CLAIMS

~~What is claimed is:~~

1. An ~~isolated~~ adeno-associated virus (AAV) or a recombinant adeno-associated virus (rAAV) expression vector comprising a transgene operably linked to a promoter sequence, wherein the transgene encodes a light-~~-~~activated ion channel polypeptide comprising an ~~the~~ amino acid sequence ~~of SEQ ID NO:2 comprising one or more amino acid modifications~~ having greater than 90% amino acid sequence identity to any one of SEQ ID NOs: 8, 9, or 10, which comprises a cysteine at a position corresponding to position 112 of SEQ ID NO:2 and either a cysteine at a position corresponding to position 139 or a glutamate at a position corresponding to position 94 in SEQ ID NO: 2, and wherein the light-~~-~~activated ion channel polypeptide has ~~a~~ at least one of a greater level of an ion flux and a greater level of proton flux compared to the light-~~-~~activated ion channel polypeptide of SEQ ID NO:2 when expressed in a cell membrane and contacted with activating light.
2. The AAV or rAAV expression vector of claim 1, wherein the transgene encodes a light-~~-~~activated ion channel ~~polypeptide of claim 1, wherein the~~ polypeptide comprise~~s~~sing the amino acid sequence of any one of SEQ ID NOs: ~~3-10~~8, 9, or 10, or an amino acid sequence having greater than 95% amino acid sequence identity thereto.
3. A~~n isolated~~ recombinant adeno-associated virus (rAAV) expression vector comprising a transgene operably linked to a promoter sequence, wherein the transgene encodes a light-activated ion channel polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: ~~3-10~~ 8, 9, or 10.
4. ~~An isolated~~ The AAV or rAAV expression vector of claim 3, wherein the transgene encodes a light-activated ion channel polypeptide comprising the amino acid sequence of ~~any one of~~ SEQ ID NO~~s~~: ~~3~~-10 ~~comprising one or more amino acid modifications~~.
5. ~~The isolated polypeptide of claim 4, wherein the one or more modification is a substitution, deletion or insertion.~~
5. A recombinant adeno-associated virus comprising a transgene operably linked to a promoter sequence, wherein the transgene encodes a light-activated ion channel

polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: 8, 9, or 10.

6. The AAV or rAAV expression vector of any one of claims 1-4, or the virus of claim 5, wherein the AAV or rAAV expression vector, or virus, is an AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10, AAV11, or AAV12 expression vector or virus.
7. The AAV or rAAV expression vector of any one of claims 1-4, or the virus of claim 5, wherein the –AAV or rAAV expression vector, or virus, is an AAV2 expression vector or virus.
8. The AAV or rAAV expression vector of any one of claims 1-4, 6 and 7, or the virus of any one of claims 5-7, wherein the promoter is a cytomegalovirus (CMV) promoter, a Rous sarcoma virus (RSV) promoter, an MMT promoter, an EF-1 alpha promoter, a UB6 promoter, a chicken beta-actin promoter, a CAG promoter, an RPE65 promoter or an opsin promoter.
9. A pharmaceutical composition comprising the AAV or rAAV expression vector of any one of claims 1-4 and 6-8.
10. A pharmaceutical composition comprising the virus of any one of claims 5-8.
11. The ~~subject in need thereof a therapeutically effective amount of the polypeptide of claims 1-5~~ pharmaceutical composition of claim 9 or 10 for use in a method of improving or restoring vision in a subject suffering from a disease or condition selected from injury, brain damage, spinal cord injury, epilepsy, a metabolic disorder, a cardiac dysfunction, vision loss, blindness, deafness, hearing loss or a neurological condition.

~~6. A cell comprising the polypeptide of an any one of the preceding claims.~~
~~7. An isolated nucleic acid molecule that encodes for the polypeptide of any one of claims 1-5.~~
~~8. An isolated nucleic acid molecule of claim 7, wherein the nucleic acid sequence is operably linked to a promoter sequence~~
~~9. A cell comprising the isolated nucleic acid molecule of claim 7 or 8.~~
~~10. A composition comprising the isolated nucleic acid molecule of claim 7 or 8.~~
~~11. The cell of claim 6 or 9 wherein the cell is in vitro, ex vivo or in vivo~~
~~12. A vector comprising the isolated nucleic acid molecule of claim 7 or 8.~~

~~13. The cell of claim 6 or 9, wherein the cell is a photoreceptor, a bipolar cell, a rod bipolar cell, an ON-type cone bipolar cell, a retinal ganglion cell, a photosensitive retinal ganglion cell, a horizontal cell, an amacrine cell, or an AII amacrine cell.~~

~~14. A method of changing the conductivity of a membrane comprising~~

~~a. expressing in a host membrane the polypeptide of any one of claim 1-5~~

~~b. contacting the polypeptide with a light under suitable conditions to change the conductivity of the host membrane.~~

~~15. The method of claim 14, wherein the host membrane is a cell membrane.~~

~~16. The method of claim 15, wherein the host membrane is a cell membrane of a neuronal cell, a nervous system cell, a cardiac cell, a circulatory cell, a visual system cell, or an auditory system cell.~~

~~17. A method of treating a disease or condition in a subject comprising administering to a subject in need thereof a therapeutically effective amount of the polypeptide of claims 1-5 or the nucleic acid of 7-8.~~

~~18.~~12. Use of the AAV or rAAV expression vector of any one of claims 1-4 and 6-8, or the pharmaceutical composition ~~The method~~ of claim ~~17~~9 or claim 10, ~~wherein~~ in the manufacture of a medicament for improving or restoring vision in a subject suffering from a disease or condition ~~is~~ selected from injury, brain damage, spinal cord injury, epilepsy, a metabolic disorder, a cardiac dysfunction, vision loss, blindness, deafness, hearing loss or a neurological condition.

13. The pharmaceutical composition of claim 9 or 10 for use in a method of improving or restoring vision in a subject.

~~19.~~14. ~~A method~~ Use of the AAV or rAAV expression vector of any one of claims 1-4 and 6-8, or the pharmaceutical composition of claim 9 or claim 10, in the manufacture of a medicament for improving or restoring vision~~, comprising administering to~~ in a subject ~~the polypeptide of claims 1-5 or the nucleic acid of 7-8~~.

~~20.~~15. The pharmaceutical composition for use ~~method~~ of claim ~~19~~ 13 or the use of claim 14, wherein the subject is suffering from an ocular disease.

~~21.~~16. The pharmaceutical composition for use or the use ~~method~~ of claim ~~20~~ 15, wherein the ocular disease is macular degeneration or retinitis pigmentosa.

~~22.~~17. The pharmaceutical composition for use of any one of claims 11, 13, 15 and 16

or the use ~~method~~ of any one of claims ~~19-21~~ 12~~1~~ and 14-16, wherein said improving or restoring vision comprises any of the following: increasing light sensitivity~~;~~, lowering the threshold light intensity required to elicit a photocurrent; and increasing visual evoked potential in the visual cortex.

18. The pharmaceutical composition of claim 9 or 10 for use in a method of treating retinitis pigmentosa or age-related macular degeneration in a subject.

~~23.~~19. ~~A method~~ Use of the AAV or rAAV expression vector of any one of claims 1-4 and 6-8, or the pharmaceutical composition of claim 9 or claim 10, in the manufacture of a medicament for treating retinitis pigmentosa or age~~-~~-related macular degeneration ~~comprising administering to~~ in a subject ~~in need thereof the polypeptide of claims 1-5 or the nucleic acid of 7-8~~.

~~24.~~20. The pharmaceutical composition for use of any one of claims 11, 13, 15-18 or the use ~~method~~ of any one of claims ~~19 to 23~~ 12, 14-17 and 19~~1-19~~, wherein the AAV or rAAV expression vector or the pharmaceutical composition is ~~administered~~ adapted for administration by intravitreal or subretinal injection.

21. An expression vector comprising a nucleic acid molecule encoding an isolated light–activated ion channel polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: 3-10, wherein the light–activated ion channel polypeptide has at least one of a greater level of an ion flux and a greater level of proton flux compared to the light–activated ion channel polypeptide of SEQ ID NO:2 when expressed in a cell membrane and contacted with activating light.