

CLAIMS:

1. ~~—— An isolated immunoglobulin heavy chain polypeptide which comprises (a) an amino acid sequence of any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217, or (b) an amino acid sequence that is at least 90% identical to any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217.~~

2. ~~—— An isolated immunoglobulin heavy chain polypeptide which binds to the same IL-33 epitope as the immunoglobulin heavy chain polypeptide of claim 1.~~

3. ~~—— An isolated immunoglobulin light chain polypeptide which comprises (a) an amino acid sequence of any one of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231, or (b) an amino acid sequence that is at least 90% identical to any one of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231.~~

4. ~~—— An isolated immunoglobulin light chain polypeptide which binds to the same IL-33 epitope as the immunoglobulin light chain polypeptide of claim 3.~~

5. ~~—— An isolated or purified nucleic acid sequence encoding the isolated immunoglobulin heavy chain polypeptide of claim 1 or claim 2.~~

6. ~~—— An isolated or purified nucleic acid sequence encoding the isolated immunoglobulin light chain polypeptide of claim 3 or claim 4.~~

7. ~~—— A vector comprising the isolated or purified nucleic acid molecule of claim 5 or claim 6.~~

81. An isolated interleukin-33 (IL-33)-binding agent comprising (a) the an immunoglobulin heavy chain variable region of SEQ ID NO: 136 or at least the CDRs thereof; polypeptide of claim 1 and/or (b) the an immunoglobulin light chain variable region of SEQ ID NO: 171 or at least the CDRs thereof; polypeptide of claim 2.

2. An isolated IL-33 binding agent, which comprises (a) an immunoglobulin heavy chain variable region of SEQ ID NO: 136; and (b) an immunoglobulin light chain variable region of SEQ ID NO: 171.

93. The isolated IL-33-binding agent of claim 81, which is an antibody, an antibody conjugate, or an antigen-binding fragment thereof.

104. The isolated IL-33-binding agent of claim 81, which is an antibody fragment selected from F(ab')₂, Fab', Fab, Fv, scFv, dsFv, dAb, and a single chain binding polypeptide.

5. The isolated IL-33-binding agent of claim 1, wherein the binding agent is an IgG1 antibody.

6. The isolated IL-33-binding agent of claim 1, wherein the IL-33-binding agent binds to IL-33 with a K_D from 1 picomolar (pM) to 1 nanomolar (nM).

7. The isolated IL-33-binding agent of claim 2, which is an antibody, an antibody conjugate, or an antigen-binding fragment thereof.

8. The isolated IL-33-binding agent of claim 2, which is an antibody fragment selected from F(ab')₂, Fab', Fab, Fv, scFv, dsFv, dAb, and a single chain binding polypeptide.

9. The isolated IL-33-binding agent of claim 2, wherein the binding agent is an IgG1 antibody.

10. The isolated IL-33-binding agent of claim 2, wherein the IL-33-binding agent binds to IL-33 with a K_D from 1 picomolar (pM) to 1 nanomolar (nM).

11. The isolated IL-33 binding agent of claim 8, which comprises an immunoglobulin heavy chain polypeptide of SEQ ID NO: 136 and an immunoglobulin light chain polypeptide of SEQ ID NO: 171.

12. — ~~An isolated IL-33 binding agent which comprises at least one complementarity determining region (CDR) of an immunoglobulin heavy chain variable region comprising any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217.~~

13. — ~~The isolated IL-33 binding agent of claim 12, which comprises one CDR of an immunoglobulin heavy chain variable region comprising any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217.~~

14. — ~~The isolated IL-33 binding agent of claim 12, which comprises two CDRs of an immunoglobulin heavy chain variable region comprising any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217.~~

15. — ~~The isolated IL-33 binding agent of claim 12, which comprises three CDRs of an immunoglobulin heavy chain variable region comprising any one of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NOs: 5-50, SEQ ID NOs: 67-140, SEQ ID NO: 176, SEQ ID NO: 177, SEQ ID NOs: 178-188, and SEQ ID NOs: 206-217.~~

16. — ~~An isolated IL-33 binding agent which comprises at least one CDR of an immunoglobulin light chain variable region comprising any one of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231.~~

17. — ~~The isolated IL-33 binding agent of claim 16, which comprises one CDR of an immunoglobulin light chain variable region comprising any one of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231.~~

18. — ~~The isolated IL-33 binding agent of claim 16, which comprises two CDRs of an immunoglobulin light chain variable region comprising any one of SEQ ID NO: 3, SEQ ID NO:~~

4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231.

19. — The isolated IL-33 binding agent of claim 16, which comprises three CDRs of an immunoglobulin light chain variable region comprising any one of SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NOs: 51-66, SEQ ID NOs: 141-175, SEQ ID NOs: 189-205, and SEQ ID NOs: 218-231.

2011. An isolated or purified nucleic acid ~~sequence~~ encoding the IL-33-binding agent of any one of claims ~~8-19~~1-10.

2112. A vector comprising ~~the an~~ isolated or purified nucleic acid sequence encoding the IL-33-binding agent of any one of claims 1-10~~of claim 20~~.

2213. An isolated cell comprising the vector of claim ~~21~~12.

23. — A composition comprising (a) the isolated IL-33 binding agent of any one of claims ~~8-19~~ or the vector of claim 21 and (b) a pharmaceutically acceptable carrier.

2414. Use of a composition comprising (a) the isolated IL-33-binding agent of any one of claims 1-10, or a vector comprising an isolated or purified nucleic acid sequence encoding the isolated IL-33-binding agent and (b) a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of an inflammatory disorder in a mammal~~A method of treating a disorder in a mammal that is responsive to IL-33 inhibition, which method comprises administering an effective amount of the composition of claim 23 to a mammal having a disorder that is responsive to IL-33 inhibition, whereupon the disorder is treated in the mammal.~~

25. — The method of claim 24, wherein the disorder is an inflammatory disorder.

2615. The ~~method-use~~ of claim ~~25~~14, wherein the inflammatory disorder is atopic dermatitis, allergic asthma, chronic obstructive pulmonary disease (COPD), food allergy, or fibrosis.

2716. The ~~method-use~~ of claim ~~26~~15, wherein the food allergy is a peanut allergy.

2817. Use of a composition comprising (a) the isolated IL-33-binding agent of any one of claims 1-10 or a vector comprising an isolated or purified nucleic acid sequence encoding the isolated IL-33-binding agent and (b) a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of an autoimmune disease in a mammal.~~The method of claim 24, wherein the disorder is an autoimmune disease.~~

2918. The method-use of claim 2817, wherein the autoimmune disease is Crohn's disease or rheumatoid arthritis.

3019. Use of a composition comprising (a) the isolated IL-33-binding agent of any one of claims 1-10 or a vector comprising an isolated or purified nucleic acid sequence encoding the isolated IL-33-binding agent and (b) a pharmaceutically acceptable carrier in the manufacture of a medicament for the treatment of cancer in a mammal.~~The method of claim 24, wherein the disorder is cancer.~~

3120. The method-use of claim 3019, wherein the cancer is an epithelial cancer, chronic myelogenous leukemia (CML), breast cancer, or gastrointestinal cancer.

21. A composition comprising (a) the isolated IL-33-binding agent of any one of claims 1-10, or a vector comprising an isolated or purified nucleic acid sequence encoding the isolated IL-33-binding agent and (b) a pharmaceutically acceptable carrier for use in the treatment of an inflammatory disorder, autoimmune disease or cancer in a mammal.

32. —The method of any one of claims 24-31, wherein the half life of the IL-33 binding agent in the mammal is between 30 minutes and 45 days.

33. —The method of any one of claims 24-32, wherein the IL-33 binding agent binds to IL-33 with a K_D between about 1 femtomolar (fM) and about 100 micromolar (μM).