[0013] Currently, there is no proven medical therapy for dry AMD, and no treatments available for advanced dry AMD. In selected cases of wet AMD, a technique known as laser photocoagulation may be effective for sealing leaky or bleeding blood vessels. Unfortunately, laser photocoagulation usually does not restore lost vision, but merely slows, and in some cases, prevents further loss. Recently, photodynamic therapy has shown to be effective in stopping abnormal blood vessel growth in about one third of wet AMD patients when treated early. In Visdyne Photodynamic Therapy (PDT), a dye is injected into the patient's eye, it accumulates in the area of vessel leakage in the retina and, when exposed to a low power laser, it reacts sealing off the leaking vessels. In addition to these two laser techniques, there are several anti-angiogenesis therapies targeting vascular endothelial growth Factor (VEGF) being developed for the treatment of wet AMD.
However, only 10% treated patients show vision improvement.
[0014] In view of these inadequate treatments for wet AMD and the total lack of treatments available for advanced dry AMD, there is a clear need for the development of new treatments for this serious disease. Our invention provides a novel approach to treating this serious disease.

SUMMARY

[0015] In one aspect, the present invention refers to the use of a complement inhibitor in the manufacture of a medicament for treating an ocular disease associated with complement activation in a subject, wherein the complement inhibitor is an antibody or an antibody-binding fragment thereof or a nucleic acid encoding the antibody or the antigen-binding fragment, wherein the antibody or the antigen-binding fragment specifically binds to Factor D, and wherein the ocular disease is age-related macular degeneration. In another aspect, the present invention refers to the use of the complement inhibitor as defined in any one of claims 1-7 in the manufacture of a medicament for use in treating an ocular disease associated with complement activation in a subject, wherein the medicament further comprises a pharmaceutically acceptable diluent or carrier, and wherein the ocular disease is age-related macular degeneration. In still another aspect, the present invention refers to the use of a complement inhibitor in the manufacture of a medicament for treating an ocular disease associated with complement activation in a subject, wherein the complement inhibitor is (i) monoclonal antibody 166-32 produced from the hybridoma deposited with the ATCC and designated HB 12476 or an antigen-binding fragment thereof, or (ii) an antibody that specifically binds to the same epitope as monoclonal antibody 166 32 or an antigen-binding fragment thereof, or (iii) a humanized antibody derived from monoclonal antibody 166-32 or an antigen-binding fragment thereof, wherein the ocular disease is age-related macular degeneration.
As disclosed herein are complement inhibitors for the treatment of ocular related conditions or diseases, such as age-related macular degeneration (AMD), diabetic retinopathy, ocular angiogenesis (such as ocular neovascularization affecting choroidal, corneal, or retinal tissue), and other ocular conditions involving complement activation. Treatment of AMD includes both the dry and wet forms of AMD.

[0016] The complement inhibitors disclosed herein include, but are not limited to, those inhibiting the alternative complement pathway, such as Factor D, properdin, Factor B, Factor Ba, and Factor Bb, and the classical complement pathway, such as C3a, C5, C5a, C5b, C6, C7, C8, C9 and C5b-9. The present disclosure also includes the use of complement inhibitors in combination with other agents, such as anti-angiogenic agents and anti-inflammatory agents such as steroids.

[0017] Another example relates to the use of C5aR and C3aR inhibitors, such as antibodies and derived fragments and single domain constructs, as well as small molecule compounds.

[0018] Another example relates to the use of recombinant soluble CR1 (TP10) and its derived proteins; use of C3 inhibiting molecules (such as Compstatin, a peptidomimetic that binds and inhibits C3 activation); siRNAs that block the synthesis of C3, C5, FD, factor P, factor B

[0019] These inhibitors can be, but not limited to, small molecule chemical compounds, nucleotides, peptides, proteins, peptidomimetics and antibodies.

[0020] Another example includes the use of human Factor H purified from human blood or recombinant human Factor H administered to patients intraocularly or by any other clinically effective route.

[0021] Antibodies described herein include whole immunoglobulins, scFv, Fab, Fab', Fv, F(ab')2, or dAb. Domain antibodies comprise either a VH domain or a VL domain.

[0022] One example describes the use of a monoclonal antibody which binds to Factor D and blocks its ability to activate the alternative complement pathway. Such antibodies are described in WO 01/70818 and US 20020081293, which are incorporated here by reference, such as monoclonal antibody 166-32 produced from the hybridoma deposited with the ATCC and designated HB 12476. The present disclosure also includes antibodies that specifically bind to the same epitope as monoclonal antibody 166-32.

[0023] One example describes the use of a monoclonal antibody which binds to complement component C5a. Such antibodies include antibody 137-26 produced from the hybridoma deposited with the ATCC and designated PTA-3650, and any antibody that specifically binds to the same epitope as 137-26.

[0024] According to the disclosure, the complement pathway inhibitor may be administered by (a) parenteral administration; (b) biocompatible or bioerodable sustained release implant; (c) implantation of an infusion pump; or (d) local administration, such as subconjunctival administration or by intravitreal administration. The complement inhibitor may also be administered by parenteral administration selected from oral administration, enteral administration and topical administration. Topical administration may include an eye wash solution, an eye ointment, an eye shield or an eye drop solution.

[0025] In addition the complement inhibitor described herein may be administered in combination with a immunomodulatory or immunosuppressive compound.

[0026] Another example relates to the administration of nucleic acid constructs that are capable of expressing the complement pathway inhibitors for gene therapy.

[0027] Another example includes a method for screening for complement inhibitors that are useful in the treatment of AMD comprising the use of an AMD model in senescent Ccl-2 or Ccr-2-deficient mice. These mice manifest

similar histopathological changes found in human dry and wet AMDs. These mice may be treated with complement inhibitors or Factor H intravitreally. Histological examination may be performed to determine protection from AMD development in mice treated with the agents to be tested.

DETAILED DESCRIPTION OF THE INVENTION