

In one aspect, the present invention refers to the use of a MASP-2 inhibitory agent in the manufacture of a medicament for preventing, treating, reverting and/or delaying angiogenesis in a mammalian subject suffering from an angiogenesis-dependent disease or condition. In another aspect, the present invention refers to the use of a MASP-2 inhibitory agent in the manufacture of a medicament for treating a subject suffering from an ocular angiogenic disease or condition selected from the group consisting of AMD, uveitis, ocular melanoma, corneal neovascularization, primary pterygium, HSV stromal keratitis, HSV-1-induced corneal lymphangiogenesis, proliferative diabetic retinopathy, retinopathy of prematurity, retinal vein occlusion, corneal graft rejection, neovascular glaucoma, and rubeosis. In still another aspect, the present invention refers to the use of a MASP-2 inhibitory agent in the manufacture of a medicament for inhibiting tumor angiogenesis in a subject with cancer. Also described herein are methods for preventing, treating, reverting and/or delaying angiogenesis in a mammalian subject suffering from, or at risk for developing, an angiogenesis-dependent disease or condition, comprising

administering to the subject an amount of a MASP-2 inhibitory agent effective to inhibit angiogenesis. In some examples of these aspects of the invention, the MASP-2 inhibitory agent is a MASP-2 antibody or fragment thereof. In further examples, the MASP-2 antibody has reduced effector function. In some examples, the MASP-2 inhibitory agent is a MASP-2 inhibitory peptide or a non-peptide MASP-2 inhibitor.

In another example, provided herein are compositions for inhibiting the adverse effects of angiogenesis, comprising a therapeutically effective amount of a MASP-2 inhibitory agent and a pharmaceutically acceptable carrier. Methods are also provided for manufacturing a medicament for use in inhibiting the adverse effects of angiogenesis in living subjects in need thereof, comprising a therapeutically effective amount of a MASP-2 inhibitory agent in a pharmaceutical carrier. Methods are also provided for manufacturing medicaments for use in inhibiting angiogenesis for treatment of each of the conditions, diseases and disorders described herein below.

The methods, compositions and medicaments described herein are useful for inhibiting the adverse effects of angiogenesis *in vivo* in mammalian subjects, including humans suffering from an acute or chronic pathological condition or injury as further described herein.

In another example described herein, methods are provided for inhibiting angiogenesis in a mammalian subject suffering from an angiogenesis-dependent disease or condition comprising administering to the subject a composition comprising an amount of a MASP-2 inhibitory agent effective to inhibit angiogenesis. In some examples, the angiogenesis-dependent disease or condition is an angiogenesis-dependent cancer, such as, for example, an angiogenesis-dependent cancer selected from the group consisting of solid tumor(s), blood borne tumors, high-risk carcinoid tumors, and tumor metastases. In some examples, the angiogenesis-dependent disease or condition is an angiogenesis-dependent benign tumor, such as, for example, an angiogenesis-dependent benign tumor selected from the group consisting of hemangiomas, acoustic neuromas, neurofibromas, trachomas, carcinoid tumors, and pyogenic granulomas. In some

examples, the angiogenesis-dependent disease or condition is an ocular angiogenic disease or condition, such as, for example, an ocular angiogenic disease or condition selected from the group consisting of age-related macular degeneration (AMD), uveitis, ocular melanoma, corneal neovascularization, primary pterygium, HSV stromal keratitis,

HSV-1-induced corneal lymphangiogenesis, proliferative diabetic retinopathy, retinopathy of prematurity, retinal vein occlusion, corneal graft rejection, neovascular glaucoma, and rubeosis.

In another example, described herein are methods of treating a subject suffering
5 from an ocular angiogenic disease or condition selected from the group consisting of AMD, uveitis, ocular melanoma, corneal neovascularization, primary pterygium, HSV stromal keratitis, HSV-1-induced corneal lymphangiogenesis, proliferative diabetic retinopathy, diabetic macular edema, retinopathy of prematurity, retinal vein occlusion, corneal graft rejection, neovascular glaucoma, vitreous hemorrhage secondary to
10 proliferative diabetic retinopathy, neuromyelitis optica and rubeosis, comprising administering to the subject an amount of a MASP-2 inhibitory agent effective to inhibit angiogenesis.

In another example, described herein are methods of inhibiting tumor angiogenesis comprising administering to a subject with cancer an amount of a MASP-2
15 inhibitory agent effective to inhibit angiogenesis.

DESCRIPTION OF THE DRAWINGS

The foregoing aspects and many of the attendant advantages of this invention will become more readily appreciated as the same become better understood by reference to
20 the following detailed description, when taken in conjunction with the accompanying drawings, wherein:

FIGURE 1 is a diagram illustrating the genomic structure of human MASP-2;

FIGURE 2A is a schematic diagram illustrating the domain structure of human MASP-2 protein;

25 FIGURE 2B is a schematic diagram illustrating the domain structure of human MASP-2 protein;

FIGURE 3 is a diagram illustrating the murine MASP-2 knockout strategy;

FIGURE 4 is a diagram illustrating the human MASP-2 minigene construct;

FIGURE 5A presents results demonstrating that MASP-2-deficiency leads to the loss of lectin-pathway-mediated C4 activation as measured by lack of C4b deposition on mannan, as described in Example 2;

CLAIMS

The embodiments of the invention in which an exclusive property or privilege is claimed are defined as follows:

1. Use of a MASP-2 inhibitory agent in the manufacture of a medicament for preventing, treating, reverting and/or delaying angiogenesis in a mammalian subject suffering from an angiogenesis-dependent disease or condition.
2. The use of Claim 1, wherein the MASP-2 inhibitory agent is a MASP-2 antibody or fragment thereof.
3. The use of Claim 2, wherein the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6.
4. The use of Claim 1, wherein the angiogenesis-dependent disease or condition is an angiogenesis-dependent cancer.
5. The use of Claim 1, wherein the angiogenesis-dependent disease or condition is a benign tumor.
6. The use of Claim 1, wherein the angiogenesis-dependent disease or condition is an ocular angiogenic disease or condition.
7. The use of Claim 4, wherein the subject is suffering from an angiogenesis-dependent cancer selected from the group consisting of: solid tumor(s), blood borne tumors, high-risk carcinoid tumors, and tumor metastases.
8. The use of Claim 7, wherein the subject is suffering from one or more solid tumors.
9. The use of Claim 8, wherein the subject is suffering from or at risk for tumor metastases.
10. The use of Claim 5, wherein the subject is suffering from an angiogenesis-dependent benign tumor(s) selected from the group consisting of hemangiomas, acoustic neuromas, neurofibromas, trachomas, carcinoid tumors, and pyogenic granulomas.

11. The use of Claim 6, wherein the ocular angiogenic disease or condition is not AMD.

12. The use of Claim 6, wherein the ocular angiogenic disease or condition is selected from the group consisting of uveitis, ocular melanoma, corneal neovascularization, primary pterygium, HSV stromal keratitis, HSV-1-induced corneal lymphangiogenesis, proliferative diabetic retinopathy, diabetic macular edema, retinopathy of prematurity, retinal vein occlusion, corneal graft rejection, neovascular glaucoma, vitreous hemorrhage secondary to proliferative diabetic retinopathy, neuromyelitis optica and rubeosis.

13. The use of Claim 2, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody and a human antibody.

14. The use of Claim 1, wherein the composition is for subcutaneous administration, intraperitoneal administration, intra-muscular administration, intra-arterial administration, intravenous administration, or as an inhalant.

15. Use of a MASP-2 inhibitory agent in the manufacture of a medicament for treating a subject suffering from an ocular angiogenic disease or condition selected from the group consisting of AMD, uveitis, ocular melanoma, corneal neovascularization, primary pterygium, HSV stromal keratitis, HSV-1-induced corneal lymphangiogenesis, proliferative diabetic retinopathy, retinopathy of prematurity, retinal vein occlusion, corneal graft rejection, neovascular glaucoma, and rubeosis.

16. The use of Claim 15, wherein the MASP-2 inhibitory agent is a MASP-2 antibody or fragment thereof.

17. The use of Claim 16, wherein the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6.

18. The use of Claim 16, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody and a human antibody.

19. Use of a MASP-2 inhibitory agent in the manufacture of a medicament for inhibiting tumor angiogenesis in a subject with cancer.

20. The use of Claim 19, wherein the MASP-2 inhibitory agent is a MASP-2 antibody or fragment thereof.

21. The use of Claim 20, wherein the MASP-2 inhibitory agent is a MASP-2 monoclonal antibody, or fragment thereof that specifically binds to a portion of SEQ ID NO:6.

22. The use of Claim 20, wherein the antibody or fragment thereof is selected from the group consisting of a recombinant antibody, an antibody having reduced effector function, a chimeric antibody, a humanized antibody and a human antibody.