

Antigen Binding Proteins that Bind CXCR5

Technical Field

The present disclosure provides compositions and methods relating to or derived from anti-CXCR5 antibodies. More specifically, the present disclosure provides human antibodies that bind CXCR5, CXCR5-binding fragments and derivatives of such antibodies, and CXCR5-binding polypeptides comprising such fragments. Further still, the present disclosure provides nucleic acids encoding such antibodies, antibody fragments and derivatives and polypeptides, cells comprising such polynucleotides, methods of making such antibodies, antibody fragments and derivatives and polypeptides, and methods of using such antibodies, antibody fragments and derivatives and polypeptides, including methods of treating or diagnosing subjects having CXCR5 related disorders or conditions, including various inflammatory disorders and various cancers.

Background

CXCR5, also known as Burkitt lymphoma receptor (BLR1), CD185, MDR15 and MGC117347, is a G protein-coupled receptor which is a member of the CXC chemokine receptor family. A ligand is BLC, also known as CXCL13, which is a B cell chemoattractant. The unprocessed CXCR5 precursor is 372 amino acids in length with a molecular weight of 42 KD- CXCR5 has a role in B cell migration and localization within particular anatomic compartments. Knockout mice lack peripheral lymph nodes, have fewer Peyer's patches and have decreased B cell levels.

Summary

The present disclosure provides a recombinant fully human anti-CXC chemokine receptor 5 (CXCR5) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising complementarity determining regions (CDRs) as set forth in a heavy chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174; and comprising a light chain variable domain comprising CDRs as set forth in a light chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO.: 137, SEQ ID NO. 139, SEQ ID NO. 150, and SEQ ID NO. 175.

The present disclosure provides a pharmaceutical composition comprising the recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, as described herein, and a pharmaceutically acceptable excipient.

The present disclosure provides a fully human antibody of an IgG class that binds to an CXCR5 epitope with a binding affinity of at least 10^{-6} M, which has a heavy chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the

group consisting of SEQ ID NO. 1, SEQ ID NO. 3, SEQ ID NO. 5, SEQ ID NO. 7,
SEQ ID NO. 9, SEQ ID NO. 11, SEQ ID NO. 13, SEQ ID NO. 15, SEQ ID NO. 17, SEQ ID
NO. 19, SEQ ID NO. 21, SEQ ID NO. 23, SEQ ID NO. 25, SEQ ID NO. 27, SEQ ID NO. 29,
SEQ ID NO. 31, SEQ ID NO. 33, SEQ ID NO. 35, SEQ ID NO. 37, SEQ ID NO. 39, SEQ ID
5 NO. 41, SEQ ID NO. 43, SEQ ID NO. 45, SEQ ID NO. 47, SEQ ID NO.50, SEQ ID NO. 52,
SEQ ID NO. 54, SEQ ID NO. 56, SEQ ID NO. 58, SEQ ID NO. 60, SEQ ID NO. 62, SEQ ID
NO. 64, SEQ ID NO. 66, SEQ ID NO. 68, SEQ ID NO. 70, SEQ ID NO. 72, SEQ ID NO. 74,
SEQ ID NO. 76, SEQ ID NO. 78, SEQ ID NO. 80, SEQ ID NO. 82, SEQ ID NO. 84, SEQ ID
NO. 87, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 94, SEQ ID NO. 96, SEQ ID NO. 98,
10 SEQ ID

We claim:

1. A recombinant fully human anti-CXC chemokine receptor 5 (CXCR5) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising complementarity determining regions (CDRs) as set forth in a heavy chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174; and comprising a light chain variable domain comprising CDRs as set forth in a light chain variable domain amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO.: 137, SEQ ID NO. 139, SEQ ID NO. 150, and SEQ ID NO. 175.

2. The recombinant fully human anti-CXCR5 antibody, or antigen binding fragment thereof, of claim 1, wherein the heavy chain variable domain is selected from the group consisting of

a) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 108 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 108;

b) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 136 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 136;

c) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 138 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 138;

d) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 149 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 149; and

e) a heavy chain variable domain comprising the CDRs as set forth in SEQ ID NO. 174 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 174; and

wherein the light chain variable domain is selected from the group consisting of

a) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 109 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 109;

b) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 137 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 137;

c) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 139 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 139

d) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 150 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 150; and

e) a light chain variable domain comprising the CDRs as set forth in SEQ ID NO. 175 and an amino acid sequence that is at least 95% identical to SEQ ID NO. 175.

3. The recombinant fully human anti-CXCR5 antibody fragment of claim 2, which is a Fab fragment.

4. The recombinant fully human anti-CXCR5 antibody, or antigen binding-fragment, of claim 1, wherein the heavy chain variable domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 108, SEQ ID NO. 136, SEQ ID NO. 138, SEQ ID NO. 149, and SEQ ID NO. 174, and the light chain variable domain comprises an amino acid sequence selected from the group consisting of SEQ ID NO. 109, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 150, and SEQ ID NO. 175.

5. The recombinant fully human anti-CXCR5 antibody of claim 1, wherein the antibody is an IgG.

6. The recombinant fully human anti-CXCR5 antibody of claim 5, wherein the antibody is an IgG1 or an IgG4.

7. The recombinant fully human anti-CXCR5 antigen-binding fragment of claim 1, wherein the fragment is a Fab fragment.

8. The recombinant fully human anti-CXCR5 antigen-binding fragment of claim 1, which is a single chain antibody.

9. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 108/SEQ ID NO. 109.

10. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 136/SEQ ID NO. 137.

11. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 138/SEQ ID NO. 139.

12. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 149/SEQ ID NO. 150.

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13. The recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, comprising heavy chain/light chain variable domain sequences as set forth in SEQ ID NO. 174/SEQ ID NO. 175.

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14. A pharmaceutical composition comprising the recombinant fully human anti-CXCR5 antibody, or antigen-binding fragment thereof, of claim 1, and a pharmaceutically acceptable excipient.

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15. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 108 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 109.

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16. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 136 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 137.

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17. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 138 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 139.

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18. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 149 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 150.

19. The recombinant, fully human antibody, or antigen-binding fragment thereof, of claim 1, wherein the antibody, or antigen-binding fragment thereof, comprises a heavy chain variable domain comprising CDRs as set forth in SEQ ID NO. 174 and comprises a light chain variable domain comprising CDRs as set forth in SEQ ID NO. 175.