CLAIMS

1. An isolated polynucleotide comprising a nucleotide sequence encoding Complement Factor I (CFI), wherein the nucleotide sequence has at least ~~85~~99% sequence identity to SEQ ID NO: 10.

2. The isolated polynucleotide of claim 1, wherein the nucleotide sequence is SEQ ID NO: 10.

~~3. An isolated polynucleotide comprising a nucleotide sequence encoding Complement Factor H-like Protein 1 (FHL1), wherein the nucleotide sequence has at least 75% sequence identity to SEQ ID NO: 12.~~

~~4. The isolated polynucleotide of claim 3, wherein the nucleotide sequence is SEQ ID NO: 12.~~

3. The isolated polynucleotide of claim 1 or 2, wherein the polynucleotide comprises an adeno-associated virus (AAV) inverted terminal repeat (ITR) at its 5' end and an AAV ITR at its 3' end.

4. The isolated polynucleotide of claim 3, wherein the AAV ITRs are AAV2 or AAV8 ITRs, preferably wherein the AAV ITRs are AAV2 ITRs.

5. The isolated polynucleotide of any one of claims 1-4, wherein the nucleotide sequence encoding CFI is operably linked to a WPRE regulatory element.

6. The isolated polynucleotide of any one of claims 1-4, wherein the nucleotide sequence encoding CFI is operably linked to a polyadenylation (poly-A) signal.

7. The isolated polynucleotide of any one of claims 1-4, wherein the nucleotide sequence encoding CFI is operably linked to a promoter, optionally wherein the promoter has the nucleotide sequence of SEQ ID NO: 5, or a nucleotide sequence having at least 75%, 80%, 85% 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 5.

8. The isolated polynucleotide of any one of claims 1-4, wherein the nucleotide sequence encoding CFI is operably linked to a CMV promoter; a WPRE regulatory element; and a poly-A signal.

9. The isolated polynucleotide of claim 8, wherein the promoter has the nucleotide sequence of SEQ ID NO: 13, or a nucleotide sequence having at least 75%, 80%, 85% 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 13.

10. The isolated polynucleotide of any one of claims 6, 8 or 9, wherein the poly-A signal is a Bovine Growth Hormone poly-A signal.

11. The isolated polynucleotide of any one of claims 6 or 8-10, wherein the poly-A signal has the nucleotide sequence of SEQ ID NO: 14 or SEQ ID NO: 6, or a nucleotide sequence that has at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: 14 or SEQ ID NO: 6.

12. The isolated polynucleotide of any one of claims 5 or 8-11, wherein the WPRE regulatory element has the nucleotide sequence of SEQ ID NO: 7 or SEQ ID NO: 15, or a nucleotide sequence that has at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identity to SEQ ID NO: ~~15~~7 or SEQ ID NO: 15~~7~~.

~~5~~13. A vector comprising the polynucleotide of any preceding claim.

~~6~~14. The vector of claim ~~5~~13, wherein the vector is an adeno-associated viral (AAV) vector.

~~7~~15. The vector of claim ~~5 or 6~~13 or 14, wherein the vector is in the form of a viral vector particle.

~~8~~16. The vector of claim ~~7~~15, wherein the viral vector particle is an AAV vector particle that comprises ~~an AAV2 or AAV8 genome, and~~ AAV2 or AAV8 capsid proteins.

17. The vector of claim 16, wherein the AAV vector particle comprises an AAV2 genome and AAV2 capsid proteins (AAV2/2), an AAV2 genome and AAV8 capsid proteins (AAV2/8) or an AAV8 genome and AAV8 capsid proteins (AAV8/8).

~~9. The vector of any one of claims 5-8, wherein the nucleotide sequence encoding the CFI or FHL1 is operably linked to a CMV promoter; a WPRE regulatory element; and/or a poly-A signal.~~

~~10~~18. A cell comprising the polynucleotide of any one of claims ~~1-4~~1-12 or a cell transduced with the vector of any one of claims ~~5-9~~13-17.

~~11~~19. A pharmaceutical composition comprising the polynucleotide, vector or cell of any preceding claim in combination with a pharmaceutically acceptable carrier, diluent or excipient.

~~12~~20. The polynucleotide~~, vector or cell~~ or vector of any one of claims 1-~~10~~ 17 for use in therapy, preferably for use in treating or preventing a complement-mediated disorder of the eye.

~~13~~21. The polynucleotide~~, vector or cell~~ or vector for use according to claim ~~12~~20, wherein the disorder is age-related macular degeneration (AMD) or diabetic retinopathy, preferably AMD.

~~14~~22. The polynucleotide~~, vector or cell~~ or vector for use according to claim ~~13~~21, wherein the AMD is dry AMD.

~~15~~23. The polynucleotide~~, vector or cell~~ or vector for use according to any one of claims ~~12~~20-~~14~~22, wherein:

(i) the formation of geographic atrophy is prevented or reduced, and/or the amount of geographic atrophy is reduced; and/or

(ii) the progression of geographic atrophy is slowed; and/or

(iii) there is at least a 10% reduction in the increase in geographic atrophy area over the 12 months following administration to a treated eye of a subject, relative to an untreated eye over the same period; and/or

(iv) administration of the polynucleotide, vector or cell increases the level of C3b-inactivating and iC3b-degradation activity in a subject, or in an eye, such as in the retinal pigment epithelium (RPE), of a subject, optionally to a level that exceeds a normal level in a subject, or eye or RPE thereof.

~~16~~24. The polynucleotide~~, vector or cell~~ or vector for use according to any one of claims ~~12-15~~20-23, wherein the polynucleotide~~, vector or cell~~ or vector is administered intraocularly.

~~17~~25. The polynucleotide~~, vector or cell~~ or vector for use according to any one of claims ~~12-16~~20-24, wherein the polynucleotide~~, vector or cell~~ or vector is administered to the eye of a subject by subretinal, direct retinal, suprachoroidal or intravitreal injection.

~~18~~26. The polynucleotide~~, vector or cell~~ or vector for use according to any one of claims ~~12-17~~20-25, wherein the polynucleotide~~, vector or cell~~ or vector is administered to the eye of a subject by subretinal injection.

~~19~~27. The use of a polynucleotide~~, vector or cell~~ or vector of any one of claims ~~1 to 10~~ 1-17 for the manufacture of a medicament for treating or preventing a complement-mediated disorder of the eye.

28. The use according to claim 27, wherein the disorder is age-related macular degeneration (AMD) or diabetic retinopathy, preferably AMD.

29. The use according to claim 28, wherein the AMD is dry AMD.

30. The use according to any one of claims 27-29, wherein:

(i) the formation of geographic atrophy is prevented or reduced, and/or the amount of geographic atrophy is reduced; and/or

(ii) the progression of geographic atrophy is slowed; and/or

(iii) there is at least a 10% reduction in the increase in geographic atrophy area over the 12 months following administration to a treated eye of a subject, relative to an untreated eye over the same period; and/or

(iv) administration of the polynucleotide, vector or cell increases the level of C3b-inactivating and iC3b-degradation activity in a subject, or in an eye, such as in the retinal pigment epithelium (RPE), of a subject, optionally to a level that exceeds a normal level in a subject, or eye or RPE thereof.

31. The use of a polynucleotide or vector of any one of claims 1-17 for the manufacture of a medicament for improving or restoring reading speed in a subject in a subject suffering from an eye disorder such as AMD and/or mitigating reduction in reading speed associated with an eye disorder such as AMD.

32. The use of a polynucleotide or vector of any one of claims 1-17 for the manufacture of a medicament for reducing or preventing loss of photoreceptors and/or the retinal pigment epithelium (RPE).

33. The use according to any one of claims 27-32, wherein the polynucleotide or vector is administered intraocularly.

34. The use according to any one of claims 27-33, wherein the polynucleotide or vector is administered to the eye of a subject by subretinal, direct retinal, suprachoroidal or intravitreal injection.

35. The use according to any one of claims 27-34, wherein the polynucleotide or vector is administered to the eye of a subject by subretinal injection.

~~20. The use of a polynucleotide, vector or cell of any one of claims 1-10 for the manufacture of a medicament for providing Complement Factor I (CFI) and/or Complement Factor~~

~~H-like Protein 1 (FHL1) to a subject, preferably wherein the polynucleotide, vector or cell is delivered to the eye of the subject.~~