

WHAT IS CLAIMED IS:

1. A multi-specific antibody comprising at least two antigen-binding domains, wherein one antigen binding domain binds to IL13 (IL13-binding domain) and the second antigen-binding domain binds to IL22 (IL22-binding domain).
2. The multi-specific antibody according to claim 1, wherein IL13 is human and/or cynomolgus IL13, and IL22 is human and/or cynomolgus IL22.
3. The multi-specific antibody according to claim 1 or 2, wherein each antigen-binding domain comprises two antibody variable domains.
4. The multi-specific antibody according to claim 3, wherein the two antibody variable domains are a VH/VL pair.
5. The multi-specific antibody according to any one of claims 1-4 wherein the IL13-binding domain and the IL22-binding domain are independently selected from a Fab, scFv, Fv, dsFv and dsscFv.
6. The multi-specific antibody according to any one of claims 1-5, wherein said multi-specific antibody neutralizes one or more IL13 and/or IL22 activities.
7. The multi-specific antibody according to claim 6, wherein said antibody is capable of inhibiting or attenuating IL22 binding to IL22 receptor 1 (IL22R1); and/or,

wherein said antibody binds to a region on IL22 such that the binding sterically blocks the interaction between IL22 and IL22R1; and/or, wherein said antibody is capable of inhibiting or attenuating IL22 binding to IL22 binding protein (IL22RA2); and/or, wherein said antibody is capable of inhibiting or attenuating IL13 binding to IL13R alpha1.
8. The multi-specific antibody according to any one of claims 1-7, wherein said antigen-binding domain that binds to IL22 has a dissociation equilibrium constant (KD) is less than 100pM for human IL22 and/or, wherein said antigen-binding domain that binds to IL13 has a dissociation equilibrium constant (KD) is less than 100pM for human IL13.
9. The multi-specific antibody according to any one of claims 1-8, wherein the IL22-binding domain binds to an epitope on IL22, said epitope comprising 5 or more residues within polypeptide VRLIGEKLFGHVSM (SEQ ID NO: 155) corresponding to residues 72-85 of the amino-acid sequence of IL22 defined by SEQ ID NO: 1.
10. The multi-specific antibody according to any one of claims 1-8 wherein the IL22-binding domain specifically binds to the polypeptide VRLIGEKLFGHVSM (SEQ ID NO: 155).
11. The multi-specific antibody according to any one of claims 1-8, wherein the IL22-binding domain binds to an epitope of human IL22, the epitope comprising 5 or more residues selected from Lys44, Phe47, Gln48, Ile75, Gly76, Glu77, Phe80, His81, Gly82, Val83, Ser84, Met85, Ser86, Arg88, Leu169,

Met172, Ser173, Arg175, Asn176 and Ile179 of human IL22 (SEQ ID NO: 1) as determined at the distance of less than 5Å contact distance between the antibody and IL22.

12. The multi-specific antibody according to any one of claims 1-11 additionally comprising a third antigen binding domain that binds to serum albumin (albumin-binding domain).

13. The multi-specific antibody according to claim 12 comprising:

a) a polypeptide chain of formula **(Ia)**:

$V_H-CH_1-X-V_1$; and

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

$V_L-C_L-Y-V_2$;

wherein:

V_H represents a heavy chain variable domain;

CH_1 represents domain 1 of a heavy chain constant region;

X represents a bond or linker;

Y represents a bond or linker;

V_1 represents a scFv, a dsScFv, or a dsFv;

V_L 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, a dsScFv or a dsFv;

wherein at least one of V_1 or V_2 is a dsScFv or a dsFv.

14. The multi-specific antibody according to claim 13, wherein:

V_L and V_H comprise the antigen-binding domain that binds to IL22,

V_2 comprises the antigen binding-domain that binds to IL13, and

V_1 comprises the antigen binding-domain that binds to serum albumin;

15. The multi-specific antibody according to any one of claims 1-11 comprising:

a) a polypeptide chain of formula **(III)**:

$VH_1-CH_1-CH_2-CH_3$;

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

VL_1-C_L ;

c) a polypeptide chain of formula **(V)**:

$VH_2-CH_1-CH_2-CH_3$; and

d) a polypeptide chain of formula **(VI)**:

VL_2-C_L ;

wherein:

VH₁ and VH₂ represent a heavy chain variable domain;
 CH₁ represents domain 1 of a heavy chain constant region;
 CH₂ represents domain 2 of a heavy chain constant region;
 CH₃ represents domain 3 of a heavy chain constant region;
 VL₁ and VL₂ represent a light chain variable domain;
 C_L represents a domain from a light chain constant region, such as Ckappa;

and wherein VH₁ and VL₁ comprise the IL22-binding domain, and VH₂ and VL₂ comprise the IL13-binding domain, and wherein the polypeptides of Formula **III** and **V** are a pair of heavy chain polypeptides in which one polypeptide comprises the knob substitution T366W in the CH₃ domain and the other polypeptide comprises the hole substitutions T366S, L368A and Y407V in the CH₃ domain, wherein the numbering is according to EU as in Kabat.

16. The multi-specific antibody according to any one of claims 1-15, wherein the IL22- binding domain comprises a light chain variable region comprising:
- a CDR-L1 comprising SEQ ID NO:8,
 - a CDR-L2 comprising SEQ ID NO:9, and
 - a CDR-L3 comprising SEQ ID NO:10;
- and a heavy chain variable region comprising:
- a CDR-H1 comprising SEQ ID NO:11,
 - a CDR-H2 comprising SEQ ID NO:12, and
 - a CDR-H3 comprising SEQ ID NO:13; and/or,, wherein the IL13- binding domain comprises a light chain variable region comprising:
- a CDR-L1 comprising SEQ ID NO:22,
 - a CDR-L2 comprising SEQ ID NO:23, and
 - a CDR-L3 comprising SEQ ID NO:24;
- and a heavy chain variable region comprising:
- a CDR-H1 comprising SEQ ID NO:25,
 - a CDR-H2 comprising SEQ ID NO:26, and
 - a CDR-H3 comprising SEQ ID NO:27; and/or, wherein the albumin- binding domain comprises a light chain variable region comprising:
- a CDR-L1 comprising SEQ ID NO:40,
 - a CDR-L2 comprising SEQ ID NO:41, and
 - a CDR-L3 comprising SEQ ID NO:42;
- and a heavy chain variable region comprising:
- a CDR-H1 comprising SEQ ID NO:43,
 - a CDR-H2 comprising SEQ ID NO:44, and

a CDR-H3 comprising SEQ ID NO:45.

optionally, wherein each CDR contains up to three amino acid substitutions, wherein such amino-acid substitutions are conservative.

17. The multi-specific antibody according to any one of claims 1-15, wherein the IL22- binding domain comprises a light chain variable region comprising the sequence given in SEQ ID NO:14 and a heavy chain variable region comprising the sequence given in SEQ ID NO:16, or, wherein the IL22-binding domain comprises CDR-L1/CDR-L2/CDR-L3/CDR-H1/CDR-H2/CDR-H3 sequences comprising SEQ ID NOs:8/9/10/11/12/13 respectively, and the remainder of the light chain and heavy chain variable regions have at least 90% identity or similarity to SEQ ID NO: 14 and 16 respectively.

18. The multi-specific antibody according to any one of claims 1-15, wherein the IL22- binding domain is a Fab comprising a light chain comprising the sequence given in SEQ ID NO:18 and a heavy chain comprising the sequence given in SEQ ID NO:20.

19. The multi-specific antibody according to any one of claims 1-15, wherein the IL13- binding domain comprises a light chain variable region comprising the sequence given in SEQ ID NO: 28 and a heavy chain variable region comprising the sequence given in SEQ ID NO:29 or, wherein the IL13-binding domain comprises CDR-L1/CDR-L2/CDR-L3/CDR-H1/CDR-H2/CDR-H3 sequences comprising SEQ ID NOs:22/23/24/25/26/27 respectively, and the remainder of the light chain and heavy chain variable regions have at least 90% identity or similarity to SEQ ID NO: 28 and 29 respectively.

20. The multi-specific antibody according to any one of claims 1-15, wherein the IL13- binding domain comprises a light chain variable region comprising the sequence given in SEQ ID NO:32 and a heavy chain variable region comprising the sequence given in SEQ ID NO:33, or, wherein the IL13-binding domain comprises CDR-L1/CDR-L2/CDR-L3/CDR-H1/CDR-H2/CDR-H3 sequences comprising SEQ ID NOs:22/23/24/25/26/27 respectively, and the remainder of the light chain and heavy chain variable regions have at least 90% identity or similarity to SEQ ID NO: 32 and 33 respectively.

21. The multi-specific antibody according to any one of claims 1-15, wherein the light chain variable region and heavy chain variable region of the IL13- binding domain are connected by a linker, said linker comprising the sequence given in SEQ ID NO:67.

22. The multi-specific antibody according to any one of claims 1-15, wherein the IL13-binding domain is a scFv comprising the sequence given in SEQ ID NO:36 or a dsScFv comprising the sequence given in SEQ ID NO:38.

23. The multi-specific antibody according to any one of claims 1-15, wherein the IL22-binding domain comprises

a light chain variable region comprising the sequence given in SEQ ID NO:14 and

a heavy chain variable region comprising the sequence given in SEQ ID NO:16; and
the IL13- binding domain comprises

a light chain variable region comprising the sequence given in SEQ ID NO:28 or 32 and

a heavy chain variable region comprising the sequence given in SEQ ID NO:29 or 33.

24. The multi-specific antibody according to any one of claims 1-15, wherein

(i) the IL22-binding domain is a Fab comprising a light chain comprising the sequence given in SEQ ID NO:18 and a heavy chain comprising the sequence given in SEQ ID NO: 20; and

(ii) the IL13- binding domain is a scFv comprising the sequence given in SEQ ID NO:36 or a dsscFv comprising the sequence given in SEQ ID NO:38.

25. The multi-specific antibody according to any one of claims 12-14, wherein the albumin- binding domain comprises a light chain variable region comprising the sequence given in SEQ ID NO:46 and a heavy chain variable region comprising the sequence given in SEQ ID NO:47, or, wherein the albumin-binding domain comprises a light chain variable region comprising the sequence given in SEQ ID NO:50 and a heavy chain variable region comprising the sequence given in SEQ ID NO:51.

26. The multi-specific antibody according to any one of claims 12-14, wherein the light chain variable region and heavy chain variable region of the albumin- binding domain are connected by a linker, said linker comprising the sequence given in SEQ ID NO:69.

27. The multi-specific antibody according to any one of claims 12-14, wherein the albumin-binding domain is a scFv comprising the sequence given in SEQ ID NO:54 or a dsscFv comprising the sequence given in SEQ ID NO:56.

28. The multi-specific antibody according to claim 13 or 14, wherein Y is a linker comprising the sequence given in SEQ ID NO:66 and/or, wherein X is a linker comprising the sequence given in SEQ ID NO: 68.

29. The multi-specific antibody according to claim 13 or 14 comprising the sequence given in SEQ ID NO:58 or SEQ ID NO: 60, or comprising the sequence given in SEQ ID NO:62 or SEQ ID NO: 64; or, comprising the sequence given in SEQ ID NO:60 and comprising the sequence given in SEQ ID NO: 64.

30. An isolated polynucleotide encoding the multi-specific antibody or a polypeptide chain thereof according to any one of claims 1-29.

31. An expression vector carrying the polynucleotide of claim 30.

32. A host cell comprising the vector as defined in claim 31.

33. A method of producing the multi-specific antibody as defined in any one of claims 1-29, comprising culturing the host cell of claim 46 under conditions permitting production of the antibody, and recovering the antibody produced.
34. A pharmaceutical composition comprising the multi-specific antibody as defined in any one of claims 1-29 and a pharmaceutically acceptable adjuvant and/or carrier.
35. The multi-specific antibody according to any one of claims 1-29 or the pharmaceutical composition according to claim 34, for use as a medicament.
36. Use of the multi-specific antibody according to any one of claims 1-29 or the pharmaceutical composition according to claim 34 for the manufacture of a medicament for the treatment of an inflammatory skin condition.
37. The use according to claim 36, wherein said inflammatory skin condition is psoriasis, psoriatic arthritis, contact dermatitis, chronic hand eczema or atopic dermatitis.