CLAIMS

1. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 11 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 12.

2. The antibody or fragment thereof of any one of claims 1 or 19-29, wherein the antibody or fragment thereof comprises one or more constant region domains.

3. The antibody or fragment thereof of any one of claims 1 or 19-29, wherein the antibody or fragment thereof comprises the constant domains C_{H1}, C_{H2}, C_{H3}, and C_L.

4. The antibody or fragment thereof of claim 2, wherein the one or more constant region is domains are from an IgG antibody.

5. The antibody or fragment thereof of Claim claim 4, wherein the IgG antibody is an IgG4 antibody.

6. An isolated nucleic add molecule encoding the antibody or fragment thereof of any one of claims 1 or 19-29.

7. A vector comprising the nucleic acid molecule of claim 6.

8. An isolated host cell comprising the vector of claim 7.

9. The antibody or fragment thereof of any one of claims 1 or 19-29, wherein the antibody or fragment thereof is a single chain Fv antibody.

10. Use of a CXCR5 antagonist in the manufacture of a medicament for the treatment of a CXCR5-related disease, wherein the CXCR5 antagonist comprises the antibody or fragment thereof of any one of claims 1 or 19-29.

11. Use of claim 10, wherein the CXCR5-related disease is rheumatoid arthritis.

12. A method of making the antibody or fragment thereof of any one of claims 1 or 19-29, comprising:

(a) identifying a human variable region homologous to a variable region of a non-human CXCR5 antibody;
(b) identifying from molecular conformations of a variable region of said non-human CXCR5 antibody, amino adds which are flexible and amino adds that flank said flexible residue and retain the molecular conformation of said variable region;
(c) identifying amino acids homologous to said identified amino acids of step (b) in said human variable region;
(d) replacing said identified amino acids of step (b) with said identified amino acids of step (c) to produce a humanized variable region; and

(e) joining said humanized variable region of step (d) with a human sequence to yield a humanized polypeptide that specifically binds CXCR5.

13. The method of claim 12, wherein said step (b) comprises molecular dynamic modeling.

14. The method of claim 12, wherein step (d) comprises not replacing amino adds more than 5 Å from a complementarity determining region.

15. The method of claim 12, further confirming said humanized variable region of step (d) resembles a human antibody by comparing said humanized variable region sequence with the sequences of a collection of human antibody sequences.

16. The method of claim 12, further confirming said humanized variable region of step (d) resembles a human antibody by comparing said humanized variable region trajectory with the sequences of a collection of human antibody trajectories.

17. The method of claim 12, wherein the humanized variable region of step (d) does not comprise a B cell epitope or a T cell epitope.

18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody or fragment thereof of any one of claims 1 to 9 or 19-29.

19. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises the amino acid sequences of RSSKSLLHSSGKTYLY, RMSNLAS, MQHLEYPYT, GFSLIDYGVN, VIWGDGTTY, and IVY.

20. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID NO: 15 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 16.

21. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLY, RLSNLAS, and MQHLEYPYT, or the amino acid sequences of RSSKSLLHSSGKTYLY, RLSSNLAS, and MQHLEYPYT; and
(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

22. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises variable light chain (V_L) comprising the amino acid sequence of SEQ ID NO: 17, SEQ ID NO: 19, or SEQ ID NO: 21 and a variable heavy chain (V_H) comprising the amino acid sequence of SEQ ID NO: 23.

23. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 29.

24. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 30, SEQ ID NO: 31, or SEQ ID NO: 32, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 33 or SEQ ID NO: 34.

25. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLY, RMSNLA, QHLEYPYT; the amino acid sequences of RSSKSLLHSSGKTYLY, RLSNLA, and MQHLEYPYT; or the amino acid sequences of RSSKSLLHSSGKTYLY, RLSSLA, and MQHLEYPYT; and

(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

26. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 35, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 37.

27. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 39, SEQ ID NO: 41, or SEQ ID NO: 43, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 45 or SEQ ID NO: 47.

28. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 55, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 56 or SEQ ID NO: 57.

29. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLYW, RMSNLA, MQHLEYPYT; and

(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

CLAIMS

1. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 11 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 12.

2. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises the amino acid sequences of RSSKSLLHSSGKTYLY, RMSNLAS, MQHLEYPYT, GFSLIDYGVN, VIWGDGTTY, and IVY.

3. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 13, SEQ ID NO: 14, or SEQ ID NO: 15 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 16.

4. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLY, RLSNLAS, and MQHLEYPYT, or the amino acid sequences of RSSKSLLHSSGKTYLY, RLSSNLAS, and MQHLEYPYT; and

(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

5. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof

comprises variable light chain (V_L) comprising the amino acid sequence of SEQ ID NO: 17, SEQ ID NO: 19, or SEQ ID NO: 21 and a variable heavy chain (V_H) comprising the amino acid sequence of SEQ ID NO: 23.

6. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 28 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 29.

7. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 30, SEQ ID NO: 31, or SEQ ID NO: 32, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 33 or SEQ ID NO: 34.

8. The isolated antibody or fragment thereof of claim 7, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 32, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 33.

9. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLY, RMSNLA MQHLEYPYT; the amino acid sequences of RSSKSLLHSSGKTYLY, RLSNLA, and MQHLEYPYT; or the amino acid sequences of RSSKSLLHSSGKTYLY, RLSSLA, and MQHLEYPYT; and

(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

10. The isolated antibody or fragment thereof of claim 9, wherein the antibody or fragment thereof comprises the amino acid sequences of RSSKSLLHSSGKTYLY, RLSSLA, MQHLEYPYT, GFSLIDYGVN, VIWGDGTTY, and IVY.

11. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 35, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 37.

12. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 39, SEQ ID NO: 41, or SEQ ID NO: 43, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 45 or SEQ ID NO: 47.

13. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises a variable light chain comprising the amino acid sequence of SEQ ID NO: 55, and a variable heavy chain comprising the amino acid sequence of SEQ ID NO: 56 or SEQ ID NO: 57.

14. An isolated antibody or fragment thereof that specifically binds to the extracellular domain of human CXCR5, wherein the antibody or fragment thereof comprises:

(a) the amino acid sequences of RSSKSLLHSSGKTYLYW, RMSNLA, MQHLEYPYT; and

(b) the amino acid sequences of GFSLIDYGVN, VIWGDGTTY, and IVY.

15. The antibody or fragment thereof of any one of claims 1-14, wherein the antibody or fragment thereof comprises one or more constant region domains.

16. The antibody or fragment thereof of any one of claims 1-14, wherein the antibody or fragment thereof comprises the constant domains C_{H1}, C_{H2}, C_{H3}, C_L or combinations thereof.

17. The antibody or fragment thereof of claim 15, wherein the one or more constant region domains are from an IgG antibody.

18. The antibody or fragment thereof of claim 17, wherein the IgG antibody is an IgG4 antibody.

19. The antibody or fragment thereof of any one of claims 1-14, wherein the antibody or fragment thereof is a single chain Fv antibody.

20. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of the antibody or fragment thereof of any one of claims 1-19.

21. Use of a CXCR5 antagonist in the manufacture of a medicament for the treatment of a CXCR5-related disease, wherein the CXCR5 antagonist comprises the antibody or fragment thereof of any one of claims 1-19.

22. Use of claim 21, wherein the CXCR5-related disease is pancreatic cancer, colon cancer, bladder cancer, T cell leukemia, B cell leukemia, lupus, Sjoren's Syndrome, myasthenia gravis, multiple sclerosis, ulcerative colitis, rheumatoid arthritis, psoriatic arthritis, chronic inflammatory diseases, or grafts undergoing rejection.

23. Use of claim 21, wherein the CXCR5-related disease is rheumatoid arthritis.

24. An isolated nucleic add molecule encoding the antibody or fragment thereof of any one of claims 1-14.

25. A vector comprising the nucleic acid molecule of claim 24.

26. An isolated host cell comprising the vector of claim 25.