

ANTI-INTERLEUKIN-33 ANTIBODIES AND USES THEREOF

FIELD OF THE INVENTION

The invention relates to anti-interleukin-33 (IL-33) antibodies, and methods of using the same, including for treatment of IL-33-mediated disorders.

BACKGROUND

Interleukin-33 (IL-33) is a member of the interleukin-1 (IL-1) cytokine family that is encoded by the *IL33* gene, and is constitutively expressed in structural cells, such as smooth muscle, epithelial, and endothelial cells. IL-33 can be induced by inflammatory factors in macrophages and dendritic cells. Cellular stress caused by environmental triggers, such as allergens, toxins, and pathogens, can lead to IL-33 release. Bioavailable IL-33 associates with a heterodimeric IL-33 receptor complex composed of suppression of tumorigenicity 2 (ST2) protein and interleukin-1 receptor accessory protein (IL-1RAcP) to activate the AP-1 and NF- κ B pathways through the adaptor protein myeloid differentiation primary response 88 (MyD88) and possibly MyD88-adaptor-like (Mal) protein. IL-33 stimulates a number of cell types, including innate type II (ILC2) cells; mast cells, basophils, eosinophils, and dendritic cells, to promote Type 2 immunity.

The IL-33 pathway has been suggested to be involved in various diseases, including allergy-related diseases for which there remains a need to develop improved compositions, including therapeutic anti-IL-33 antagonists, and methods for treatment.

SUMMARY

The present disclosure relates to anti-IL-33 antibodies, including bispecific anti-IL-33/anti-IL-13 antibodies, and methods of using the same.

In one embodiment, the disclosure features an isolated antibody that specifically binds both human and cynomolgus monkey (cyno) interleukin-33 (IL-33) with a K_D of about 500 pM or lower. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 100 fM and about 500 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 1 pM and about 200 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 15 pM and about 180 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 15 and about 140 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 100 fM and about 500 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 1 pM and about 500 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 100 and about 500 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 125 and about 500 pM. In some embodiments, the antibody the antibody specifically binds both human and cyno IL-33 with a K_D of between about 1 pM and about 500 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D of between about 1 pM and about 200 pM.

In some embodiments, any one of the preceding antibodies is capable of inhibiting the binding of IL-33 to an IL-33 receptor (e.g., ST2 and/or IL-1RAcP). In some embodiments, the inhibiting is measured using a cell-based blocking assay. In some embodiments, the antibody inhibits the binding of human IL-33 to an IL-33 receptor with a 90% inhibitory concentration (IC90) of between about 0.001 µg/ml and about 0.5 µg/ml. In some embodiments, the IC90 is between about 0.002 µg/ml and about 0.25 µg/ml. In some embodiments, the IC90 is about 0.17 µg/ml. In some embodiments, the IC90 is about 0.004 µg/ml. In some embodiments, the antibody inhibits the binding of human IL-33 to an IL-33 receptor with a 50% inhibitory concentration (IC50) of between about 800 fM and about 10 pM. In some embodiments, the IC50 is between about 1 pM and about 5 pM. In some embodiments, the IC50 is about 2.5 pM. In some embodiments, the antibody inhibits the binding of cyno IL-33 to an IL-33 receptor with an IC50 of between about 1 nM and about 5 nM. In some embodiments, IC50 is about 4 nM. In some embodiments, HEK-BLUE™ IL-33/IL-1β cells are used in the cell-based blocking assay. In some embodiments, the HEK-BLUE™ IL-33/IL-1β cells comprise a nucleic acid comprising the sequence of SEQ ID NO: 311. In some embodiments, the assay comprises treating HEK-BLUE™ IL-33/IL-1β cells with IL-33. In some embodiments, the IL-33 comprises the amino acid sequence of any one of SEQ ID NOs: 313-318. In some embodiments, sST2-LZ is used as a positive control in the cell-based blocking assay. In some embodiments, the sST2-LZ comprises the amino acid sequence of SEQ ID NO: 310.

In some embodiments, the antibody comprises a binding domain comprising: (a) an HVR-H1 comprising the amino acid sequence of SFSMS (SEQ ID NO: 1); (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDSVKG (SEQ ID NO: 2); and (c) an HVR-H3 comprising the amino acid sequence of ANYGNWFFEY (SEQ ID NO: 3). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 12); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 13); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKNTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 14); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVVSS (SEQ ID NO: 15). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of DVNLVESGGGSVKPGGSLKLSCVASGFTFS (SEQ ID NO: 16); (b) an FR-H2 comprising the amino acid sequence of WVRQTPEKRLEWVA (SEQ ID NO: 17); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDAKNTLYLQMSSLESEDAMYYCTR (SEQ ID NO: 18); and (d) an FR-H4 comprising the amino acid sequence of WGAGTTVAVSS (SEQ ID NO: 19). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 12) or EVQLVESGGGLVKPGGSLRLSCAASGFTFS (SEQ ID NO: 20); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 13) or WVRQAPGKGLEWVS (SEQ ID NO: 21); (c) an FR-H3 comprising the amino acid sequence of RFTISRDNKNTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 22), RFTISRDDAKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 23), RFTISRDNKNSLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 24), or RFTISRDDSKNTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 14); and (d) an FR-H4 comprising the

amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 15). In some embodiments, the binding domain further comprises: (a) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLLN (SEQ ID NO: 4); (b) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and (c) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6). In some embodiments, the binding domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 25); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQPPRLLIF (SEQ ID NO: 26); (c) an FR-L3 comprising the amino acid sequence of GIPARFSGSGSGTDFTLTISSELPEDFAVYYC (SEQ ID NO: 27); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 28). In some embodiments, the binding domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIVLTQSPGFLVSLGQRATISC (SEQ ID NO: 29); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIF (SEQ ID NO: 30); (c) an FR-L3 comprising the amino acid sequence of GVPARFSGSGSGTDFTSLNIHPMEEDDTAMYFC (SEQ ID NO: 31); and (d) an FR-L4 comprising the amino acid sequence of FGSGTKLEIK (SEQ ID NO: 32). In some embodiments, the binding domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 25); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQPPRLLIF (SEQ ID NO: 26); (c) an FR-L3 comprising the amino acid sequence of GIPARFSGSGSGTDFTLTISSELPEDFAVYYC (SEQ ID NO: 27), GVPARFSGSGSGTDFTLTISSELPEDFAVYFC (SEQ ID NO: 33), GVPARFSGSGSGTDFTLTISSELPEDFAVYYC (SEQ ID NO: 34), or GIPARFSGSGSGTDFTLTISSELPEDFAVYFC (SEQ ID NO: 35); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 28).

In some embodiments, the antibody comprises a binding domain comprising: (a) an HVR-H1 comprising the amino acid sequence of SSIFYWG (SEQ ID NO: 65); (b) an HVR-H2 comprising the amino acid sequence of SIYYSGRTYYNPSLKS (SEQ ID NO: 66) or SIYYSGRTYYNPALKS (SEQ ID NO: 67); and (c) an HVR-H3 comprising the amino acid sequence of AGGLYNWNDESFSFYMDV (SEQ ID NO: 68). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of ELQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 72); (b) an FR-H2 comprising the amino acid sequence of WIRQPPGKGLEWIG (SEQ ID NO: 73); (c) an FR-H3 comprising the amino acid sequence of RVTISVDTSKNQFSLMLTSVTAADTAVYYCAR (SEQ ID NO: 74); and (d) an FR-H4 comprising the amino acid sequence of WGQGTTVTVSS (SEQ ID NO: 75). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of QLQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 76); (b) an FR-H2 comprising the amino acid sequence of WIRQPPGKGLEWIG (SEQ ID NO: 73); (c) an FR-H3 comprising the amino acid sequence of RVTISVDTSKNQFSLMLTSVTAADTAVYYCAR (SEQ ID NO: 74); and (d) an FR-H4 comprising the amino acid sequence of WGNQTTVTVSS (SEQ ID NO: 78). In some embodiments, the binding domain further comprises: (a) an FR-H1 comprising the amino acid sequence of ELQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 72),

QLQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 76) or

QVQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 77); (b) an FR-H2 comprising the amino acid sequence of WIRQPPGKGLEWIG (SEQ ID NO: 73); (c) an FR-H3 comprising the amino acid sequence of RVTISVDTSKNQFSLMLTSVTAADTAVYYCAR (SEQ ID NO: 74); and (d) an FR-H4 comprising the amino acid sequence of WGQGTTVTVSS (SEQ ID NO: 75) or WGNGTTVTVSS (SEQ ID NO: 78). In some embodiments, the binding domain further comprises: (a) an HVR-L1 comprising the amino acid sequence of RASQSFSSSYLA (SEQ ID NO: 69); (b) an HVR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO: 70); and (c) an HVR-L3 comprising the amino acid sequence of QQYDRSPLT (SEQ ID NO: 71). In some embodiments, the binding domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPGTLSPGERATLSC (SEQ ID NO: 79); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLLIY (SEQ ID NO: 80); (c) an FR-L3 comprising the amino acid sequence of GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 81); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 82).

In one aspect, the invention features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SFSX₁S (SEQ ID NO: 62), wherein X₁ is Met, Leu, or Val; (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDX₁VKG (SEQ ID NO: 63), wherein X₁ is Ser or Ala; (c) an HVR-H3 comprising the amino acid sequence of ANYGX₁X₂FFEY (SEQ ID NO: 64), wherein X₁ is Asn or Asp, and X₂ is Trp or Phe; (d) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLLN (SEQ ID NO: 4); (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SFSMS (SEQ ID NO: 1); (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDSVKG (SEQ ID NO: 2); (c) an HVR-H3 comprising the amino acid sequence of ANYGNWFFEY (SEQ ID NO: 3); (d) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLLN (SEQ ID NO: 4); (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6).

In another aspect, the invention features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 37; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 12); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 13); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKNTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 14); and (d) an FR-H4 comprising the amino acid sequence of WGQGTTLTVSS (SEQ ID NO: 15). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 36. In some

VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 37.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 38 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 39.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 40 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 41.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SSIFYWG (SEQ ID NO: 65); (b) an HVR-H2 comprising the amino acid sequence of SIYYSGRTYYNPX₁LKS (SEQ ID NO: 90), wherein X₁ is Ser or Ala; (c) an HVR-H3 comprising the amino acid sequence of AGGLYNWNDESFYMDV (SEQ ID NO: 68); (d) an HVR-L1 comprising the amino acid sequence of RASQSFSSSYLA (SEQ ID NO: 69); (e) an HVR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO: 70); and (f) an HVR-L3 comprising the amino acid sequence of QQYDRSPLT (SEQ ID NO: 71). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SSIFYWG (SEQ ID NO: 65); (b) an HVR-H2 comprising the amino acid sequence of SIYYSGRTYYNP₁SLKS (SEQ ID NO: 66); (c) an HVR-H3 comprising the amino acid sequence of AGGLYNWNDESFYMDV (SEQ ID NO: 68); (d) an HVR-L1 comprising the amino acid sequence of RASQSFSSSYLA (SEQ ID NO: 69); (e) an HVR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO: 70); and (f) an HVR-L3 comprising the amino acid sequence of QQYDRSPLT (SEQ ID NO: 71). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SSIFYWG (SEQ ID NO: 65); (b) an HVR-H2 comprising the amino acid sequence of SIYYSGRTYYNPALKS (SEQ ID NO: 67); (c) an HVR-H3 comprising the amino acid sequence of AGGLYNWNDESFYMDV (SEQ ID NO: 68); (d) an HVR-L1 comprising the amino acid sequence of RASQSFSSSYLA (SEQ ID NO: 69); (e) an HVR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO: 70); and (f) an HVR-L3 comprising the amino acid sequence of QQYDRSPLT (SEQ ID NO: 71).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 84; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 85; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of ELQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 72); (b) an FR-H2

comprising the amino acid sequence of WIRQPPGKGLEWIG (SEQ ID NO: 73); (c) an FR-H3 comprising the amino acid sequence of RVTISVDTSKNQFSLMLTSVTAADTAVYYCAR (SEQ ID NO: 74); and (d) an FR-H4 comprising the amino acid sequence of WGQGTTTVTVSS (SEQ ID NO: 75). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 84. In some

5 embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPGTLSSLSPGERATLSC (SEQ ID NO: 79); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLLIY (SEQ ID NO: 80); (c) an FR-L3 comprising the amino acid sequence of GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 81); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 82). In some embodiments, the VL domain comprises the

10 amino acid sequence of SEQ ID NO: 85. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 86. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPGTLSSLSPGERATLSC (SEQ ID NO: 79); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLLIY (SEQ ID NO: 80); (c) an FR-L3 comprising the amino acid sequence of GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 81);

15 and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 82). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 87. In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of QLQLQESGPGLVKPSETLSLTCTVSGGSIR (SEQ ID NO: 76); (b) an FR-H2 comprising the amino acid sequence of WIRQPPGKGLEWIG (SEQ ID NO: 73); (c) an FR-H3 comprising the amino acid sequence

20 of RVTISVDTSKNQFSLMLTSVTAADTAVYYCAR (SEQ ID NO: 74); and (d) an FR-H4 comprising the amino acid sequence of WGNQTTTVTVSS (SEQ ID NO: 78). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 88. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPGTLSSLSPGERATLSC (SEQ ID NO: 79); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQAPRLLIY (SEQ ID NO:

25 80); (c) an FR-L3 comprising the amino acid sequence of GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO: 81); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 82). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 89.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid

30 sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 84 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 85.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid

35 sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 86 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 87.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid

sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 88 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 89.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of NYX₁MN (SEQ ID NO: 97), wherein X₁ is Trp, Phe, or Tyr; (b) an HVR-H2 comprising the amino acid sequence of EITLKFNX₁YX₂THYAESVKG (SEQ ID NO: 98), wherein X₁ is Asn, Asp, Ser, or Ala, and X₂ is Ser or Ala; (c) an HVR-H3 comprising the amino acid sequence of RNYGX₁X₂YINV (SEQ ID NO: 99), wherein X₁ is Asp or Asn, and X₂ is Trp or Phe; (d) an HVR-L1 comprising the amino acid sequence of RASESVDKFGX₁SFLN (SEQ ID NO: 100), wherein X₁ is Met, Val, or Leu; (e) an HVR-L2 comprising the amino acid sequence of VASSQGS (SEQ ID NO: 113); and (f) an HVR-L3 comprising the amino acid sequence of QQSKDIPYT (SEQ ID NO: 114). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of NYWMN (SEQ ID NO: 101); (b) an HVR-H2 comprising the amino acid sequence of EITLKFN₁NYSTHYAESVKG (SEQ ID NO: 104); (c) an HVR-H3 comprising the amino acid sequence of RNYGDWYINV (SEQ ID NO: 109); (d) an HVR-L1 comprising the amino acid sequence of RASESVDKFGMSFLN (SEQ ID NO: 112); (e) an HVR-L2 comprising the amino acid sequence of VASSQGS (SEQ ID NO: 113); and (f) an HVR-L3 comprising the amino acid sequence of QQSKDIPYT (SEQ ID NO: 114). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of NYWMN (SEQ ID NO: 101); (b) an HVR-H2 comprising the amino acid sequence of EITLKFN₁NYSTHYAESVKG (SEQ ID NO: 104); (c) an HVR-H3 comprising the amino acid sequence of RNYGNWYINV (SEQ ID NO: 110); (d) an HVR-L1 comprising the amino acid sequence of RASESVDKFGMSFLN (SEQ ID NO: 112); (e) an HVR-L2 comprising the amino acid sequence of VASSQGS (SEQ ID NO: 113); and (f) an HVR-L3 comprising the amino acid sequence of QQSKDIPYT (SEQ ID NO: 114). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of NYWMN (SEQ ID NO: 101); (b) an HVR-H2 comprising the amino acid sequence of EITLKFN₁DYSTHYAESVKG (SEQ ID NO: 105); (c) an HVR-H3 comprising the amino acid sequence of RNYGNWYINV (SEQ ID NO: 110); (d) an HVR-L1 comprising the amino acid sequence of RASESVDKFGVSFLN (SEQ ID NO: 115); (e) an HVR-L2 comprising the amino acid sequence of VASSQGS (SEQ ID NO: 113); and (f) an HVR-L3 comprising the amino acid sequence of QQSKDIPYT (SEQ ID NO: 114).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 134; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 135; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVKLEESGGGLVQPGGSMKLSVASGFTFS (SEQ ID NO: 117); (b) an FR-H2 comprising the amino acid sequence of WVRQSPEKGLEWMA (SEQ ID NO: 119); (c) an

FR-H3 comprising the amino acid sequence of RFSISRDDSKSTVYLQMNNLRAEDTGIYYCAR (SEQ ID NO: 121); and (d) an FR-H4 comprising the amino acid sequence of WGAGTTVTVSS (SEQ ID NO: 124). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 134. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of
5 DIVLTQSPTSLAVSLGQRATISC (SEQ ID NO: 126); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQPPKLLIF (SEQ ID NO: 128); (c) an FR-L3 comprising the amino acid sequence of GVPARFSGSGSGTDFSLNIHPVEEDDTAMYFC (SEQ ID NO: 130); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKLEIK (SEQ ID NO: 132). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 135.

10 In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 136; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 137; or (c) a VH domain as in (a)
15 and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 118); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWMA (SEQ ID NO: 120); (c) an FR-H3 comprising the amino acid sequence of RFTISRDN SKNTVYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 122) or RFTISRDDSKNTVYLQMNSLRAEDTAVYYCAR (SEQ ID NO: 123); and (d) an FR-H4
20 comprising the amino acid sequence of WGQGTTLTVSS (SEQ ID NO: 125). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 138. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIVMTQSPDSLAVSLGERATINC (SEQ ID NO: 127); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGQPPKLLIF (SEQ ID NO: 129); (c) an FR-L3 comprising the amino acid sequence of
25 GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYC (SEQ ID NO: 131); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 133). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 139.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid
30 sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 134 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 135.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid
35 sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 136 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 137.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid

sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 138 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 139.

5 In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of KFWMN (SEQ ID NO: 158); (b) an HVR-H2 comprising the amino acid sequence of EIRLX₁X₂INYVKDYAESVKG (SEQ ID NO: 161), wherein X₁ is Asn or Ser, and X₂ is Ser or Ala; (c) an HVR-H3 comprising the amino acid sequence of RNYGNWFFEI (SEQ ID NO: 160); (d) an HVR-L1 comprising the amino acid sequence of RASESVDRYGISFMN (SEQ ID NO: 164); (e) an HVR-L2 comprising the amino acid sequence of AASNQGS (SEQ ID NO: 165); and (f) an HVR-L3 comprising the amino acid sequence of QHSKEVPYT (SEQ ID NO: 166). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of KFWMN (SEQ ID NO: 158); (b) an HVR-H2 comprising the amino acid sequence of EIRLNSINYVKDYAESVKG (SEQ ID NO: 159); (c) an HVR-H3 comprising the amino acid sequence of RNYGNWFFEI (SEQ ID NO: 160); (d) 15 an HVR-L1 comprising the amino acid sequence of RASESVDRYGISFMN (SEQ ID NO: 164); (e) an HVR-L2 comprising the amino acid sequence of AASNQGS (SEQ ID NO: 165); and (f) an HVR-L3 comprising the amino acid sequence of QHSKEVPYT (SEQ ID NO: 166). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of KFWMN (SEQ ID NO: 158); (b) an HVR-H2 comprising the amino acid sequence of 20 EIRLSSINYVKDYAESVKG (SEQ ID NO: 162); (c) an HVR-H3 comprising the amino acid sequence of RNYGNWFFEI (SEQ ID NO: 160); (d) an HVR-L1 comprising the amino acid sequence of RASESVDRYGISFMN (SEQ ID NO: 164); (e) an HVR-L2 comprising the amino acid sequence of AASNQGS (SEQ ID NO: 165); and (f) an HVR-L3 comprising the amino acid sequence of QHSKEVPYT (SEQ ID NO: 166). In some embodiments, the binding domain comprises the following six HVRs: (a) an 25 HVR-H1 comprising the amino acid sequence of KFWMN (SEQ ID NO: 158); (b) an HVR-H2 comprising the amino acid sequence of EIRLNAINYVKDYAESVKG (SEQ ID NO: 163); (c) an HVR-H3 comprising the amino acid sequence of RNYGNWFFEI (SEQ ID NO: 160); (d) an HVR-L1 comprising the amino acid sequence of RASESVDRYGISFMN (SEQ ID NO: 164); (e) an HVR-L2 comprising the amino acid sequence of AASNQGS (SEQ ID NO: 165); and (f) an HVR-L3 comprising the amino acid sequence of 30 QHSKEVPYT (SEQ ID NO: 166).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 183; (b) a light chain variable (VL) domain comprising an amino acid sequence having at 35 least 95% sequence identity to the amino acid sequence of SEQ ID NO: 184; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVKLEESGGGLVQPGGSMKLSVASGFTFN (SEQ ID NO: 167); (b) an FR-H2 comprising the amino acid sequence of WVRQSPEKGLEWVA (SEQ ID NO: 168); (c) an 40 FR-H3 comprising the amino acid sequence of RFTISRDDSKNSVYQLQMNNLRAEDTGIYYCIR (SEQ ID

NO: 169); and (d) an FR-H4 comprising the amino acid sequence of WGAGTTVTVSS (SEQ ID NO: 170). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 183. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIVLTQSPASLAVSLGQRATISC (SEQ ID NO: 175); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQSPKLLIY (SEQ ID NO: 176); (c) an FR-L3 comprising the amino acid sequence of GVPARFSGSGSGTDFSLNIHPLEDDAAMYFC (SEQ ID NO: 177); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKLEIK (SEQ ID NO: 178). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 184.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 185; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 186; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFN (SEQ ID NO: 171); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 172); (c) an FR-H3 comprising the amino acid sequence of RFTISRDNAKNSVYLQMNSLRAEDTAVYYCIR (SEQ ID NO: 173); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 174). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 185. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 179); (b) an FR-L2 comprising the amino acid sequence of WFQQKPGKAPKLLIY (SEQ ID NO: 180); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 181); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 182). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 186. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 187. In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 188. In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 189. In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 190.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 183 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 184.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 185 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 186.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 187 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 188.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 189 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 190.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DYNMN (SEQ ID NO: 191); (b) an HVR-H2 comprising the amino acid sequence of DINPKX₁X₂DTFYNQNFKD (SEQ ID NO: 192), wherein X₁ is Asn or Ser, and X₂ is Gly or Ala; (c) an HVR-H3 comprising the amino acid sequence of HYYYGSSYGGFVY (SEQ ID NO: 196); (d) an HVR-L1 comprising the amino acid sequence of HASQNINWLS (SEQ ID NO: 197); (e) an HVR-L2 comprising the amino acid sequence of AASKLHT (SEQ ID NO: 198); and (f) an HVR-L3 comprising the amino acid sequence of QQGQSYPLT (SEQ ID NO: 199). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DYNMN (SEQ ID NO: 191); (b) an HVR-H2 comprising the amino acid sequence of DINPKNGDTFYNQNFKD (SEQ ID NO: 193); (c) an HVR-H3 comprising the amino acid sequence of HYYYGSSYGGFVY (SEQ ID NO: 196); (d) an HVR-L1 comprising the amino acid sequence of HASQNINWLS (SEQ ID NO: 197); (e) an HVR-L2 comprising the amino acid sequence of AASKLHT (SEQ ID NO: 198); and (f) an HVR-L3 comprising the amino acid sequence of QQGQSYPLT (SEQ ID NO: 199). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DYNMN (SEQ ID NO: 191); (b) an HVR-H2 comprising the amino acid sequence of DINPKSGDTFYNQNFKD (SEQ ID NO: 194) or DINPKNADTFYQNFKD (SEQ ID NO: 195); (c) an HVR-H3 comprising the amino acid sequence of HYYYGSSYGGFVY (SEQ ID NO: 196); (d) an HVR-L1 comprising the amino acid sequence of HASQNINWLS (SEQ ID NO: 197); (e) an HVR-L2 comprising the amino acid sequence of AASKLHT (SEQ ID NO: 198); and (f) an HVR-L3 comprising the amino acid sequence of QQGQSYPLT (SEQ ID NO: 199).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 216; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 217; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVLLQQSGPELVKPGASVKISCNASGYTFS (SEQ ID NO: 200); (b) an FR-H2 comprising the amino acid sequence of WVKQSHGKSLESIG (SEQ ID NO: 201); (c) an FR-

H3 comprising the amino acid sequence of KATLTIDKSSSTVYMELRSLTSEDAMYYCAR (SEQ ID NO: 202); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVAA (SEQ ID NO: 203). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 216. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMNQSPSSLSASLGDTITITC (SEQ ID NO: 208); (b) an FR-L2 comprising the amino acid sequence of WYQQKAGNNPKLLIY (SEQ ID NO: 209); (c) an FR-L3 comprising the amino acid sequence of GVPSRFTGSGSGTLFTLTISLQPEDATYYC (SEQ ID NO: 210); and (d) an FR-L4 comprising the amino acid sequence of FGSGTNLELK (SEQ ID NO: 211). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 217.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 218; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 219; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVQSGAEVKKPGASVKVSCKASGYTFS (SEQ ID NO: 204); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGQGLESIG (SEQ ID NO: 205); (c) an FR-H3 comprising the amino acid sequence of RATLTIDKSTSTAYLELSSLRSEDATVYYCAR (SEQ ID NO: 206); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 207). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 218. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRTITC (SEQ ID NO: 212); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKNPCKLLIY (SEQ ID NO: 213); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 214); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 215). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 219.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 216 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 217. In another embodiment, the VH domain comprises the amino acid sequence of SEQ ID NO: 220. In another embodiment, the VL domain comprises the amino acid sequence of SEQ ID NO: 219.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 218 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 219.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 220 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 219.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SYWIN (SEQ ID NO: 222); (b) an HVR-H2 comprising the amino acid sequence of RIAPGSGFISYNELFKD (SEQ ID NO: 223); (c) an HVR-H3 comprising the amino acid sequence of EFYYGSFYGGFAY (SEQ ID NO: 224); (d) an HVR-L1 comprising the amino acid sequence of HASQNIHWLS (SEQ ID NO: 225); (e) an HVR-L2 comprising the amino acid sequence of KASTLHT (SEQ ID NO: 226); and (f) an HVR-L3 comprising the amino acid sequence of QQGQSSPLT (SEQ ID NO: 227).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 236; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 237; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of QVQLQQSGNDLVKPGASVKLSCKASGYTFT (SEQ ID NO: 228); (b) an FR-H2 comprising the amino acid sequence of WIKQRPQGQGLEWIG (SEQ ID NO: 229); (c) an FR-H3 comprising the amino acid sequence of KATLTVDTSSSTAYIQLGSLSSEDSAVYFCAR (SEQ ID NO: 230); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSA (SEQ ID NO: 231). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 236. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMNQSPSSLSASLGDTITITC (SEQ ID NO: 232); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGNIPKLLIY (SEQ ID NO: 233); (c) an FR-L3 comprising the amino acid sequence of GVPSRFNGSGSGTGTFTLTISSLQPEDIATYYC (SEQ ID NO: 234); and (d) an FR-L4 comprising the amino acid sequence of FGAGTKLEVK (SEQ ID NO: 235). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 237.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 246; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 247; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVQSGAEVKKPGASVKVSCKASGYTFT (SEQ ID NO: 238); (b) an FR-H2 comprising the amino acid sequence of WVRQAPQGQGLEWIG (SEQ ID NO: 239); (c) an FR-H3 comprising the amino acid sequence of RVTITRDTSTSTAYLELSSLRSEDVAVYYCAR (SEQ ID

NO: 240); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 241). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 246. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 242); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKLLIY (SEQ ID NO: 243); (c) an FR-L3 comprising the amino acid sequence of GVPSRFGSGSGTDFLTISLQPEDFATYYC (SEQ ID NO: 244); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 245). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 247.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 236 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 237.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 246 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 247.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of GSAX₁H (SEQ ID NO: 248), wherein X₁ is Met or Ile; (b) an HVR-H2 comprising the amino acid sequence of RIRSX₁X₂NX₃YATX₄YX₅ASVKG (SEQ ID NO: 249), wherein X₁ is Arg or Lys, X₂ is Asn, Thr, or Gly, X₃ is Asn or Ser, X₄ is Ala or Glu, and X₅ is Ala or Asp; (c) an HVR-H3 comprising the amino acid sequence of X₁X₂X₃X₄PFDY (SEQ ID NO: 250), wherein X₁ is Leu or Gln, X₂ is Gln, Gly, or Phe, X₃ is Gln or Gly, and X₄ is Pro or Asp; (d) an HVR-L1 comprising the amino acid sequence of RASQGIRNDLD (SEQ ID NO: 251); (e) an HVR-L2 comprising the amino acid sequence of AASSLQS (SEQ ID NO: 252); and (f) an HVR-L3 comprising the amino acid sequence of LQHX₁X₂YPX₃T (SEQ ID NO: 253), wherein X₁ is Asp or Ser, X₂ is Ser or Ile, and X₃ is Leu or Pro. In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of GSAMH (SEQ ID NO: 254); (b) an HVR-H2 comprising the amino acid sequence of RIRSRNNNYATAYAASVKG (SEQ ID NO: 255); (c) an HVR-H3 comprising the amino acid sequence of LQQPPFDY (SEQ ID NO: 256); (d) an HVR-L1 comprising the amino acid sequence of RASQGIRNDLD (SEQ ID NO: 251); (e) an HVR-L2 comprising the amino acid sequence of AASSLQS (SEQ ID NO: 252); and (f) an HVR-L3 comprising the amino acid sequence of LQHDSYPLT (SEQ ID NO: 257). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of GSAIH (SEQ ID NO: 258); (b) an HVR-H2 comprising the amino acid sequence of RIRSRTNNYATEYDASVKG (SEQ ID NO: 259); (c) an HVR-H3 comprising the amino acid sequence of LGQPPFDY (SEQ ID NO: 260); (d) an HVR-L1 comprising the amino acid sequence of RASQGIRNDLD (SEQ ID NO: 251); (e) an HVR-L2 comprising the amino acid sequence of AASSLQS

(SEQ ID NO: 252); and (f) an HVR-L3 comprising the amino acid sequence of LQHSIYPPT (SEQ ID NO: 261). In some embodiments, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of GSAMH (SEQ ID NO: 254); (b) an HVR-H2 comprising the amino acid sequence of RIRSKGNSYATAYAASVKG (SEQ ID NO: 262); (c) an HVR-H3 comprising the amino acid sequence of QFGDPFDY (SEQ ID NO: 263); (d) an HVR-L1 comprising the amino acid sequence of RASQGIRNDLD (SEQ ID NO: 251); (e) an HVR-L2 comprising the amino acid sequence of AASSLQS (SEQ ID NO: 252); and (f) an HVR-L3 comprising the amino acid sequence of LQHDSYPLT (SEQ ID NO: 257).

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 282; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 283; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of QVQLVQSGGGLVQPGGSLKLSAASGFTFS (SEQ ID NO: 264); (b) an FR-H2 comprising the amino acid sequence of WVRQASGKGLEWVG (SEQ ID NO: 267); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKRTTYLQMNSLKTEDTAVYYCTR (SEQ ID NO: 269); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 272). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 282. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 273); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKRLIY (SEQ ID NO: 276); (c) an FR-L3 comprising the amino acid sequence of GVPSRFNGSGSGTEFTLTISLQPEDFATYYC (SEQ ID NO: 277); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 280). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 283.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 284; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 285; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGDLVQPGGSLKLSAASGFTFS (SEQ ID NO: 265); (b) an FR-H2 comprising the amino acid sequence of WVRQASGKGLEWVG (SEQ ID NO: 267); (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKRTAYLQMNSLKTEDTAVYYCTR (SEQ ID NO: 270); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLTVSS (SEQ ID NO: 272). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 284. In some embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of AIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 274); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKRLIY (SEQ ID NO: 276); (c) an FR-L3 comprising the amino acid sequence of

GVPSRFGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 278); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 281). In some embodiments, the VL domain comprises the amino acid sequence of SEQ ID NO: 285.

5 In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 286; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 287; or (c) a VH domain as in (a) and a VL domain as in (b). In some embodiments, the VH domain further comprises: (a) an FR-H1
10 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLKLSAASGFTFS (SEQ ID NO: 266); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVG (SEQ ID NO: 268); (c) an FR-H3 comprising the amino acid sequence of RFSISRDDSKRTAYLQMSSLKTEDSAVYYCAR (SEQ ID NO: 271); and (d) an FR-H4 comprising the amino acid sequence of WGQGLTVTVSS (SEQ ID NO: 272). In some embodiments, the VH domain comprises the amino acid sequence of SEQ ID NO: 286. In some
15 embodiments, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of AIRITQSPSSLSASVGDRVTITC (SEQ ID NO: 275); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKRLIY (SEQ ID NO: 276); (c) an FR-L3 comprising the amino acid sequence of GVPSRFGSGSGSGTEFTLTISLQPEDFATYYC (SEQ ID NO: 279); and (d) an FR-L4 comprising the amino acid sequence of FGGGTKVEIK (SEQ ID NO: 280). In some embodiments, the VL domain
20 comprises the amino acid sequence of SEQ ID NO: 287.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 282 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino
25 acid sequence of SEQ ID NO: 283.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 284 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino
30 acid sequence of SEQ ID NO: 285.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 286 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino
35 acid sequence of SEQ ID NO: 287.

In another aspect, the invention features an isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 288 and (b) a light chain comprising

an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 289.

In another aspect, the invention features an isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 290 and (b) a light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 291.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 292 and (b) a light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 293.

In another embodiment, the disclosure features an isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 294 and (b) a light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 295.

In some embodiments of any of the preceding aspects, the antibody specifically binds human or cyno IL-33. In some embodiments, the antibody specifically binds both human and cyno IL-33. In some embodiments, the antibody specifically binds both human and cyno IL-33 with a K_D of about 1 nM or lower. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 100 fM and about 1 nM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 1 pM and about 200 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 75 pM and about 180 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D between about 75 and about 140 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 100 fM and about 1 nM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 1 pM and about 500 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 200 and about 500 pM. In some embodiments, the antibody specifically binds cyno IL-33 with a K_D between about 250 and about 500 pM. In some embodiments, the antibody specifically binds both human and cyno IL-33 with a K_D of between about 1 pM and about 500 pM. In some embodiments, the antibody specifically binds human IL-33 with a K_D of between about 1 pM and about 200 pM.

In some embodiments of any of the preceding aspects, the antibody is capable of inhibiting the binding of IL-33 to an IL-33 receptor. In some embodiments, the inhibiting is measured using a cell-based blocking assay. In some embodiments, the antibody inhibits the binding of human IL-33 to an IL-33 receptor with a 90% inhibitory concentration (IC90) of between about 0.001 μ g/ml and about 0.5 μ g/ml. In some embodiments, the IC90 is between about 0.002 μ g/ml and about 0.25 μ g/ml. In some embodiments, the IC90 is about 0.17 μ g/ml. In some embodiments, the IC90 is about 0.004 μ g/ml.

comprising the amino acid sequence of RASESVAKYGLSLN (SEQ ID NO: 4); (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6); and a second binding domain that specifically binds IL-13 comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of AYSVN (SEQ ID NO: 296); (b) an HVR-H2 comprising the amino acid sequence of MIWGDGKIVYNSALKS (SEQ ID NO: 297); (c) an HVR-H3 comprising the amino acid sequence of DGYYPYAMDND (SEQ ID NO: 298); (d) an HVR-L1 comprising the amino acid sequence of RASKSVDSYGNFSMH (SEQ ID NO: 299); (e) an HVR-L2 comprising the amino acid sequence of LASNLES (SEQ ID NO: 300); and (f) an HVR-L3 comprising the amino acid sequence of QQNNEDPRT (SEQ ID NO: 301).

In another embodiment, the disclosure features an isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises a first binding domain that specifically binds IL-33 comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SSIFYWG (SEQ ID NO: 65); (b) an HVR-H2 comprising the amino acid sequence of SIYYSGRITYNPSLKS (SEQ ID NO: 66); (c) an HVR-H3 comprising the amino acid sequence of AGGLYNWNDESFYMDV (SEQ ID NO: 68); (d) an HVR-L1 comprising the amino acid sequence of RASQSFSSSYLA (SEQ ID NO: 69); (e) an HVR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO: 70); and (f) an HVR-L3 comprising the amino acid sequence of QQYDRSPLT (SEQ ID NO: 71); and a second binding domain that specifically binds IL-13 comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of AYSVN (SEQ ID NO: 296); (b) an HVR-H2 comprising the amino acid sequence of MIWGDGKIVYNSALKS (SEQ ID NO: 297); (c) an HVR-H3 comprising the amino acid sequence of DGYYPYAMDND (SEQ ID NO: 298); (d) an HVR-L1 comprising the amino acid sequence of RASKSVDSYGNFSMH (SEQ ID NO: 299); (e) an HVR-L2 comprising the amino acid sequence of LASNLES (SEQ ID NO: 300); and (f) an HVR-L3 comprising the amino acid sequence of QQNNEDPRT (SEQ ID NO: 301).

In another embodiment, the disclosure features an isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises a first binding domain that specifically binds IL-33 comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 36 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 37, and a second binding domain that specifically binds IL-13 comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 302 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 303.

In another embodiment, the disclosure features an isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises a first binding domain that specifically binds IL-33 comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 84 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 85, and a second binding

domain that specifically binds IL-13 comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 302 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 303.

5 In another embodiment, the disclosure features an isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises: (a) a first heavy chain and a first light chain that specifically bind IL-33, wherein the first heavy chain comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 306 and the first light chain comprises
10 an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 307, and (b) a second heavy chain and a second light chain that specifically bind IL-13, wherein the second heavy chain comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 304 and the second light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 305.

15 In another embodiment, the disclosure features an isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises: (a) a first heavy chain and a first light chain that specifically bind IL-33, wherein the first heavy chain comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 308 and the first light chain comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID
20 NO: 309, and (b) a second heavy chain and a second light chain that specifically bind IL-13, wherein the second heavy chain comprises an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 304 and the second light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 305.

In some embodiments of any of the preceding aspects, the antibody is an antigen-binding antibody fragment. In some embodiments, the antigen-binding antibody fragment is selected from the
25 group consisting of Fab, Fab'-SH, Fv, scFv, and (Fab')₂ fragments. In some embodiments, the antigen-binding antibody fragment is an Fab.

In another aspect, the invention features an isolated nucleic acid encoding any of the antibodies described herein. In another aspect, the invention features a vector comprising the preceding isolated nucleic acid. In some embodiments, the disclosure features a vector (e.g., an expression vector)
30 comprising the isolated nucleic acid for expressing the antibody. In another aspect, the invention features a host cell comprising the preceding vector. In some embodiments, the disclosure features host cells comprising the preceding nucleic acids and/or vectors. In some embodiments, the host cell is a mammalian cell. In some embodiments, the mammalian cell is a Chinese hamster ovary (CHO) cell. In some embodiments, the host cell is a prokaryotic cell. In some embodiments, the prokaryotic cell is *E. coli*.
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In another aspect, the invention features a method of producing any of the antibodies described herein, the method comprising culturing a host cell described herein in a culture medium. In some
40 embodiments, the disclosure features a method of producing any of the antibodies described herein, the method comprising culturing a host cell that comprises any of the preceding vectors (e.g., expression vectors) in a culture medium. In some embodiments, the method further comprises recovering the antibody from the host cell or the culture medium.

In another aspect, the invention features a composition comprising any one of the preceding antibodies. In some embodiments, the composition further comprises a pharmaceutically acceptable

carrier, excipient, or diluent. In some embodiments, the composition is a pharmaceutical composition. In some embodiments, the pharmaceutical composition further comprises an ST2 binding antagonist, a Factor D binding antagonist, an HtrA1 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. In some embodiments, the pharmaceutical composition comprises a Factor D binding antagonist. In some embodiments, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof. In some embodiments, the pharmaceutical composition comprises an HtrA1 antagonist. In some embodiments, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof. In some embodiments, the pharmaceutical composition comprises a VEGF antagonist. In some embodiments, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In some embodiments, any one of the preceding antibodies can be used as a medicament.

In some embodiments, any one of the preceding antibodies can be used in treating an IL-33-mediated disorder. In some embodiments, the IL-33-mediated disorder is selected from the group consisting of an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, a solid tumor, and an ophthalmologic disorder. In some embodiments, the inflammatory condition is selected from the group consisting of asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, and chronic obstructive pulmonary disease (COPD). In some embodiments, the immune disorder is selected from the group consisting of asthma, rheumatoid arthritis, allergic rhinitis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, diabetes, and liver disease. In some embodiments, the fibrotic disease is idiopathic pulmonary fibrosis (IPF). In some embodiments, the eosinophilic disorder is an eosinophil-associated gastrointestinal disorder (EGID). In some embodiments, the EGID is eosinophilic esophagitis. In some embodiments, the infection is a helminth infection, a protozoan infection, or a viral infection. In some embodiments, the protozoan infection is a *Leishmania major* infection. In some embodiments, the viral infection is a respiratory syncytial virus (RSV) infection or an influenza infection. In some embodiments, the pain is inflammatory pain. In some embodiments, the central nervous system disorder is Alzheimer's disease. In some embodiments, the solid tumor is selected from the group consisting of breast tumor, colon tumor, prostate tumor, lung tumor, kidney tumor, liver tumor, pancreas tumor, stomach tumor, intestinal tumor, brain tumor, bone tumor, and skin tumor. In some embodiments, the ophthalmologic disorder is selected from the group consisting of 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, and conjunctivitis. In some embodiments, the AMD is wet AMD, dry AMD, or geographic atrophy (GA). In some embodiments, the AMD is intermediate AMD or advanced AMD. In some embodiments, the retinopathy of the eye is diabetic retinopathy (DR) or retinopathy of prematurity (ROP). In some embodiments, the retinopathy of the eye is high-altitude DR. In some embodiments, the

conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis. In some embodiments, the conjunctivitis is allergic conjunctivitis.

In some aspects, the invention features use of any one of the preceding antibodies in the manufacture of a medicament for treating an IL-33-mediated disorder in a subject. In some
5 embodiments, the IL-33-mediated disorder is selected from the group consisting of an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, a solid tumor, and an ophthalmologic disorder. In some embodiments, the inflammatory condition is selected from the group consisting of asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, and chronic obstructive pulmonary disease (COPD). In
10 some embodiments, the immune disorder is selected from the group consisting of asthma, rheumatoid arthritis, allergic rhinitis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, diabetes, and liver disease. In some embodiments, the fibrotic disease is idiopathic pulmonary fibrosis (IPF). In some embodiments, the eosinophilic disorder is an eosinophil-associated gastrointestinal disorder (EGID). In some embodiments, the EGID is eosinophilic esophagitis. In some embodiments, the infection is a
15 helminth infection, a protozoan infection, or a viral infection. In some embodiments, the protozoan infection is a *Leishmania major* infection. In some embodiments, the viral infection is a respiratory syncytial virus (RSV) infection or an influenza infection. In some embodiments, the pain is inflammatory pain. In some embodiments, the central nervous system disorder is Alzheimer's disease. In some
embodiments, the solid tumor is selected from the group consisting of breast tumor, colon tumor, prostate
20 tumor, lung tumor, kidney tumor, liver tumor, pancreas tumor, stomach tumor, intestinal tumor, brain tumor, bone tumor, and skin tumor. In some embodiments, the ophthalmologic disorder is selected from the group consisting of 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,
25 traumatic eye injury, and conjunctivitis. In some embodiments, the AMD is wet AMD, dry AMD, or geographic atrophy (GA). In some embodiments, the AMD is intermediate AMD or advanced AMD. In some embodiments, the retinopathy of the eye is diabetic retinopathy (DR) or retinopathy of prematurity (ROP). In some embodiments, the retinopathy of the eye is high-altitude DR. In some embodiments, the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis. In some embodiments, the
30 conjunctivitis is allergic conjunctivitis. In some embodiments, 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 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
35 antagonist. In some embodiments, the medicament is formulated for use in combination with a Factor D binding antagonist. In some embodiments, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof. In some embodiments, the medicament is formulated for use in combination with an HtrA1 binding antagonist. In some embodiments, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof. In some embodiments, the medicament is
40 formulated for use in combination with a VEGF

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

In another embodiment, the disclosure provides for the use of a bispecific antibody that specifically binds both IL-33 and Factor D or an antigen-binding antibody fragment thereof in the manufacture of a medicament for treating geographic atrophy (GA). In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, any one of the preceding antibodies can be used in the manufacture of a medicament for treating geographic atrophy (GA), wherein the medicament is formulated for use in combination with a Factor D binding antagonist. In some embodiments, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure provides for the use of a bispecific antibody that specifically binds both IL-33 and HtrA1 or an antigen-binding antibody fragment thereof in the manufacture of a medicament for treating geographic atrophy (GA), AMD (wet or dry), DR, PCV, or ROP. In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, any one of the preceding antibodies can be used in the manufacture of a medicament for treating geographic atrophy (GA), AMD (wet or dry), DR, PCV, or ROP, wherein the medicament is formulated for use in combination with an HtrA1 binding antagonist. In some embodiments, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure provides for the use of a bispecific antibody that specifically binds both IL-33 and VEGF or an antigen-binding antibody fragment thereof in the manufacture of a medicament for treating wet AMD. In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, any one of the preceding antibodies can be used in the manufacture of a medicament for treating wet AMD, wherein the medicament is formulated for use in combination with a VEGF antagonist. In some embodiments, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure features 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 preceding antibodies. In some embodiments, the IL-33-mediated disorder is selected from the group consisting of an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, a solid tumor, and an ophthalmologic disorder. In some embodiments, the inflammatory condition is selected from the group consisting of asthma, sepsis, septic shock, atopic dermatitis, allergic rhinitis, rheumatoid arthritis, and chronic obstructive pulmonary disease (COPD). In some embodiments, the immune disorder is selected from the group consisting of asthma, rheumatoid arthritis, allergic rhinitis, psoriasis, inflammatory bowel disease (IBD), Crohn's disease, diabetes, and liver disease. In some embodiments, the fibrotic disease is idiopathic pulmonary fibrosis (IPF). In some embodiments, the eosinophilic disorder is an eosinophil-associated gastrointestinal disorder (EGID). In some embodiments, the EGID is eosinophilic esophagitis.

In some embodiments, the infection is a helminth infection, a protozoan infection, or a viral infection. In some embodiments, the protozoan infection is a *Leishmania major* infection. In some embodiments, the viral infection is a respiratory syncytial virus (RSV) infection or an influenza infection. In some embodiments, the pain is inflammatory pain. In some embodiments, the central nervous system disorder is Alzheimer's disease. In some embodiments, the solid tumor is selected from the group consisting of breast tumor, colon tumor, prostate tumor, lung tumor, kidney tumor, liver tumor, pancreas tumor, stomach tumor, intestinal tumor, brain tumor, bone tumor, and skin tumor. In some embodiments, the ophthalmologic disorder is selected from the group consisting of 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, and conjunctivitis. In some embodiments, the AMD is wet AMD, dry AMD, or geographic atrophy (GA). In some embodiments, the AMD is intermediate AMD or advanced AMD. In some embodiments, the retinopathy of the eye is diabetic retinopathy (DR) or retinopathy of prematurity (ROP). In some embodiments, the retinopathy of the eye is high-altitude DR. In some embodiments, the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis. In some embodiments, the conjunctivitis is allergic conjunctivitis. In some embodiments, the method further comprises administering to the subject 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. In some embodiments, the method further comprises administering to the subject a Factor D binding antagonist. In some embodiments, the Factor D binding antagonist is anti-Factor D antibody or an antigen-binding fragment thereof. In some embodiments, the method further comprises administering to the subject an HtrA1 binding antagonist. In some embodiments, the HtrA1 binding antagonist is anti-HtrA1 antibody or an antigen-binding fragment thereof. In some embodiments, the method further comprises administering to the subject a VEGF antagonist. In some embodiments, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure features a method of treating geographic atrophy (GA) in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a bispecific antibody that specifically binds both IL-33 and Factor D or an antigen-binding antibody fragment thereof. In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, the disclosure features a method of treating geographic atrophy (GA) in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one of the preceding antibodies and a therapeutically effective amount of a Factor D binding antagonist. In some embodiments, the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure features a method of treating geographic atrophy (GA), AMD (wet or dry), DR, PCV, or ROP in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a bispecific antibody that specifically binds both IL-33 and HtrA1 or an antigen-binding antibody fragment thereof. In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, the disclosure features a method of treating geographic atrophy (GA), AMD (wet or dry), DR, PCV, or ROP in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one of the preceding antibodies and a therapeutically effective amount of a HtrA1 binding antagonist. In some embodiments, the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.

In another embodiment, the disclosure features a method of treating wet AMD in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a bispecific antibody that specifically binds both IL-33 and VEGF or an antigen-binding antibody fragment thereof. In some embodiments, the antigen-binding antibody fragment is a (Fab')₂ fragment.

In another embodiment, the disclosure features a method of treating wet AMD in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of any one of the preceding antibodies and a therapeutically effective amount of a VEGF antagonist. In some embodiments, the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

In some embodiments of any of the preceding methods, the antibody is administered subcutaneously, intravenously, intramuscularly, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, intranasally, intravitreally, intraocularly, periocularly, conjunctivally, subconjunctivally, subtenonally, intracamerally, subretinally, retrobulbarly, or intracanalicularly. In some embodiments, the subject is a human.

Brief Description of the Drawings

FIGURE 1A is a diagram showing a schematic of a cell-based IL-33 blocking assay. SEAP is used as a reporter gene for NF-κB/AP-1 secreted alkaline phosphatase. Soluble ST2 (sST2) is used as a positive control.

FIGURE 1B is a graph showing the results of a cell-based IL-33 blocking assay for human IL-33.

FIGURE 1C is a graph showing the results of a cell-based IL-33 blocking assay for cynomolgus monkey (cyno) IL-33.

FIGURE 2 is a graph showing the results of a cell-based IL-33 blocking assay for the indicated anti-IL-33 antibody clones.

FIGURE 3 is a table showing the results of cell-based IL-33 blocking assays (IC₅₀ and IC₉₀) for the indicated parental and humanized anti-IL-33 antibodies.

FIGURE 4A is an image showing the macular and peripheral retina dissected for RNA-seq analysis. The macular area between the superior and inferior temporal vascular arcades was separated from the peripheral fundus using dissecting scissors. RNA was isolated from both macular and peripheral retina tissues for RNA-seq. The dashed outline indicates the area of the macula, and the solid circle

WHAT IS CLAIMED IS:

1. An isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising the following six HVRs:
 - (a) an HVR-H1 comprising the amino acid sequence of SFSX₁S (SEQ ID NO: 62), wherein X₁ is Met, Leu, or Val;
 - (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDX₁VKG (SEQ ID NO: 63), wherein X₁ is Ser or Ala;
 - (c) an HVR-H3 comprising the amino acid sequence of ANYGX₁X₂FFEY (SEQ ID NO: 64), wherein X₁ is Asn or Asp, and X₂ is Trp or Phe;
 - (d) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLLN (SEQ ID NO: 4);
 - (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6).
2. The antibody of claim 1, wherein the binding domain comprises the following six HVRs:
 - (a) an HVR-H1 comprising the amino acid sequence of SFSMS (SEQ ID NO: 1);
 - (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDSVKG (SEQ ID NO: 2);
 - (c) an HVR-H3 comprising the amino acid sequence of ANYGNWFFEY (SEQ ID NO: 3);
 - (d) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLLN (SEQ ID NO: 4);
 - (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6).
3. An isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 36; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 37; or (c) a VH domain as in (a) and a VL domain as in (b).
4. The antibody of claim 3, wherein the VH domain further comprises:
 - (a) an FR-H1 comprising the amino acid sequence of EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO: 12);
 - (b) an FR-H2 comprising the amino acid sequence of WVRQAPGKGLEWVA (SEQ ID NO: 13);
 - (c) an FR-H3 comprising the amino acid sequence of RFTISRDDSKNTLYLQMNSLRAEDTAVYYCTR (SEQ ID NO: 14); and
 - (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 15).
5. The antibody of claim 4, wherein the VH domain comprises the amino acid sequence of SEQ ID NO: 36.
6. The antibody of any one of claims 3-5, wherein the VL domain further comprises:
 - (a) an FR-L1 comprising the amino acid sequence of EIVLTQSPATLSLSPGERATLSC (SEQ ID NO: 25);

- (b) an FR-L2 comprising the amino acid sequence of WFQQKPGQPPRLIF (SEQ ID NO: 26);
- (c) an FR-L3 comprising the amino acid sequence of GIPARFSGSGSGTDFTLTSSLEPEDFAVYYC (SEQ ID NO: 27); and
- (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 28).

7. The antibody of claim 6, wherein the VL domain comprises the amino acid sequence of SEQ ID NO: 37.

8. An isolated antibody that specifically binds IL-33, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 36 and (b) a VL domain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 37.

9. An isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 288 and (b) a light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 289.

10. An isolated antibody that specifically binds IL-33, wherein the antibody comprises (a) a heavy chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 290 and (b) a light chain comprising an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 291.

11. The antibody of any one of claims 1-10, wherein the antibody specifically binds human or cynomolgus monkey (cyno) IL-33.

12. The antibody of claim 11, wherein the antibody specifically binds both human and cyno IL-33.

13. The antibody of claim 12, wherein the antibody specifically binds both human and cyno IL-33 with a K_D of about 1 nM or lower.

14. The antibody of claim 13, wherein the antibody specifically binds human IL-33 with a K_D between about 1 pM and about 500 pM.

15. The antibody of claim 14, wherein the antibody specifically binds human IL-33 with a K_D between about 15 pM and about 140 pM.

16. The antibody of claim 13, wherein the antibody specifically binds cyno IL-33 with a K_D between about 1 pM and about 500 pM.

17. The antibody of claim 16, wherein the antibody specifically binds cyno IL-33 with a K_D between about 125 pM and about 500 pM.

18. The antibody of claim 14 or 16, wherein the antibody specifically binds both human and cyno IL-33 with a K_D of between about 1 pM and about 500 pM.
19. The antibody of claim 18, wherein the antibody specifically binds human IL-33 with a K_D of between about 1 pM and about 200 pM.
20. The antibody of any one of claims 1-19, wherein the antibody is capable of inhibiting the binding of IL-33 to an IL-33 receptor.
21. The antibody of claim 20, wherein the inhibiting is measured using a cell-based blocking assay.
22. The antibody of claim 21, wherein the antibody inhibits the binding of human IL-33 to an IL-33 receptor with a 90% inhibitory concentration (IC90) of between about 0.001 μ g/ml and about 0.5 μ g/ml.
23. The antibody of claim 22, wherein the IC90 is between about 0.002 μ g/ml and about 0.25 μ g/ml.
24. The antibody of claim 23, wherein the IC90 is about 0.004 μ g/ml.
25. The antibody of any one of claims 1-24, wherein the antibody inhibits binding of human IL-33 to an IL-33 receptor with an IC50 of between about 800 fM and about 10 pM.
26. The antibody of claim 25, wherein the IC50 is between about 1 pM and about 5 pM.
27. The antibody of claim 26, wherein the IC50 is about 2.5 pM.
28. The antibody of any one of claims 1-27, wherein the antibody inhibits binding of cyno IL-33 to an IL-33 receptor with an IC50 of between about 1 nM and about 5 nM.
29. The antibody of claim 28, wherein the IC50 is about 4 nM.
30. The antibody of any one of claims 1-29, wherein the antibody comprises an aglycosylation site mutation.
31. The antibody of any one of claims 1-30, wherein the antibody is monoclonal, human, humanized, or chimeric.
32. The antibody of any one of claims 1-31, wherein the antibody is an antibody fragment that binds IL-33.
33. The antibody of claim 32, wherein the antibody fragment is selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and (Fab')₂ fragments.

34. The antibody of claim 33, wherein the antibody fragment is an Fab fragment.
35. The antibody of any one of claims 1-31, wherein the antibody is a full-length antibody.
36. The antibody of claim 35, wherein the antibody is an IgG antibody.
37. The antibody of claim 36, wherein the IgG antibody is an IgG1 antibody.
38. The antibody of claim 36, wherein the IgG antibody is an IgG4 antibody.
39. The antibody of claim 38, wherein the IgG4 antibody comprises a mutation in the hinge region.
40. The antibody of claim 39, wherein the mutation is a substitution mutation.
41. The antibody of claim 40, wherein the substitution mutation is at amino acid residue S228 (EU numbering).
42. The antibody of claim 41, wherein the substitution mutation is an S228P mutation.
43. The antibody of any one of claims 1-42, wherein the antibody is a monospecific antibody.
44. The antibody of any one of claims 1-42, wherein the antibody is a multispecific antibody.
45. The antibody of claim 44, wherein the antibody is a bispecific antibody.
46. The antibody of claim 45, wherein the bispecific antibody comprises a second binding domain that binds to a second biological molecule, wherein the second biological molecule is selected from the group consisting of interleukin-13 (IL-13), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, and a VEGF receptor.
47. The antibody of claim 46, wherein the second biological molecule is IL-13.
48. The antibody of claim 47, wherein the second binding domain comprises the following six HVRs:
 - (a) an HVR-H1 comprising the amino acid sequence of AYSVN (SEQ ID NO: 296);
 - (b) an HVR-H2 comprising the amino acid sequence of MIWGDGKIVYNSALKS (SEQ ID NO: 297);
 - (c) an HVR-H3 comprising the amino acid sequence of DGYYPYAMDN (SEQ ID NO: 298);
 - (d) an HVR-L1 comprising the amino acid sequence of RASKSVDSYGNSFMH (SEQ ID NO: 299);
 - (e) an HVR-L2 comprising the amino acid sequence of LASNLES (SEQ ID NO: 300); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQNNEDPRT (SEQ ID NO: 301).

49. An isolated antibody that specifically binds both IL-33 and IL-13, wherein the antibody comprises a first binding domain that specifically binds IL-33 comprising the following six HVRs:
- (a) an HVR-H1 comprising the amino acid sequence of SFSMS (SEQ ID NO: 1);
 - (b) an HVR-H2 comprising the amino acid sequence of TISGGKTFTDYVDSVKG (SEQ ID NO: 2);
 - (c) an HVR-H3 comprising the amino acid sequence of ANYGNWFFEY (SEQ ID NO: 3);
 - (d) an HVR-L1 comprising the amino acid sequence of RASESVAKYGLSLN (SEQ ID NO: 4);
 - (e) an HVR-L2 comprising the amino acid sequence of AASNRGS (SEQ ID NO: 5); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQSKEVPFT (SEQ ID NO: 6); and
- a second binding domain that specifically binds IL-13 comprising the following six HVRs:
- (a) an HVR-H1 comprising the amino acid sequence of AYSVN (SEQ ID NO: 296);
 - (b) an HVR-H2 comprising the amino acid sequence of MIWGDGKIVYNSALKS (SEQ ID NO: 297);
 - (c) an HVR-H3 comprising the amino acid sequence of DGYYPYAMDN (SEQ ID NO: 298);
 - (d) an HVR-L1 comprising the amino acid sequence of RASKSVDSYGNSFMH (SEQ ID NO: 299);
 - (e) an HVR-L2 comprising the amino acid sequence of LASNLES (SEQ ID NO: 300); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQNNEDPRT (SEQ ID NO: 301).
50. An isolated nucleic acid encoding the antibody of any one of claims 1-49.
51. A vector comprising the isolated nucleic acid of claim 50.
52. A host cell comprising the vector of claim 51.
53. The host cell of claim 52, wherein the host cell is a mammalian cell.
54. The host cell of claim 53, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.
55. The host cell of claim 52, wherein the host cell is a prokaryotic cell.
56. The host cell of claim 55, wherein the prokaryotic cell is *E. coli*.
57. A method of producing the antibody of any one of claims 1-49, the method comprising culturing the host cell of claim 52 in a culture medium.
58. The method of claim 57, wherein the method further comprises recovering the antibody from the host cell or the culture medium.
59. A composition comprising the antibody of any one of claims 1-49.
60. The composition of claim 59, further comprising a pharmaceutically acceptable carrier, excipient, or diluent.
61. The composition of claim 60, wherein the composition is a pharmaceutical composition.

62. The composition of any one of claims 59-61, 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.
63. The composition of claim 62, wherein the pharmaceutical composition comprises a Factor D binding antagonist.
64. The composition of claim 63, wherein the Factor D binding antagonist is an anti-Factor D antibody or an antigen-binding fragment thereof.
65. The composition of claim 62, wherein the pharmaceutical composition comprises an HtrA1 binding antagonist.
66. The composition of claim 65, wherein the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.
67. The composition of claim 62, wherein the pharmaceutical composition comprises a VEGF antagonist.
68. The composition of claim 67, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.
69. Use of the antibody of any one of claims 1-49 in the manufacture of a medicament for treating an IL-33-mediated disorder in a subject.
70. The use of claim 69, wherein the IL-33-mediated disorder is selected from the group consisting of an inflammatory condition, an immune disorder, a fibrotic disorder, an eosinophilic disorder, an infection, pain, a central nervous system disorder, a solid tumor, and an ophthalmologic disorder.
71. The use of claim 70, wherein the ophthalmologic disorder is selected from the group consisting of AMD, retinopathy of the eye, PCV, diabetic macular edema (DME), dry eye disease, Behcet's disease, retina detachment, glaucoma, uveitis, retinitis pigmentosa, Leber Congenital Amaurosis, Stargardt's disease, traumatic eye injury, and conjunctivitis.
72. The use of claim 71, wherein the AMD is wet AMD.
73. The use of claim 71, wherein the AMD is dry AMD.

74. The use of claim 71, wherein the AMD is geographic atrophy (GA).
75. The use of claim 71, wherein the AMD is intermediate AMD or advanced AMD.
76. The use of claim 71, wherein the retinopathy of the eye is diabetic retinopathy (DR) or ROP.
77. The use of claim 76, wherein the retinopathy of the eye is DR.
78. The use of claim 77, wherein the DR is high-altitude DR.
79. The use of claim 71, wherein the conjunctivitis is infectious conjunctivitis or non-infectious conjunctivitis.
80. The use of claim 79, wherein the conjunctivitis is allergic conjunctivitis.
81. The use of claim 71, wherein the ophthalmologic disorder is DME.
82. The use of any one of claims 69-81, wherein 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 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.
83. The use of claim 82, wherein the medicament is formulated for use in combination with a Factor D binding antagonist.
84. The use of claim 83, wherein the Factor D binding antagonist is anti-Factor D antibody or an antigen-binding fragment thereof.
85. The use of claim 82, wherein the medicament is formulated for use in combination with an HtrA1 binding antagonist.
86. The use of claim 85, wherein the HtrA1 binding antagonist is an anti-HtrA1 antibody or an antigen-binding fragment thereof.
87. The use of claim 82, wherein the medicament is formulated for use in combination with a VEGF antagonist.
88. The use of claim 87, wherein the VEGF antagonist is an anti-VEGF antibody or an antigen-binding fragment thereof.

89. The use of any one of claims 69-88, wherein the antibody is a bispecific antibody comprising a second binding domain that binds to a second biological molecule, wherein the second biological molecule is selected from the group consisting of interleukin-13 (IL-13), interleukin-4 (IL-4), interleukin-5 (IL-5), interleukin-17 (IL-17), Factor D, HtrA1, VEGF, and a VEGF receptor.

90. The use of any one of claims 69-89, wherein the antibody is one that is formulated for administration subcutaneously, intravenously, intramuscularly, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, intranasally, intravitreally, intraocularly, periocularly, conjunctivally, subconjunctivally, subtenonly, intracamerally, subretinally, retrobulbarly, or intracanalicularly.

91. The use of any one of claims 69-90, wherein the subject is a human.