

SUMMARY

[0005] Sema3A is an endogenous secreted protein that belongs to the class 3 semaphorin family (Sema3), which were originally identified as axonal guidance molecules and were implicated in vessel pathfinding and network formation. Neuropilin 1 and 2 (Nrp1 and Nrp2) and the type A/D plexins (Plxns) act as the ligands binding and the signal transducing subunits of the Sema3 receptor complexes on the surface of endothelial cells (ECs). As a special member of the Sema3 family, Sema3A binds to Nrp1 exclusively at first and then combines with PlexinA1–4 as a complex (Nrp1/PlexA1–4). In this receptor complex, Nrp1 acts as a binding element, while PlexA1–4 acts as a signal-transducing element.

[0006] Human Semaphorin 3A is a protein as disclosed in SEQ ID NO: 22 and available under the NCBI Reference Sequence NP_006071.1. Further, human Sema3A is encoded by the Gene ID: 10371 (NCBI).

[0007] Sema3A has been studied in tumor angiogenesis and metastasis for years, but its effects on retinal neovascularization are still unclear. The inventors have exemplified that Semaphorin 3A is secreted by hypoxic retinal ganglion cells and acts as a vasorepulsive cue. Sema3A repels neovessels away from ischemic region by inducing a cytoskeletal collapse in these cells. Without wishing to be bound by theory, the inventors have hypothesized that this would explain why revascularization of ischemic regions does not occur and instead the up-regulation of Sema3A leads to a pathological neovascularisation into the vitreous region.

[0008] Semaphorin 3A is secreted by hypoxic neurons in ischemic/avascular retina, thereby inhibiting vascular regeneration of the retina and enhancing pathologic preretinal neovascularization.

[0009] The inventors have addressed this pathological situation by developing antibodies targeting Sema3A. The present disclosure thus provides monoclonal antibodies that specifically bind to Sema3A, preferably human Sema3A.

[0010] In one aspect, the present disclosure provides an anti-Sema3A 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).

[0011] In another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- 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 SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; 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, SEQ ID NO: 12 or SEQ ID NO: 13;

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 comprises 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).

[0012] In another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- 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 SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; 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, SEQ ID NO: 12 or SEQ ID NO: 13.

[0013] In yet another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a heavy chain variable region comprising the amino acid sequences of SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and
- a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13.

[0014] In another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 7 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: 8 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: 9 and SEQ ID NO: 12, respectively; or
- d. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 10 and SEQ ID NO: 13, respectively.

[0015] In yet another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a heavy chain comprising, preferably consisting of, the amino acid sequence of SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19; and
- a light chain comprising, preferably consisting of, the amino acid sequence of SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20.

[0016] In a particular example, the disclosure relates to an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a. a heavy chain comprising the amino acid sequence of SEQ ID NO: 14 and a light chain comprising the amino acid sequence of SEQ ID NO: 15;
- b. a heavy chain comprising the amino acid sequence of SEQ ID NO: 16 and a light chain comprising the amino acid sequence of SEQ ID NO: 15;
- c. a heavy chain comprising the amino acid sequence of SEQ ID NO: 17 and a light chain comprising the amino acid sequence of SEQ ID NO: 18; or
- d. a heavy chain comprising the amino acid sequence of SEQ ID NO: 19 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

[0017] In a particular preferred example, the anti-Sema3A antibody is a humanized anti-Sema3A antibody.

[0018] **In another aspect**, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof that binds to at least one amino acid residue within amino acid regions 370-382 of the human Sema3A as set forth in SEQ ID NO: 22.

[0019] In one example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof that binds to at least one amino acid residue within amino acid regions as set forth in SEQ ID NO: 21 (DSTKDLPPDDVITF). In a preferred example, the present disclosure provides an anti-Sema3A antibody or an

antigen-binding fragment thereof that binds the amino acid regions as set forth in SEQ ID NO: 21. **In another aspect**, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof that binds to SEQ ID NO: 21.

[0020] The present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use as a medicament. **In another aspect**, the present disclosure provides an antibody or an antigen-binding fragment according to the disclosure for use as a medicament.

[0021] In one example, the present disclosure provides an anti-Sema3A or an antigen-binding fragment for inhibiting the vasorepressive effect of SemaA, and/or for improving revascularisation of the retina.

[0022] In one example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use in the treatment or prevention of a retinal or eye disease. **In another aspect**, the present disclosure provides the antibody or the antigen-binding fragment according to the disclosure for use for treating or preventing an eye or a retinal disease.

[0022a] **In another aspect**, the present disclosure provides use of the antibody or the antigen-binding fragment according to the disclosure in the manufacture of a medicament for treating or preventing an eye or a retinal disease.

[0023] In another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use in the treatment or prevention of a disease selected from the group consisting of retinopathy, 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 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.

[0024] In another example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use in the treatment or prevention of a disease 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. Preferably, said disease is diabetic macular edema and/or diabetic macular ischemia.

[0025] In a preferred example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use in the treatment of diabetic macular ischemia, by promoting vascular regeneration within the ischemic retina (revascularization) and preventing pathological neovascularization of the vitreous region of the eye.

[0026] In another preferred example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for use in the treatment of diabetic macular edema, by reducing permeability of blood retinal barrier.

[0027] In another preferred example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof for inhibiting Sema3A-induced permeability of the blood retinal barrier and/or Sema3A-induced vasoregression from ischemic areas.

[0028] The present disclosure provides a pharmaceutical composition comprising an anti-Sema3A antibody or an antigen-binding fragment thereof and a pharmaceutically acceptable carrier. **In another aspect**, the present disclosure provides a pharmaceutical composition comprising an antibody or an antigen-binding fragment according to the disclosure and a pharmaceutically acceptable carrier.

[0029] In one example, the present disclosure provides an anti-Sema3A antibody or an antigen-binding fragment thereof or a pharmaceutical composition comprising an anti-Sema3A antibody or an antigen-binding fragment thereof, wherein said antibody or an antigen-binding fragment thereof is administered by a parenteral route, intravenous route, intravitreal route or subcutaneous route of administration, preferably by intravitreal route.

[0030] In another aspect, the present disclosure provides an isolated polynucleotide or polynucleotides comprising:

- a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and

- a sequence encoding a light chain as shown in SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13.

[0031] The present disclosure provides an expression vector comprising an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and a sequence encoding a light chain as shown in SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13. **In another aspect**, the present disclosure provides an expression vector comprising the isolated polynucleotide or polynucleotides of the disclosure.

[0032] In one example, the present disclosure provides a viral vector comprising an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and a sequence encoding a light chain as shown in SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13.

[0033] The present disclosure provides a host cell comprising an expression vector or an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and a sequence encoding a light chain as shown in SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13. **In another aspect**, the present disclosure provides a host cell comprising an isolated polynucleotide or polynucleotides according to the disclosure or an expression vector according to the disclosure.

[0034] The present disclosure provides a method for producing an anti-Sema3A antibody or an antigen-binding fragment thereof comprising obtaining a host cell comprising an expression vector or an isolated polynucleotide or polynucleotides comprising a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable

region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and a sequence encoding a light chain as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13; and cultivating the host cell.

[0034a] In another aspect, the present disclosure provides a method for producing an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a. obtaining a host cell according to the disclosure; and
- b. cultivating the host cell.

[0035] In one example, the method for producing an anti-Sema3A antibody or an antigen-binding fragment thereof further comprises recovering and purifying the anti-Sema3A antibody or an antigen-binding fragment thereof.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] **FIGURE 1:** Localization of Sema3A in human eyes.

This figure shows the localization of Sema3A in human eyes in prespecified retinal samples from human donors with a history of Diabetic Retinopathy or primary open angle glaucoma (POAG) in comparison to age matched controls (Age ctrl) and subjects with Diabetes, but no ocular pathology (DM ctrl). Sema3A was found in the vasculature wall of retinal blood vessels. Additionally, unidentified but distinctive Sema3A fluorescent objects were observed in the retinal ganglion cell layer.

[0037] **FIGURE 2:** Efficacy in cellular permeability assay.

Permeation of FITC-dextran in human retinal microvascular endothelial cells is measured in a transwell assay. Anti-TNP is a control antibody against trinitrophenol. Anti-Sema3A is an antibody according to the invention (clone I). Significance is shown vs. recombinant human Sema3A.

[0038] **FIGURE 3:** Cytoskeletal collapse in HRMEC (Xcelligence).

Sema3A-F all induce a cytoskeletal collapse in human retinal endothelial cells. The antibody of the invention (clone I) is specific for Sema3A and prevents only the Sema3A-induced collapse.

[0039] **FIGURE 4:** Efficacy on tip cell density and avascular area in vivo.

CLAIMS

1. An anti-Sema3A 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-Sema3A 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 SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; 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, SEQ ID NO: 12 or SEQ ID NO: 13.

3. The anti-Sema3A 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 SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; 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, SEQ ID NO: 12 or SEQ ID NO: 13;

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 comprises 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-Sema3A 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: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10 and
- a light chain variable region comprising the amino acid sequence of SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13.

5. The anti-Sema3A 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: 7 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: 8 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: 9 and SEQ ID NO: 12, respectively; or
- d. a variable heavy chain and a variable light chain comprising the amino acid sequences of SEQ ID NO: 10 and SEQ ID NO: 13, respectively.

6. The anti-Sema3A 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: 14, SEQ ID NO: 15, SEQ ID NO: 17 or SEQ ID NO: 19; and
- a light chain comprising, preferably consisting of, the amino acid sequence of SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20.

7. The anti-Sema3A 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: 14 and a light chain comprising the amino acid sequence of SEQ ID NO: 15;
- b. a heavy chain comprising the amino acid sequence of SEQ ID NO: 16 and a light chain comprising the amino acid sequence of SEQ ID NO: 15;
- c. a heavy chain comprising the amino acid sequence of SEQ ID NO: 17 and a light chain comprising the amino acid sequence of SEQ ID NO: 18; or
- d. a heavy chain comprising the amino acid sequence of SEQ ID NO: 19 and a light chain comprising the amino acid sequence of SEQ ID NO: 20.

8. An anti-Sema3A antibody or an antigen-binding fragment thereof that binds to at least one amino acid residue within amino acid regions 370-382 of human Sema3A as set forth in SEQ ID NO: 22.

9. An anti-Sema3A antibody or an antigen-binding fragment thereof that binds to SEQ ID NO: 21.

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 for use according to claim **10** for inhibiting the vasorepressive effect of SemaA3.

12. An antibody or an antigen-binding fragment for use according to claim **10** for improving revascularisation of the retina.

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

14. Use of the antibody or the 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.

15. The antibody or the antigen-binding fragment for use according to claim **13** or the use according to claim **14**, wherein said disease is selected from the group consisting of retinopathy, 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 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.

16. The antibody or the antigen-binding fragment for use according to any one of claims **13 or 15**, or the use according to claim **14 or 15**, 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.

17. The antibody or the antigen-binding fragment for use according to any one of claims **13**, **15** and **16**, or the use according to any one of claims **14** to **16**, wherein said disease is diabetic macular edema and/or diabetic macular ischemia.

18. The antibody or the antigen-binding fragment for use according to any one of claims **13**, **15** and **16**, or the use according to any one of claims **14** to **16**, wherein:

- said disease is diabetic macular ischemia, and
- said antibody or an antigen-binding fragment promotes vascular regeneration within the ischemic retina (revascularization) and prevents pathological neovascularization of the vitreous region of the eye.

19. The antibody or the antigen-binding fragment for use according to any one of claims **13**, **15** and **16**, or the use according to any one of claims **14** to **16**, wherein:

- said disease is diabetic macular edema, and
- said antibody or an antigen-binding fragment reduces permeability of blood retinal barrier.

20. The antibody or the antigen-binding fragment for use or the use according to claim **19**, wherein said antibody or an antigen-binding fragment inhibits Sema3A-induced permeability of the blood retinal barrier and/or Sema3A-induced vasoregression from ischemic areas.

21. A pharmaceutical composition comprising an antibody or an antigen-binding fragment according to any of claims **1** to **13** and **15** to **20** and a pharmaceutically acceptable carrier.

22. The antibody or the antigen-binding fragment thereof according to any of claims **1** to **13** and **15** to **20**, the use according to any one of claims **14** to **20** or the pharmaceutical composition according to claim **21**, 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.

23. The antibody or the antigen-binding fragment thereof according to any of claims **1** to **13** and **15** to **20**, the use according to any one of claims **14** to **20** or the pharmaceutical composition according to claim **21**, wherein said antibody or an antigen-binding fragment thereof is to be administered by intravitreal route.

24. An isolated polynucleotide or polynucleotides comprising:

- a sequence encoding a heavy chain as shown in SEQ ID NO: 14, SEQ ID NO: 16, SEQ ID NO: 17, or SEQ ID NO: 19 or a heavy chain variable region as shown in SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 or SEQ ID NO: 10; and
- a sequence encoding a light chain as shown in SEQ ID NO: 15, SEQ ID NO: 18 or SEQ ID NO: 20 or a light chain variable region as shown in SEQ ID NO: 11, SEQ ID NO: 12 or SEQ ID NO: 13.

25. An expression vector comprising the isolated polynucleotide or polynucleotides of claim **24**.

26. A host cell comprising an isolated polynucleotide or polynucleotides according to claim **24** or an expression vector according to claim **25**.

27. A method for producing an anti-Sema3A antibody or an antigen-binding fragment thereof comprising:

- a. obtaining a host cell according to claim **26**; and
- b. cultivating the host cell.

28. The method according to claim **27**, further comprising recovering and purifying the antibody or an antigen-binding fragment thereof.