CLAIMS

WHAT IS CLAIMED IS:

1. A recombinant adeno-associated viral (rAAV) vector comprising at least a first polynucleotide that comprises a photoreceptor-specific human rhodopsin kinase promoter operably linked to at least a first nucleic acid segment that encodes at least a first biologically-active, retinal-specific human guanylate cyclase protein, peptide, or polypeptide that comprises a first contiguous amino acid sequence region that is at least about 95% identical to an at least 80-contiguous-amino-acid sequence from SEQ ID NO: 1, wherein the rAAV vector is contained within a AAV5 or AAV8 particle.

2. The rAAV vector according to claim 1, wherein the at least a first mammalian guanylate cyclase protein, peptide, or polypeptide first biologically-active, retinal-specific human guanylate cyclase protein, peptide, or polypeptide comprises at least a first contiguous amino acid sequence region that is at least about 98% identical to an at least 140-contiguous-amino-acid sequence from SEQ ID NO: 1.

3. The rAAV vector according to any preceding claim, wherein the at least first biologically-active, retinal-specific human guanylate cyclase protein, peptide, or polypeptide comprises an amino acid sequence that is at least about 98% identical to SEQ ID NO: 1.

4. The rAAV vector according to any preceding claim, wherein the at least first biologically-active, retinal-specific human guanylate cyclase protein, peptide, or polypeptide comprises the amino acid sequence of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or SEQ ID NO:11.

5. The rAAV vector according to any preceding claim, wherein the at least first biologically-active, retinal-specific human guanylate cyclase protein, peptide, or

polypeptide consists essentially of an amino acid sequence that is at least 98% identical to the sequence of SEQ ID NO:1.

6. The rAAV vector according to any preceding claim, wherein the rAAV vector is contained with a AAV5 particle.

7. The rAAV vector according to any preceding claim, wherein the vector is a self-complementary rAAV (scAAV).

8. The rAAV vector according to any preceding claim, wherein the photoreceptor-specific human rhodopsin kinase promoter comprises a nucleic acid sequence that consists essentially of an at least 30 contiguous base pair sequence from SEQ ID NO:12.

9. The rAAV vector according to any preceding claim, wherein the photoreceptor- specific human rhodopsin kinase promoter comprises a nucleic acid sequence that consists essentially of an at least 40 contiguous basepair sequence from SEQ ID NO:12.

10. The rAAV vector according to any preceding claim, wherein the photoreceptor- specific human rhodopsin kinase promoter comprises a nucleic acid sequence that consists essentially of an at least 60 contiguous basepair sequence from SEQ ID NO:12.

11. The rAAV vector according to any preceding claim, wherein the photoreceptor- specific human rhodopsin kinase promoter comprises the nucleic acid sequence of SEQ ID NO:12.

12. The rAAV vector according to any preceding claim, further comprising at least a first enhancer operably linked to the at least a first nucleic segment.

13. The rAAV vector according to any preceding claim, further comprising at least a first mammalian intron sequence operably linked to the at least a first nucleic segment.

14. An isolated mammalian host cell comprising:

the rAAV vector in accordance with any one of claims 1 to 13.

15. The isolated mammalian host cell according to claim 14, wherein the cell is a human host cell.

16. A composition comprising:

(1) (a) the rAAV vector in accordance with any one of claims 1 to 13; or

(b) an isolated mammalian host cell comprising the vector; and

(2) a pharmaceutically-acceptable buffer, carrier, vehicle, or diluent.

17. The composition according to claim 16, further comprising a lipid, a liposome, a lipid complex, an ethosome, a niosome, a nanoparticle, a microparticle, a liposphere, a nanocapsule, or any combination thereof.

18. The composition according to claim 16 or claim 17, formulated for administration to the human eye.

19. The composition according to any one of claims 16 to 18, for use in the therapy or prophylaxis of Leber congenital amaurosis-1 (LCA1).

20. A kit comprising:

(1) a component selected from the group consisting of:

(a) the rAAV vector in accordance with any one of claims 1 to 13;

(b) the isolated mammalian host cell in accordance with claim 14 or claim 15; or

(c) the composition in accordance with any one of claims 16 to 19; and

(2) instructions for using the component in the diagnosis, prevention, treatment, or amelioration of one or more symptoms of a retinal dystrophy, disease, disorder, or abnormal condition in a human.

21. The kit according to claim 20, wherein the retinal dystrophy is diagnosed as Leber congenital amaurosis-1 (LCA-1).

22. Use of a composition in accordance with claim 16, in the manufacture of a medicament for treating or ameliorating one or more symptoms of Leber congenital amaurosis-1 (LCA-1) in a human.

23. A method for preventing, treating or ameliorating Leber congenital amaurosis-1 (LCA1) in a mammal, or one or more symptoms thereof, the method comprising administering to the mammal a composition comprising the rAAV vector in accordance with any one of claims 1 to 13, in an amount and for a time sufficient to prevent, treat or ameliorate the LCA1 in the mammal, or one or more symptoms thereof.

24. The method according to claim 23, wherein the mammal is a human neonate, newborn, infant, or juvenile that is at risk for developing or has been diagnosed with Leber congenital amaurosis-1 (LCA-1).

25. A method for providing a mammal with a therapeutically-effective amount of a biologically-active mammalian guanylate cyclase peptide, polypeptide, or protein to a mammal in need thereof, comprising introducing into suitable cells of a mammal in need thereof, an effective amount of the rAAV vector in accordance with any one of claims 1 to 13, for a time sufficient to produce a biologically-active guanylate cyclase peptide, polypeptide or protein therefrom in at least a first population of cells or at least a first tissue of the mammal into which the rAAV vector has been introduced.

26. The method according to claim 25, wherein the mammal in need thereof has a defect, deficiency, or substantial absence of biologically-active retGC1 protein in at least a first tissue of the mammal, when compared to the level of biologically-active retGC1 protein in a normal mammal.

27. The method according to claim 25 or claim 26, wherein a plurality of cells from the mammal are provided with the rAAV vector *ex vivo* or *in vitro,* and the method further comprises introducing the plurality of provided cells into at least a first tissue site within or about the body of the mammal.

28. The method according to any one of claims 25 to 27, wherein the plurality of obtained cells is introduced into at least a first site within one or both eyes of the mammal.

29. The method according to any one of claims 25 to 28, wherein the plurality of obtained cells is introduced into at least a first site within one or both eyes of the mammal by direct injection into the retina or the surrounding tissue.

30. The method according to any one of claims 25 to 29, wherein introduction of the rAAV vector preserved cone photoreceptors, and restored cone-mediated function and visual behavior in the eye of the mammal.

31. The method according to any one of claims 25 to 30, wherein a single introduction of the rAAV vector into the eye of the mammal preserved cone photoreceptors, and restored cone-mediated function and visual behavior in the mammal for a period of at least three months.

32. The method according to any one of claims 25 to 31, wherein a single introduction of the rAAV vector into the eye of the mammal preserved cone photoreceptors, and restored cone-mediated function and visual behavior in the mammal for a period of at least six months.

33. The method according to any one of claims 25 to 32, wherein a single introduction of the rAAV vector into the eye of the mammal preserved cone photoreceptors, and restored cone-mediated function and visual behavior in the mammal for a period of at least ten months.

34. A method for increasing the level of biologically-active retGC1 protein in one or more retinal cells of a mammal that has, is suspected of having, is diagnosed with, or is at risk for developing, LCA1, comprising introducing the rAAV vector in accordance with any one of claims 1 to 13, into at least a first population of retinal cells of the mammal, in an amount and for a time effective to increase the level of biologically-active retGCl protein in one or more retinal cells of the mammal.

35. A method for treating or ameliorating one or more symptoms of retinal dystrophy in a mammal, the method comprising directly administering to the retina or sub-retinal space of the mammal an rAAV vector in accordance with any one of claims 1 to 13, in an amount and for a time sufficient to treat or ameliorate the one or more symptoms of retinal dystrophy in the mammal, wherein the mammal has been diagnosed with Leber congenital amaurosis-1 (LCA-1).