

CLAIMS:

1. A polypeptide which binds to human CXCR4, comprising a scaffold region and complementarity determining regions (CDR1 and CDR3) contained therein, the scaffold region comprising a sequence which has at least 75% identity to the scaffold region defined by amino acids 1 to 26, 33 to 79 and 88 to 97 of SEQ ID NO: 1; and
wherein the CDR1 and CDR3 region defined by amino acids 27 to 32 and 80-87 respectively of SEQ ID NO: 1 are modified by amino acid addition or substitution therein; and
wherein the CDR3 region comprises or consists of a sequence having at least 70% identity to SEQ ID NO: 13, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 28, or SEQ ID NO: 31.
2. The polypeptide according to claim 1, wherein the scaffold region comprises between 1 and 5 amino acid additions or substitutions within the sequence set forth in SEQ ID NO: 2 or comprises the sequence set forth in SEQ ID NO: 2.
3. The polypeptide according to claim 2, wherein the amino acid designated by A' at position 23 of SEQ ID NO: 2 is the amino acid residue glutamine (Q) or lysine (K); and the amino acid designated by B' at position 24 of SEQ ID NO: 2 is the amino acid residue valine (V) or alanine (A).
4. The polypeptide according to any preceding claim, which is an antagonist of human CXCR4.
5. The polypeptide according to any preceding claim, wherein the CDR3 region comprises or consists of a sequence having at least one, two, three, four or five amino acid substitutions within a sequence selected from SEQ ID NO: 13, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 28, or SEQ ID NO: 31.
6. The polypeptide according to any preceding claim wherein the CDR1 region comprises or consists of a sequence having at least 50% identity to SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 24, SEQ ID NO: 27, or SEQ ID NO: 30.

7. The polypeptide according to any preceding claim, wherein the CDR1 region comprises or consists of a sequence having at least one, two, three, four or five amino acid substitutions within SEQ ID NO: 12, SEQ ID NO: 15, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 24, SEQ ID NO: 27, or SEQ ID NO: 30.
8. The polypeptide according to any preceding claim, wherein the polypeptide comprises:
 - (i) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 12 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 13;
 - (ii) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 15 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 16;
 - (iii) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 18 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 19;
 - (iv) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 21 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 22;
 - (v) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 24 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 25;
 - (vi) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 27 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 28; or
 - (vii) a CDR1 region sequence having at least 50% identity to SEQ ID NO: 30 and a CDR3 region sequence having at least 70% identity to SEQ ID NO: 31.
9. The polypeptide according any preceding claim, wherein the polypeptide comprises:
 - (i) a sequence that has at least 80% identity to SEQ ID NO: 11, SEQ ID NO: 14, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 26, or SEQ ID NO: 29; or
 - (ii) the sequence set forth in any one of SEQ ID NO: 11, SEQ ID NO: 14, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 26, or SEQ ID NO: 29.
10. The polypeptide according to any preceding claim, comprising one, two, three, four, five, six, seven, eight, nine or ten substitutions within the sequence selected from the group consisting of SEQ ID NO: 11, SEQ ID NO: 14, SEQ ID NO: 17, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 40, SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 52, SEQ ID NO: 56, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 68, SEQ ID NO: 72, or SEQ ID NO: 76.

11. A polypeptide which binds to human CXCR4 , comprising a scaffold region and complementarity determining regions (CDR1 and CDR3) contained therein, the scaffold region comprising a sequence which has at least 75% identity to the scaffold region defined by amino acids 1 to 26, 33 to 79 and 88 to 97 of SEQ ID NO: 1; and
 wherein the CDR1 region comprises a sequence represented by the formula $SX_1SX_2X_3R$ wherein
 X_1 is G, K, L or Y;
 X_2 is D, H, G or N; and
 X_3 is I, V, M, F, Q or Y; or
 a conservative amino acid substitution thereof
 and/or
 wherein the CDR3 region comprises a sequence represented by the formula $Y'_1RY'_2GY'_3YRHR Y'_4LY'_5LG$ wherein
 Y'_1 is Y or W;
 Y'_2 is T, V or I;
 Y'_3 is G or A;
 Y'_4 is A or Y; and
 Y'_5 is V, R or K; or
 a conservative amino acid substitution thereof.
12. The polypeptide according to claim 11, wherein the CDR1 region comprises or consists of the sequence set forth in any one of SEQ ID NO: 41, SEQ ID NO: 45, SEQ ID NO: 49, SEQ ID NO: 53, SEQ ID NO: 57, SEQ ID NO: 61, SEQ ID NO: 65, SEQ ID NO: 69, SEQ ID NO: 73, or SEQ ID NO: 77; and/or
 wherein the CDR3 region comprises or consists of the sequence set forth in any one of SEQ ID NO: 42, SEQ ID NO: 46, SEQ ID NO: 50, SEQ ID NO: 54, SEQ ID NO: 58, SEQ ID NO: 62, SEQ ID NO: 66, SEQ ID NO: 70, SEQ ID NO: 74, or SEQ ID NO: 78.
13. The polypeptide according to claim 11 or 12, comprising a sequence at least 75% identical to the sequence selected from the group consisting of SEQ ID NO: 40, SEQ ID NO: 44, SEQ ID NO: 48, SEQ ID NO: 52, SEQ ID NO: 56, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 68, SEQ ID NO: 72 or SEQ ID NO: 76.
14. The polypeptide according to any one of claims 11 to 13, comprising or consisting of the sequence set forth in any one of SEQ ID NO: 40, SEQ ID NO:

44, SEQ ID NO: 48, SEQ ID NO: 52, SEQ ID NO: 56, SEQ ID NO: 60, SEQ ID NO: 64, SEQ ID NO: 68, SEQ ID NO: 72 or SEQ ID NO: 76.

15. The polypeptide according to any preceding claim which binds to one or more residues of CXCR4 selected from the group consisting of C28, E32, V112, Y184, F189, P191, D193, W195, D262, L266, E268 and E288 of human CXCR4 (SEQ ID NO:105).
16. An expression construct comprising the nucleic acid molecule encoding the polypeptide according to any preceding claim.
17. A conjugate comprising a polypeptide according to any preceding claim and an agent selected from a therapeutic agent, a toxin, a detectable label or an agent which extends the half-life of the polypeptide.
18. A pharmaceutical composition comprising the polypeptide according to any one of claims 1 to 15 or the conjugate of claim 17 and an acceptable carrier.
19. A polypeptide according to any one of claims 1 to 15, or the conjugate of claim 17, for use in the treatment or prevention of a CXCR4-related disease or disorder.
20. Use of a polypeptide according to any one of claims 1 to 15 or the conjugate of claim 17 or the pharmaceutical composition of claim 18 in the manufacture of a medicament for the prevention or treatment of a CXCR4-related disease or disorder or a disease or disorder associated with CXCR4 signalling or a pathway or mechanism in which CXCR4 is involved.
21. A method for detecting CXCR4 in a sample obtained from a subject, the method comprising contacting the sample with the polypeptide according to any one of claims 1 to 15 such that a CXCR4-polypeptide complex forms and detecting the complex, wherein detecting the complex is indicative of CXCR4 in the sample.