys Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
195 200 205

Ser Lys Ser Pro Gly Lys
210

<210> 198

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG7 Fc, S(63)P

<400> 198

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Asn Asn Pro Thr
50 55 60

Tyr Arg Val Val Ser Ile Leu Ala Ile Gln His Lys Asp Trp Leu Ser
65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro
85 90 95

Val Gln Lys Thr Ile Ser Lys Pro Thr Gly Gln Pro Arg Glu Pro Gln
100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys

180

185

190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
 195 200 205

Ser Lys Ser Pro Gly Lys
 210

<210> 199

<211> 214

<212> PRT

<213> Artificial Sequence

<220>

<223> Aglycosyl variant equine IgG7 Fc, T(64)X

<220>

<221> MISC_FEATURE

<222> (64)..(64)

<223> X = any amino acid except T or S

<400> 199

Val Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Pro Lys Asp Val Leu
 1 5 10 15

Met Ile Ser Arg Thr Pro Thr Val Thr Cys Val Val Val Asp Val Gly
 20 25 30

His Asp Phe Pro Asp Val Gln Phe Asn Trp Tyr Val Asp Gly Val Glu
 35 40 45

Thr His Thr Ala Thr Thr Glu Pro Lys Gln Glu Gln Asn Asn Ser Xaa
 50 55 60

Tyr Arg Val Val Ser Ile Leu Ala Ile Gln His Lys Asp Trp Leu Ser
 65 70 75 80

Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Gln Ala Leu Pro Ala Pro

85

90

95

Val Gln Lys Thr Ile Ser Lys Pro Thr Gly Gln Pro Arg Glu Pro Gln
 100 105 110

Val Tyr Val Leu Ala Pro His Pro Asp Glu Leu Ser Lys Asn Lys Val
 115 120 125

Ser Val Thr Cys Leu Val Lys Asp Phe Tyr Pro Pro Asp Ile Asp Ile
 130 135 140

Glu Trp Lys Ser Asn Gly Gln Pro Glu Pro Glu Thr Lys Tyr Ser Thr
 145 150 155 160

Thr Pro Ala Gln Leu Asp Gly Asp Gly Ser Tyr Phe Leu Tyr Ser Lys
 165 170 175

Leu Thr Val Glu Thr Asn Arg Trp Gln Gln Gly Thr Thr Phe Thr Cys
 180 185 190

Ala Val Met His Glu Ala Leu His Asn His Tyr Thr Glu Lys Ser Val
 195 200 205

Ser Lys Ser Pro Gly Lys
 210