

induced by interferon- γ) and i-TAC (interferon-inducible T cell chemoattractant). These three chemokines belong to the structural subfamily of "CXC" chemokines, in which a single amino acid residue separates the first two of four highly conserved Cys residues. Historically, CD183 is the third CXC chemokine receptor discovered and, therefore, CD 183 is commonly designated as "CXCR3. " Binding of chemokines to CXCR3 induces cellular responses that are involved in leukocyte traffic, most notably integrin activation, cytoskeletal changes and chemotactic migration. CXCR3 is expressed on effector/memory T cells and/or in T cells present in many types of inflamed tissues (e.g., T-helper 1 cells or Th1 cells and CD8⁺ Tc1 cells). In addition, IP10, Mig and I-TAC are commonly produced by local cells in inflammatory lesions, suggesting that CXCR3 and its chemokines participate in the recruitment of white blood cells to sites of inflammation. Therefore, CXCR3 is a target for the development of antibodies and antagonists, which may be used in the treatment and diagnosis of diverse inflammatory and immune diseases and disorders, such as rheumatoid arthritis, multiple sclerosis, Crohn's disease, inflammatory bowel disease, chronic obstructive pulmonary disease, psoriasis, type 1 diabetes and transplant rejection. Because CXCR3 is expressed on a subset of B-cell lymphomas, CXCR3 may also be a target for treating and diagnosing lymphomas and leukemias.

Therefore, there is a need in the art for an improved anti-CXCR3 antibodies that can be used as therapeutic agents.

Summary

The present disclosure provides an anti-CXCR3 fully human antibody Fab fragment comprising a heavy chain variable domain comprising an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO. 17, and comprising complementarity determining regions (CDRs) as set forth in the heavy chain variable domain amino acid sequence of SEQ ID NO: 17, and comprising a light chain variable domain comprising an amino acid sequence that is at least 95% identical to the amino acid set forth in SEQ ID NO. 18, and comprising CDRs as set forth in the light chain variable domain amino acid sequence of SEQ ID NO: 18.

The present disclosure provides a recombinant fully human anti-C-X-C chemokine receptor-3 (CXCR3) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising complementarity determining regions (CDRs) as set forth in the heavy chain variable domain amino acid sequence of SEQ ID NO: 17; and comprising a light chain variable domain comprising CDRs as set forth in the light chain variable domain amino acid sequence of SEQ ID NO: 18.

The present disclosure provides a pharmaceutical composition comprising the recombinant fully human anti-CXCR3 antibody as described herein, and a pharmaceutically acceptable excipient.

The present disclosure provides a fully human antibody of an IgG class that binds to an CXCR3 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
5 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, and combinations thereof, and that has a light chain variable domain sequence that is at least 95% identical to the amino acid sequences selected from the group consisting of SEQ ID NO.2, SEQ ID NO.4, SEQ ID NO. 6, SEQ ID NO. 8, SEQ ID NO. 10,
10 SEQ ID NO. 12, SEQ ID NO. 14, SEQ ID NO. 16, SEQ ID NO. 18, SEQ ID NO. 20, SEQ ID NO. 22, SEQ ID NO. 24, SEQ ID NO. 26, SEQ ID NO. 28, SEQ ID NO. 30, SEQ ID NO. 32, SEQ ID NO. 33, SEQ ID NO. 34, SEQ ID NO. 35, SEQ ID NO. 36, SEQ ID NO. 37, and combinations thereof. Preferably, the fully human antibody has both a heavy chain and a light chain wherein the antibody has a heavy chain/light chain variable domain sequence selected

We claim:

1. An anti-CXCR3 fully human antibody Fab fragment comprising a heavy chain variable domain comprising an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO. 17, and comprising complementarity determining regions (CDRs) as set forth in the heavy chain variable domain amino acid sequence of SEQ ID NO: 17, and comprising a light chain variable domain comprising an amino acid sequence that is at least 95% identical to the amino acid set forth in SEQ ID NO. 18, and comprising CDRs as set forth in the light chain variable domain amino acid sequence of SEQ ID NO: 18.
2. A recombinant fully human anti-C-X-C chemokine receptor-3 (CXCR3) antibody, or an antigen-binding fragment thereof, comprising a heavy chain variable domain comprising complementarity determining regions (CDRs) as set forth in the heavy chain variable domain amino acid sequence of SEQ ID NO: 17; and comprising a light chain variable domain comprising CDRs as set forth in the light chain variable domain amino acid sequence of SEQ ID NO: 18.
3. The recombinant fully human anti-CXCR3 antibody, or antigen binding fragment thereof, of claim 2, wherein the heavy chain variable domain comprises an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO. 17, and the light chain variable domain comprises an amino acid sequence that is at least 95% identical to the amino acid sequence set forth in SEQ ID NO. 18.
4. The recombinant fully human anti-CXCR3 antibody, or antigen binding-fragment thereof, of claim 2, comprising a heavy chain variable domain comprising an amino acid sequence as set forth in SEQ ID NO. 17, and a light chain variable domain comprising an amino acid sequence as set forth in SEQ ID NO. 18.
5. The recombinant fully human anti-CXCR3 antibody of claim 2, wherein the antibody is an IgG.
6. The recombinant fully human anti-CXCR3 antibody of claim 2, wherein the antibody is an IgG1 or an IgG4.
7. The recombinant fully human antigen binding fragment of claim 2, wherein the fragment is a Fab fragment or a single chain antibody.
8. A pharmaceutical composition comprising the recombinant fully human anti-CXCR3 antibody, or antigen-binding fragment thereof, of claim 2, and a pharmaceutically acceptable excipient.

9. A pharmaceutical composition comprising the recombinant fully human anti-CXCR3 antibody of claim 2, and a pharmaceutically acceptable excipient.
10. The recombinant fully human anti-CXCR3 antibody of claim 2, comprising a heavy chain variable domain comprising the amino acid sequence as set forth in SEQ ID NO: 17; and comprising
- 5 a light chain variable domain comprising the amino acid sequence as set forth in SEQ ID NO: 18, wherein the antibody is an IgG.
11. The antibody of claim 10, where the IgG antibody is an IgG1 isotype or an IgG4 isotype.