CLAIMS

1. Use of a non-naturally occurring nuclease system comprising one or more vectors comprising:

i) a promoter operably linked to at least one nucleotide sequence encoding a nuclease system guide RNA (gRNA), wherein the gRNA hybridizes with a target sequence of a DNA molecule in a cell of a subject, and wherein the DNA molecule encodes one or more gene products expressed in the cell, wherein the one or more gene products are selected from the group consisting of rhodopsin, CEP290, Dual Leucine Zipper Kinase (DLK), and Leucine Zipper Kinase (LZK); and

ii) a regulatory element operable in a cell operably linked to a nucleotide sequence encoding a genome-targeted nuclease,

in the manufacture of a medicament for the treatment of a retinal degeneration in a subject in need thereof, wherein components (i) and (ii) are located on the same or different vectors of the system, wherein the gRNA targets and hybridizes with the target sequence and the nuclease cleaves one or two strands of the DNA molecule to alter expression of the one or more gene products.

2. An *in vitro* method of altering expression of one or more gene products in a cell, wherein the cell comprises a DNA molecule encoding the one or more gene products, the method comprising introducing into the cell a non-naturally occurring nuclease system comprising one or more vectors comprising:

a) a promoter operably linked to at least one nucleotide sequence encoding a nuclease system guide RNA (gRNA), wherein the gRNA hybridizes with a target sequence of the DNA molecule; and

b) a regulatory element operable in the cell operably linked to a nucleotide sequence encoding a genome-targeted nuclease,

wherein components (a) and (b) are located on the same or different vectors of the system, wherein the gRNA targets and hybridizes with the target sequence and the nuclease cleaves the DNA molecule to alter expression of the one or more gene products selected from the group consisting of rhodopsin, CEP290, Dual Leucine Zipper Kinase (DLK), and Leucine Zipper Kinase (LZK).

3. The use of claim 1 or the method of claim 2, wherein the system is CRISPR.

4. The use of claim 1 or the method of claim 2, wherein the system is packaged into a single adeno-associated virus (AAV) particle.

5. The use of claim 1 or the method of claim 2, wherein the system inactivates one or more gene products.

6. The use of claim 1 or the method of claim 2, wherein the nuclease system excises at least one gene mutation.

7. The use of claim 1 or the method of claim 2, wherein the promoter is a bidirectional promoter.

8. The use or method of claim 7, wherein the bidirectional promoter is H1.

9. The use or method of claim 8, wherein the H1 promoter comprises:

a) control elements that provide for transcription in one direction of the at least one nucleotide sequence encoding the gRNA; and

b) control elements that provide for transcription in the opposite direction of the nucleotide sequence encoding the genome-targeted nuclease.

10. The use of claim 1 or the method of claim 2, wherein the genome-targeted nuclease is Cas9 protein.

11. The use or method of claim 10, wherein the Cas9 protein is codon optimized for expression in the cell.

12. The use or method of claim 7 or claim 8, wherein the promoter is operably linked to at least one, two, three, four, five, six, seven, eight, nine, or ten gRNA.

13. The use of claim 1, wherein the retinal area is the retina.

14. The method of claim 2, wherein the cell is a eukaryotic or non-eukaryotic cell.

15. The method of claim 2, wherein the eukaryotic cell is a mammalian or human cell.

16. The use of claim 1 or the method of claim 2, wherein the cell is a retinal photoreceptor cell.

17. The use of claim 1 or the method of claim 2, wherein the cell is a retinal ganglion cell.

18. The use of claim 1 or the method of claim 2, wherein the retinal degeneration is selected from the group consisting of Leber's congenital amaurosis (LCA), retinitis pigmentosa (RP), and glaucoma.

19. The use or method of claim 18, wherein the retinal degeneration is LCA1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, or 18.

20. The use or method of claim 19, wherein the target sequence is in the LCA10 CEP290 gene.

21. The use or method of claim 19 or claim 20, wherein the target sequence is a mutation in the CPE290 gene selected from the group consisting of the nucleotide sequences set forth in SEQ ID NO: 1-109, 164-356, 735-738, or 788-1397, or combinations thereof.

22. The use or method of claim 21, wherein the target sequence comprises SEQ ID NOs: 1, 2, 3, and 4 operably linked.

23. The use of claim 1 or the method of claim 2, wherein the vector comprises the nucleotide sequence set forth in SEQ ID NO: 110.

24. The use or method of claim 18, wherein the retinal degeneration is an autosomal dominant form of retinitis pigmentosa (ADRP).

25. The use of claim 1 or the method of claim 2, wherein the target sequence is a mutation in the rhodopsin gene.

26. The use of claim 1 or the method of claim 2, wherein the target sequence is a mutation at R135 of the rhodopsin gene.

27. The use or method of claim 26, wherein the mutation at R135 is selected from the group consisting of R135G, R135W, R135L.

28. The use or method of any one of claims 25-27, wherein the target sequence is selected from the group consisting of the nucleotide sequences set forth in SEQ ID NO: 111-126, or combinations thereof.

29. The use of claim 1 or the method of claim 2, wherein the gRNA sequence is selected from the group consisting of the nucleotide sequences set forth in SEQ ID NO: 131-142, or combinations thereof.

30. The use or method of claim 18, wherein the retinal degeneration is glaucoma.

31. The use of claim 1 or the method of claim 2, wherein the target sequence is selected from the group consisting of the nucleotide sequences set forth in SEQ ID NO: 143-163, or combinations thereof.

32. A non-naturally occurring nuclease system comprising one or more vectors comprising:

i) a promoter operably linked to at least one nucleotide sequence encoding a nuclease system guide RNA (gRNA), wherein the gRNA hybridizes with a target sequence of a DNA molecule in a cell of a subject, and wherein the DNA molecule encodes one or more gene products expressed in the cell, wherein the one or more gene products are selected from the group consisting of rhodopsin, CEP290, Dual Leucine Zipper Kinase (DLK), and Leucine Zipper Kinase (LZK); and

ii) a regulatory element operable in a cell operably linked to a nucleotide sequence encoding a genome-targeted nuclease,

for use in the treatment of a retinal degeneration in a subject in need thereof, wherein components (i) and (ii) are located on the same or different vectors of the system, wherein the gRNA targets and hybridizes with the target sequence and the nuclease cleaves one or two strands of the DNA molecule to alter expression of the one or more gene products.