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 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.

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 within a AAV5 particle.

7. The rAAV vector according to any preceding claim, wherein the rAAV vector is contained within a AAV8 particle.

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

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 30 contiguous base pair 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 40 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 a nucleic acid sequence that consists essentially of an at least 60 contiguous basepair sequence from SEQ ID NO:12.

12. 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.

13. 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.

14. 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.

15. An isolated mammalian host cell comprising:

the rAAV vector in accordance with any one of claims 1 to 14.

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

17. A composition comprising:

(1) (a) the rAAV vector in accordance with any one of claims 1 to 14; or

(b) an isolated mammalian host cell comprising the rAAV vector in accordance with any one of claims 1 to 14; and

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

18. The composition according to claim 17, 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.

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

20. The composition according to any one of claims 17 to 19, for use in the therapy or prophylaxis of Leber congenital amaurosis-1 (LCA1).

21. 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 14;

(b) the isolated mammalian host cell in accordance with claim 15 or claim 16; or

(c) the composition in accordance with any one of claims 17 to 20; 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.

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

23. Use of a composition in accordance with claim 17, in the manufacture of a medicament for treating or ameliorating one or more symptoms of Leber congenital amaurosis-1 (LCA-1) in a human.

24. An rAAV vector in accordance with any one of claims 1 to 14 for use in a method for preventing, treating or ameliorating Leber congenital amaurosis-1 (LCA1) in a mammal, or one or more symptoms thereof, wherein the method comprises administering to the mammal a composition comprising the rAAV vector, in an amount and for a time sufficient to prevent, treat or ameliorate the LCA1 in the mammal, or one or more symptoms thereof.

25. The rAAV vector according to claim 24, 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).

26. An rAAV vector in accordance with any one of claims 1 to 14 for use in 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, wherein the method comprises introducing into suitable cells of a mammal in need thereof, an effective amount of the rAAV vector, 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.

27. The rAAV vector according to claim 26, 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.

28. The rAAV vector according to claim 26 or claim 27, 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.

29. The rAAV vector according to any one of claims 26 to 28, wherein the plurality of obtained cells is introduced into at least a first site within one or both eyes of the mammal.

30. The rAAV vector according to any one of claims 26 to 29, 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.

31. The rAAV vector according to any one of claims 26 to 30, wherein introduction of the rAAV vector preserved cone photoreceptors, and restored cone-mediated function and visual behavior in the eye of the mammal.

32. The rAAV vector according to any one of claims 26 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 three months.

33. The rAAV vector according to any one of claims 26 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 six months.

34. The rAAV vector according to any one of claims 26 to 33, 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.

35. An rAAV vector in accordance with any one of claims 1 to 14 for use in 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, wherein the method comprises introducing the rAAV vector, 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.

36. An rAAV vector in accordance with any one of claims 1 to 14 for use in a method for treating or ameliorating one or more symptoms of retinal dystrophy in a mammal, wherein the method comprises directly administering to the retina or sub-retinal space of the mammal the rAAV vector, 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).