

Annex 1

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Claims

1. An antagonist of an IL-17A/F polypeptide, wherein the antagonist is an anti-IL-17A/F antibody, wherein the antibody is a humanized or human antibody, and wherein the IL-17A/F polypeptide is:
an isolated polypeptide comprising:
 - (a) the amino acid sequence of an IL-17A/F polypeptide comprising SEQ ID NO:3 and SEQ ID NO:4; or
 - (b) the amino acid sequence of an IL-17A/F polypeptide comprising SEQ ID NO:3 and SEQ ID NO:4 lacking their associated signal peptides.
2. The antagonist anti-IL-17A/F antibody according to claim 1, wherein said IL-17A/F polypeptide comprises a heterodimeric complex comprising SEQ ID NO:3 and SEQ ID NO:4 or SEQ ID NO:3 and SEQ ID NO:4 lacking their associated signal peptides.
3. The antagonist anti-IL-17A/F antibody according to claim 2, wherein said heterodimeric complex comprises two interchain disulfide linkages between SEQ ID NO:3 and SEQ ID NO:4 or between SEQ ID NO:3 and SEQ ID NO:4 lacking their associated signal peptides
4. The antagonist anti-IL-17A/F antibody according to any preceding claim, wherein the isolated polypeptide comprises SEQ ID NO:3 and SEQ ID NO:4, lacking their associated signal peptides.
5. The antagonist anti-IL-17A/F antibody according to any one of the claims 1 to 4, wherein the isolated polypeptide is a mature IL-17A/F heterodimeric polypeptide consisting of:
 - (i) an IL-17A chain consisting of the amino acid sequence of SEQ ID NO:3 lacking its signal peptides; and
 - (ii) an IL-17F chain consisting of the amino acid sequence of SEQ ID NO:4 lacking its signal peptides.and having disulfide bridges:
 - (a) between IL-17F chain residue 47 and IL-17A chain residue 129;
 - (b) between IL-17F chain residue 137 and IL-17A chain residue 33;
 - (c) between IL-17F chain residues 102 and 152;
 - (d) between IL-17F chain residues 107 and 154;
 - (e) between IL-17A chain residues 94 and 144; and
 - (f) between IL-17A chain residues 99 and 146;wherein the residue numbering is from the initiating methionine residue of each chain.
6. The antagonist anti-IL-17A/F antibody according to any preceding claim, which partially or fully blocks, inhibits or neutralizes a biological activity of said IL-17A/F polypeptide selected from the group consisting of:
 - (a) activation of NF- κ B and stimulation of the production of the proinflammatory chemokines IL-8 and IL-6;
 - (b) stimulation of peripheral blood mononuclear cells or CD4+ cells;
 - (c) stimulation of the proliferation of T-lymphocytes;

- (d) release of TNF- α from THP1 cells;
 - (e) enhancement of matrix synthesis in articular cartilage;
 - (f) promoting breakdown of articular cartilage matrix as well as inhibiting matrix synthesis; and
 - (g) modulating the level of the interleukin-17 signalling pathway during mild to severe stages of inflammatory bowel disease or during stroke.
7. The antagonist anti-IL-17A/F antibody according to claim 6, which partially or fully blocks, inhibits or neutralizes the biological activity of said IL-17A/F polypeptide or activation of NF- κ B and stimulation of the production of the proinflammatory chemokines IL-8 and IL-6.
8. The antagonist anti-IL-17A/F antibody according to any one of claims 1 to 5, which partially or fully blocks, inhibits or neutralizes the biological activity of said IL-17A/F polypeptide to induce the production of IL-8 and IL-6.
9. The antagonist anti-IL-17A/F antibody according to any one of claims 1 to 8, wherein said antibody has a Kd for said IL-17A/F polypeptide of at least about 10^{-8} , 10^{-9} , 10^{-10} , 10^{-11} , or 10^{-12} M.
10. The antagonist anti-IL-17A/F antibody according to any one of claims 1 to 9 for use in the treatment of psoriasis.
- 9-11. The antagonist anti-IL-17A/F antibody according to any one of claims 1 to 9 for use to partially or fully block, inhibit, or neutralize a biological activity of said IL-17A/F polypeptide in the treatment of psoriasis.