[0022] The present invention provides a method in which the viral vector is delivered to a retinal cell. The retinal cell is a retinal ganglion cell, a retinal horizontal cell, a retinal bipolar cell, an amacrine cell, a photoreceptor cell, a Müller glial cell, or a retinal pigment epithelial cell.

[0023] In one aspect, the proteasome inhibitor and the viral vector is administered to the vitreous of the eye.

[0024] In other aspects, the proteasome inhibitor and the viral vector are administered by a route wherein the administration is by injection or infusion.

[0025] In a further aspect, the proteasome inhibitor and the viral vector are administered by a route that is not subretinal.

[0026] The present invention further provides a method of increasing or restoring light sensitivity in a subject comprising administering the proteasome inhibitor and the viral vector that encodes an opsin to the vitreous of the eye. The present invention also provides a method of improving or restoring vision in a subject comprising administering a proteasome inhibitor and the viral vector that encodes an opsin to the vitreous of the eye.

[0027] Uses of a composition comprising a proteasome inhibitor for treating an ocular disease or disorder in a subject are also provided herein.

[0028] The subject is suffering from an ocular disease or disorder. The ocular disease is retinoblastoma, ocular melanoma, diabetic retinopathy, hypertensive retinopathy, any inflammation of the ocular tissues. Preferably, the ocular disease or disorder is associated with photoreceptor degeneration.

[0029] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used in the practice of the present invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are expressly incorporated by reference in their entirety. In cases of conflict, the present specification, including definitions, will control.

[0030] In addition, the materials, methods, and examples described herein are illustrative only and are not intended to be limiting.

[0031] Other features and advantages of the invention will be apparent from and are encompassed by the following detailed description and claims.

DETAILED DESCRIPTION

inhibitor, when the population of cells is brought into contact with a gene delivery vehicle, such as an adenovirus, the cells are transduced with the gene delivery vehicle at a higher transduction efficiency, defined as the percentage of cells which are transduced with the gene delivery vehicle, compared to a similar population of cells that is brought into contact with a similar gene delivery vehicle, in the absence a proteasome inhibitor.

[0114] As used herein, the term "transduction efficiency" refers to the percentage of cells cultured with a compound that increases prostaglandin signaling that are transduced with a gene delivery vehicle, compared to a similar population of cells that is brought into contact with a similar gene delivery vehicle, in the absence of the compound that increases prostaglandin signaling.

[0115] A "small molecule," "small organic molecule," or "small molecule compound" refers to a low molecular weight compound that has a molecular weight of less than about 5 kD, less than about 4 kD, less than about 3 kD, less than about 2 kD, less than about 1 kD, or less than about 0.5 kD. In particular aspects, small molecules can include, nucleic acids, peptides, peptidomimetics, peptoids, other small organic compounds or drugs, and the like. Libraries of chemical and/or biological mixtures, such as fungal, bacterial, or algal extracts, are known in the art and can be screened with any of the assays of the invention. Examples of methods for the synthesis of molecular libraries can be found in: (Carell et al., 1994a; Carell et al., 1994b; Cho et al., 1993; DeWitt et al., 1993; Gallop et al., 1994; Zuckermann et al., 1994).

[0116] As used herein, the terms "polynucleotide" or "nucleic acid" refers to messenger RNA (mRNA), RNA, genomic RNA (gRNA), plus strand RNA (RNA(+)), minus strand RNA (RNA(-)), genomic DNA (gDNA), complementary DNA (cDNA) or DNA. Polynucleotides include single and double stranded polynucleotides. Preferably, polynucleotides of the invention include polynucleotides or variants having at least about 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to any of the reference sequences described herein (see, e.g., Sequence Listing), typically where the variant maintains at least one biological activity of the reference sequence. In various illustrative aspects, the present invention contemplates, in part, viral vector and transfer plasmid polynucleotide sequences and compositions comprising the same. In particular aspects, the invention provides polynucleotides encoding one or more therapeutic polypeptides and/or other genes of interest.

[0117] As used herein, the terms "polynucleotide variant" and "variant" and the like refer to

two, three, four, five or more nucleic acid cassettes. The nucleic acid cassette is positionally and sequentially oriented within the vector such that the nucleic acid in the cassette can be transcribed into RNA, and when necessary, translated into a protein or a polypeptide, undergo appropriate post-translational modifications required for activity in the transformed cell, and be translocated to the appropriate compartment for biological activity by targeting to appropriate intracellular compartments or secretion into extracellular compartments. Preferably, the cassette has its 3' and 5' ends adapted for ready insertion into a vector, e.g., it has restriction endonuclease sites at each end. In a preferred aspect of the invention, the nucleic acid cassette contains the sequence of a therapeutic gene used to treat, prevent, or ameliorate a genetic disorder, such as an ocular disorder. The cassette can be removed and inserted into a plasmid or viral vector as a single unit.

[0122] Polynucleotides include a polynucleotide(s)-of-interest. As used herein, the term "polynucleotide(s)-of-interest" refers to one or more polynucleotides, e.g., a polynucleotide encoding a polypeptide (i.e., a polypeptide-of-interest), inserted into an expression vector.

[0123] The term "expression control sequence" refers to a polynucleotide sequence that comprises one or more promoters, enhancers, or other transcriptional control elements or combinations thereof that are capable of directing, increasing, regulating, or controlling the transcription or expression of an operatively linked polynucleotide. In particular aspects, vectors of the invention comprise one or more expression control sequences that are specific to particular cells, cell types, or cell lineages e.g., target cells; that is, expression of polynucleotides operatively linked to an expression control sequence specific to particular cells, cell types, or cell lineages is expressed in target cells and not in other non-target cells. Each one of the one or more expression control sequences in a vector that are cell specific may express in the same or different cell types depending on the therapy desired. In preferred aspects, vectors comprise one or more expression control sequences specific to hematopoietic cells, e.g., hematopoietic stem or progenitor cells. In other preferred aspects, vectors comprise one or more expression control sequences specific to erythroid cells.

[0124] The term "promoter" as used herein refers to a recognition site of a polynucleotide (DNA or RNA) to which an RNA polymerase binds. The term "enhancer" refers to a segment of DNA which contains sequences capable of providing enhanced transcription and in some instances can function independent of their orientation relative to another control sequence. An enhancer can function cooperatively or additively with promoters and/or other