CLAIMS

1. A multi-specific antibody molecule comprising a binding domain specific to human TNF-alpha and a binding domain specific to human IL-17A and human IL-17F, wherein the antibody molecule is capable of neutralising the biological activity of human TNF-alpha, human IL-17A and human IL-17F.
2. A multi-specific antibody molecule according to claim 1, wherein the antibody has a binding affinity for human TNF-alpha of 200pM or better.
3. A multi-specific antibody molecule according to claim 1 or claim 2, wherein the antibody has a binding affinity for human IL-17A of 100pM or better.
4. A multi-specific antibody molecule according to claim 3, wherein the antibody has a binding affinity for human IL-17A of 20pM or better.
5. A multi-specific antibody molecule according to any one of claims 1 to 4, wherein the antibody has a binding affinity for IL-17F of 100pM or better.
6. A multi-specific antibody molecule according to claim 5, wherein the antibody has a binding affinity for IL-17 F of 20pM or better.
7. A multi-specific antibody molecule according to any one of claims 1 to 6, wherein the binding domain specific to human IL-17A and human IL-17F also binds the IL-17A/IL-17F heterodimer.
8. A multispecific antibody molecule according to any one of claims 1 to 7, wherein each binding domain comprises two antibody variable domains.
9. A multispecific antibody molecule according to claim 8, wherein the two antibody variable domains are a VH/VL pair.
10. A multispecific antibody molecule according to any one of claims 1 to 9, wherein the molecule format is selected from diabody, scdiabody, triabody, tandem scFv, FabFv, Fab'Fv, FabdsFv, Fab-scFv, Fab-dsscFv, Fab-$(dsscFv)_2$ diFab, diFab', tribody, tandem scFv-Fc, scFv-Fc-scFv, scdiabody-Fc, scdiabody-CH3, Ig-scFv, scFv-Ig, V-Ig, Ig-V, Duobody and DVD-Ig.
11. A multispecific antibody molecule according to any one of claims 1 to 9 wherein the binding domain which is specific to human TNF-alpha and the binding domain which is specific to IL-17A and human IL-17F are independently selected from a Fab, scFv, Fv, dsFv and dsscFv.
12. A multi-specific antibody molecule according to any one of claims 1 to 9 comprising or consisting of:
    a) a polypeptide chain of formula (**I**):

$$\mathbf{V_{H1}\text{-}CH_1\text{-}X\text{-}V_1}; \text{ and}$$

b) a polypeptide chain of formula (**II**):

$$\mathbf{V_{L1}\text{-}C_L\text{-}Y\text{-}V_2};$$

wherein:

V_{H1} represents a heavy chain variable domain;

CH_1 represents a domain of a heavy chain constant region, for example domain 1 thereof;

X represents a bond or linker;

Y represents a bond or linker;

V_1 represents a scFv or a dsscFv;

V_{L1} represents a light chain variable domain;

C_L represents a domain from a light chain constant region, such as Ckappa;

V_2 represents a scFv or a dsscFv.

13. A multi-specific antibody molecule according to claim 12, wherein V1 is a dsscFv and V2 is a dsscFv.
14. A multi-specific antibody molecule according to claim 12 or 13, wherein V1 is a scFv or dsscFv, and V1 comprises a polypeptide chain of:
    a. formula (III): VH2-Z1-VL2 and VH2 is attached to X, for example through a peptide bond; or
    b. formula (IV): VL2-Z1-VH2 and VL2 is attached to X, for example through a peptide bond;

    wherein VH2 represents a heavy chain variable domain, Z1 represents a peptide linker and VL2 represents a light chain variable domain.
15. A multispecific antibody molecule according to any one of claims 12 to 14, wherein V2 is a scFv or dsscFv, and V2 comprises a polypeptide chain of:
    a. formula (V): VH3-Z2-VL3 and VH3 is attached to Y, for example through a peptide bond; or
    b. formula (VI): VL3-Z2-VH3 and VL3 is attached to Y, for example through a peptide bond;

    wherein VH3 represents a heavy chain variable domain, Z2 represents a peptide linker and VL3 represents a light chain variable domain.
16. A multispecific antibody according to claim 14 or 15, wherein Z1 and/or Z2 are a peptide linker of 12 to 25 amino acids in length, for example the sequence given in SEQ ID NO: 68.
17. A multi-specific antibody molecule according to any one of claims 12 to 16, wherein X is a peptide linker, for example the sequence given in SEQ ID NO: 1 or 2.

18. A multi-specific antibody molecule according to any one of claims 12 to 17, wherein Y is a peptide linker, for example the sequence given in SEQ ID NO: 1 or 2.
19. A multi-specific antibody molecule according to claim 17 or claim 18, wherein X is the sequence given in SEQ ID NO: 2 and Y is the sequence given in SEQ ID NO:2.
20. A multi-specific antibody molecule according to claim 17 or claim 18, wherein X is the sequence given in SEQ ID NO: 1 and Y is the sequence given in SEQ ID NO:2.
21. A multi-specific antibody molecule according to any one of claims 12 to 20 wherein at least one of V1 and V2 is a dsscFv or dsFv; and the light chain and heavy chain variable domains of V_1 and/or the light chain and heavy chain variable domains of V_2 are linked by a disulfide bond between two engineered cysteine residues.
22. A multi-specific antibody molecule according to any one of claims 12-21, wherein at least one of V1 and V2 is a dsscFv or dsFv; and the heavy chain and light chain variable domains of V_1 and/or V_2 are linked by a disulfide bond between two cysteine residues, wherein the position of the pair of cysteine residues is selected from the group comprising or consisting of: V_H37 and V_L95, V_H44 and V_L100, V_H44 and V_L105, V_H45 and V_L87, V_H100 and V_L50, V_H100b and V_L49, V_H98 and V_L46, V_H101 and V_L46, V_H105 and V_L43 and V_H106 and V_L57, wherein the V_H and V_L values are independently selected within a given V_1 or V_2.
23. A multi-specific antibody molecule according to claim 22, wherein the position of the pair of engineered cysteine residues is V_H44 and V_L100.
24. A multi-specific antibody molecule according to any one of claims 12 to 23, wherein VH1 and VL1 comprise the binding domain specific to human IL-17A and human IL-17F and V1 and/or V2 comprise the binding domain specific to human TNF-alpha.
25. A multi-specific antibody molecule according to any one of claims 1 to 24 which comprises three binding domains.
26. A multi-specific antibody molecule according to claim 25 wherein each of the three binding domains bind different antigens.
27. A multi-specific antibody molecule according to claim 26, wherein the antibody molecule comprises a binding domain specific to a human serum carrier protein.
28. A multi-specific antibody molecule according to claim 27, wherein the human serum carrier protein is selected from the group consisting of thyroxine-binding protein, transthyretin, α1-acid glycoprotein, transferrin, fibrinogen and albumin, or a fragment of any thereof.
29. A multi-specific antibody molecule according to any one of claims 12 to 28, wherein:
    a. VH1 and VL1 comprise the binding domain specific to human IL-17A and human IL-17F; and

b. V1 comprises the binding domain specific to human TNF-alpha and V2 comprises a binding domain specific to a human serum carrier protein, for example human serum albumin; or V2 comprises the binding domain specific to human TNF-alpha and V1 comprises a binding domain specific to a human serum carrier protein, for example human serum albumin.

30. A multispecific antibody molecule according to any one of claims 1 to 29 wherein the antibody molecule comprises no more than one binding domain which is specific to human TNF-alpha and no more than one binding domain which is specific to human IL-17A and human IL-17F.
31. A multispecific antibody molecule according to any one of claims 1 to 30, wherein the antibody molecule does not comprise a CH2 domain and/or a CH3 domain.
32. A multi-specific antibody molecule according to any one of claims 1 to 31, wherein the binding domain specific for human TNF-alpha comprises at least one of a CDR having the sequence given in SEQ ID NO:85 for CDRH1, a CDR having the sequence given in SEQ ID NO:86 for CDRH2 and a CDR having the sequence given in SEQ ID NO:87 for CDRH3.
33. A multi-specific antibody molecule according to claim 32, wherein the binding domain specific for human TNF-alpha comprises 3 heavy chain CDRs having the sequence given in SEQ ID NO:85 for CDRH1, SEQ ID NO:86 for CDRH2 and SEQ ID NO:87 for CDRH3.
34. A multi-specific antibody molecule according to any one of claims 1 to 33, wherein the binding domain specific for human TNF-alpha comprises at least one of a CDR having the sequence given in SEQ ID NO: 88 for CDRL1, a CDR having the sequence given in SEQ ID NO:89 for CDRL2 and a CDR having the sequence given in SEQ ID NO:90 for CDRL3.
35. A multi-specific antibody molecule according to claim 34, wherein the binding domain specific for human TNF-alpha comprises 3 light chain CDRs having the sequence given in SEQ ID NO:88 for CDRL1, SEQ ID NO:89 for CDRL2 and SEQ ID NO:90 for CDRL3.
36. A multi-specific antibody molecule according to any one of claims 1 to 35, wherein the binding domain specific for human TNF-alpha comprises a heavy chain variable domain comprising the sequence given in SEQ ID NO:92 or SEQ ID NO:96; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:92 or SEQ ID NO:96; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO: 92 or SEQ ID NO:96 wherein CDRH1, CDRH2 and CDRH2 have the sequences given in claim 33.

37. A multispecific antibody molecule according to any one of claims 1 to 36, wherein the binding domain specific for human TNF-alpha comprises a light chain variable domain comprising the sequence given in SEQ ID NO:91 or SEQ ID NO:95 ; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:91 or SEQ ID NO:95 ; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:91 or SEQ ID NO:95 wherein CDRL1, CDRL2 and CDRL3 have the sequences given in claim 35.
38. A multispecific antibody molecule according to any one of claims 1 to 37, wherein the antibody comprises a dsscFv specific for human TNF-alpha and the dsscFv comprises the sequence given in SEQ ID NO:101 ; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO: 101; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:101 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 33 and CDRL1, CDRL2 and CDRL3 have the sequences given in claim 35.
39. A multispecific antibody molecule according to any one of claims 1 to 37, wherein the antibody comprises a scFv specific for human TNF-alpha and the scFv comprises the sequence given in SEQ ID NO:99; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:99 ; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:99 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 33 and CDRL1, CDRL2 and CDRL3 have the sequences given in claim 35.
40. A multi-specific antibody molecule according to any one of claims 1 to 39, wherein the binding domain specific for human IL-17A and human IL-17F comprises 3 heavy chain CDRs having the sequence given in SEQ ID NO: 71 for CDRH1, SEQ ID NO: 72 for CDRH2 and SEQ ID NO: 73 for CDRH3.
41. A multi-specific antibody molecule according to any one of claims 1 to 40, wherein the binding domain specific for human IL-17A and human IL-17F comprises 3 light chain CDRs having the sequence given in SEQ ID NO:74 for CDRL1, SEQ ID NO:75 for CDRL2 and SEQ ID NO:76 for CDRL3.
42. A multi-specific antibody molecule according to any one of claims 1 to 41, wherein the binding domain specific for human IL-17A and human IL-17F comprises a heavy chain variable domain comprising the sequence given in SEQ ID NO:78; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:78; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:78 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 40.

43. A multi-specific antibody molecule according to any one of claims 1 to 42, wherein the binding domain specific for human IL-17A and human IL-17F comprises a light chain variable domain comprising the sequence given in SEQ ID NO:77; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:77; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:77 wherein CDRL1, CDRL2 and CDRL3 have the sequences given in claim 41.
44. A multi-specific antibody molecule according to any one of claims 1 to 43, wherein the antibody comprises a heavy chain comprising the sequence given in SEQ ID NO:82; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:82; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:82 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 40.
45. A multi-specific antibody molecule according to any one of claims 1 to 44, wherein the antibody comprises a light chain comprising the sequence given in SEQ ID NO:81; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:81; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:81 wherein CDRL1, CDRL2 and CDRL3 have the sequences given in claim 41.
46. A multi-specific antibody molecule according to any one of claims 1 to 45, wherein the antibody molecule comprises a binding domain specific for human serum albumin which comprises 3 heavy chain CDRs having the sequence given in SEQ ID NO: 103 for CDRH1, SEQ ID NO: 104 for CDRH2 and SEQ ID NO: 105 for CDRH3.
47. A multi-specific antibody molecule according to any one of claims 1 to 46, wherein the antibody molecule comprises a binding domain specific for human serum albumin which comprises 3 light chain CDRs having the sequence given in SEQ ID NO:106 for CDRL1, SEQ ID NO:107 for CDRL2 and SEQ ID NO:108 for CDRL3.
48. A multi-specific antibody molecule according to any one of claims 1 to 47, wherein the binding domain specific for human serum albumin comprises a heavy chain variable domain comprising the sequence given in SEQ ID NO:110 or SEQ ID NO:114; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:110 or SEQ ID NO:114; or having at least 80% identity or similarity to the sequence given in SEQ ID NO:110 or SEQ ID NO:114 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 46.
49. A multispecific antibody molecule according to any one of claims 1 to 48, wherein the binding domain specific for human serum albumin comprises a light chain variable domain comprising the sequence given in SEQ ID NO:109 or SEQ ID NO:113 a

sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:109 or SEQ ID NO:113; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:109 or SEQ ID NO:113 wherein CDRL1, CDRL2 and CDRL3 have sequences given in claim 47.

50. A multispecific antibody according to any one of claims 1 to 49, wherein the antibody comprises a dsscFv specific for human serum albumin and the dsscFv comprises the sequence given in SEQ ID NO:119; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:119; or a sequence having at least 80% identity or similarity to the sequence of SEQ ID NO:119 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 46 and CDRL1, CDRL2 and CDRL3 have the sequences given in claim 47.
51. A multispecific antibody according to any one of claims 1 to 49, wherein the antibody comprises a scFv specific for human serum albumin and the scFv comprises the sequence given in SEQ ID NO:117; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:117; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:117 wherein CDRH1, CDRH2 and CDRH3 have the sequences given in claim 46 and CDRL1, CDRL2 and CDRL3 have the sequences given in claim 47.
52. A tri-specific antibody molecule comprising a binding domain specific to human TNF-alpha, a binding domain specific to human IL-17A and human IL-17F and a binding domain specific to human serum albumin, wherein the antibody molecule comprises or consists of:
    a. a first polypeptide comprising or consisting of the sequence given in SEQ ID NO:125; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:125; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:125 wherein the CDRs have the sequences given in claims 33, 35 and 40; and
    b. a second polypeptide comprising or consisting of the sequence given in SEQ ID NO:131; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:131; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:131 wherein the CDRs have the sequences given in claims 41, 46 and 47.
53. A tri-specific antibody molecule comprising a binding domain specific to human TNF-alpha, a binding domain specific to human IL-17A and human IL-17F and a binding domain specific to human serum albumin, and comprises or consists of:

a. a first polypeptide comprising or consisting of the sequence given in SEQ ID NO:127; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:127; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:127 wherein the CDRs have the sequences given in claims 33, 35 and 40; and
b. a second polypeptide comprising or consisting of the sequence given in SEQ ID NO:131; a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:131; or a sequence having at least 80% identity or similarity to the sequence given in SEQ ID NO:131 wherein the CDRs have the sequences given in claims 41, 46 and 47.

54. A tri-specific antibody molecule according to claim 52 or claim 53, wherein the antibody molecule is capable of neutralising the biological activity of human TNF-alpha, human IL-17A and human IL-17F.
55. A polynucleotide encoding a multi-specific antibody molecule or polypeptide chain thereof according to any one of claims 1 to 54.
56. A vector comprising a polynucleotide or polynucleotides defined in claim 55.
57. A host cell comprising one or more polynucleotides or vectors of claim 55 or 56 respectively.
58. A host cell comprising two vectors each vector comprising a polynucleotide encoding a different polypeptide chain of a multi-specific antibody molecule according to any one of claims 1 to 54.
59. A process comprising expressing a multi-specific antibody molecule from a host cell defined in claim 57 or claim 58.
60. A pharmaceutical composition comprising a multi-specific antibody molecule according to any one of claims 1 to 54 and at least one excipient.
61. A multi-specific antibody molecule according to any one of claims 1 to 54 or a pharmaceutical composition according to claim 60 for use in therapy.
62. A multi-specific antibody molecule according to any one of claims 1 to 54 or a pharmaceutical composition according to claim 60 for use in the treatment of an inflammatory disease, autoimmune disease or cancer.
63. Use of a multi-specific antibody molecule according to any one of claims 1 to 54 or a pharmaceutical composition according to claim 60 in the manufacture of a medicament for the treatment of an inflammatory disease, autoimmune disease or cancer.
64. A multi-specific antibody molecule according to any one of claims 1 to 54 or a pharmaceutical composition according to claim 60 for use in the treatment of one or more of arthritis, psoriatic arthritis, systemic onset juvenile idiopathic arthritis (JIA),

Crohn's disease, inflammatory bowel disease, Ulcerative colitis, ankylosing spondylitis and other spondyloarthropathies, psoriasis, hidradenitis suppurativa, Behcet's disease, rheumatoid arthritis, systemic lupus erythematosus (SLE), asthma, myocarditis, uveitis, atopic dermatitis, vasculitis, immune mediated inflammatory disorders of the central and peripheral nervous system such as multiple sclerosis and Guillain-Barr syndrome, other autoimmune disorders, osteoporosis, bone resorption, gout, sarcoidosis, Sjogren syndrome and pyoderma gangrenosum.

65. Use of a multi-specific antibody molecule according to any one of claims 1 to 54 or a pharmaceutical composition according to claim 60 in the manufacture of a medicament for the treatment of one or more of arthritis, psoriatic arthritis, systemic onset juvenile idiopathic arthritis (JIA), Crohn's disease, inflammatory bowel disease, Ulcerative colitis, ankylosing spondylitis and other spondyloarthropathies, psoriasis, hidradenitis suppurativa, Behcet's disease, rheumatoid arthritis, systemic lupus erythematosus (SLE), asthma, myocarditis, uveitis, atopic dermatitis, vasculitis, immune mediated inflammatory disorders of the central and peripheral nervous system such as multiple sclerosis and Guillain-Barr syndrome, other autoimmune disorders, osteoporosis, bone resorption, gout, sarcoidosis, Sjogren syndrome and pyoderma gangrenosum.
66. A tri-specific antibody molecule comprising a binding domain specific to human TNF-alpha, a binding domain specific to human IL-17A and human IL-17F and a binding domain specific to human serum albumin, and comprises or consists of a first polypeptide encoded by the polynucleotide sequence given in SEQ ID NO:126 and a second polypeptide encoded by the polynucleotide sequence given in SEQ ID NO:132.