

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 90% 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 regions are defined by amino acids 27 to 32 and 80-87 respectively of SEQ ID NO: 1; and
wherein the CDR3 region comprises or consists of the sequence set forth in any one of SEQ ID NO: 13, SEQ ID NO: 16, SEQ ID NO: 19, SEQ ID NO: 28, or SEQ ID NO: 31.
2. The polypeptide according to claim 1, which is an antagonist of human CXCR4.
3. The polypeptide according to claim 1 or 2 wherein the CDR1 region comprises or consists of the sequence set forth in any one of 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.
4. The polypeptide according to any preceding claim, wherein the CDR1 region comprises or consists of a sequence having at least one, two or three 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.
5. The polypeptide according to any preceding claim, wherein the polypeptide comprises:
 - (i) a CDR1 region sequence set forth in SEQ ID NO: 12 and a CDR3 region sequence set forth in SEQ ID NO: 13;
 - (ii) a CDR1 region sequence set forth in SEQ ID NO: 15 and a CDR3 region sequence set forth in SEQ ID NO: 16;
 - (iii) a CDR1 region sequence set forth in SEQ ID NO: 18 and a CDR3 region sequence set forth in SEQ ID NO: 19;
 - (iv) a CDR1 region sequence set forth in SEQ ID NO: 27 and a CDR3 region sequence set forth in SEQ ID NO: 28; or
 - (v) a CDR1 region sequence set forth in SEQ ID NO: 30 and a CDR3 region sequence set forth in SEQ ID NO: 31.

6. The polypeptide according any preceding claim, wherein the polypeptide comprises:
 - (i) a sequence that has at least 90% identity to SEQ ID NO: 11, SEQ ID NO: 14, SEQ ID NO: 17, 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: 26, or SEQ ID NO: 29.

7. 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 90% 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;
 and
 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.

8. The polypeptide according to claim 7, 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
 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.

9. The polypeptide according to claim 7 or 8, comprising a sequence at least 90% 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.

10. The polypeptide according to any one of claims 7 to 9, 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.
11. 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).
12. An expression construct comprising the nucleic acid molecule encoding the polypeptide according to any preceding claim.
13. A conjugate comprising the polypeptide according to any one of claims 1 to 11 and an agent selected from a therapeutic agent, a toxin, a detectable label or an agent which extends the half-life of the polypeptide.
14. A pharmaceutical composition comprising the polypeptide according to any one of claims 1 to 11 or the conjugate of claim 13 and an acceptable carrier.
15. The polypeptide according to any one of claims 1 to 11, or the conjugate of claim 13, for use in the treatment or prevention of a CXCR4-mediated disease or disorder.
16. Use of the polypeptide according to any one of claims 1 to 11 or the conjugate of claim 13 or the pharmaceutical composition of claim 14 in the manufacture of a medicament for the prevention or treatment of a CXCR4-mediated disease or disorder.
17. 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 11 such that a CXCR4-polypeptide complex forms and detecting the complex, wherein detecting the complex is indicative of CXCR4 in the sample.