

In one aspect, the present disclosure refers to an isolated multispecific antibody comprising a first domain specifically binding IL-17A, a second domain specifically binding TNF α , and a third domain specifically binding to human serum albumin (HSA), wherein (a) said first domain comprises (i) a set of CDRs: HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 1, 2, and 3, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 12, 13, and 14, respectively; wherein said first domain selectively binds to human IL-17A over human IL-17B, IL-17C, IL-17D, IL-17E and IL-17F as measured by ELISA; and (b) said second domain comprises a set of CDRs: HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 63, 64, and 65, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 76, 77, and 78, respectively; and (c) said third domain comprises a set of CDRs: (i) HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 90, 91, and 92, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 100, 101, and 102, respectively. In one example, the present disclosure refers to isolated multispecific antibody comprising a first domain specifically binding IL-17A and a second domain specifically binding TNF α , and, optionally, a third domain specifically binding human serum albumin.

In one aspect, the present disclosure refers to a pharmaceutical composition comprising the multispecific antibody as disclosed herein and a pharmaceutically acceptable carrier.

In a further aspect, the present disclosure refers to the multispecific antibody as disclosed herein or the pharmaceutical composition as disclosed herein for use as a medicament.

In a further example, the present disclosure describes the multispecific antibody of the invention or the pharmaceutical composition of the disclosure for use in treatment of a disorder mediated by IL-17A and/or TNF α or a disorder that can be treated by inhibiting Gro- α secretion, in particular for use in the treatment of an inflammatory condition or an autoimmune disease.

In one example, the present disclosure describes the use of the multispecific antibody of the invention or the pharmaceutical composition of the disclosure for the treatment of a disorder mediated by IL-17A and/or TNF α or a disorder that

CLAIMS

1. An isolated multispecific antibody comprising a first domain specifically binding IL-17A, a second domain specifically binding TNF α , and a third domain specifically binding to human serum albumin (HSA), wherein
 - (a) said first domain comprises (i) a set of CDRs: HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 1, 2, and 3, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 12, 13, and 14, respectively, wherein said first domain selectively binds to human IL-17A over human IL-17B, IL-17C, IL-17D, IL-17E and IL-17F as measured by ELISA; and
 - (b) said second domain comprises a set of CDRs: HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 63, 64, and 65, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 76, 77, and 78, respectively; and
 - (c) said third domain comprises a set of CDRs: (i) HCDR1, HCDR2, and HCDR3 sequences of SEQ ID NOs: 90, 91, and 92, respectively, and LCDR1, LCDR2, and LCDR3 sequences of SEQ ID NOs: 100, 101, and 102, respectively;
2. The multispecific antibody of claim 1, wherein said antibody comprises only one domain specifically binding IL-17A and/or only one domain specifically binding TNF α , and/or, optionally, comprises only one domain specifically binding human serum albumin.
3. The multispecific antibody of claim 1 or claim 2, wherein said first domain specifically binding IL-17A, said second domain specifically binding TNF α , and said third domain specifically binding to HSA are capable of binding to their respective antigens IL-17A, TNF α and HSA simultaneously.
4. The multispecific antibody of any one of the preceding claims, wherein said antibody has the following properties
 - (a) has a melting temperature (T_m), determined by differential scanning fluorimetry, of at least 60°C in phosphate-citrate buffer at pH 6.4, 150 mM NaCl;

- (b) has a loss in monomer content, after five consecutive freeze-thaw cycles, of less than 1%, when said multispecific antibody is at a starting concentration of 10 mg/ml in phosphate buffered saline (PBS), pH 7.4;
- (c) has a loss in monomer content, after storage for at least two weeks at 4°C, of less than 5%, when said multispecific antibody is at a starting concentration of 10 mg/ml in phosphate buffered saline (PBS), pH 7.4; and/or
- (d) has a loss in monomer content, after storage for at least two weeks at 37°C, of less than 15%, when said multispecific antibody is at a starting concentration of 10 mg/ml in phosphate buffered saline (PBS), pH 7.4.

5. The multispecific antibody of any one of the preceding claims, wherein said first domain and/or said second domain, and/or said third domain, comprise(s) a heavy chain variable region VH and wherein said VH is VH3 or VH4.

6. The multispecific antibody of any one of the preceding claims, wherein said first domain and/or said second domain, and/or said third domain, comprise(s) a light chain variable region VL and wherein said VL comprises V κ frameworks FR1, FR2 and FR3, particularly V κ 1 or V κ 3 FR1 to FR3, preferably V κ 1 FR1 to FR3, and a framework FR4, which is selected from a V κ FR4, particularly V κ 1 FR4, V κ 3 FR4, and V λ FR4, particularly V λ FR4 comprising the amino acid sequence having at least 60, 70, 80, 90 percent identity to an amino acid sequence selected from any of SEQ ID NO: 26 to SEQ ID NO: 32, preferably V λ FR4 as set forth in any of SEQ ID NO: 26 to SEQ ID NO: 32, preferably V λ FR4 as set forth in SEQ ID NO: 26 or 27, more preferably V λ FR4 as set forth in SEQ ID NO: 27.

7. The multispecific antibody of claim 5 or 6, wherein said VH of the first domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence SEQ ID NO: 10; and/or said VL of the first domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence SEQ ID NO: 21, preferably wherein said VH of the first domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 10 and 11; and/or said VL of the first domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 21 and 22,

more preferably wherein said VH of the first domain is as set forth in SEQ ID NO: 10 and/or said VL of the first domain is as set forth in of SEQ ID NO: 21.

8. The multispecific antibody of any one of claims 5 to 7, wherein said VH of the second domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 72, 73, 74 or 75, preferably SEQ ID NO: 72; and/or said VL of the second domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence selected from the group consisting of SEQ ID NOs: 85, 86, 87, 88 and 89, preferably SEQ ID NO: 85, preferably wherein said VH of the second domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 72, 73, 74 or 75; and/or said VL of the second domain comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 85, 86, 87, 88 and 89, more preferably wherein said VH of the second domain is as set forth in SEQ ID NO: 72 and/or said VL of the second domain is as set forth SEQ ID NO: 85.

9. The multispecific antibody of any one of claims 5 to 8, wherein said VH of the third domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence SEQ ID NO: 99; and/or said VL of the third domain comprises an amino acid sequence that is at least 90 percent identical to the amino acid sequence SEQ ID NO: 108, preferably wherein said VH of the third domain is as set forth in sequence of SEQ ID NO: 99 and/or a VL of the third domain is as set forth in SEQ ID NO: 108

10. The multispecific antibody of any one of the preceding claims, wherein said multispecific antibody is in a format selected from the group consisting of a single-chain diabody (scDb), a tandem scDb (Tandab), a linear dimeric scDb (LD-scDb), a circular dimeric scDb (CD-scDb), a bispecific T-cell engager (BiTE; tandem di-scFv), a tandem tri-scFv, a tribody (Fab-(scFv)₂) or bibody (Fab-(scFv)₁), Fab, Fab-Fv₂, Morrison (IgG CH3-scFv fusion (Morrison L) or IgG CL-scFv fusion (Morrison H)), triabody, scDb-scFv, bispecific Fab₂, di-miniantibody, tetrabody, scFv-Fc-scFv fusion, scFv-HSA-scFv fusion, di-diabody, DVD-Ig, COVD, IgG-scFab, scFab-dsscFv, Fv₂-Fc, IgG-scFv fusions, such as bsAb (scFv linked to C-terminus of light chain), Bs1Ab (scFv linked to N-terminus of light chain), Bs2Ab (scFv linked to N-terminus of heavy chain), Bs3Ab (scFv linked to C-terminus of heavy chain), Ts1Ab (scFv linked to N-terminus of both heavy

chain and light chain), Ts2Ab (dsScFv linked to C-terminus of heavy chain), Bispecific antibodies based on heterodimeric Fc domains, such as Knob-into-Hole antibodies (KiHs); an Fv, scFv, scDb, tandem-di-scFv, tandem tri-scFv, Fab-(scFv)₂, Fab-(scFv)₁, Fab, Fab-Fv₂, COVD fused to the N- and/or the C-terminus of either chain of a heterodimeric Fc domain or any other heterodimerization domain, a MATCH and DuoBodies, preferably is tribody or scDb-scFv.

11. The multispecific antibody of any of the preceding claims, wherein the antibody comprises an amino acid sequence having at least 80% identity, preferably at least 90% identity, to the sequence selected from any of SEQ ID NOs: 136, 137, 138, 139, 140, 141, 142, 143, 144, preferably to the sequence of SEQ ID NO: 143.

12. The multispecific antibody of claim 11, wherein the antibody comprises (a) a combination of amino acid sequences selected from any of: SEQ ID NO: 136 and SEQ ID NO: 137; SEQ ID NO: 138 and SEQ ID NO: 139; and SEQ ID NO: 140 and SEQ ID NO: 141; or an amino acid sequence selected from any of SEQ ID NOs: 142, 143, and 144.

13. The multispecific antibody of claim 12, wherein the antibody comprises the amino acid sequence of SEQ ID NO: 143.

14. A pharmaceutical composition comprising the multispecific antibody of any one of the preceding claims and a pharmaceutically acceptable carrier.

15. The multispecific antibody of any one of claims 1 to 13, or the pharmaceutical composition of claim 14, for use as a medicament.

16. A kit comprising the multispecific antibody of any one of claims 1 to 13, or the pharmaceutical composition of claim 14.