The demonstrated *in vivo* activities of both IL-17A and IL-17F illustrate the clinical and/or therapeutic potential of, and need for, IL-17A and IL-17F antagonists. Specifically, antibodies that bind to both IL-17A and IL-17F and inhibit (antagonist antibodies) one or more of the immunological activities of both IL-17A and Il-17F would be beneficial. Thus, there remains a need in the art for an antagonist ~~to are~~that is cross reactive to both IL-17A and IL-17F and IL-17A/IL-17F heterodimeric complex.

SUMMARY ~~OF THE INVENTION~~

The present disclosure ~~invention~~ provides monoclonal antibodies such as fully human monoclonal antibodies which specifically bind to IL-17F, the IL-17F homodimer, IL-17A, the IL-17A homodimer and/or the heterodimeric IL-17A/IL-17F complex. The antibodies of the disclosure~~invention~~ are capable of modulating, *e.g.*, blocking, inhibiting, reducing, antagonizing, neutralizing or otherwise interfering with IL-17, IL-17A and/or IL-17A/IL-17F mediated pro-inflammatory cytokine and/or chemokine production.

Exemplary monoclonal antibodies of the disclosure~~invention~~ include, for example, the 30D12 antibody, the 29D8 antibody, the 1E4 antibody, the 31A3 antibody, the 39F12 antibody, the 12B12 antibody, the 15B7 antibody, the 4H11 antibody, 4B11 antibody, the 8B11 antibody, the 38B1 antibody, the 15E6 antibody, the 5E12 antibody, the 41B10 antibody, and variants thereof. Variants of such antibodies include the 30D12BF antibody (a variant of the 30D12 antibody having a modified heavy chain variable region), the 39F12A antibody (a variant of the 39F12 antibody having a modified heavy chain variable region), and the 15E6FK antibody (a variant of the 15E6 antibody having a modified light chain variable region). Alternatively, the monoclonal antibody is an antibody that binds to the same epitope as the 30D12 antibody, the 29D8 antibody, the 1E4 antibody, the 31A3 antibody, the 39F12 antibody, the 12B12 antibody, the 15B7 antibody, the 4H11 antibody, the 4B11 antibody, the 8B11 antibody, the 38B1 antibody, the 15E6 antibody, the 5E12 antibody, the 41B10 antibody, and variants thereof, including the 30D12BF antibody, the 39F12A antibody and the 15E6FK antibody. Each of these antibodies are respectively referred to herein as "huIL-17A/F" antibodies. The huIL-17A/F antibodies include fully human monoclonal antibodies, as well as humanized monoclonal antibodies and chimeric antibodies. Preferably, the antibodies are IgG_1.

These antibodies show specificity for human IL-17F, IL-17-A and/or the IL-17A/IL-17F heterodimeric complex, and they have been shown to inhibit IL-17F, IL-17A and/or IL-

17A/IL-17F mediated cytokine production. These antibodies have distinct specificities. In some embodiments the huIL-17A/F antibodies of the disclosure~~invention~~ specifically bind~~s~~ both IL-17F and IL-17A alone (*i.e.*, when not complexed together). In some embodiments, the huIL-17A/F antibodies of the disclosure~~invention~~ 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~~invention~~ specifically bind~~s~~ 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~~invention~~ 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~~invention~~ 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 or variant thereof, wherein said antibody comprises: (a) a V_H CDR1 region comprising the amino acid sequence of SEQ ID NO: 57, 60, 69, or 85; (b) a V_H CDR2 region comprising the amino acid sequence of SEQ ID NO: 58, 61, 70, 86, 93 or 94; (c) a V_H CDR3 region comprising the amino acid sequence of SEQ ID NO: 59, 62, 71, 87, or 95; (d) a V_L CDR1 region comprising the amino acid sequence of SEQ ID NO: 96, 104, or 110; (e) a V_L CDR2 region comprising the amino acid sequence of SEQ ID NO: 97, 102 or 105; and (f) a V_L CDR3 region comprising the amino acid sequence of SEQ ID NO: 98, 99, 106, or 111, wherein said antibody, antigen-binding fragment or variant binds IL-17F and IL-17A, and wherein said variant comprises heavy and light chain CDRs having at least 92% sequence identity to the CDRs of said antibody. In another aspect, there is provided an antibody or an antigen-binding fragment thereof, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence having at least 95% sequence identity to the sequence selected from SEQ ID NO: 2, 6, 18, 38, 52, and 54, wherein said antibody or antigen-binding fragment binds IL-17F and IL-17A.

Antibodies of the disclosure~~invention~~ 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-

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

The huIL-17A/F antibodies bind to a common epitope that is found on both the IL-17F homodimer, the IL-17A homodimer and the IL-17A/IL-17F heterodimeric complex. Unlike antibodies that bind to an epitope at the interface or otherwise spans the IL-17A/IL-17F heterodimeric complex, the huIL-17A/F antibodies specifically bind the IL-17A/IL-17F heterodimeric complex and also recognize and bind IL-17F and IL-17A when not complexed together. Thus, the huIL-17A/F antibodies do not require the formation of the IL-17A/IL-17F complex to recognize IL-17F and/or IL-17A.

The huIL-17A/F antibodies exhibit a neutralizing ability and inhibit one or more biological functions of IL-17F, IL-17A and/or the IL-17A/IL-17F heterodimeric complex. The huIL-17A/F antibodies are able to bind each IL-17F including the IL-17F homodimer, IL-17A including the IL-17A homodimer, and the IL-17A/IL-17F heterodimeric complex.

The huIL-17A/IL-17F antibodies bind IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, and these antibodies exhibit (i) a binding affinity of at least 100 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 300 pM or less against the IL-17F homodimer, (iii) a binding affinity of at least 400 pM or less against the IL-17A/IL-17F heterodimeric complex, (iv) a neutralizing ability of at least 40 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 120 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 31 nM or less against the IL-17A/IL-17F heterodimeric complex.

In some embodiments, the huIL-17A/IL-17F antibodies bind IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, and these antibodies exhibit (i) a binding affinity of at least 40 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 10 pM or less against the IL-17F homodimer, and (iii) a binding affinity of at least 50 pM or less against the IL-17A/IL-17F heterodimer.

In some embodiments, the huIL-17A/IL-17F antibodies bind IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, and these antibodies exhibit (i) a binding affinity of at least 15 pM or less against the IL-17A homodimer, (ii) a

epitope as the 15E6 antibody or otherwise cross-competes with the binding site of the 15E6FK antibody. In a most preferred embodiment, the huIL-17A/IL-17F antibody has the *binding affinity and neutralizing conditions described above, and binds to the same epitope* as the 15E6 antibody or otherwise competes with the binding site of the 15E6 antibody.

Preferably, the huIL-17A/IL-17F antibodies bind to the same epitope as the 15E6 antibody or otherwise competes with the binding site of the 15E6 antibody, and the huIL-17A/IL-17F antibodies also bind IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, and these antibodies exhibit (i) a binding affinity of at least 40 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 10 pM or less against the IL-17F homodimer, (iii) a binding affinity of at least 50 pM or less against the IL-17A/IL-17F heterodimeric complex, (iv) a neutralizing ability of at least 1.6 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 1.7 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 1.1 nM or less against the IL-17A/IL-17F heterodimeric complex.

Preferably, the huIL-17A/IL-17F antibodies bind to the same epitope as the 15E6FK antibody or otherwise competes with the binding site of the 15E6FK antibody, and the huIL-17A/IL-17F antibodies also bind IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, and these antibodies exhibit (i) a binding affinity of at least 15 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 10 pM or less against the IL-17F homodimer, (iii) a binding affinity of at least 30 pM or less against the IL-17A/IL-17F heterodimeric complex, (iv) a neutralizing ability of at least 0.2 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 1.2 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 0.2 nM or less against the IL-17A/IL-17F heterodimeric complex.

Antibodies of the disclosure~~invention~~ also include fully human antibodies that specifically bind IL-17F, IL-17A and or IL-17A/IL-17F wherein the antibody exhibits greater than 50% inhibition of IL-17F, IL-17A and/or IL-17A/IL-17F mediated pro-inflammatory cytokine production *in vitro*. For example, antibodies of the disclosure~~invention~~ exhibit greater than 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 92%, 95%, 97%, 98%, or 99% inhibition of IL-6 secretion by IL-17 stimulated cells. As used herein, the term "pro-inflammatory cytokine" refers to those immunoregulatory cytokines that promote inflammation and/or are associated with inflammation. Pro-inflammatory cytokines and chemokines include, for example, IL-6, IL-8, G-CSF, and GM-CSF. Pro-inflammatory chemokines include, for

example, GRO-α, GRO-b, LIX, GCP-2, MIG, IP10, I-TAC, ,and MCP-1, RANTES, Eotaxin, SDF-1, and MIP3a.

The present disclosure~~invention~~ also provides methods of treating or preventing pathologies associated with aberrant IL-17, IL-17A and/or IL-17A/IL-17F activity (*e.g.*, aberrant pro-inflammatory cytokine production such as aberrant IL-6 production), or alleviating a symptom associated with such pathologies, by administering a monoclonal antibody of the disclosure~~invention~~ (*e.g.*, fully human monoclonal antibody) to a subject in which such treatment or prevention is desired. The subject to be treated is, *e.g.*, human. The monoclonal antibody is administered in an amount sufficient to treat, prevent or alleviate a symptom associated with the pathology. The amount of monoclonal antibody sufficient to treat or prevent the pathology in the subject is, for example, an amount that is sufficient to reduce IL-17F, IL-17A and/or IL-17A/IL-17F signaling (*e.g.*, IL-17F induced production of one or more pro-inflammatory cytokines (*e.g.*, IL-6)). As used herein, the term "reduced" refers to a decreased production of a pro-inflammatory cytokine in the presence of a monoclonal antibody of the disclosure~~invention~~, wherein the production is, for example, local pro-inflammatory cytokine production (*e.g.*, at a site of inflamed tissue) or systemic pro-inflammatory cytokine production. IL-17F, IL-17A and/or IL-17A/IL-17F signaling (*e.g.*, IL-17F induced pro-inflammatory cytokine such as IL-6) is decreased when the level of pro-inflammatory cytokine (*e.g.*, IL-6) production in the presence of a monoclonal antibody of the disclosure~~invention~~ is greater than or equal to 5%, 10%, 20%, 25%, 30%, 40%, 50%, 60%, 70%, 75%, 80%, 90%, 95%, 99%, or 100% lower than a control level of pro-inflammatory cytokine production (*i.e.*, the level of pro-inflammatory cytokine production in the absence of the monoclonal antibody). Level of pro-inflammatory cytokine production (*e.g.*, IL-6) is measured, *e.g.*, using the IL-17-stimulated Mouse Embryonic Fibroblasts (MEF) cellular assays described herein. Those skilled in the art will appreciate that the level of pro-inflammatory cytokine production can be measured using a variety of assays, including, for example, commercially available ELISA kits.

Pathologies treated and/or prevented using the monoclonal antibodies of the disclosure ~~invention~~ (*e.g.*, fully human monoclonal antibody) include, for example, acute inflammation, chronic inflammation (*e.g.*, chronic inflammation associated with allergic conditions and asthma), autoimmune diseases (*e.g.*, Crohn's disease, multiple sclerosis), inflammatory bowel disease, and transplant rejection.

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

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

The present disclosure~~invention~~ 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, antigen-binding fragment or variant, 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, antigen-binding fragment or variant, 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~~invention~~ can include an antibody of the disclosure~~invention~~ 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~~invention~~ have a variety of uses. For example, the proteins of the disclosure~~invention~~ 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~~invention~~ 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 or variant thereof, wherein said antibody comprises:

(a) a V_H CDR1 region comprising the amino acid sequence of SEQ ID NO: 57, 60, 69, or 85;

(b) a V_H CDR2 region comprising the amino acid sequence of SEQ ID NO: 58, 61, 70, 86, 93 or 94;

(c) a V_H CDR3 region comprising the amino acid sequence of SEQ ID NO: 59, 62, 71, 87, or 95;

(d) a V_L CDR1 region comprising the amino acid sequence of SEQ ID NO: 96, 104, or 110;

(e) a V_L CDR2 region comprising the amino acid sequence of SEQ ID NO: 97, 102 or 105; and

(f) a V_L CDR3 region comprising the amino acid sequence of SEQ ID NO: 98, 99, 106, or 111,

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

wherein said variant comprises heavy and light chain CDRs having at least 92% sequence identity to the CDRs of said antibody.

2. The antibody, antigen-binding fragment or variant, of claim 1, wherein said variant comprises heavy and light chain CDRs having at least 95% sequence identity to the CDRs of said antibody.

3. The antibody, antigen-binding fragment or variant, of claim 1, wherein said variant comprises heavy and light chain CDRs having at least 98% sequence identity to the CDRs of said antibody.

4. The antibody, antigen-binding fragment or variant, of claim 1, wherein said variant comprises heavy and light chain CDRs having at least 99% sequence identity to the CDRs of said antibody.

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

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

7. The antibody, antigen-binding fragment or variant, of claim 6, which is an IgG1 or IgG4 isotype.

8. The antibody, antigen-binding fragment or variant, of claim 7, which is an IgG1 isotype.

9. The antibody, antigen-binding fragment or variant, of claim 7, which is an IgG4 isotype.

10. The antibody, antigen-binding fragment or variant, 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.

11. The antibody, antigen-binding fragment or variant, 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.

12. The antibody, antigen-binding fragment or variant, of claim 1, wherein said variant comprises a VH CDRl region comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 region having at least 92% amino acid sequence identity to 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.

13. The antibody, antigen-binding fragment or variant, 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.

14. The antibody, antigen-binding fragment or variant, of claim 1, which is fully human, humanized, bispecific, or chimeric.

15. The antibody, antigen-binding fragment or variant, of claim 14, which is bispecific.

16. The antibody, antigen-binding fragment or variant, of claim 14, 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.

17. The antibody, antigen-binding fragment or variant, of claim 14, which is an IgG isotype.

18. The antibody, antigen-binding fragment or variant, of claim 17, which is an IgG1 isotype or IgG4 isotype.

19. The antibody, antigen-binding fragment or variant, of claim 18, which is an IgG1 isotype.

20. The antibody, antigen-binding fragment or variant, of claim18, which is an IgG4 isotype.

21. An antibody or an antigen-binding fragment thereof, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence having at least 95% sequence identity to the sequence selected from SEQ ID NO: 2, 6, 18, 38, 52, and 54, wherein said antibody or antigen-binding fragment binds IL-17F and IL-17A.

22. The antibody or antigen-binding fragment of claim 21, wherein said antibody further comprises a light chain variable region comprising an amino acid sequence having at least 95% sequence identity to the sequence selected from SEQ ID NO: 4, 12, 22, 40 and 56.

23. The antibody or antigen-binding fragment of claim 22, wherein the heavy chain variable region comprises an amino acid sequence having at least 98% sequence identity to the sequence selected from SEQ ID NO: 2, 6, 18, 38, 52, and 54 and/or the light chain variable region comprises an amino acid sequence having at least 98% sequence identity to the sequence selected from SEQ ID NO: 4, 12, 22, 40 and 56.

24. The antibody or antigen-binding fragment of claim 22, wherein the heavy chain variable region comprises an amino acid sequence having at least 99% sequence identity to the sequence selected from SEQ ID NO: 2, 6, 18, 38, 52, and 54 and/or the light chain variable region comprises an amino acid sequence having at least 99% sequence identity to the sequence selected from SEQ ID NO: 4, 12, 22, 40 and 56.

25. The antibody or antigen-binding fragment of claim 24, 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.

26. The antibody or antigen-binding fragment of claim 24, 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.

27. The antibody or antigen-binding fragment of any one of claims 21-26, which is monoclonal.

28. The antibody or antigen-binding fragment, of any one of claims 21-26, which is fully human, humanized, bispecific or chimeric.

29. The antibody or antigen-binding fragment of claim 28, which is bispecific.

30. The antibody or antigen-binding fragment of claim 28, 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.

31. The antibody or antigen-binding fragment of claim 27, which is an IgG isotype.

32. The antibody or antigen-binding fragment of claim 31, which is an IgG1 isotype.

33. The antibody or antigen-binding fragment of claim 31, which is an IgG4 isotype.

34. An immunoconjugate comprising an antibody, antigen-binding fragment or variant, of any one of claims 1-33, conjugated to a cytotoxic agent.

35. A pharmaceutical composition comprising an antibody, antigen-binding fragment or variant, of any one of claims 1-33, or an immunoconjugate of claim 34, and a carrier.

36. Use of an antibody, antigen-binding fragment or variant, of any one of claims 1-33, or an immunoconjugate of claim 34, 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.

37. The use of claim 36, wherein the subject is a human.

38. The use of claim 36 or claim 37, wherein the autoimmune disease is selected from the group consisting of Acquired Immunodeficiency Syndrome (AIDS), alopecia areata, ankylosing spondylitis, antiphospholipid syndrome, autoimmune Addison's disease, autoimmune hemolytic anemia, autoimmune hepatitis, autoimmune inner ear disease (AIED), autoimmune lymphoproliferative syndrome (ALPS), autoimmune thrombocytopenic purpura (ATP), Behcet's disease, cardiomyopathy, celiac sprue-dermatitis hepetiformis; chronic fatigue immune dysfunction syndrome (CFIDS), chronic inflammatory demyelinating polyneuropathy (CIPD), cicatricial pemphigold, cold agglutinin disease, crest syndrome, Crohn's disease, Degos' disease, dermatomyositis-juvenile, discoid lupus, essential mixed cryoglobulinemia, fibromyalgia-fibromyositis, Graves' disease, Guillain-Barré syndrome, Hashimoto's thyroiditis, idiopathic pulmonary fibrosis, idiopathic thrombocytopenia purpura (ITP), IgA nephropathy, insulin-dependent diabetes mellitus, juvenile chronic arthritis (Still's disease), juvenile rheumatoid arthritis, Ménière's disease, mixed connective tissue disease, multiple sclerosis, myasthenia gravis, pernacious anemia, polyarteritis nodosa, polychondritis, polyglandular syndromes, polymyalgia rheumatica, polymyositis and dermatomyositis, primary agammaglobulinemia, primary biliary cirrhosis, psoriasis, psoriatic arthritis, Raynaud's phenomena, Reiter's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, scleroderma (progressive systemic sclerosis (PSS), also known as systemic sclerosis (SS)), Sjögren's syndrome, stiff-man syndrome, systemic lupus erythematosus, Takayasu arteritis, temporal arteritis/giant cell arteritis, ulcerative colitis, uveitis, vitiligo and Wegener's granulomatosis.

39. The use of claim 36 or claim 37, wherein the inflammatory disorder is selected from the group consisting of chronic and acute inflammatory disorders.

40. The use of claim 39, wherein the inflammatory disorder is selected from the group consisting of Alzheimer's disease, asthma, atopic allergy, allergy, atherosclerosis, bronchial asthma, eczema, glomerulonephritis, graft vs. host disease, hemolytic anemias, osteoarthritis, sepsis, stroke, transplantation of tissue and organs, vasculitis, diabetic retinopathy and ventilator induced lung injury.

41. The use of claim 36 or claim 37, wherein the neoplastic disorder is selected from the group consisting of malignant lesions and cancer metastasis.

42. The use of claim 41, wherein the malignant lesion is selected from the group consisting of carcinoma, sarcoma, lymphoma, or leukemia.

43. Use of an antibody, antigen-binding fragment or variant, of any one of claims 1-33, or an immunoconjugate of claim 34 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.

44. The use of any one of claims 38-43, wherein said subject is a human.

What is claimed is:

1. An isolated fully human monoclonal antibody that binds IL-17A homodimer, IL-17F homodimer and the IL-17A/IL-17F heterodimeric complex, wherein the antibody exhibits (i) a binding affinity of at least 100 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 300 pM or less against the IL-17F homodimer, (iii) a binding affinity of at least 400 pM or less against the IL-17A/IL-17F heterodimeric complex, (iv) a neutralizing ability of at least 13 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 120 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 31 nM or less against the IL-17A/IL-17F heterodimeric complex.

2. The antibody of claim 1, wherein the antibody exhibits (i) a binding affinity of at least 40 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 10 pM or less against the IL-17F homodimer, and (iii) a binding affinity of at least 50 pM or less against the IL-17A/IL-17F heterodimer.

3. The antibody of claim 1, wherein the antibody exhibits (i) a binding affinity of at least 15 pM or less against the IL-17A homodimer, (ii) a binding affinity of at least 10 pM or less against the IL-17F homodimer, and (iii) a binding affinity of at least 30 pM or less against the IL-17A/IL-17F heterodimer.

4. The antibody of claim 1, wherein the antibody exhibits, (iv) a neutralizing ability of at least 13 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 1.9 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 11 nM or less against the IL-17A/IL-17F heterodimeric complex.

5. The antibody of claim 1, wherein the antibody exhibits, (iv) a neutralizing ability of at least 1.6 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 1.7 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 1.1 nM or less against the IL-17A/IL-17F heterodimeric complex.

6. The antibody of claim 1, wherein the antibody exhibits, (iv) a neutralizing ability of at least 0.2 nM or less against the IL-17A homodimer, (v) a neutralizing ability of at least 1.2 nM or less against the IL-17F homodimer, and (vi) a neutralizing ability of at least 0.2 nM or less against the IL-17A/IL-17F heterodimeric complex.

7. The antibody of claim 1, wherein the antibody is 15E6 and comprises a VH CDR1 sequence comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 sequence comprising the amino acid sequence of SEQ ID NO: 86, a VH CDR3 sequence comprising the amino acid sequence of SEQ ID NO: 87, a VL CDR1 sequence comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 sequence comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 sequence comprising the amino acid sequence of SEQ ID NO: 111.

8. The antibody of claim 1, wherein the antibody is 15E6FK and comprises a VH CDR1 sequence comprising the amino acid sequence of SEQ ID NO: 85, a VH CDR2 sequence comprising the amino acid sequence of SEQ ID NO: 94, a VH CDR3 sequence comprising the amino acid sequence of SEQ ID NO: 95, a VL CDR1 sequence comprising the amino acid sequence of SEQ ID NO: 110, a VL CDR2 sequence comprising the amino acid sequence of SEQ ID NO: 97 and a VL CDR3 sequence comprising the amino acid sequence of SEQ ID NO: 111..

9. The antibody of claim 1, wherein the antibody binds to the same epitope as the 15E6 antibody.

10. The antibody of claim 1, wherein the antibody binds to the same epitope as the 15E6FK antibody.

11. The antibody of claim 1, wherein the antibody binds IL-17A, IL-17F and the 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.

12. An isolated fully human monoclonal antibody, or fragment thereof, wherein said antibody comprises:

(a) a V_H CDR1 region comprising the amino acid sequence of SEQ ID NO: 57, 60, 66, 69, 76, 79, 82, or 85;

(b) a V_H CDR2 region comprising the amino acid sequence of SEQ ID NO: 58, 61, 63, 65, 67, 70, 72, 74, 77, 80, 83, 86, 93 or 94;

(c) a V_H CDR3 region comprising the amino acid sequence of SEQ ID NO: 59, 62, 64, 68, 71, 73, 75, 78, 81, 84, 87, or 95;

(d) a V_L CDR1 region comprising the amino acid sequence of SEQ ID NO: 96, 101, 104, 107 or 110;

(e) a V_L CDR2 region comprising the amino acid sequence of SEQ ID NO: 97, 102, 105 or 108; and

(f) a V_L CDR3 region comprising the amino acid sequence of SEQ ID NO: 98, 99, 100, 103, 106, 109, or 111,

wherein said antibody binds IL-17F and IL-17A.

13. The antibody of claim 12, wherein said antibody also binds the IL-17A/IL-17F heterodimeric complex.

14. The antibody of claim 12, wherein said antibody is an IgG isotype.

15. The antibody of claim 12, wherein said antibody is an IgG1 isotype.

16. The antibody of claim 12, wherein said antibody comprises a heavy chain variable sequence comprising an amino acid sequence selected from SEQ ID NO: 2, 6, 8, 10, 14, 18, 20, 24, 28, 32, 34, 38, 52, and 54.

17. The antibody of claim 12, wherein said antibody further comprises a light chain variable sequence comprising the amino acid sequence selected from SEQ ID NO: 4, 12, 16, 22, 26, 30, 36, 40 and 56.

18. An isolated fully human monoclonal antibody comprising a heavy chain variable sequence comprising the amino acid sequence of SEQ ID NO: 2, 6, 8, 10, 14, 18, 20, 24, 28, 32, 38, 52, or 54, and a light chain variable sequence comprising the amino acid sequence of

SEQ ID NO: 4, 12, 16, 22, 26, 30, 36, 40, or 56, wherein said antibody binds IL-17F and IL-17A.

19. The antibody of claim 18, wherein said antibody is an IgG isotype.

20. The antibody of claim 18, wherein said antibody is an IgG1 isotype.

21. An isolated fully human monoclonal antibody, or fragment thereof, wherein said antibody comprises:

(a) a V_H CDR1 region comprising the amino acid sequence of SEQ ID NO: 85 or 90;

(b) a V_H CDR2 region comprising the amino acid sequence of SEQ ID NO: 88 or 91;

(c) a V_H CDR3 region comprising the amino acid sequence of SEQ ID NO: 89 or 92;

(d) a V_L CDR1 region comprising the amino acid sequence of SEQ ID NO: 101 or 107;

(e) a V_L CDR2 region comprising the amino acid sequence of SEQ ID NO: 102 or 108; and

(f) a V_L CDR3 region comprising the amino acid sequence of SEQ ID NO: 112 or 113,

wherein said antibody binds IL-17F.

22. The antibody of claim 21, wherein said antibody does not bind IL-17A or IL-17A homodimer.

23. The antibody of claim 21, wherein said antibody is an IgG isotype.

24. The antibody of claim 21, wherein said antibody comprises a heavy chain variable sequence comprising an amino acid sequence selected from SEQ ID NO: 44 and 48.

25. The antibody of claim 21, wherein said antibody further comprises a light chain variable sequence comprising the amino acid sequence of SEQ ID NO: 46 and 50.

26. A pharmaceutical composition comprising an antibody of any one of the preceding claims and a carrier.

27. A method of alleviating a symptom of a clinical indication associated rheumatoid arthritis, Crohn's disease, psoriasis, multiple sclerosis chronic obstructive pulmonary disease, or asthma in a subject, the method comprising administering an antagonist of the IL-17A/IL-17F heterodimeric complex to a subject in need thereof in an amount sufficient to alleviate the symptom of the clinical indication associated with rheumatoid arthritis, Crohn's disease, psoriasis, multiple sclerosis chronic obstructive pulmonary disease, or asthma.

28. The method of claim 27, wherein said subject is a human.

29. The method of claim 27, wherein said antagonist is a monoclonal antibody or fragment thereof.

30. The method of claim 29, wherein said monoclonal antibody is an antibody according to any one of claims 1 to 20 or fragment thereof.

31. A method of alleviating a symptom of an autoimmune disease, inflammatory disorder or cell proliferation disorder, wherein the method comprises administering an antibody according to any one of claims 1 to 25 to a subject in need thereof in an amount sufficient to alleviate the symptom of the autoimmune disease, inflammatory disorder or cell proliferation disorder in the subject.

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