CLAIMS

1. A polypeptide that binds to human serum albumin (HSA) with a K_d of $1x10^{-6}$ M or less at pH 7.4, and at pH 6 binds to HSA with a K_d that is at least half a log less than the K_d for binding to HSA at pH 7.4.

2. The polypeptide of claim 1, wherein the polypeptide at pH 6 binds to HSA with a K_d that is at least one log less than the K_d for binding to HSA at pH 7.4.

3. The polypeptide of claim 1, wherein the polypeptide has a serum half-life in human patients of greater than 10 hours.

4. The polypeptide of claim 1, wherein the polypeptide has a serum half-life in human patients of greater than 50% of the serum half-life of HSA.

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

$$FR1\text{-}(Xaa)_n\text{-}FR2\text{-}(Xaa)_m\text{-}FR3 \quad (I),$$

wherein

FR1 is an amino acid sequence having at least 90% identity to MIPGGLSEAK PATPEIQEIV DKVKPQLEEK TNETYGKLEA VQYKTQVLA (SEQ ID NO: 1);

FR2 is an amino acid sequence having at least 90% identity to GTNYYIKVRA GDNKYMHLKV FKSL (SEQ ID NO: 2);

FR3 is an amino acid sequence having at least 90% identity to EDLVLTGYQV DKNKDDELTG F (SEQ ID NO: 3); and

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

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

6. The polypeptide of claim 5, wherein:

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

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

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

7. The polypeptide of claim 5, wherein the amino acid sequence is represented in general formula (II)

MIP-Xaa1-GLSEAKPATPEIQEIVDKVKPQLEEKTNETYGKLEAVQYKTQVLA-$(Xaa)_n$-Xaa2-TNYYIKVRAGDNKYMHLKVF-Xaa3-Xaa4-Xaa5-$(Xaa)_m$-Xaa6-D-Xaa7-VLTGYQVDKNKDDELTGF (SEQ ID NO: 166) (II),

wherein

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

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

Xaa1 is Gly, Ala, Val, Arg, Lys, Asp, or Glu;

Xaa2 is Gly, Ala, Val, Ser or Thr;

Xaa3 is Arg, Lys, Asn, Gln, Ser, Thr;

Xaa4 is Gly, Ala, Val, Ser or Thr;

Xaa5 is Ala, Val, Ile, Leu, Gly or Pro;

Xaa6 is Gly, Ala, Val, Asp or Glu; and

Xaa7 is Ala, Val, Ile, Leu, Arg or Lys.

8. The polypeptide of claim 7, wherein the amino acid sequence is represented in general formula (III)

MIPRGLSEAKPATPEIQEIVDKVKPQLEEKTNETYGKLEAVQYKT
QVLA-(Xaa)n-STNYYIKVRAGDNKYMHLKVFNGP-(Xaa)m-ADR
VLTGYQVDKNKDDELTGF (SEQ ID NO: 167) (III),

wherein

Xaa, individually for each occurrence, is an amino acid; n is an integer from 3 to 20; and m is an integer from 3 to 20.

9. The polypeptide of claim 5 wherein

(a) $(Xaa)_n$ is an amino acid sequence having at least 90% identity to the amino acid sequence of any one of SEQ ID NOS: 4-55; and/or

(b) $(Xaa)_m$ is an amino acid sequence having at least 90% identity to the amino acid sequence of any one of SEQ ID NOS: 57-108.

10. The polypeptide of claim 9, wherein

(a) $(Xaa)_n$ is the amino acid sequence of any one of SEQ ID NOS: 4-55; and/or

(b) $(Xaa)_m$ is the amino acid sequence of any one of SEQ ID NOS: 57-108.

11. The polypeptide of claim 10, wherein

(a) $(Xaa)_n$ is an amino acid sequence of any one of SEQ ID NOS: 22, 24, 26, 35, 40, 41, and 45; and/or

(b) $(Xaa)_m$ is an amino acid sequence of any one of SEQ ID NOS: 75, 77, 79, 88, 93, 94, and 98.

12. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that has at least 90% identity to an amino acid sequence of any one of SEQ ID NOS: 110-116 and 138.

13. The polypeptide of claim 12, wherein the polypeptide comprises an amino acid sequence of any one of SEQ ID NOS: 110-116 and 138.

14. The polypeptide of claim 1, wherein the polypeptide comprises an amino acid sequence that comprises a cysteine located at the C-terminal end or the N-terminal end of the polypeptide.

15. The polypeptide of claim 1 further comprising a heterologous polypeptide covalently linked through an amide bond to form a contiguous fusion protein.

16. The polypeptide of claim 15, wherein the heterologous polypeptide is

(a) selected from the group consisting of polypeptide hormones, polypeptide cytokines, polypeptide chemokines, growth factors, hemostasis active polypeptides, enzymes, and toxins;

(b) selected from the group consisting of receptor traps and receptor ligands;

(c) selected from the group consisting of angiogenic agents and anti-angiogenic agents;

(d) a neurotransmitter;

(e) an erythropoiesis-stimulating agent; or

(f) an incretin.

17. A pharmaceutical composition suitable for therapeutic use in a human patient, comprising a polypeptide of claim 1 and a pharmaceutically acceptable excipient.

18. A polynucleotide comprising a sequence encoding the polypeptide of claim 1.

19. A viral vector, a plasmid or minicircle comprising the polynucleotide of claim 18.

20. A fusion protein comprising a polypeptide of claim 1.

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