

CLAIMS

1. An anti-Nrp1A antibody or an antigen-binding fragment thereof comprising:

- a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 1 (H-CDR1); the amino acid sequence of SEQ ID NO: 2 (H-CDR2); and the amino acid sequence of SEQ ID NO: 3 (H-CDR3); and
- a light chain variable region comprising the amino acid sequence of SEQ ID NO: 4 (L-CDR1); the amino acid sequence of SEQ ID NO: 5 (L-CDR2); and the amino acid sequence of SEQ ID NO: 6 (L-CDR3).

2. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**, wherein the antibody or the antigen-binding fragment thereof comprises:

- a heavy chain variable region comprising an amino acid sequence at least 80%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 or SEQ ID NO: 17; and
- a light chain variable region comprising an amino acid sequence at least 80%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 11.

3. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**:

- a heavy chain variable region comprising an amino acid sequence at least 80%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino

acid sequence of SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 or SEQ ID NO: 17 and

- a light chain variable region comprising an amino acid sequence at least 80%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 11;

wherein

- the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 1 (H-CDR1), the amino acid sequence of SEQ ID NO: 2 (H-CDR2), and the amino acid sequence of SEQ ID NO: 3 (H-CDR3); and
- the light chain variable region comprising the amino acid sequence of SEQ ID NO: 4 (L-CDR1), the amino acid sequence of SEQ ID NO: 5 (L-CDR2), and the amino acid sequence of SEQ ID NO: 6 (L-CDR3).

4. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**, wherein the antibody or the antigen-binding fragment thereof comprises:

- a heavy chain variable region comprising the amino acid sequences of SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 or SEQ ID NO: 17; and
- a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11.

5. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**, wherein the antibody or the antigen-binding fragment thereof comprises:

- a. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 10 and SEQ ID NO: 11, respectively;
- b. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 12 and SEQ ID NO: 11, respectively;
- c. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 13 and SEQ ID NO: 11, respectively;
- d. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 14 and SEQ ID NO: 11, respectively;
- e. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 15 and SEQ ID NO: 11, respectively;
- f. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 16 and SEQ ID NO: 11, respectively; or
- g. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 17 and SEQ ID NO: 11, respectively.

6. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**, wherein the antibody or the antigen-binding fragment thereof comprises:

- a heavy chain comprising, preferably consisting of, the amino acid sequence of SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25; and
- a light chain comprising, preferably consisting of, the amino acid sequence of SEQ ID NO: 19.

7. The anti-Nrp1A antibody or the antigen-binding fragment thereof according to claim **1**, wherein the antibody or the antigen-binding fragment thereof comprises:

- a. a heavy chain comprising the amino acid sequence of SEQ ID NO: 18 and a light chain comprising the amino acid sequence of SEQ ID NO: 19;
- b. a heavy chain comprising the amino acid sequence of SEQ ID NO: 20 and a light chain comprising the amino acid sequence of SEQ ID NO: 19;
- c. a heavy chain comprising the amino acid sequence of SEQ ID NO: 21 and a light chain comprising the amino acid sequence of SEQ ID NO: 19;
- d. a heavy chain comprising the amino acid sequence of SEQ ID NO: 22 and a light chain comprising the amino acid sequence of SEQ ID NO: 19;
- e. a heavy chain comprising the amino acid sequence of SEQ ID NO: 23 and a light chain comprising the amino acid sequence of SEQ ID NO: 19;
- f. a heavy chain comprising the amino acid sequence of SEQ ID NO: 24 and a light chain comprising the amino acid sequence of SEQ ID NO: 19; or
- g. a heavy chain comprising the amino acid sequence of SEQ ID NO: 25 and a light chain comprising the amino acid sequence of SEQ ID NO: 19.

8. An anti-Nrp1A antibody or an antigen-binding fragment thereof that binds to at least one amino acid residue within amino acid regions 68-77 of human Nrp1A as set forth in SEQ ID NO: 26.

9. An anti-Nrp1A antibody or an antigen-binding fragment thereof that binds to the sequence set forth in SEQ ID NO: 27.

10. An antibody or an antigen-binding fragment according to any one of claims **1 to 9** for use as a medicament.

11. An antibody or an antigen-binding fragment according to any one of claims **1 to 9** for use in treating or preventing an eye or a retinal disease.

12. Use of an antibody or an antigen-binding fragment according to any one of claims **1 to 9** in the manufacture of a medicament for treating or preventing an eye or a retinal disease.

13. The antibody or the antigen-binding fragment for use according to claim **11**, or the use according to claim **12**, wherein said disease is selected from the group consisting of retinopathy, proliferative retinopathy such as retinopathy of prematurity, ischemic retinopathy, diabetic retinopathy including proliferative diabetic retinopathy and non-proliferative diabetic retinopathy, diabetic macular edema, diabetic macular ischemia, age-related macular degeneration, retinitis pigmentosa, inherited retinal dystrophy, myopic degeneration, retinal vein occlusions, retinal artery occlusions, endophthalmitis, uveitis, cystoid macular edema, choroidal neovascular membrane secondary to any retinal diseases, optic neuropathies, glaucoma, retinal detachment, toxic retinopathy, radiation retinopathy, traumatic retinopathy, drug-induced retinal vasculopathy, retinal neovascularisation, polypoidal choroidal vasculopathy, retinal vasculitis, retinal microaneurysm, Fuch's dystrophy, macular telangiectasia, usher syndrome, and Stargardt disease.

14. The antibody or the antigen-binding fragment for use according to any one of claims **11 or 13**, or the use according to claim **12 or 13**, wherein said disease is selected from the group consisting of diabetic retinopathy including proliferative diabetic retinopathy and non-proliferative diabetic retinopathy, ischemic retinopathy, diabetic macular edema, diabetic macular ischemia, age-related macular edema, retinal neovascularization, glaucoma and choroidal neovascularization.

15. The antibody or the antigen-binding fragment for use according to any one of claims **11, 13 or 14**, or the use according to any one of claims **12 to 14**, wherein said disease is diabetic macular edema and/or diabetic macular ischemia.

16. The antibody or the antigen-binding fragment for use according to any one of claims **11, 13 or 14**, or the use according to any one of claims **12 to 14**, wherein:

- said disease is diabetic macular ischemia, and
- vascular regeneration within the ischemic retina (revascularization) is to be promoted by said antibody or said antigen binding fragment and pathological neovascularization of the vitreous region of the eye is to be prevented by said antibody or said antigen binding fragment.

17. The antibody or the antigen-binding fragment for use, or the use according to claim **16**, wherein the angiogenesis induced by VEGF-A is not to be inhibited by said antibody or said antigen binding fragment.

18. The antibody or the antigen-binding fragment for use according to any one of claims **11, 13 or 14**, or the use according to any one of claims **12 to 14**, wherein:

- said disease is diabetic macular edema;
- permeability of the blood retinal barrier induced by Sema3A is to be reduced by said antibody or said antigen binding fragment; and
- permeability of the blood retinal barrier induced by VEGF-A is to be reduced by said antibody or said antigen binding fragment.

19. A pharmaceutical composition comprising an antibody or an antigen-binding fragment according to any of claims **1 to 11 or 13 to 18** and a pharmaceutically acceptable carrier.

20. The antibody or the antigen-binding fragment thereof according to any of claims **1 to 11 or 13 to 18**, the use according to any one of claims **12 to 18** or the pharmaceutical composition according to claim **19**, wherein said antibody or an antigen-

binding fragment thereof is to be administered by a parenteral route, intravenous route, intravitreal route or subcutaneous route of administration.

21. The antibody or the antigen-binding fragment thereof according to any of claims **1 to 11 or 13 to 18**, the use according to any one of claims **12 to 18** or the pharmaceutical composition according to claim **19**, wherein said antibody or an antigen-binding fragment thereof is to be administered by intravitreal route.

22. An isolated polynucleotide or polynucleotides comprising:

- a sequence encoding a heavy chain as shown in SEQ ID NO: 18, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25 or a heavy chain variable region as shown in SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, SEQ ID NO: 16 or SEQ ID NO: 17; and
- a sequence encoding a light chain as shown in SEQ ID NO: 19 or a light chain variable region as shown in SEQ ID NO: 11.

23. An expression vector comprising the isolated polynucleotide or polynucleotides of claim **22**.

24. A host cell comprising an isolated polynucleotide or polynucleotides according to claim **22** or an expression vector according to claim **23**.

25. A method for producing an anti-Nrp1A antibody or an antigen-binding fragment thereof comprising:

- a. obtaining a host cell according to claim **24**; and
- b. cultivating the host cell.

26. The method according to claim **25**, further comprising recovering and purifying the antibody or an antigen-binding fragment thereof.