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 example, disclosed herein are methods of treating retinal degeneration by administering ~~SB623~~ cells to the eye of a subject in need thereof, wherein said cells are descendants of marrow adherent stem cells that have been

engineered to express an exogenous Notch intracellular domain. The present invention disclosed herein refers to the use of ~~SB623~~ cells in the manufacture of a medicament for treating retinal degeneration in a subject in need thereof, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

[0007] In another example, 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, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

[0008] In another example, 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, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

[0009] In another example, 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, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

[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 the~~SB623~~ cells, in the same or different formulations.

[0011] Accordingly, the present disclosure describes, *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, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

2. The method of example 1, wherein ~~SB623~~ said 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

What is claimed is:

1. Use of ~~SB623~~ cells in the manufacture of a medicament for treating retinal degeneration in a subject in need thereof, wherein said cells are descendants of marrow adherent stem cells that have been engineered to express an exogenous Notch intracellular domain.

2. The use of claim 1, wherein said ~~SB623~~ cells are to be transplanted into the eye of the subject.

3. The use of claim 2, wherein the transplantation is intravitreal.

4. The use of claim 2, wherein the transplantation is subretinal.

5. The use of any of claims 1 to 4, wherein the retinal degeneration occurs in retinitis pigmentosa.

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

7. The use of claim 1, wherein the retinal degeneration occurs in Usher syndrome, Stargardt`s disease, Leber Congenital Amaurosis, choroidermia, Bardet-Biedl syndrome, or Refsum disease.

8. The use of claim 1, wherein the retinal degeneration occurs in 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).

9. The use of claim 8, 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.