CLAIMS

What is claimed is:

Claim 1. Use of a therapeutically effective amount of an inhibitor of a lymphatic formation factor associated with the Schlemm's canal, in the manufacture of a medicament for treating glaucoma.

Claim 2. Use of a therapeutically effective amount of an inhibitor of a pro-lymphatic formation factor in the manufacture of a medicament for:

(a) preventing glaucoma;

(b) inhibiting lymphangiogenesis in a subject at risk of development of glaucoma or suffering from elevated intraocular pressure (IOP);

(c) increasing Schlemm's canal permeability in a subject suffering from elevated IOP;

(d) inhibiting Schlemm's canal cellular activity in a subject suffering from elevated IOP;

(e) increasing aqueous humor outflow in Schlemm's canal of a subject suffering from elevated IOP;

(f) reducing corneal edema;

(g) reducing retinal nerve fiber layer thinning; or

(h) for reducing retinal ganglion cell (RGC) death.

Claim 3. The use of claim 1 or 2, wherein the pro-lymphatic formation factor is a VEGF/VEGFR family member.

Claim 4. The use of claim 3, wherein the VEGF/VEGFR family member is selected from the group consisting of VEGF-A, VEGF-B, VEGF-C, VEGF-D, VEGF-E, PIGF, VEGFR-1, VEGFR-2, and VEGFR-3.

Claim 5. The use of claim 1 or 2, wherein the pro-lymphatic formation factor is an integrin family member.

Claim 6. The use of claim 5, wherein the integrin family member is selected from the group consisting of very late antigen-1 (VLA-1), integrin alpha 5 (ITGA5), and integrin alpha 9 (ITGA9).

Claim 7. The use of claim 1 or 2, wherein the pro-lymphatic formation factor is an angiopoietin family member.

Claim 8. The use of claim 7, wherein the angiopoietin family member is selected from the group consisting of angiopoietin- 1 (ANGPT1), angiopoietin-2 (ANGPT2 or Ang-2), and Tie2/TEK.

Claim 9. The use of claim 1 or 2, wherein the pro-lymphatic formation factor is selected from the group consisting of:

(i) a cytokine or chemokine;

(ii) an extracellular matrix protein;

(iii) a transcription factor;

(iv) a guidance molecule;

(v) a fibroblast growth factor (FGF);

(vi) a protein tyrosine phosphatase (PTP);

(vii) a platelet factor member or (viii) a platelet-derived growth factor;

(ix) a LEC polarity factor;

(x) a Notch family member; and

(xi) a combination of any of (i)-(xi).

Claim 10. The use of claim 1 or 2, wherein the pro- lymphatic formation factor is selected from the group consisting of:

(i) a cytokine/chemokine, wherein the cytokine or chemokine is selected from the group consisting of interleukin 8, interferon gamma, CCR7, and SLC;

(ii) an extracellular matrix protein, wherein the extracellular matrix protein is CCBE1;

(iii) a transcription factor, wherein the transcription factor is selected from the group consisting of Soxl8 and Hhex;

(iv) a guidance molecule, wherein the guidance molecule is selected from the group consisting of neuropilin 2 and SEMA7A;

(v) an FGF, wherein the FGF is FGF-2;

(vi) a protein tyrosine phosphatase (PTP), wherein the PTP is PTPN14;

(vii) a member of platelet factors, wherein the platelet factor member is platelet factor 4 or (viii) a platelet-derived growth factor comprising PDGF-BB;

(ix) a LEC polarity factor, wherein the LEC polarity factor is selected from the group consisting of Celsrl, Vangl2, Pdk2, and Fat4;

(x) a member of Notch family;

(xi) ARAF, SOS1, Apelin, KIF11, REELIN, CALCRL, GJC2 (gap junction protein gamma-2), Rasipl, or FBXL7 (F-box and leucine-rich repeat protein 7); and,

(xii) a combination of any one of (i)-(xi).

Claim 11. The use of any of claims 1-10, wherein the inhibitor of the pro-lymphatic formation factor is selected from the group consisting of:

(i) an agent capable of disrupting the pro-lymphatic formation factor's gene, thereby eliminating or reducing expression of the pro-lymphatic formation factor;

(ii) an siRNA capable of degrading the mRNA of a pro-lymphatic formation factor, thus reducing expression of the pro-lymphatic factor;

(iii) an antagonist antibody against the pro-lymphatic formation factor which inhibits or prevents the function of the pro-lymphatic formation factor;

(iv) a small molecule capable of inhibiting or preventing the function of the prolymphatic formation factor; and

(v) a combination of any of (i)-(iv).

Claim 12. Use of a therapeutically effective amount of an inhibitor of a pro-lymphatic formation factor selected from the group consisting of VEGFR-3, VLA-1, ITGA5, and Ang-2 in the manufacture of a medicament for treating glaucoma.

Claim 13. Use of a therapeutically effective amount of an inhibitor of a pro-lymphatic formation factor selected from the group consisting of VEGFR-3, VLA-1, ITGA5, and Ang-2 in the manufacture of a medicament for:

(a) preventing glaucoma;

(b) inhibiting lymphangiogenesis in a subject at risk of development of glaucoma;

(c) inhibiting lymphangiogenesis in a subject suffering from elevated intraocular pressure (IOP);

(d) increasing Schlemm's canal permeability in a subject suffering from elevated IOP;

(e) inhibiting Schlemm's canal cellular activity in a subject suffering from elevated IOP;

(f) inhibiting Schlemm's canal cellular activity in a subject suffering from elevated IOP;

(g) increasing aqueous humor outflow in Schlemm's canal of a subject suffering from elevated IOP;

(h) reducing corneal edema;

(i) reducing corneal edema in an eye of a subject;

(j) reducing retinal nerve fiber layer (RNFL) thinning;

(k) reducing corneal edema;

(l) reducing retinal nerve fiber layer (RNFL) thinning;

(m) reducing retinal ganglion cell (RGC) death; or

(n) reducing retinal ganglion cell (RGC) death.

Claim 14. The use of any of claims 12-13, wherein the inhibitor of the pro-lymphatic formation factor is selected from the group consisting of:

(i) an agent capable of disrupting the pro-lymphatic formation factor's gene, thereby eliminating or reducing expression of the pro-lymphatic formation factor;

(ii) an siRNA capable of degrading the mRNA of a pro-lymphatic formation factor, thus reducing expression of the pro-lymphatic factor;

(iii) an antagonist antibody against the pro-lymphatic formation factor which inhibits or prevents the function of the pro-lymphatic formation factor;

(iv) a small molecule capable of inhibiting or preventing the function of the prolymphatic formation factor; and

(v) a combination of any of (i)-(iv).

Claim 15. The use of any of claims 12-14, wherein the pro-lymphatic formation factor is VEGFR-3, VLA-1, ITAG5 or Ang-2.

Claim 16. The method of any of claims 1-15, wherein the inhibitor is an siRNA or an antagonist antibody or disrupts the pro-lymphatic formation factor's gene's expression.

Claim 17. Use of a therapeutically effective amount of an agent that activates or stimulates a lymphatic factor that inhibits or prevents lymphangiogenesis, in the manufacture of a medicament for treating glaucoma.

Claim 18. Use of a therapeutically effective amount of an agent that activates or stimulates an anti-lymphatic formation factor in the manufacture of a medicament for preventing glaucoma.

Claim 19. Use of a therapeutically effective amount of an agent that activates or stimulates an anti-lymphatic formation factor, in the manufacture of a medicament for:

(a) inhibiting lymphangiogenesis in a subject at risk for development of glaucoma;

(b) inhibiting lymphangiogenesis in a subject suffering from elevated intraocular pressure (IOP);

(c) inhibiting Schlemm's canal cellular activity in a subject suffering from elevated IOP;

(d) increasing aqueous humor outflow of Schlemm's canal in a subject suffering from elevated IOP;

(e) reducing corneal edema;

(f) reducing retinal nerve fiber layer (RNFL) thinning;

(g) reducing retinal ganglion cell (RGC) death.

Claim 20. The use of any one of claims 17-19, wherein the agent to be administered is selected from the group consisting of:

(i) an anti-lymphatic formation factor;

(ii) an agent that activates the expression of the anti-lymphatic formation factor;

(iii) an agonist antibody activating the anti-lymphatic formation factor;

(iv) a microRNA or mimics inhibiting lymphatic formation, and

(v) a small molecule activating the function of the anti-lymphatic formation factor.

Claim 21. The use of any one of claims 10-20, wherein the anti-lymphatic formation factor is selected from the group consisting of: microRNA184, microRNA126, miR-31, miR-181a, microRNA132, miR-194, miR-186, miR-99a, miR-92a, and miR-466, endostatin, and a VEGF family inhibitor (e.g. soluble VEGFR-2, soluble VEGFR-3).

Claim 22. The use of any one of claims 1, 2, 12, 13 or 17, wherein the glaucoma is primary glaucoma.

Claim 23. The use of claim 22, wherein the primary glaucoma is any one of primary open angle glaucoma primary angle-closure glaucoma primary congenital glaucoma, or primary normal tension glaucoma.

Claim 24. The use of any of claims 1-23, wherein the agent or medicament is formulated to be administered topically, via intracameral injection, via subconjunctival injection, via intravitreal injection, via suprachoroidal injection, via peribulbar injection, or via retrobulbar injection.

Claim 25. The use of any of claims 1-24, wherein the agent or medicament is formulated as eye drop, depot, bolus, inhibitor-loaded contact lens, suspension, solution, ophthalmic gel, or ointment.