CLAIMS

That which is claimed is:

1. A recombinant adeno-associated virus (rAAV) variant comprising a polynucleotide of interest for use in delivering the polynucleotide of interest to a cone photoreceptor in a subject, wherein said rAAV variant is to be delivered into the vitreous of the eye.

2. The rAAV variant for use according to claim 1, wherein the rAAV variant comprises a variant AAV capsid protein comprising an insertion of an amino acid peptide in the GH loop of the parental AAV capsid protein.

3. The rAAV variant for use according to claim 2, wherein the GH loop of the parental capsid protein consists essentially of amino acids 571-612 of AAV1 VP1 (SEQ ID NO:1), about amino acids 570-611 of AAV2 VP1 (SEQ ID NO:2), about amino acids 571-612 of AAV3 VP1 (SEQ ID NO:3), about amino acids 569-610 of AAV4 VP1 (SEQ ID NO:4), about amino acids 560-601 of AAV5 VP1 (SEQ ID NO:5), about amino acids 571 to 612 of AAV6 VP1 (SEQ ID NO:6), about amino acids 572 to 613 of AAV7 VP1 (SEQ ID NO:7), about amino acids 573 to 614 of AAV8 VP1 (SEQ ID NO:8), about amino acids 571 to 612 of AAV9 VP1 (SEQ ID NO:9), about amino acids 573 to 614 of AAV10 VP1 (SEQ ID NO:10); or the corresponding amino acid range of a variant thereof.

4. The rAAV variant for use according to claim 2, wherein the parental capsid is AAV2 VP1, wherein the insertion site is between amino acids 580 and 581, amino acids 581 and 582, amino acids 582 and 583, amino acids 583 and 584, amino acids 584 and 585, amino acids 585 and 586, amino acids 586 and 587, amino acids 587 and 588, amino acids 588 and 589, amino acids 589 and 590, amino acids 590 and 591, amino acids 591 and 592, amino acids 592 and 593, amino acids 593 and 594, or amino acids 594 and 595 of AAV2 VP1.

5. The rAAV variant for use according to claim 2, wherein the peptide is of the formula:

$Y_1Y_2X_1X_2X_3X_4X_5X_6X_7Y_3Y_4$

wherein:

each of Y1 –Y4, if present, is independently selected from Ala, Leu, Gly, Ser, and Thr;

X1, if present, is selected from Leu, Asn, and Lys;

X2 is selected from Gly, Glu, Ala, and Asp;
X3 is selected from Glu, Thr, Gly, and Pro;
X4 is selected from Thr, Ile, Gln, and Lys;
X5 is selected from Thr and Ala;
X6 is selected from Arg, Asn, and Thr;
X7, if present, is selected from Pro and Asn.

6. The rAAV variant for use according to claim 5, wherein the peptide comprises the amino acid sequence LGETTRP (SEQ ID NO:11).

7. The rAAV variant for use according to claim 1, wherein the cone photoreceptor is a foveal cone.

8. The rAAV variant for use according to claim 1, wherein the subject is a primate.

9. A recombinant adeno-associated virus (rAAV) variant comprising a polynucleotide that encodes a gene product for use in expressing a gene product in a cone photoreceptor in a subject, wherein said rAAV is to be delivered into the vitreous of the eye.

10. The rAAV for use according to claim 9, wherein the rAAV variant comprises a variant AAV capsid protein comprising an insertion of an amino acid peptide in the GH loop of the parental AAV capsid protein.

11. The rAAV for use according to claim 10, wherein the GH loop of the parental capsid protein consists essentially of amino acids 571-612 of AAV1 VP1 (SEQ ID NO:1), about amino acids 570-611 of AAV2 VP1 (SEQ ID NO:2), about amino acids 571-612 of AAV3 VP1 (SEQ ID NO:3), about amino acids 569-610 of AAV4 VP1 (SEQ ID NO:4), about amino acids 560-601 of AAV5 VP1 (SEQ ID NO:5), about amino acids 571 to 612 of AAV6 VP1 (SEQ ID NO:6), about amino acids 572 to 613 of AAV7 VP1 (SEQ ID NO:7), about amino acids 573 to 614 of AAV8 VP1 (SEQ ID NO:8), about amino acids 571 to 612 of AAV9 VP1 (SEQ ID NO:9), about amino acids 573 to 614 of AAV10 VP1 (SEQ ID NO:10); or the corresponding amino acid range of a variant thereof.

12. The rAAV for use according to claim 10, wherein the parental capsid is AAV2 VP1, wherein the insertion site is between amino acids 580 and 581, amino acids 581 and 582, amino acids 582 and 583, amino acids 583 and 584, amino acids 584 and 585, amino acids 585 and 586, amino acids 586 and 587, amino acids 587 and 588, amino acids 588 and 589, amino acids 589 and 590, amino acids 590 and 591, amino acids 591 and 592, amino acids 592 and 593, amino acids 593 and 594, or amino acids 594 and 595 of AAV2 VP1.

13. The rAAV for use according to claim 10, wherein the peptide is of the formula:

$Y_1Y_2X_1X_2X_3X_4X_5X_6X_7Y_3Y_4$

wherein:

each of Y1 –Y4, if present, is independently selected from Ala, Leu, Gly, Ser, and Thr;

X1, if present, is selected from Leu, Asn, and Lys;

X2 is selected from Gly, Glu, Ala, and Asp;

X3 is selected from Glu, Thr, Gly, and Pro;

X4 is selected from Thr, Ile, Gln, and Lys;

X5 is selected from Thr and Ala;

X6 is selected from Arg, Asn, and Thr;

X7, if present, is selected from Pro and Asn.

14. The rAAV for use according to claim 13, wherein the peptide comprises the amino acid sequence LGETTRP (SEQ ID NO:11).

15. The rAAV for use according to claim 9, wherein the polynucleotide is operably linked to the MNTC promoter.

16. The rAAV for use according to claim 9, wherein the method further comprises detecting the expression of the polynucleotide in the cone photoreceptor.

17. The rAAV for use according to claim 9, wherein the cone photoreceptor is a foveal cone.

18. The rAAV for use according to claim 9, wherein the subject is a primate.

19. Use of a recombinant adeno-associated virus (rAAV) variant in the manufacture of a medicament for treating or preventing a cone-associated retinal disorder in a subject having or at risk for developing a cone-associated retinal disorder, wherein said rAAV comprises a therapeutic polynucleotide in an amount effective to treat or prevent the cone-associated retinal disorder and wherein the medicament is to be administered intravitreally.

20. The use according to claim 19, wherein the rAAV variant comprises a variant AAV capsid protein comprising an insertion of an amino acid peptide in the GH loop of the parental AAV capsid protein.

21. The use according to claim 20, wherein the GH loop of the parental capsid protein consists essentially of amino acids 571-612 of AAV1 VP1 (SEQ ID NO:1), about amino acids 570-611 of AAV2 VP1 (SEQ ID NO:2), about amino acids 571-612 of AAV3 VP1 (SEQ ID NO:3), about amino acids 569-610 of AAV4 VP1 (SEQ ID NO:4), about amino acids 560-601 of AAV5 VP1 (SEQ ID NO:5), about amino acids 571 to 612 of AAV6 VP1 (SEQ ID NO:6), about amino acids 572 to 613 of AAV7 VP1 (SEQ ID NO:7), about amino acids 573 to 614 of AAV8 VP1 (SEQ ID NO:8), about amino acids 571 to 612 of AAV9 VP1 (SEQ ID NO:9), about amino acids 573 to 614 of AAV10 VP1 (SEQ ID NO:10); or the corresponding amino acid range of a variant thereof.

22. The use according to claim 20, wherein the parental capsid is AAV2 VP1, wherein the insertion site is between amino acids 580 and 581, amino acids 581 and 582, amino acids 582 and 583, amino acids 583 and 584, amino acids 584 and 585, amino acids 585 and 586, amino acids 586 and 587, amino acids 587 and 588, amino acids 588 and 589, amino acids 589 and 590, amino acids 590 and 591, amino acids 591 and 592, amino acids 592 and 593, amino acids 593 and 594, or amino acids 594 and 595 of AAV2 VP1.

23. The use according to claim 20, wherein the peptide is of the formula:

$Y_1Y_2X_1X_2X_3X_4X_5X_6X_7Y_3Y_4$

wherein:

each of Y1 –Y4, if present, is independently selected from Ala, Leu, Gly, Ser, and Thr;

X1, if present, is selected from Leu, Asn, and Lys;

X2 is selected from Gly, Glu, Ala, and Asp;

X3 is selected from Glu, Thr, Gly, and Pro;
X4 is selected from Thr, Ile, Gln, and Lys;
X5 is selected from Thr and Ala;
X6 is selected from Arg, Asn, and Thr;
X7, if present, is selected from Pro and Asn.

24. The use according to claim 20, wherein the peptide comprises the amino acid sequence LGETTRP (SEQ ID NO:11).

25. The use according to claim 19, wherein the retinal disorder is a cone-associated disorder.

26. The use according to claim 25, wherein the cone-associated disorder is selected from the group consisting of rod-cone dystrophy; cone-rod dystrophy; progressive cone dystrophy; retinitis pigmentosa (RP); Stargardt Disease; macular telangiectasia, Leber hereditary optic neuropathy, Best's disease; adult vitelliform macular dystrophy; X-linked retinoschisis; a color vision disorder; age-related macular degeneration; wet age-related macular degeneration; geographic atrophy; diabetic retinopathy; a retinal vein occlusion; retinal ischemia; Familial Exudative Vitreoretinopathy (FEVR); COATs disease; and Sorsby's fundus dystrophy.

27. The use according to claim 19, wherein the method further comprises identifying the subject as having a cone-associated disorder.

28. The use according to claim 19, wherein the method further comprises detecting an improvement in vision following the administration step.

29. The use according to claim 19, wherein the subject is a primate.