Claims

1. Use of a recombinant viral vector comprising nucleic acid encoding Factor I, or a fragment or derivative thereof that retains C3b-inactivating and iC3b-degradation activity in the manufacture of a medicament for preventing, treating, or ameliorating a complement-mediated disorder in a subject in need thereof, wherein the usecomprises that the medicament is to be administered to the subject such that a therapeutically effective amount of the encoded Factor I, or the fragment or derivative thereof, is expressed from the nucleic acid in the subject, thereby increasing the level of C3b-inactivating and iC3b-degradation activity in the subject.

2. The use according to claim 1, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that exceeds a normal level.

3. The use according to claim 1 or claim 2, wherein the subject is to be administered with a recombinant virus particle that encapsidates the recombinant viral vector.

4. The use according to claim 3, wherein the recombinant virus particle infects the liver of the subject following administration, resulting in expression of the Factor I, or the fragment or derivative thereof, from the liver.

5. The use according to claim 3 or 4, wherein the recombinant virus particle is a recombinant adeno-associated virus (rAAV) particle encapsidating a rAAV vector.

6. The use according to claim 5, wherein the rAAV particle is pseudotyped to confer liver tropism.

7. The use according to claim 5 or 6, wherein the rAAV particle comprises one or two AAV2 ITRs, or derivatives thereof wherein each derivative AAV2 ITR comprises nucleotide sequence that is at least 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical over its entire length with the nucleotide sequence of a naturally occurring AAV2 ITR, and wherein the rAAV particle is pseudotyped with AAV8 capsid protein (rAAV2/8), or AAV2 pseudotyped with AAV9 capsid protein (rAAV2/9), or a derivative thereof comprising amino acid sequence that is at least 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% identical over its entire length to the amino acid sequence of a naturally occurring AAV8 or AAV9 capsid protein.

8. The use according to any preceding claim, wherein the recombinant virus particle is to be administered intravenously to the subject.

9. The use according to any preceding claim, wherein the recombinant viral vector is a non-integrating, episomal viral vector.

10. The use according to any preceding claim, wherein the encoded Factor I, or the fragment or derivative thereof, is expressed from a liver-specific promoter, such as a human alpha-1-anti-trypsin (hAAT) promoter.

11. The use according to any preceding claim, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is up to twice the normal level.

12. The use according to any preceding claim, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is up to 80%, or up to 60%, above the normal level.

13. The use according to any preceding claim, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is up to 40%, or up to 20% above the normal level.

14. The use according to any preceding claim, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is at least 5%, 10%, 15%, 20%, or 25% above the normal level.

15. The use according to any preceding claim, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is the level in serum of the subject.

16. The use according to any preceding claim, wherein the normal level of C3b-inactivating and iC3b-degradation activity in the subject is equivalent to that provided by 30-40μg/ml Factor I in serum of the subject.

17. The use according to any preceding claim, wherein the complement-mediated disorder is a disorder associated with over-activity of the complement C3b feedback cycle.

18. The use according to any preceding claim, wherein the complement-mediated disorder is age-related macular degeneration (AMD) (particularly early (dry) AMD, or geographic atrophy), dense deposit disease (DDD), atypical haemolytic uraemic syndrome (aHUS), C3 glomerulopathies, membranoproliferative glomerulonephritis Type 2 (MPGN2), atherosclerosis, chronic cardiovascular disease, Alzheimer's disease, systemic vasculitis,

paroxysmal nocturnal haemoglobinuria (PNH), inflammatory or autoinflammatory diseases of old age, membranoproliferative glomerulonephritis type I (MPGN type I), membranoproliferative glomerulonephritis type III (MPGN type III), Guillain-Barré syndrome, Henoch-Schonlein purpura, IgA nephropathy, or membranous glomerulonephritis.

19. The use according to claim 18, wherein the subject is at risk of developing AMD.

20. The use according to claim 19, wherein the subject is homozygous or heterozygous susceptible for one or more SNPs associated with AMD.

21. The use according to claim 19 or 20, which further comprises determining whether the subject is at risk of developing AMD.

22. The use according to claim 21, wherein it is determined whether the subject is at risk of developing AMD by determining whether the subject is homozygous or heterozygous susceptible for one or more SNPs associated with AMD.

23. The use according to claim 20 or 22, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is at least 10% above the normal level if the subject is heterozygous susceptible for one or more SNPs associated with AMD.

24. The use according to claim 20 or 22, wherein the level of C3b-inactivating and iC3b-degradation activity in the subject is increased to a level that is at least 50% above the normal level if the subject is homozygous susceptible for one or more SNPs associated with AMD.

25. The use according to any preceding claim, which further comprises determining the level of C3b-inactivating and iC3b-degradation activity in the subject at least a week after the administration, and repeating the administration if the level of activity is found to be at, or below the normal level.

26. The use according to any preceding claim, wherein the Factor I is human Factor I with an amino acid sequence of SEQ ID NO: 2 or 4.

27. The use according to any preceding claim, wherein the fragment or derivative of Factor I is a polypeptide that has at least 60%, 70%, 80%, 90%, 95%, 96%, 97%, 98%, or 99% amino acid identity across its entire length to human Factor I with an amino acid sequence of SEQ ID NO: 2 or 4.

28. The use according to any preceding claim, wherein the subject is a human subject.