METHODS AND COMPOSITIONS FOR TREATMENT OF RETINAL DEGENERATION

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 61/711,665, filed October 9, 2012, the disclosure of which is hereby incorporated by reference herein in its entirety.

STATEMENT REGARDING FEDERAL SUPPORT

[0002] Not applicable.

FIELD

[0003] The present application is in the field of cell therapies for retinal degeneration as occurs, for example, in retinitis pigmentosa and in age-related macular degeneration (AMD).

BACKGROUND

[0004] Retinal degeneration, resulting, for example, from choroidal neovascularization ("wet AMD") or from buildup of cellular debris between the retina and the choroid ("dry AMD"), is one of the major causes of blindness in the world today. Cai et al. (2012) *Front Biosci.* **17:**1976-95. Similarly, degeneration and death of photoreceptor cells (rods and cones), as occurs in Retinitis pigmentosa, can also lead to deterioration and/or loss of vision. Accordingly, treatments that block and/or reverse retinal degeneration, in particular treatments that restore photoreceptor function, are needed.

SUMMARY

[0005] Disclosed herein are methods and compositions for treating retinal degeneration, using cells descended from marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain. Such cells are denoted SB623 cells for the purposes of the present disclosure.

[0006] In one aspect, the present invention provides a use of cells in the manufacture of a medicament for enhancing transmission of visual signals from the retina to the visual cortex in a subject, wherein said cells are descendents of marrow

adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

[0006A] In another aspect, the present invention provides a use of cells in the manufacture of a medicament for increasing electrical activity of photoreceptor cells in a subject, wherein said cells are descendants of marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

[0006B] In yet another aspect, the present invention provides a use of cells in the manufacture of a medicament for preventing loss of cells of the outer nuclear layer of the retina in a subject, wherein said cells are descendants of marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

[0006C] Also disclosed herein are methods of treating retinal degeneration by administering SB623 cells to the eye of a subject in need thereof.

[0007] Also disclosed herein are methods of increasing photoreceptor activity in the eye of a subject, the methods comprising administering SB623 cells to the eye of the subject such that photoreceptor activity is increased.

[0008] Also disclosed herein are methods of enhancing photoreceptor function in the eye of a subject, the methods comprising administering SB623 cells to the eye of the subject such that photoreceptor function is enhanced.

[0009] Also disclosed herein are methods of enhancing transmission of visual signals from the retina to the visual cortex of the brain, the methods comprising administering SB623 cells to the eye of the subject such that transmission of visual signals from the retina to the visual cortex of the brain is enhanced.

[0010] In any of the methods described herein, the cells can be administered by any delivery method, including direct injection, topical administration and the like. In certain examples, the SB623 cells are administered as a composition (or formulation) comprising the cells, for example in combination with one or more pharmaceutical carriers. In addition, the methods can involve repeated administration of SB623 cells, in the same or different formulations.

[0011] Accordingly, the present disclosure provides, *inter alia*, the following examples:

1. A method for treating retinal degeneration in a subject in need thereof, the method comprising administering SB623 cells to the subject.

2. The method of example 1, wherein SB623 cells are transplanted into the eye of the subject.

3. The method of either of examples 1 or 2, wherein the transplantation is intravitreal.

4. The method of either of example 1 or 2, wherein the transplantation is subretinal.

5. The method of any of examples 1-4, wherein the retinal degeneration occurs in retinitis pigmentosa.

6. The method of any of examples 1-4, wherein the retinal degeneration occurs in age-related macular degeneration (AMD).

[0012] These and other aspects will be readily apparent to the skilled artisan in light of disclosure as a whole.

Claims

1. Use of cells in the manufacture of a medicament for enhancing transmission of visual signals from the retina to the visual cortex in a subject, wherein said cells are descendents of marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

2. Use of cells in the manufacture of a medicament for increasing electrical activity of photoreceptor cells in a subject, wherein said cells are descendants of marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

3. Use of cells in the manufacture of a medicament for preventing loss of cells of the outer nuclear layer of the retina in a subject, wherein said cells are descendants of marrow adherent stem cells (MASCs) that have been engineered to express an exogenous Notch intracellular domain.

4. The use of any of claims 1-3, wherein the cells are for transplantation into the eye of the subject.

5. The use of claim 4, wherein the transplantation is intravitreal.

6. The use of claim 4, wherein the transplantation is subretinal.

7. The use of any of claims 1-6; wherein the transmission of visual signals is enhanced, the electrical activity is increased, or loss of cells in the outer nuclear layer is prevented, in an individual having retinitis pigmentosa.

8. The use of any of claims 1-6; wherein the transmission of visual signals is enhanced, the electrical activity is increased, or loss of cells in the outer nuclear layer is prevented, in an individual having age-related macular degeneration (AMD).

9. The use of claim 8, wherein the AMD is dry AMD

10. The use of claim 8, wherein the AMD is wet AMD

11. The use of any of claims 1-6; wherein the transmission of visual signals is enhanced, the electrical activity is increased, or loss of cells in the outer nuclear layer is prevented, in an individual having Usher syndrome, Stargardt's disease, Leber Congenital Amaurosis, choroidermia, Bardet-Biedl syndrome, or Refsum disease.

12. The use of any of claims 1-6; wherein the transmission of visual signals is enhanced, the electrical activity is increased, or loss of cells in the outer nuclear layer is prevented, in an individual having having Best's disease, cone-rod retinal dystrophy, gyrate atrophy, Oguchi disease, juvenile retinoschisis, Bassen-Kornzweig disease (abetalipoproteinemia), blue cone monochromatism disease, dominant drusen, Goldman-Favre vitreoretinal dystrophy (enhanced S-cone syndrome), Kearns-Sayre syndrome, Laurence-Moon syndrome, peripapillary choroidal dystrophy, pigment pattern dystrophy, Sorsby macular dystrophy, Stickler's syndrome or Wagner's syndrome (vitreoretinal dystrophy).

13. The use of claim 12, wherein the pigment pattern dystrophy is selected from the group consisting of Butterfly-shaped pigment dystrophy of the fovea, North Carolina macular dystrophy, macro-reticular dystrophy, spider dystrophy and Sjogren reticular pigment epithelium dystrophy.