

and it is most frequently characterized as an epithelial cytokine that promotes type 2 or T helper 2 (Th2) immune responses. There are a number of antibodies that bind to and neutralize IL-33 known in the art. For example, United States Publication No. 20160168242A1 and International Publication No. WO2015/106080A2 disclose certain
5 antibodies that bind human IL-33. However, there is a need for alternative antibodies that bind human IL-33 with high affinity and are therapeutically effective in treating allergic diseases such as atopic dermatitis. Improved affinity and superior IC₅₀ may enable dosing benefits.

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Summary

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In one aspect of the present disclosure, there is provided an antibody that binds human IL-33, comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, and wherein the amino acid sequence of LCDR1 is SEQ ID NO: 16, the amino acid sequence of LCDR2 is SEQ ID NO: 17, the amino acid sequence of LCDR3 is SEQ ID NO: 18, the amino acid sequence of HCDR1 is SEQ ID NO: 13, the amino acid sequence of HCDR2 is SEQ ID NO: 14, and the amino acid sequence of HCDR3 is SEQ ID NO: 15, and wherein Xaa at position 6 of SEQ ID NO: 13 is Ser or Phe, Xaa at position 2 of SEQ ID NO: 15 is Leu or Ile, Xaa at position 6 of SEQ ID NO: 17 is Ala or Leu, and Xaa at position 6 of SEQ ID NO: 18 is Ser or Pro.

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In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the antibody disclosed herein, and one or more pharmaceutically acceptable carriers, diluents, or excipients.

In a further aspect of the present disclosure, there is provided the antibody disclosed herein for use in therapy.

In another aspect of the present disclosure, there is provided the antibody disclosed herein for use in the treatment of one or more allergic disease.

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In a further aspect of the present disclosure, there is provided the antibody disclosed herein for use in the treatment of eosinophilic esophagitis,

scleroderma/systemic sclerosis, ulcerative colitis, or chronic obstructive pulmonary disease.

5 In another aspect of the present disclosure, there is provided the antibody disclosed herein for use in the treatment of Crohn's disease.

 In a further aspect of the present disclosure, there is provided the use of the antibody disclosed herein in the manufacture of a medicament for the treatment of one or more allergic disease.

10 In another aspect of the present disclosure, there is provided the use of the antibody disclosed herein in the manufacture of a medicament for the treatment of eosinophilic esophagitis, scleroderma/systemic sclerosis, ulcerative colitis, or chronic obstructive pulmonary disease.

 In a further aspect of the present disclosure, there is provided the use of the
15 antibody disclosed herein in the manufacture of a medicament for the treatment of Crohn's disease.

 In a further aspect of the present disclosure, there is provided a DNA molecule comprising a polynucleotide sequence encoding a HC, wherein the amino acid sequence of the HC is SEQ ID NO: 9.

20 In another aspect of the present disclosure, there is provided a DNA molecule comprising a polynucleotide sequence encoding a LC, wherein the amino acid sequence of the LC is SEQ ID NO: 10.

 In a further aspect of the present disclosure, there is provided a DNA molecule comprising a polynucleotide sequence encoding a HC having the amino acid sequence of
25 SEQ ID NO: 9, and comprising a polynucleotide sequence encoding a LC having the amino acid sequence of SEQ ID NO: 10.

 In a further aspect of the present disclosure, there is provided a mammalian cell transformed with the DNA molecule comprising a polynucleotide sequence encoding a HC, wherein the amino acid sequence of the HC is SEQ ID NO: 9 and the DNA molecule
30 comprising a polynucleotide sequence encoding a LC, wherein the amino acid sequence of the LC is SEQ ID NO: 10, wherein the cell is capable of expressing an antibody comprising a

HC given by the amino acid sequence of SEQ ID NO: 9 and a LC given by the amino acid sequence of SEQ ID NO: 10.

5 In another aspect of the present disclosure, there is provided a mammalian cell transformed with the DNA molecule comprising a polynucleotide sequence encoding a HC having the amino acid sequence of SEQ ID NO: 9, and comprising a polynucleotide sequence encoding a LC having the amino acid sequence of SEQ ID NO: 10, wherein the cell is capable of expressing an antibody comprising a HC given by the amino acid sequence of SEQ ID NO: 9 and a LC given by the amino acid sequence of SEQ ID NO: 10.

10 In a further aspect of the present disclosure, there is provided a process for producing an antibody, which antibody comprises two HCs and two LCs, in which the amino acid sequence of each of the two HCs is given by the amino acid sequence of SEQ ID NO: 9 and the amino acid sequence of each of the two LCs is given by the amino acid sequence of SEQ ID NO: 10, and which process comprises:

- 15 a. cultivating the mammalian cell disclosed herein under conditions such that the antibody expressed, and
- b. recovering the expressed antibody.

In another aspect of the present disclosure, there is provided an antibody produced by the process disclosed herein.

20 **Description**

The present invention addresses the need for an alternative antibody therapy for patients having allergic diseases such as atopic dermatitis, food allergy, allergic rhinitis, and asthma. In some embodiments, the allergic disease is atopic dermatitis. The present invention also addresses the need for an alternative antibody therapy for patients having 25 persistent inflammatory diseases including eosinophilic esophagitis, scleroderma/systemic sclerosis, ulcerative colitis, and chronic obstructive pulmonary disease. The present invention also addresses the need for an alternative antibody therapy for patients having Crohn's disease.

30 The present invention provides antibodies that bind human IL-33. In some embodiments, the antibody comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity

determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, and wherein the amino acid sequence of LCDR1 is SEQ ID NO: 16, the amino acid sequence of LCDR2 is SEQ ID NO: 17, the amino acid sequence of LCDR3 is SEQ ID NO: 18, the amino acid sequence of HCDR1 is SEQ ID NO: 13, the amino acid sequence of HCDR2 is SEQ ID NO: 14, and the amino acid sequence of HCDR3 is SEQ ID NO: 15. In some such embodiments, Xaa at position 6 of SEQ ID NO: 13 is Ser, Xaa at position 2 of SEQ ID NO: 15 is Leu, Xaa at position 6 of SEQ ID NO: 17 is ala, and Xaa at position 6 of SEQ ID NO: 18 is Ser. In other such embodiments, Xaa at position 6 of SEQ ID NO: 13 is Phe, Xaa at position 2 of SEQ ID NO: 15 is Leu, Xaa at position 6 of SEQ ID NO: 17 is Leu, and Xaa at position 6 of SEQ ID NO: 18 is Pro. In other such embodiments, Xaa at position 6 of SEQ ID NO: 13 is

WE CLAIM:

1. An antibody that binds human IL-33, comprising a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, and wherein the amino acid sequence of LCDR1 is SEQ ID NO: 16, the amino acid sequence of LCDR2 is SEQ ID NO: 17, the amino acid sequence of LCDR3 is SEQ ID NO: 18, the amino acid sequence of HCDR1 is SEQ ID NO: 13, the amino acid sequence of HCDR2 is SEQ ID NO: 14, and the amino acid sequence of HCDR3 is SEQ ID NO: 15, and wherein Xaa at position 6 of SEQ ID NO: 13 is Ser or Phe, Xaa at position 2 of SEQ ID NO: 15 is Leu or Ile, Xaa at position 6 of SEQ ID NO: 17 is Ala or Leu, and Xaa at position 6 of SEQ ID NO: 18 is Ser or Pro.
2. The antibody of Claim 1, wherein:
 - a. Xaa at position 6 of SEQ ID NO: 13 is Ser;
 - b. Xaa at position 2 of SEQ ID NO: 15 is Leu;
 - c. Xaa at position 6 of SEQ ID NO: 17 is Ala; and
 - d. Xaa at position 6 of SEQ ID NO: 18 is Ser.
3. The antibody of Claim 1, wherein:
 - a. Xaa at position 6 of SEQ ID NO: 13 is Phe;
 - b. Xaa at position 2 of SEQ ID NO: 15 is Leu;
 - c. Xaa at position 6 of SEQ ID NO: 17 is Leu; and
 - d. Xaa at position 6 of SEQ ID NO: 18 is Pro.
4. The antibody of Claim 1, wherein:
 - a. Xaa at position 6 of SEQ ID NO: 13 is Phe;
 - b. Xaa at position 2 of SEQ ID NO: 15 is Ile;
 - c. Xaa at position 6 of SEQ ID NO: 17 is Leu; and

- d. Xaa at position 6 of SEQ ID NO: 18 is Pro.
- 5. The antibody of Claim 1, wherein the amino acid sequence of the LCVR is SEQ ID NO: 4, and the amino acid sequence of the HCVR is SEQ ID NO: 3.
- 6. The antibody of Claim 1, wherein the amino acid sequence of the LCVR is SEQ ID NO: 8, and the amino acid sequence of the HCVR is SEQ ID NO: 7.
- 7. The antibody of Claim 1, wherein the amino acid sequence of the LCVR is SEQ ID NO: 12, and the amino acid sequence of the HCVR is SEQ ID NO: 11.

8. The antibody of Claim 1, comprising a light chain (LC) and a heavy chain (HC), wherein the amino acid sequence of the LC is SEQ ID NO: 2, and the amino acid sequence of the HC is SEQ ID NO: 1.
9. The antibody of Claim 1, comprising a LC and a HC, wherein the amino acid sequence of the LC is SEQ ID NO: 6, and the amino acid sequence of the HC is SEQ ID NO: 5.
10. The antibody of Claim 1, comprising a comprising a LC and a HC, wherein the amino acid sequence of the LC is SEQ ID NO: 10, and the amino acid sequence of the HC is SEQ ID NO: 9.
11. A pharmaceutical composition comprising the antibody of any one of Claims 1-10, and one or more pharmaceutically acceptable carriers, diluents, or excipients.
12. The antibody of any one of Claims 1-10 for use in therapy.
13. The antibody of any one of Claims 1-10 for use in the treatment of one or more allergic disease.

14. The antibody of Claim 13, wherein the allergic disease is atopic dermatitis, asthma, allergic rhinitis, or food allergy.
15. The antibody of Claim 14, wherein the allergic disease is atopic dermatitis.
16. The antibody of any one of Claims 1-10 for use in the treatment of eosinophilic esophagitis, scleroderma/systemic sclerosis, ulcerative colitis, or chronic obstructive pulmonary disease.
17. The antibody of any one of Claims 1-10 for use in the treatment of Crohn's disease.
18. Use of the antibody of any one of Claims 1-10 in the manufacture of a medicament for the treatment of one or more allergic disease.
19. The use of Claim 18, wherein the allergic disease is atopic dermatitis, asthma, allergic rhinitis, or food allergy.
20. The use of Claim 19, wherein the allergic disease is atopic dermatitis.
21. Use of the antibody of any one of Claims 1-10 in the manufacture of a medicament for the treatment of eosinophilic esophagitis, scleroderma/systemic sclerosis, ulcerative colitis, or chronic obstructive pulmonary disease.
22. Use of the antibody of any one of Claims 1-12 in the manufacture of a medicament for the treatment of Crohn's disease.
23. A DNA molecule comprising a polynucleotide sequence encoding a HC, wherein the amino acid sequence of the HC is SEQ ID NO: 9.
24. A DNA molecule comprising a polynucleotide sequence encoding a LC, wherein the amino acid sequence of the LC is SEQ ID NO: 10.
25. A DNA molecule comprising a polynucleotide sequence encoding a HC having the amino acid sequence of SEQ ID NO: 9, and comprising a polynucleotide sequence encoding a LC having the amino acid sequence of SEQ ID NO: 10.
26. A mammalian cell transformed with the DNA molecule of claim 23 and the DNA molecule of claim 24, wherein the cell is capable of expressing an antibody

comprising a HC given by the amino acid sequence of SEQ ID NO: 9 and a LC given by the amino acid sequence of SEQ ID NO: 10.

27. A mammalian cell transformed with the DNA molecule of claim 25, wherein the cell is capable of expressing an antibody comprising a HC given by the amino acid sequence of SEQ ID NO: 9 and a LC given by the amino acid sequence of SEQ ID NO: 10.
28. A process for producing an antibody, which antibody comprises two HCs and two LCs, in which the amino acid sequence of each of the two HCs is given by the amino acid sequence of SEQ ID NO: 9 and the amino acid sequence of each of the two LCs is given by the amino acid sequence of SEQ ID NO: 10, and which process comprises:
 - a. cultivating the mammalian cell of claim 26 or the mammalian cell of claim 27 under conditions such that the antibody expressed, and
 - b. recovering the expressed antibody.
29. An antibody produced by the process of claim 28.