

WHAT IS CLAIMED IS:

1. An isolated IL-33 protein or an active fragment thereof stabilized in a reduced form by a modification that reduces or eliminates the formation of disulphide bridges between the native cysteines within the IL-33 protein.
2. An isolated IL-33 protein or an active fragment thereof stabilized in a reduced form by a modification wherein
 - (i) one or more native cysteines is replaced with an alternative amino acid;
 - (ii) one or more native cysteines is deleted;
 - (iii) one or more native cysteines is conjugated to a chemical entity.
3. The isolated IL-33 protein or an active fragment thereof according to claim 1 or 2, wherein the protein is mutated such that one or more cysteines are replaced with a non-cysteine amino acid, for example wherein one, two, three or four cysteines selected from Cys-208, Cys-227, Cys-232 and Cys-259 are replaced.
4. The isolated IL-33 protein or an active fragment thereof according to claim 3, wherein one or more cysteine residues is/are replaced by a serine residue.
5. An isolated antibody or antigen-binding fragment thereof which attenuates or inhibits activity of redIL-33 protein.
6. The isolated antibody or antigen-binding fragment thereof according to claim 5, which catalyzes oxidation of redIL-33 to IL-33 DSB.
7. The isolated antibody or antigen-binding fragment thereof according to claim 6, wherein the molecule binds IL-33-DSB.
8. The isolated antibody or antigen-binding fragment thereof according to any one of claims 5 to 7, which comprises an antibody or antigen-binding fragment thereof.

9. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 to 8, comprising a variable heavy domain (VH) and a variable light domain (VL) having VH CDRs 1-3 of SEQ ID NO:183, SEQ ID NO: 184 and SEQ ID NO: 185, wherein one or more VHCDRs have 3 or fewer single amino acid substitutions.
10. The isolated antibody or antigen-binding fragment thereof of claim 8, comprising VHCDRs 1-3 of SEQ ID NO:183, SEQ ID NO: 184 and SEQ ID NO: 185.
11. The isolated antibody or antigen-binding fragment thereof of any one of claims 5-10, comprising a VL and a VH having VLCDRs 1-3 of SEQ ID NO:188, SEQ ID NO: 189 and SEQ ID NO: 190, wherein one or more VLCDRs have 3 or fewer single amino acid substitutions.
12. The isolated antibody or antigen-binding fragment thereof of claim 11, comprising VLCDRs 1-3 of SEQ ID NO:188, SEQ ID NO: 189 and SEQ ID NO: 190.
13. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 to 12, comprising a VHCDR1 having the sequence of SEQ ID NO: 183, a VHCDR2 having the sequence of SEQ ID NO: 184, a VHCDR3 having the sequence of SEQ ID NO: 185, a VLCDR1 having the sequence of SEQ ID NO: 188, a VLCDR2 having the sequence of SEQ ID NO: 189, and a VLCDR3 having the sequence of SEQ ID NO: 190.
14. The isolated antibody or antigen-binding fragment thereof which specifically binds to IL-33 of any one of claims 5 to 13, wherein the VH and VL of said antibody or antigen-binding fragment thereof comprise amino acid sequences at least 95%, 90%, or 85% identical to SEQ ID NO: 182 and SEQ ID NO: 187, respectively.
15. The antibody or antigen-binding fragment thereof according to claim 14, comprising a VH having the sequence of SEQ ID NO: 182 and a VL having the sequence of SEQ ID NO: 187.
16. The isolated antibody or antigen-binding fragment thereof according to claim 5, wherein said molecule binds to the IL-33 protein of any one of claims 1 to 4.

17. The isolated antibody or antigen-binding fragment thereof according to claim 5 or 16, wherein said molecule is cross-reactive to wild-type redIL-33.
18. The isolated antibody or antigen-binding fragment thereof according to claim 17, which specifically binds wild-type redIL-33.
19. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 or 16 to 18 comprising a variable heavy domain (VH) and a variable light domain (VL) having VH CDRs of SEQ ID NO: 543, SEQ ID NO: 544 and SEQ ID NO: 545, wherein one or more of the VHCDRs have 3 or fewer single amino acid substitutions.
20. The isolated antibody or antigen-binding fragment thereof of claim 19, comprising VHCDRs 1-3 of SEQ ID NO: 543, SEQ ID NO: 544 and SEQ ID NO: 545.
21. The isolated antibody or antigen-binding fragment thereof of any one of claims 5, 16 to 20, comprising a VL and a VH having VLCDRs 1-3 of SEQ ID NO: 548, SEQ ID NO: 549 and SEQ ID NO: 550, wherein one or more VLCDRs have 3 or fewer single amino acid substitutions.
22. The isolated antibody or antigen-binding fragment thereof of claim 21, comprising VLCDRs 1-3 of SEQ ID NO: 548, SEQ ID NO: 549 and SEQ ID NO: 550.
23. The isolated antibody or antigen-binding fragment thereof of claims 20 and 22, comprising a VHCDR1 having the sequence of SEQ ID NO: 543, a VHCDR2 having the sequence of SEQ ID NO: 544, a VHCDR3 having the sequence of SEQ ID NO: 545, a VLCDR1 having the sequence of SEQ ID NO: 548, a VLCDR2 having the sequence of SEQ ID NO: 549, and a VLCDR3 having the sequence of SEQ ID NO: 550.
24. The isolated antibody or antigen-binding fragment thereof according to claim 23 which specifically binds to IL-33, wherein the VH and VL of said antibody or

antigen-binding fragment thereof comprise amino acid sequences at least 95%, 90%, or 85% identical to SEQ ID NO: 542 and SEQ ID NO: 547, respectively.

25. The antibody or antigen-binding fragment thereof according to claim 24, comprising a VH having the sequence of SEQ ID NO: 542 and a VL having the sequence of SEQ ID NO: 547.
26. An isolated antibody or antigen-binding fragment thereof which attenuates activity of IL-33DSB protein.
27. The isolated antibody or antigen-binding fragment thereof according to claim 26, which prevents or reduces binding of IL-33 DSB to receptor for advanced glycation end products (RAGE).
28. The isolated antibody or antigen-binding fragment thereof of claim 26 or 27, which comprises an antibody or antigen binding fragment thereof.
29. The isolated antibody or antigen-binding fragment thereof of any one of claims 25 to 27, wherein the binding molecule is that of any one of claims 5 to 8 and 16 to 25.
30. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 to 29 or an antigen-binding fragment thereof, which is selected from the group consisting of a human antibody, a chimeric antibody, and a humanized antibody.
31. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 to 29 or the antibody or an antigen-binding fragment thereof, which is selected from the group consisting of a naturally-occurring antibody, an scFv fragment, an Fab fragment, an F(ab')₂ fragment, a minibody, a diabody, a triabody, a tetrabody, and a single chain antibody.
32. The isolated antibody or antigen-binding fragment thereof of any one of claims 5 to 29, or an antibody or antigen-binding fragment thereof, which is a monoclonal antibody.

33. A polynucleotide encoding the binding molecule of any one of claims 5 to 32 or an antibody or antigen-binding fragment thereof.
34. A polynucleotide encoding the VH of the binding molecule of any one of claims 5 to 32, antigen-binding fragment thereof.
35. A polynucleotide encoding the VL of the binding molecule of any one of claims 5 to 32, antigen-binding fragment thereof.
36. A vector comprising the polynucleotide of any one of claims 33 to 35.
37. A composition comprising the polynucleotide of any one of claims 33 to 35 or the vector of claim 36.
38. A host cell comprising the polynucleotide of any one of claims 33 to 35 or the vector of claim 36.
39. A host cell comprising at least a first and a second vector, wherein said first and said second vectors are non-identical, wherein said first vector comprises the polynucleotide of claim 34, which encodes an immunoglobulin heavy chain variable region, and wherein said second vector comprises the polynucleotide of claim 35 which encodes an immunoglobulin light chain variable region.
40. A method of producing an anti-IL33 antibody or antigen-binding fragment thereof, comprising culturing the host cell of claim 38 or 39, and recovering said antibody or antigen-binding fragment thereof.
41. An anti-IL33 antibody or antigen-binding fragment thereof, produced by the method of claim 40.
42. A method for detecting redIL-33 expression in a sample comprising:
 - (a) isolating a cell-containing sample;

- (b) contacting said sample with the binding molecule of any one of claims 5 to 32, or an antigen-binding fragment thereof; and
 - (c) detecting binding of said binding molecule in said sample.
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- 43. A pharmaceutical composition comprising the binding molecule of any one of claims 5 to 32 or an antigen-binding fragment thereof and a carrier.
 - 44. A combination product comprising the binding molecule of any one of claims 5 to 32 or an antigen-binding fragment thereof and a second therapeutic agent.
 - 45. Use of the binding molecule of any one of claims 5 to 32 or an antigen-binding fragment thereof or the pharmaceutical composition of claim 43 or the combination product of claim 44 in therapy.
 - 46. The use of an isolated antibody or antigen-binding fragment thereof as defined in any one of claims 5 to 32 or the composition of claim 43 in the manufacture of a medicament for the treatment of a subject with an inflammatory condition comprising administering to the subject an effective amount of.
 - 47. The use according to claim 46, wherein the isolated antibody or antigen-binding fragment thereof inhibits IL-33 driven cytokine production.
 - 48. The use according to claim 46 or 47, wherein the isolated antibody or antigen-binding fragment thereof inhibits RAGE mediated effects.
 - 49. The use according to any one of claims 46 to 48 wherein the isolated antibody or antigen-binding fragment thereof inhibits IL-33 driven cytokine production and/or RAGE mediated effects.
 - 50. The use of any one of claims 46 to 49 wherein said inflammatory condition is an allergic disorder.

51. The use of any one of claims 46 to 49, wherein said inflammatory condition is asthma or COPD.
52. The use of claim 46 to 49, wherein said inflammatory response is in the airway of said subject.
53. A method of identifying a therapeutic antibody or antigen-binding fragment thereof comprising selecting for an antibody or antigen-binding fragment thereof that binds to redIL-33, wherein said antibody or antigen-binding fragment thereof attenuates activity of redIL-33 protein.
54. The method of claim 53, wherein said therapeutic antibody or antigen-binding fragment thereof is selected from the group consisting of a human antibody, a chimeric antibody, and a humanized antibody.
55. The method of claim 53 or 54, wherein said therapeutic antibody or antigen-binding fragment thereof is selected from the group consisting of a naturally-occurring antibody, an scFv fragment, an Fab fragment, an F(ab')₂ fragment, a minibody, a diabody, a triabody, a tetrabody, and a single chain antibody.
56. The method of any one of claims 53 to 55, wherein said therapeutic antibody or antigen-binding fragment thereof is a monoclonal antibody.
57. The method of any one of claims 53 to 56, wherein said therapeutic antibody or antigen-binding fragment thereof is effective for treating or preventing an inflammatory condition in a subject.
58. The method of claim 57, wherein said inflammatory condition is asthma or chronic obstructive pulmonary disease.