

CLAIMS:

1. A molecule that specifically binds human thymic stromal lymphopoietin (TSLP) selected from any one of the following:

a) a molecule 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;

b) a molecule 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; and

c) a molecule 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.

2. The molecule 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 molecule 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 molecule 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 molecule of any of claims 1-4, wherein the molecule comprises a paratope comprising at least one of the following residues: Thr28, Asp31, Tyr32, Trp33, Asp56, Glu101, Ile102, 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. A molecule that specifically binds an epitope in human TSLP, wherein the epitope comprises at least one of the following residues: Lys38, Ala41, Leu44, Ser45, Thr46, Ser48, Lys49, Ile52, Thr53, Ser56, Gly57, Thr58, Lys59, Lys101, Gln145, and Arg149 of SEQ ID NO: 38.

7. The molecule of claim 6, wherein the epitope comprises at least one of the following sets of residues of SEQ ID NO: 38:

- (a) Lys49 and Ile52,
- (b) Gly57 and Lys59,
- (c) Lys101,
- (d) Gln145 and Arg149.

8. The molecule of any of claims 1-7, wherein the molecule is a monoclonal antibody.

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

10. The molecule of any of claims 1-7, wherein the molecule is a Fab.

11. The molecule of claim 10, wherein the molecule is a human or humanized Fab.

12. The molecule of any of claims 1-8, wherein the molecule is a human immunoglobulin.

13. The molecule of any of claims 1-12, wherein the molecule binds human TSLP with a dissociation constant (K_D) of less than 100 pM.

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

15. A pharmaceutical composition comprising the molecule of any of claims 1-14 and at least one pharmaceutically acceptable excipient.

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

17. The pharmaceutical composition of any of claims 15-16, wherein the composition comprises a shell-forming agent.

18. The pharmaceutical composition of claim 17, wherein the shell-forming agent is trileucine or leucine.

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

20. The pharmaceutical composition of claim 19, 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.

21. The pharmaceutical composition of any of claims 15-20, wherein the composition comprises at least one glass-forming excipient.

22. The pharmaceutical composition of claim 21, wherein the at least one glass-forming excipient is selected from histidine, trehalose, mannitol, sucrose, or sodium citrate.

23. The pharmaceutical composition of claim 22, wherein the at least one glass-forming excipient is selected from trehalose or a mixture of trehalose and mannitol.

24. The pharmaceutical composition of any of claims 21-23, wherein the glass-forming excipient is about 15-35% (w/w) of the composition.

25. The pharmaceutical composition of any of claims 15-24, wherein the composition comprises a buffer.

26. The pharmaceutical composition of claim 25, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

27. The pharmaceutical composition of any of claims 25-26, wherein the buffer is about 5-13% of the composition.

28. The pharmaceutical composition of any of claims 15-27, wherein the composition is formulated as a dry powder formulation.

29. The pharmaceutical composition of claim 28, wherein the composition is formulated as a dry powder formulation suitable for inhalation.

30. The pharmaceutical composition of claim 11, 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 molecule, trehalose, mannitol, and a buffer; or
- ii) the molecule, trehalose, buffer, and HCl.

31. The pharmaceutical composition of claim 30, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

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

i) a core comprising trehalose, mannitol, histidine, and a TSLP-binding molecule, or a core comprising trehalose, histidine, HCl, and a TSLP-binding molecule, wherein the TSLP-binding molecule 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; 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; 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; and
- ii) a shell comprising trileucine or leucine.

33. The pharmaceutical composition of claim 32 comprising:

- a) 40% (w/w) TSLP-binding molecule, 25% (w/w) trileucine, 30% (w/w) combined weight of trehalose and mannitol, and 5% (w/w) histidine;
- b) 50% (w/w) TSLP-binding molecule, 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 molecule, 15% (w/w) trileucine, 19.4% (w/w) trehalose, 13.04% (w/w) histidine, and 2.56% (w/w) HCl.

34. A kit comprising the molecule of any of claims 1-14, or the pharmaceutical composition of any of claims 15-33, and a device for delivering the molecule or pharmaceutical composition to a subject.

35. The kit of claim 34, wherein the device delivers the molecule or pharmaceutical composition in an aerosolized form.

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

37. The molecule of any one of claims 1-14, or the pharmaceutical composition of any one of claims 15-33 for use in treating a TSLP-related condition in a subject in need thereof.

38. Use of the molecule of any one of claims 1-14 in the manufacture of a medicament for use in the treatment of a TSLP-related condition in a subject in need thereof.

39. The use of claim 38, 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.

40. The use of claim 38, wherein the TSLP-related inflammatory condition is asthma.

41. The use of claims 38 to 40, wherein the medicament is formulated as a dry powder formulation suitable for inhalation.

42. The use of claims 38 to 41, wherein the medicament is to be administered to the subject orally or intranasally.

43. The use of claims 38 to 42, wherein the medicament is to be administered to the subject in an aerosolized form.

44. The use of claims 38 to 43, wherein the medicament is to be administered to the subject by a dry powder inhaler.

45. use of claims 38 to 44, wherein the subject is a human.

46. The use of claim 38 to 45 further comprising the administration of a second agent to the subject.

47. The use of claim 46, wherein the second agent is selected from the group consisting of corticosteroids, bronchodilators, antihistamines, antileukotrienes, and PDE-4 inhibitors.

48. A nucleic acid encoding the molecule of any of claims 1-14, or a fragment thereof.

49. The nucleic acid of claim 48, 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.

50. A vector comprising the nucleic acid of any of claims 48-49.

51. A host cell comprising the nucleic acid of any of claims 48-49 or the vector of claim 50.

52. A method of producing the molecule of any of claims 1-14, the method comprising: culturing a host cell expressing a nucleic acid encoding the molecule; and collecting the molecule from the culture medium.

53. A method for making a dry powder formulation comprising the molecule of any of claims 1-14, the method comprising:

(a) providing an aqueous solution comprising the molecule of any of claims 1-14, 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.

54. The method of claim 53, wherein the buffer is selected from a histidine, glycine, acetate, or phosphate buffer.

55. The method of any of claims 53 or 54, wherein the glass forming excipient is selected from histidine, histidine HCl, trehalose, mannitol, sucrose, or sodium citrate.

56. The pharmaceutical composition of claim 15, wherein the excipient:molecule mass ratio is greater than 0.5.