17A/IL-17F mediated cytokine production. These antibodies have distinct specificities. In some embodiments the huIL-17A/F antibodies of the disclosure specifically bind both IL-17F and IL-17A alone (*i.e.*, when not complexed together). In some embodiments, the huIL-17A/F antibodies of the disclosure specifically bind IL-17F, the IL-17F homodimer, and the IL-17A/IL-17F heterodimeric complex. In some embodiments, the huIL-17A/F antibodies of the disclosure specifically bind IL-17F, the IL-17F homodimer, IL-17A, the IL-17A homodimer, and the IL-17A/IL-17F heterodimeric complex. For example, 30D12, 29D8, 1E4, 31A3, 39F12, 12B12, 15B7, 4H11, 38B1, 15E6, 30D12BF, 4B11, 15E6FK, and 39F12A bind IL-17F and cross-react with IL-17A, and these antibodies also bind the IL-17A/IL-17F heterodimeric complex. The 5E12 and 41B10 antibodies bind IL-17F and the IL-17F homodimer, but do not bind IL-17A or the IL-17A homodimer. The 41B10 antibody also binds the IL-17A/IL-17F heterodimeric complex.

The fully human antibodies of the disclosure contain a heavy chain variable region having the amino acid sequence of SEQ ID NOS: 2, 6, 8, 10, 14, 18, 20, 24, 28, 32, 34, 38, 44, 48, 52, and 54. The fully human antibodies of the disclosure contain a light chain variable region having the amino acid sequence of SEQ ID NOS: 4, 12, 16, 22, 26, 30, 36, 40, 46, and 56. The three heavy chain CDRs include a CDR1 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOS: 57, 60, 66, 69, 76, 79, 82, 85 and 90; a CDR2 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOs: 58, 61, 63, 65, 67, 70, 72, 74, 77, 80, 83, 86, 88, 91, 93 and 94; and a CDR3 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOs: 59, 62, 64, 68, 71, 73, 75, 78, 81, 84, 87, 89, 92, and 95. The three light chain CDRs include a CDR1 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOs: 96, 101, 104, 107 and 110; a CDR2 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOs: 97, 102, 105 and 108; and a CDR3 region comprising an amino acid sequence at least 90%, 92%, 95%, 97% 98%, 99% or more identical to a sequence selected from the group consisting of SEQ ID NOs: 98, 99, 100, 103, 106, 109, 111, 112 and 113.

In one aspect, there is provided an antibody, or an antigen-binding fragment thereof, wherein said antibody comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 86, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 87, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 111; or

(b) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 94, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 95, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO : 111, wherein said antibody, or antigen-binding fragment, binds IL-17F and IL-17A. In another aspect, there is provided an antibody or an antigen-binding fragment thereof, wherein the antibody comprises:

(a) a heavy chain variable region sequence of SEQ ID NO: 38 and a light chain variable region sequence of SEQ ID NO: 40; or

(b) a heavy chain variable region sequence of SEQ ID NO: 54 and a light chain variable region sequence of SEQ ID NO: 40,wherein said antibody or antigen-binding fragment binds IL-17F and IL-17A.

Antibodies of the disclosure that specifically bind IL-17F, IL-17A and the IL-17A/IL-17F heterodimeric complex recognize and bind to an epitope that is shared by IL-

In another aspect, there is provided an immunoconjugate comprising an antibody, or antigen-binding fragment, described herein, conjugated to a cytotoxic agent.

In another aspect, there is provided a pharmaceutical composition comprising an antibody, or antigen-binding fragment, or an immunoconjugate, described herein and a carrier. Pharmaceutical compositions according to the disclosure can include an antibody of the disclosure and a carrier. These pharmaceutical compositions can be included in kits, such as, for example, diagnostic kits.

The present disclosure also provides soluble IL-17F proteins, methods for expressing IL-17F proteins, and methods for purifying such proteins in a soluble form.

In another aspect, there is provided a use of an antibody, or antigen-binding fragment, or an immunoconjugate, described herein in the preparation of a medicament for the treatment of a disease or condition selected from the group consisting of an autoimmune disease, inflammatory disorder, and neoplastic disorder in a subject.

In some embodiments, the pathology to be treated is one or more autoimmune diseases inflammatory disorders and cancer. For example, without limitation, the pathology is rheumatoid arthritis, Crohn's disease, psoriasis, multiple sclerosis chronic obstructive pulmonary disease, asthma, angiogenesis and cancer. In another aspect, there is provided a use of an antibody, or antigen-binding fragment, or an immunoconjugate, described herein in the preparation of a medicament for the treatment of rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, multiple sclerosis, chronic obstructive pulmonary disease, or asthma in a subject.

Pharmaceutical compositions according to the disclosure can include an antibody of the disclosure and a carrier. These pharmaceutical compositions can be included in kits, such as, for example, diagnostic kits.

One skilled in the art will appreciate that the antibodies of the disclosure have a variety of uses. For example, the proteins of the disclosure are used as therapeutic agents to prevent the activation of IL-17 receptor and/or IL-17 receptor complexes in disorders such as, for example, rheumatoid arthritis, Crohn's disease, psoriasis, multiple sclerosis chronic obstructive pulmonary disease, asthma, angiogenesis and cancer. The antibodies of the disclosure are also used as reagents in diagnostic kits or as diagnostic tools, or these antibodies can be used in competition assays to generate therapeutic reagents.

DETAILED DESCRIPTION

The present invention provides monoclonal antibodies that specifically bind IL-17F. The invention further provides monoclonal antibodies that specifically bind IL-17F and IL-17A when not complexed together (*i.e.*, cross-reactive monoclonal antibodies). The invention further provides monoclonal antibodies that specifically bind IL-17F and the heterodimeric IL-17A/IL-17F complex (also referred to herein as the IL-17A/IL-17F heterodimer). The present invention even further provides cross-reactive monoclonal antibodies that bind IL-17F, IL-17A and the heterodimeric IL-17A/IL-17F complex. These antibodies are collectively referred to herein as "huIL-17A/F" antibodies. The antibody is *e.g.*, a fully human antibody.

Antibodies of the invention specifically bind IL-17F, wherein the antibody binds to an epitope that includes one or more amino acid residues of human IL-17F. Antibodies of the invention specifically bind both IL-17F and IL-17A wherein the antibody binds an

What is claimed is:

1. An antibody, or an antigen-binding fragment thereof, wherein said antibody comprises:

(a) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 86, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 87, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 111; or

(b) a VH CDR1 region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 94, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 95, a VL CDR1 region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO : 111,

wherein said antibody, or antigen-binding fragment, binds IL-17F and IL-17A.

2. The antibody, or antigen-binding fragment, of claim 1, which also binds IL-17A/IL-17F heterodimeric complex.

3. The antibody, or antigen-binding fragment, of claim 1, which is an IgG isotype.

4. The antibody, or antigen-binding fragment, of claim 3, which is an IgG1 or IgG4 isotype.

5. The antibody, or antigen-binding fragment, of claim 4, which is an IgG1 isotype.

6. The antibody, or antigen-binding fragment, of claim 4, which is an IgG4 isotype.

7. The antibody, or antigen-binding fragment, of claim 1, wherein the antibody comprises a VH CDRl region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 86, a VH CDR3 region comprising the amino acid sequence of SEQ ID NO: 87, a VL CDRl region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO: 111.

8. The antibody, or antigen-binding fragment, of claim 1, wherein the antibody comprises a VH CDRl region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region comprising the amino acid sequence of SEQ ID NO: 94, a VH CDR3 region

comprising the amino acid sequence of SEQ ID NO: 95, a VL CDRl region comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 region comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 region comprising the amino acid sequence of SEQ ID NO : 111.

9. The antibody, or antigen-binding fragment, of claim 1, which binds IL-17A, IL-17F and IL-17A/IL-17F heterodimeric complex and prevents one or more of IL-17F, IL-17A or the IL-17A/IL-17F heterodimeric complex from binding with its receptor.

10. The antibody, or antigen-binding fragment of any one of claims 1-9, which is fully human, humanized, bispecific, or chimeric.

11. The antibody, or antigen-binding fragment, of claim 10, which is bispecific.

12. The antibody, or antigen-binding fragment, of claim 10, wherein the antigen-binding fragment is selected from the group consisting of Fab, Fab', $F(ab')_2$, and scFv fragments, diabodies, and single-chain antibody molecules.

13. The antibody, or antigen-binding fragment, of claim 10, which is an IgG isotype.

14. The antibody, or antigen-binding fragment, of claim 13, which is an IgG1 isotype or IgG4 isotype.

15. The antibody, or antigen-binding fragment, of claim 14, which is an IgG1 isotype.

16. The antibody, or antigen-binding fragment, of claim 14, which is an IgG4 isotype.

17. An antibody, or an antigen-binding fragment thereof, wherein the antibody comprises:

(a) a heavy chain variable region sequence of SEQ ID NO: 38 and a light chain variable region sequence of SEQ ID NO: 40; or

(b) a heavy chain variable region sequence of SEQ ID NO: 54 and a light chain variable region sequence of SEQ ID NO: 40,

wherein said antibody or antigen-binding fragment binds IL-17F and IL-17A.

18. The antibody, or antigen-binding fragment, of claim 17, wherein the antibody comprises the heavy chain variable region sequence of SEQ ID NO: 38 and the light chain variable region sequence of SEQ ID NO: 40.

19. The antibody, or antigen-binding fragment, of claim 17, wherein the antibody comprises the heavy chain variable region sequence of SEQ ID NO: 54 and the light chain variable region sequence of SEQ ID NO: 40.

20. The antibody, or antigen-binding fragment, of any one of claims 17-19, which is monoclonal.

21. The antibody, or antigen-binding fragment, of any one of claims 17-19, which is fully human, humanized, bispecific or chimeric.

22. The antibody, or antigen-binding fragment, of claim 21, which is bispecific.

23. The antibody, or antigen-binding fragment, of claim 21, wherein the antigen-binding fragment is selected from the group consisting of Fab, Fab', $F(ab')_2$, and scFv fragments, diabodies, and single-chain antibody molecules.

24. The antibody, or antigen-binding fragment, of claim 21, which is an IgG isotype.

25. The antibody, or antigen-binding fragment, of claim 24, which is an IgG1 isotype.

26. The antibody, or antigen-binding fragment, of claim 24, which is an IgG4 isotype.

27. An immunoconjugate comprising an antibody, or antigen-binding fragment, of any one of claims 1-26, conjugated to a cytotoxic agent.

28. A pharmaceutical composition comprising an antibody, or antigen-binding fragment, of any one of claims 1-26, or an immunoconjugate of claim 27, and a carrier.

29. Use of an antibody, or antigen-binding fragment, of any one of claims 1-26, or an immunoconjugate of claim 27, in the preparation of a medicament for the treatment of a disease or condition selected from the group consisting of an autoimmune disease, inflammatory disorder, and neoplastic disorder in a subject.

30. The use of claim 29, wherein the subject is a human.

31. Use of an antibody, or antigen-binding fragment, of any one of claims 1-26, or an immunoconjugate of claim 27 in the preparation of a medicament for the treatment of rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, multiple sclerosis, chronic obstructive pulmonary disease, or asthma in a subject.

32. The use of claim 31, wherein said subject is a human.