

The IL-33 pathway has been suggested to be involved in various diseases, including ocular diseases (e.g, GA) for which there remains a need to develop improved compositions, and methods for treatment.

5

SUMMARY

The present disclosure relates, *inter alia*, to anti-IL-33 antibodies and methods of making and using the same.

In one example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, the binding domain comprising the following six complementarity-determining regions (CDRs): (a) a CDR-H1 comprising the amino acid sequence of NYWMT (SEQ ID NO: 1); (b) a CDR-H2 comprising the amino acid sequence of SITYTGGGTYYPDSVKG (SEQ ID NO: 2); (c) a CDR-H3 comprising the amino acid sequence of ANYYYNTYGGFPY (SEQ ID NO: 3); (d) a CDR-L1 comprising the amino acid sequence of LASEGFSNDLA (SEQ ID NO: 4); (e) a CDR-L2 comprising the amino acid sequence of AASRLQD (SEQ ID NO: 5); and (f) a CDR-L3 comprising the amino acid sequence of QQGSKYPLT (SEQ ID NO: 6).

In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 7; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 8; or (c) a VH domain as in (a) and a VL domain as in (b).

In some examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVX₁SGX₂X₃X₄X₅X₆PGX₇SX₈X₉X₁₀SCX₁₁ASGFTFN (SEQ ID NO: 9), wherein X₁ is E or Q; X₂ is G or A; X₃ is G or E; X₄ is L or V; X₅ is V or K; X₆ is Q or K; X₇ is G, A, or T; X₈ is L or V; X₉ is R or K; X₁₀ is L or V; and X₁₁ is A, K, or L; (b) an FR-H2 comprising the amino acid sequence of WX₁RQAPGX₂GLEWX₃X₄ (SEQ ID NO: 10), wherein X₁ is I or V; X₂ is K or Q; X₃ is V, M, or I; and X₄ is A or G; (c) an FR-H3 comprising the amino acid sequence of RX₁TX₂X₃RDX₄X₅X₆X₇X₈X₉YX₁₀X₁₁X₁₂X₁₃SLRX₁₄EDTAX₁₅YYCTR (SEQ ID NO: 11), wherein X₁ is F or V; X₂ is I or M; X₃ is S or T; X₄ is D, N, or T; X₅ is A or S; X₆ is K or T; X₇ is S or N; X₈ is S or T; X₉ is L or V; X₁₀ is L or M; X₁₁ is Q or E; X₁₂ is M or L; X₁₃ is N or S; X₁₄ is A or S; and X₁₅ is V or T; and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

In some examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWVA (SEQ ID NO: 18); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 19); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 12).

In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 7.

In some examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 17); (b) an FR-H2 comprising the amino

In some examples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of X₁IX₂X₃TQSPX₄X₅LSX₆SX₇GX₈X₉X₁₀X₁₁X₁₂X₁₃C (SEQ ID NO: 13), wherein X₁ is D or E; X₂ is Q or V; X₃ is M or L; X₄ is S or A; X₅ is S or T; X₆ is A or L; X₇ is V, P, or L; X₈ is D or E; X₉ is R or T; X₁₀ is V or A; X₁₁ is T or S; X₁₂ is I or L; and X₁₃ is T, S, or E; (b) an FR-L2 comprising the amino acid sequence of WX₁QQKX₂GX₃X₄PX₅X₆LIY (SEQ ID NO: 14), wherein X₁ is Y or F; X₂ is P or S; X₃ is K or Q; X₄ is S or A; X₅ is K, R, or Q; and X₆ is L or S; (c) an FR-L3 comprising the amino acid sequence of GX₁PX₂RFSGSGSGTX₃FX₄LX₅ISX₆X₇X₈PEDX₉AX₁₀YX₁₁C (SEQ ID NO: 15), wherein X₁ is V or I; X₂ is S or A; X₃ is D or R; X₄ is T or S; X₅ is T or K; X₆ is S or G; X₇ is L or M; X₈ is Q or E; X₉ is F, V, or E; X₁₀ is T, V, or D; and X₁₁ is F or Y; and (d) an FR-L4 comprising the amino acid sequence of FGX₁GTX₂EIK (SEQ ID NO: 16), wherein X₁ is G or S and X₂ is V or L.

In some examples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKSPKLLIY (SEQ ID NO: 22); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 8.

In one aspect, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 7 and/or wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 8. In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 7 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8.

In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 25 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 26.

In some examples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 54); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 55.

In some examples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKSLIY (SEQ ID NO: 56); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYFC (SEQ ID NO: 23); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 24).

In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 57.

In some examples, the VL domain comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 21); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKSLIY (SEQ ID NO: 53); (c) an FR-L3 comprising the amino acid sequence of

In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58.

5 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

10 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

15 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

20 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59.

25 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61.

30 In another example, provided herein is an isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 35; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; or (c) a VH domain as in (a) and a VL domain as in (b).

35 In some examples, the VH domain comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGTSLKLSCLASGFTFN (SEQ ID NO: 27); (b) an FR-H2 comprising the amino acid sequence of WIRQAPGKGLEWIA (SEQ ID NO: 28); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKSTLYLQMNSLRSEDATYYCTR (SEQ ID NO: 29); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 12).

40 In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 35.

In some examples, the antibody fragment is an Fab.
 In some examples, the antibody is a full-length antibody.
 In some examples, the antibody is an IgG antibody.
 In some examples, the IgG antibody is an IgG1 antibody.
 5 In some examples, the IgG antibody is an IgG4 antibody.
 In some examples, the antibody is a monospecific antibody.
 In some examples, the antibody is a multispecific antibody.
 In some examples, the antibody is a bispecific antibody.
 In some examples, the bispecific antibody comprises a second binding domain that binds to a
 10 second biological molecule, wherein the second biological molecule is interleukin-13 (IL-13), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, or a VEGF receptor.
 In one aspect, provided herein is an isolated nucleic acid encoding the antibody as disclosed herein or a set of isolated nucleic acids together encoding the antibody as disclosed herein. In another example, provided herein is an isolated nucleic acid encoding any one of the antibodies disclosed herein
 15 or a set of isolated nucleic acids together encoding the antibody.
 In another aspect, provided herein is a vector or a set of vectors comprising the isolated nucleic acid or set of isolated nucleic acids as disclosed herein. In another example, provided herein is a vector or a set of vectors comprising any of the isolated nucleic acids or set of isolated nucleic acids disclosed herein.
 20 In another aspect, provided herein is a host cell comprising the vector or the set of vectors as disclosed herein. In another example, provided herein is a host cell comprising any one of the vectors or the set of vectors disclosed herein.
 In some examples, the host cell is a mammalian cell.
 In some examples, the mammalian cell is a Chinese hamster ovary (CHO) cell.
 25 In some examples, the host cell is a prokaryotic cell.
 In some examples, the prokaryotic cell is *E. coli*.
 In one aspect, provided herein is a method of producing an antibody that specifically binds to IL-33, the method comprising culturing the host cell as disclosed herein in a culture medium, preferably wherein the method further comprises recovering the antibody from the host cell or the culture medium. In
 30 another example, provided herein is a method of producing an antibody that specifically binds to IL-33, the method comprising culturing any one of the host cells disclosed herein in a culture medium.
 In some examples, the method further comprises recovering the antibody from the host cell or the culture medium.
 In one aspect, provided herein is a pharmaceutical composition comprising the antibody as
 35 disclosed herein, preferably further comprising a pharmaceutically acceptable carrier, excipient, or diluent.
 In another example, provided herein is a composition comprising any one of the antibodies disclosed herein.
 In some examples, the composition further comprises a pharmaceutically acceptable carrier,
 40 excipient, or diluent.
 In some examples, the composition is a pharmaceutical composition.
 In some examples, the pharmaceutical composition further comprises an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTH2) binding
 45 antagonist, an interleukin-13 (IL-13) binding antagonist, an interleukin-17 (IL-17) binding antagonist, a JAK1 antagonist, and/or an interleukin-5 (IL-5) binding antagonist.
 In some examples, the pharmaceutical composition comprises a Factor D binding antagonist.
 In some examples, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.
 50 In some examples, the pharmaceutical composition comprises an HtrA1 binding antagonist.

In some examples, the immune disorder is asthma, rheumatoid arthritis, allergy, anaphylaxis, anaphylactic shock, allergic rhinitis, psoriasis, IBD, Crohn's disease, diabetes, or liver disease.

In some examples, the fibrotic disease is IPF.

In some examples, the eosinophilic disorder is an EGID.

5 In some examples, the EGID is eosinophilic esophagitis.

In some examples, the infection is a helminth infection, a protozoan infection, or a viral infection.

In some examples, the protozoan infection is a *Leishmania major* infection.

In some examples, the viral infection is an RSV infection or an influenza infection.

In some examples, the pain is inflammatory pain.

10 In some examples, the central nervous system disorder is Alzheimer's disease.

In some examples, the solid tumor is a breast tumor, a colon tumor, a prostate tumor, a lung tumor, a kidney tumor, a liver tumor, a pancreas tumor, a stomach tumor, an intestinal tumor, a brain tumor, a bone tumor, and a skin tumor.

15 In some examples, the medicament is formulated for use in combination with an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.

In some examples, the medicament is formulated for use in combination with a Factor D binding antagonist.

20 In some examples, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.

In some examples, the medicament is formulated for use in combination with an HtrA1 binding antagonist.

25 In some examples, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In some examples, the medicament is formulated for use in combination with a VEGF antagonist.

In some examples, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

30 In one aspect, provided herein is the antibody as disclosed herein or the pharmaceutical composition as disclosed herein for use as a medicament.

35 In one aspect, provided herein is use of the antibody as disclosed herein or the pharmaceutical composition as disclosed herein, in the manufacture of a medicament for treating an IL-33-mediated ocular disorder, preferably wherein the ocular disorder is age-related macular degeneration (AMD), retinopathy of the eye, polypoidal choroidal vasculopathy (PCV), diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis. In another example, provided herein is a method of treating an IL-33-mediated disorder in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one of the antibodies disclosed herein or any one of the compositions disclosed herein.

40 In some examples, the IL-33-mediated disorder is an ocular disorder, an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, or a solid tumor.

45 In some examples, the ocular disorder is AMD, retinopathy of the eye, PCV, diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.

In some examples, the AMD is GA, wet AMD, or dry AMD.

In some examples, the AMD is GA.

In some examples, the AMD is intermediate AMD or advanced AMD.

WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises a binding domain comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 7 and/or wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 8.

2. The isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, according to claim 1, wherein the antibody comprises a binding domain comprising (a) a heavy chain (HC) comprising an amino acid sequence of SEQ ID NO: 25 and (b) a light chain (LC) comprising an amino acid sequence of SEQ ID NO: 26.

3. An isolated antibody that specifically binds IL-33, or an antigen-binding fragment thereof, wherein the antibody comprises:

(i) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;

(ii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 55;

(iii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 41 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(iv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(v) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(vi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(vii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 8;

(viii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(ix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(x) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 57;

(xiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xiv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xv) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xvi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xvii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 58;

(xviii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 43 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xix) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 44 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xx) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 46 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xxi) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 48 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59;

(xxii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 50 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 59; or

(xxiii) a binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 52 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 61.

4. The antibody of any one of claims 1-3, wherein the antibody

- (i) specifically binds both human and cynomolgus monkey (cyno) interleukin-33 (IL-33) with a K_D of 1 nM or lower;
- (ii) inhibits binding of human IL-33 to an IL-33 receptor with a 50% inhibitory concentration (IC₅₀) of between 800 fM and 100 pM;
- (iii) has a viscosity of less than 5 centipoise (cP) at a concentration of about 180 mg/mL; and
- (iv) has a turbidity (optical density (OD)) of 0.5 or lower at a concentration of 150 mg/mL or higher in phosphate-buffered saline (PBS) pH 7.4.

5. The antibody of any one of claims 1-4, wherein the antibody is monoclonal, human, humanized, or chimeric.

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

- a) an antibody fragment that binds IL-33, preferably, wherein the antibody fragment is an Fab, Fab'-SH, Fv, scFv, or (Fab')₂ fragment; or
- b) a full-length antibody, preferably an IgG1 antibody, or an IgG4 antibody.

7. The antibody of any one of claims 1-6, wherein the antibody is

- a) a monospecific antibody; or
 - b) is a multispecific antibody, or a bispecific antibody, preferably wherein the bispecific antibody comprises a second binding domain that binds to a second biological molecule, wherein the second biological molecule is interleukin-13 (IL-13), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, or a VEGF receptor.
8. An isolated nucleic acid encoding the antibody of any one of claims 1-7 or a set of isolated nucleic acids together encoding the antibody of any one of claims 1-7.
9. A vector or a set of vectors comprising the isolated nucleic acid or set of isolated nucleic acids of claim 8.
10. A host cell comprising the vector or the set of vectors of claim 9.
11. A method of producing an antibody that specifically binds to IL-33, the method comprising culturing the host cell of claim 10 in a culture medium, preferably wherein the method further comprises recovering the antibody from the host cell or the culture medium.
12. A pharmaceutical composition comprising the antibody of any one of claims 1-7, preferably further comprising a pharmaceutically acceptable carrier, excipient, or diluent.
13. The pharmaceutical composition of claim 12, wherein the pharmaceutical composition further comprises an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a chemoattractant receptor-homologous molecule expressed on Th2 cells (CRTH2) binding antagonist, an interleukin-13 (IL-13) binding antagonist, an interleukin-17 (IL-17) binding antagonist, a JAK1 antagonist, and/or an interleukin-5 (IL-5) binding antagonist.
14. The antibody of any one of claims 1-7 or the pharmaceutical composition of any one of claims 12-13 for use as a medicament.
15. Use of the antibody of any one of claims 1-7 or the pharmaceutical composition of any one of claims 12-13, in the manufacture of a medicament for treating an IL-33-mediated ocular disorder, preferably wherein the ocular disorder is age-related macular degeneration (AMD), retinopathy of the eye, polypoidal choroidal vasculopathy (PCV), diabetic macular edema, dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, or conjunctivitis.

16. The use of claim 15, wherein the AMD is geographic atrophy (GA), wet AMD, or dry AMD.

17. The use of claim 15, wherein the antibody or pharmaceutical composition is to be administered directly to the eye; preferably the antibody or pharmaceutical composition is to be administered using intravitreal, intraocular, periocular, conjunctival, subconjunctival, subtenon, intracameral, subretinal, retrobulbar, or intracanalicular injections, by direct application to the eye, by topical ocular drops or ointments, or by a slow-release device in the cul-de-sac or implanted adjacent to the sclera or in the sclera or within the eye.

18. The use of any one of claims 14-17, wherein the medicament is for administration in combination with an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 binding antagonist, a VEGF antagonist, a tryptase-beta binding antagonist, a CRTH2 binding antagonist, an IL-13 binding antagonist, an IL-17 binding antagonist, a JAK1 antagonist, and/or an IL-5 binding antagonist.