

Claims:

1. An antibody or antibody fragment that specifically binds human thymic stromal lymphopoietin (TSLP) selected from any one of the following:

a) an antibody or antibody fragment that comprises:

a heavy chain complementarity determining region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 4;

a heavy chain complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 2;

a heavy chain complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 3;

a light chain complementarity determining region 1 (LCDR1) comprising the amino acid sequence of SEQ ID NO: 11;

a light chain complementarity determining region 2 (LCDR2) comprising the amino acid sequence of SEQ ID NO: 12; and

a light chain complementarity determining region 3 (LCDR3) comprising the amino acid sequence of SEQ ID NO: 13,

wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are defined according to the Kabat numbering scheme;

b) an antibody or antibody fragment that comprises:

a HCDR1 comprising the amino acid sequence of SEQ ID NO: 5;

a HCDR2 comprising the amino acid sequence of SEQ ID NO: 6;

a HCDR3 comprising the amino acid sequence of SEQ ID NO: 3;

a LCDR1 comprising the amino acid sequence of SEQ ID NO: 14;

a LCDR2 comprising the amino acid sequence of SEQ ID NO: 15;

and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,

wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are defined according to the Chothia numbering scheme;
and

c) an antibody or antibody fragment that comprises

a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1;

a HCDR2 comprising the amino acid sequence of SEQ ID NO: 2;

a HCDR3 comprising the amino acid sequence of SEQ ID NO: 3;

a LCDR1 comprising the amino acid sequence of SEQ ID NO: 11;

a LCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and

a LCDR3 comprising the amino acid sequence of SEQ ID NO: 13,
wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are defined according to the combination of the Chothia and Kabat numbering schemes.

2. The antibody or antibody fragment of claim 1 that comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7, and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 17.

3. The antibody or antibody fragment of claim 1 that comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 22, and a light chain comprising the amino acid sequence of SEQ ID NO: 25;

4. The antibody or antibody fragment of claim 1 that comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 9, and a light chain comprising the amino acid sequence of SEQ ID NO: 19;

5. The antibody or antibody fragment of any of claims 1-4, wherein the antibody or antibody fragment comprises a paratope comprising at least one of the following residues: Thr28, Asp31, Tyr32, Trp33, Asp56, Glu101, 11e102, Tyr103, Tyr104, Tyr105 of a heavy chain sequence of SEQ ID NO:22 or Gly28, Ser29, Lys30, Tyr31, Tyr48, Asp50, Asn51, Glu52, Asn65, and Trp92 of a light chain sequence of SEQ ID NO:25.

6. The antibody of any of claims 1-5, wherein the antibody is a monoclonal antibody.

7. The antibody fragment of any of claims 1-5, wherein the antibody fragment is selected from a Fab, Fab', F(ab')₂, scFv, minibody, or diabody.

8. The antibody fragment of any of claims 1-5, wherein the antibody fragment is a Fab.

9. The antibody fragment of claim 8, wherein the antibody fragment is a human or humanized Fab.

10. The antibody of any of claims 1-6, wherein the antibody is a human immunoglobulin.

11. The antibody or antibody fragment of any of claims 1-10, wherein the antibody or antibody fragment binds human TSLP with a dissociation constant (K_D) of less than 100 pM.

12. The antibody or antibody fragment of any of claims 1-11, wherein the antibody or antibody fragment binds human TSLP with a dissociation constant (K_D) of less than 10 pM.

13. A pharmaceutical composition comprising the antibody or antibody fragment of any of claims 1-12 and at least one pharmaceutically acceptable excipient.

14. The pharmaceutical composition of claim 13, wherein the antibody or antibody fragment is 5% to 95%, or 10% to 90%, or 15% to 85%, or 20% to 80%, or 25% to 75%, or 30% to 70%, or 40 % to 60%, or 40-50% (w/w) of the composition.

15. The pharmaceutical composition of any of claims 13-14, wherein the composition comprises a shell-forming agent.

16. The pharmaceutical composition of claim 15, wherein the shell-forming agent is trileucine or leucine.

17. The pharmaceutical composition of claim 16, wherein the trileucine or leucine is about 10-75% (w/w) of the composition.

18. The pharmaceutical composition of claim 17, wherein the trileucine is about 10-30% (w/w) of the composition, or wherein the leucine is about 50-75% (w/w) of the composition.

19. The pharmaceutical composition of any of claims 13-18, wherein the composition comprises at least one glass-forming excipient.

20. The pharmaceutical composition of claim 19, wherein the at least one glass-forming excipient is selected from histidine, trehalose, mannitol, sucrose, or sodium citrate.

21. The pharmaceutical composition of claim 20, wherein the at least one glass-forming excipient is selected from trehalose or a mixture of trehalose and mannitol.

22. The pharmaceutical composition of any of claims 19-21, wherein the glass-forming excipient is about 15-35% (w/w) of the composition.

23. The pharmaceutical composition of any of claims 13-22, wherein the composition comprises a buffer.

24. The pharmaceutical composition of claim 23, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

25. The pharmaceutical composition of any of claims 23-24, wherein the buffer is about 5-13% of the composition.

26. The pharmaceutical composition of any of claims 13-25, wherein the composition is formulated as a dry powder formulation.

27. The pharmaceutical composition of claim 26, wherein the composition is formulated as a dry powder formulation suitable for inhalation.

28. The pharmaceutical composition of claim 13, wherein the composition comprises: spray-dried particles comprising a shell and a core, wherein the shell comprises trileucine or leucine and the core comprises:

- i) the antibody or antibody fragment, trehalose, mannitol, and a buffer; or
- ii) the antibody or antibody fragment, trehalose, buffer, and HCl.

29. The pharmaceutical composition of claim 28, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

30. A pharmaceutical composition comprising spray-dried particles comprising:

i) a core comprising trehalose, mannitol, histidine, and a TSLP-binding antibody or antibody fragment, or a core comprising trehalose, histidine, HCl, and a TSLP-binding antibody or antibody fragment, wherein the TSLP-binding antibody or antibody fragment is an antibody Fab comprising:

- a) a HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 11; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 13, wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are defined according to the Kabat numbering scheme; or
- b) a HCDR1 comprising the amino acid sequence of SEQ ID NO: 5; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 6; a

HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; a

LCDR1 comprising the amino acid sequence of SEQ ID NO: 14; a

LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and

a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16,
wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are defined
according to the Chothia numbering scheme; or

c) a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; a

HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; a

HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; a

LCDR1 comprising the amino acid sequence of SEQ ID NO: 11; a

LCDR2 comprising the amino acid sequence of SEQ ID NO: 12; and

a LCDR3 comprising the amino acid sequence of SEQ ID NO: 13,
wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2 and LCDR3 are
defined according to the combination of the Chothia and Kabat numbering
schemes; and

ii) a shell comprising trileucine or leucine.

31. The pharmaceutical composition of claim 30 comprising:

a) 40% (w/w) TSLP-binding antibody or antibody fragment , 25% (w/w) trileucine, 30%
(w/w) combined weight of trehalose and mannitol, and 5% (w/w) histidine;

b) 50% (w/w) TSLP-binding antibody or antibody fragment , 15% (w/w) trileucine, 2.6%
(w/w) HCl, 5.6% (w/w) histidine, and 26.8% (w/w) combined weight of trehalose and a base; or

c) 50% (w/w) TSLP-binding antibody or antibody fragment , 15% (w/w) trileucine,
19.4% (w/w) trehalose, 13.04% (w/w) histidine, and 2.56% (w/w) HCl.

32. A kit comprising the antibody or antibody fragment of any of claims 1-12, or the pharmaceutical composition of any of claims 13-31, and a device for delivering the antibody or antibody fragment or pharmaceutical composition to a subject.

33. The kit of claim 32, wherein the device delivers the antibody or antibody fragment or pharmaceutical composition in an aerosolized form.

34. The kit of claim 32, wherein the device is a dry powder inhaler.

35. The antibody or antibody fragment of any one of claims 1-12, or the pharmaceutical composition of any one of claims 13-31 for use in treating a TSLP-related condition in a subject in need thereof, wherein the TSLP-related inflammatory condition is selected from asthma, chronic obstructive pulmonary disease, allergic rhinitis, allergic rhinosinusitis, allergic conjunctivitis, eosinophilic esophagitis, and atopic dermatitis..

36. Use of the antibody or antibody fragment of any one of claims 1-12 in the manufacture of a medicament for use in the treatment of a TSLP-related condition in a subject in need thereof, wherein the TSLP-related inflammatory condition is selected from asthma, chronic obstructive pulmonary disease, allergic rhinitis, allergic rhinosinusitis, allergic conjunctivitis, eosinophilic esophagitis, and atopic dermatitis.

37. The use of claim 36, wherein the TSLP-related inflammatory condition is asthma.

38. The use of claims 36 to 37, wherein the medicament is formulated as a dry powder formulation suitable for inhalation.

39. The use of claims 36 to 38, wherein the medicament is to be administered to the subject orally or intranasally.

40. The use of claims 36 to 39, wherein the medicament is to be administered to the subject in an aerosolized form.

41. The use of claims 36 to 40, wherein the medicament is to be administered to the subject by a dry powder inhaler.

42. The Use of claims 36 to 41, wherein the subject is a human.

43. The use of claim 36 to 42, wherein a second agent is to be administered to the subject.

44. The use of claim 43, wherein the second agent is selected from the group consisting of corticosteroids, bronchodilators, antihistamines, antileukotrienes, and PDE-4 inhibitors.

45. A nucleic acid encoding the antibody or antibody fragment of any of claims 1-12.

46. The nucleic acid of claim 45, comprising:

- a) SEQ ID NO: 8;
- b) SEQ ID NO: 18;
- c) SEQ ID NO: 8 and SEQ ID NO: 18;
- d) SEQ ID NO: 10;
- e) SEQ ID NO: 20;
- f) SEQ ID NO: 10 and SEQ ID NO: 20;
- g) SEQ ID NO: 21;
- h) SEQ ID NO: 24;
- i) SEQ ID NO: 21 and SEQ ID NO: 24;
- j) SEQ ID NO: 23;
- k) SEQ ID NO: 26; or
- l) SEQ ID NO: 23 and SEQ ID NO: 26.

47. A vector comprising the nucleic acid of any of claims 45-46.

48. A host cell comprising the nucleic acid of any of claims 45-46 or the vector of claim 47.

49. A method of producing the antibody or antibody fragment of any of claims 1-12, the method comprising:

culturing a host cell expressing a nucleic acid encoding the antibody or antibody fragment; and

collecting the antibody or antibody fragment from the culture medium.

50. A method for making a dry powder formulation comprising the antibody or antibody fragment of any of claims 1-12, the method comprising:

(a) providing an aqueous solution comprising the antibody or antibody fragment of any of claims 1-12, trileucine or leucine, a glass forming excipient, and a buffer;

(b) spray drying the aqueous solution of step (a) at a temperature between about 120°C to about 200°C (inlet) range and 55°C to about 75 °C (outlet) range to produce dry powder particles; and

(c) collecting the dry power particles.

51. The method of claim 50, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

52. The method of any of claims 50 or 51, wherein the glass forming excipient is selected from histidine, histidine HCl, trehalose, mannitol, sucrose, or sodium citrate.

53. The pharmaceutical composition of claim 13, wherein the excipient : antibody or antibody fragment mass ratio is greater than 0.5.