

examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 21. In some examples, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 17); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKPLIS (SEQ ID NO: 18); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 19); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 20). In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 22.

In another example, there is provided an isolated antibody that specifically binds HtrA1, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DSEX₁H (SEQ ID NO: 1), wherein X₁ is Met or Leu; (b) an HVR-H2 comprising the amino acid sequence of GVDPETX₂GAAYNQKFKG (SEQ ID NO: 2), wherein X₂ is Glu or Asp; (c) an HVR-H3 comprising the amino acid sequence of GYDYDYALDY (SEQ ID NO: 3); (d) an HVR-L1 comprising the amino acid sequence of RASSSVX₃FIH (SEQ ID NO: 4), wherein X₃ is Glu or Asn; (e) an HVR-L2 comprising the amino acid sequence of ATSX₄LAS (SEQ ID NO: 5), wherein X₄ is Asn, His or Glu; and (f) an HVR-L3 comprising the amino acid sequence of QQWX₅SX₆PWT (SEQ ID NO: 6), wherein X₅ is Ser or Tyr and X₆ is Ala or Asn. In some examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DSEMH (SEQ ID NO: 7); (b) an HVR-H2 comprising the amino acid sequence of GVDPETEGAAYNQKFKG (SEQ ID NO: 8); (c) an HVR-H3 comprising the amino acid sequence of GYDYDYALDY (SEQ ID NO: 3); (d) an HVR-L1 comprising the amino acid sequence of RASSSVEFIH (SEQ ID NO: 9); (e) an HVR-L2 comprising the amino acid sequence of ATSNLAS (SEQ ID NO: 10); and (f) an HVR-L3 comprising the amino acid sequence of QQWSSAPWT (SEQ ID NO: 11). In one aspect, the present disclosure refers to an isolated antibody that specifically binds HtrA1, wherein the antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of DSEMH (SEQ ID NO: 7); (b) an HVR-H2 comprising the amino acid sequence of GVDPETEGAAYNQKFKG (SEQ ID NO: 8); (c) an HVR-H3 comprising the amino acid sequence of GYDYDYALDY (SEQ ID NO: 3); (d) an HVR-L1 comprising the amino acid sequence of RASSSVEFIH (SEQ ID NO: 9); (e) an HVR-L2 comprising the amino acid sequence of ATSNLAS (SEQ ID NO: 10); and (f) an HVR-L3 comprising the amino acid sequence of QQWSSAPWT (SEQ ID NO: 11).

In another example, there is provided an isolated antibody that specifically binds HtrA1, wherein the antibody comprises a binding domain comprising (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 21; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 22; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain further comprises: (a) an FR-H1 comprising the amino acid sequence of EVQLVQSGAEVKKPGASVKVSCKASGYKFT (SEQ ID NO: 16); (b) an FR-H2 comprising the amino acid sequence of WVRQAPGQGLEWIG (SEQ ID NO: 13); (c) an FR-H3 comprising the amino acid sequence of RATITRDTSTSTAYLELSSLRSEDTAVYYCTR (SEQ ID NO: 14); and (d) an FR-H4 comprising the amino acid sequence of WGQGTLVTVSS (SEQ ID NO: 15). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 21. In some examples, the VL domain further comprises: (a) an FR-L1 comprising the amino acid sequence of DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO: 17); (b) an FR-L2 comprising the amino acid sequence of WYQQKPGKAPKPLIS (SEQ ID NO: 18); (c) an FR-L3 comprising the amino acid sequence of GVPSRFSGSGSGTDFTLTISLQPEDFATYYC (SEQ ID NO: 19); and (d) an FR-L4 comprising the amino acid sequence of FGQGTKVEIK (SEQ ID NO: 20). In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 22.

CLAIMS

What is claimed is:

1. An isolated antibody that specifically binds HtrA1, wherein the antibody comprises a binding domain comprising the following six HVRs:
 - (a) an HVR-H1 comprising the amino acid sequence of DSEMH (SEQ ID NO: 7);
 - (b) an HVR-H2 comprising the amino acid sequence of GVDPETEGAAYNQKFKG (SEQ ID NO: 8);
 - (c) an HVR-H3 comprising the amino acid sequence of GYDYDYALDY (SEQ ID NO: 3);
 - (d) an HVR-L1 comprising the amino acid sequence of RASSSVEFIH (SEQ ID NO: 9);
 - (e) an HVR-L2 comprising the amino acid sequence of ATSNLAS (SEQ ID NO: 10); and
 - (f) an HVR-L3 comprising the amino acid sequence of QQWSSAPWT (SEQ ID NO: 11).

2. The antibody of claim 1, wherein the antibody comprises a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 21 and/or a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 22.

3. The antibody of claim 2, wherein the antibody comprises a VH domain comprising the amino acid sequence of SEQ ID NO: 21 and/or a VL domain comprising the amino acid sequence of SEQ ID NO: 22.

4. The antibody of any one of claims 1-3, wherein:
 - (i) the antibody is monoclonal, humanized, or chimeric; wherein optionally
 - (ii) the antibody is an antibody fragment that binds to HtrA1; wherein optionally
 - (iii) the antibody fragment is selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and (Fab')₂ fragments; wherein optionally
 - (iv) the antibody fragment is a Fab; wherein optionally
 - (v) the Fab comprises a truncation in the upper hinge of the heavy chain constant region; and wherein optionally
 - (vi) the heavy chain constant region terminates at position 221 (EU numbering).

5. The antibody of any one of claims 1-3, wherein the antibody comprises the heavy chain amino acid sequence of SEQ ID NO: 160 and the light chain amino acid sequence of SEQ ID NO: 159.

6. The antibody of any one of claims 1-5, wherein said antibody specifically binds to an HtrA1 epitope, wherein the HtrA1 epitope comprises at least one amino acid of the HtrA1 protein selected from the group consisting of Arg190, Leu192, Pro193, Phe194, and Arg197.

7. The antibody of claim 6, wherein the HtrA1 epitope comprises at least one amino acid of the HtrA1 protein selected from the group consisting of Leu192, Pro193, and Arg197; wherein optionally the HtrA1 epitope comprises the HtrA1 amino acids Leu192, Pro193, and Arg197; and wherein optionally the HtrA1 epitope comprises the HtrA1 amino acids Arg190, Leu192, Pro193, Phe194, and Arg197.
8. The antibody of any one of claims 1-7, wherein the antibody is a bispecific antibody.
9. An isolated nucleic acid encoding the antibody of any one of claims 1-8.
10. A method of producing an antibody, the method comprising culturing a host cell comprising a vector comprising an isolated nucleic acid according to claim 9 and recovering the antibody from the host cell or the host cell culture medium.
11. A pharmaceutical composition comprising an antibody of any one of claims 1-8 and further comprising at least one pharmaceutically acceptable carrier, excipient, or diluent.
12. The pharmaceutical composition of claim 11, wherein the composition is lyophilized.
13. The antibody of any one of claims 1-8 for use as a medicament.
14. The antibody of any one of claims 1-8 for use in treating an HtrA1-associated disorder or an ocular disorder in a subject in need thereof, wherein the HtrA1-associated disorder or the ocular disorder is age-related macular degeneration (AMD), diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy, wherein optionally the HtrA1-associated disorder or the ocular disorder is early dry AMD, intermediate dry AMD, or advanced dry AMD, wherein optionally the advanced dry AMD is geographic atrophy.
15. The antibody for use of claim 14, wherein the antibody is to be administered to the subject with a Factor D antagonist.
16. The antibody for use of claim 15, wherein the Factor D antagonist is an anti-Factor D antibody.
17. The antibody for use of claim 16, wherein the anti-Factor D antibody is lampalizumab.
18. The antibody for use of any one of claims 15-17, wherein the anti-Factor D antagonist is to be administered sequentially.

19. Use of the antibody of any one of claims 1-8 in the manufacture of a medicament for treating an HtrA1-associated disorder or an ocular disorder in a subject in need thereof, wherein the HtrA1-associated disorder or the ocular disorder is AMD, diabetic retinopathy, retinopathy of prematurity, or polypoidal choroidal vasculopathy, wherein optionally the HtrA1-associated disorder or the ocular disorder is early dry AMD, intermediate dry AMD, or advanced dry AMD, wherein optionally the advanced dry AMD is geographic atrophy; wherein optionally the medicament is to be administered with a Factor D antagonist, wherein the Factor D antagonist is an anti-Factor D antibody, and wherein optionally the anti-Factor D antibody is lampalizumab.

20. The use of claim 19, wherein the medicament is to be administered intravitreally, ocularly, intraocularly, juxtasclerally, subtenonly, superchoroidally, or topically, wherein optionally the medicament is to be administered intravitreally by injection; or wherein the medicament is to be administered by a long-acting delivery system, wherein optionally the long-acting delivery system is a PLGA-based solid implant or an implantable port delivery system.