

Claims

We claim:

1. A nucleic acid comprising:
 - (a) a template nucleic acid set forth in any one of SEQ ID NOs: 1-8;
 - (b) a nucleic acid encoding a PMP22 artificial inhibitory RNA at least 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the polynucleotide sequence set forth in any one of SEQ ID NOs: 9-16,
 - (c) a nucleic acid encoding a PMP22 artificial inhibitory RNA set forth in any one of SEQ ID NOs: 9-16;
 - (d) a nucleic acid encoding a PMP22 antisense guide strand at least 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the polynucleotide sequence set forth in any one of SEQ ID NOs: 17-24; or
 - (e) a nucleic acid encoding a PMP22 antisense guide strand set forth in any one of SEQ ID NOs: 17-24.
2. A viral vector comprising the nucleic acid of claim 1 or a combination of any one or more thereof.
3. The viral vector of claim 2, wherein the viral vector is an adeno-associated virus (AAV), adenovirus, lentivirus, retrovirus, poxvirus, baculovirus, herpes simplex virus, vaccinia virus, or a synthetic virus.
4. The viral vector of claim 3, wherein the viral vector is an AAV.
5. The viral vector of claim 4, wherein the AAV lacks rep and cap genes.
6. The viral vector of claim 4 or 5, wherein the AAV is a recombinant AAV (rAAV) or a self-complementary recombinant AAV (scAAV).
7. The viral vector of any one of claims 4-6, wherein the AAV has a capsid serotype of: AAV-1, AAV-2, AAV-3, AAV-4, AAV-5, AAV-6, AAV-7, AAV-8, AAV-9, AAV-10, AAV-11, AAV-12, AAV-13, AAV-anc80, or AAV rh.74.

8. The viral vector of any one of claims 4-7, wherein the AAV has a capsid serotype of AAV-9.
9. The viral vector of any one of claims 4-8, wherein the AAV is a pseudotyped AAV.
10. The viral vector of claim 9, wherein the AAV is AAV2/8 or AAV2/9.
11. The viral vector of any one of claims 4-10, wherein expression of the nucleic acid encoding the PMP22 artificial inhibitory RNA is under the control of a U6 promoter.
12. A composition comprising the nucleic acid of claim 1 and a pharmaceutically acceptable carrier.
13. A composition comprising the viral vector of any one of claims 2-11 and a pharmaceutically acceptable carrier.
14. A composition comprising a delivery vehicle capable of delivering agents to a Schwann cell and a nucleic acid encoding an artificial inhibitory RNA, wherein the artificial inhibitory RNA binds a segment of a messenger RNA (mRNA) encoded by a human peripheral myelin protein-22 (*PMP22*) gene, and, optionally, a pharmaceutically acceptable carrier.
15. The composition of claim 14, wherein the human *PMP22* gene comprises the sequence of SEQ ID NO: 25, or a variant thereof at least 70%, 75%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, identical to the sequence of SEQ ID NO: 25.
16. The composition of claim 14 or 15, wherein the mRNA segment is complementary to a sequence within nucleotides 1 to 2423 of SEQ ID NO: 25.
17. The composition of claim 16, wherein the mRNA segment is complementary to a sequence within nucleotides 1412-1433 or 1415-1436 of SEQ ID NO: 25.
18. The composition of any one of claims 14-17, wherein the delivery vehicle is a viral vector.

19. The composition of claim 18, wherein the viral vector is an adeno-associated virus (AAV), adenovirus, lentivirus, retrovirus, poxvirus, baculovirus, herpes simplex virus, vaccinia virus, or a synthetic virus.

20. The composition of claim 19, wherein the viral vector is an AAV.

21. The composition of claim 20, wherein the AAV lacks rep and cap genes.

22. The composition of claim 20 or 21, wherein the AAV is a recombinant AAV (rAAV), a recombinant single-stranded AAV (ssAAV), or a self-complementary recombinant AAV (scAAV).

23. The composition of any one of claims 20-22, wherein the AAV has a capsid serotype selected from the group consisting of: AAV-1, AAV-2, AAV-3, AAV-4, AAV-5, AAV-6, AAV-7, AAV-8, AAV-9, AAV-10, AAV-11, AAV-12, AAV-13, AAV-anc80, and AAV rh.74.

24. The composition of any one of claims 20-23, wherein the AAV has a capsid serotype of AAV-9.

25. The composition of any one of claims 20-24, wherein the AAV is a pseudotyped AAV.

26. The composition of claim 25, wherein the AAV is AAV2/8 or AAV2/9.

27. The composition of any one of claims 12-26, wherein expression of the nucleic acid encoding the PMP22 artificial inhibitory RNA is under the control of a U6 promoter.

28. Use of

- (a) the nucleic acid of claim 1;
- (b) the vector of any one of claims 2-11; or
- (c) the composition of any one of claims 12-27 for use in therapy.

29. Use of

- (a) a nucleic acid according to claim 1,
- (b) a vector according to any one of claims 2-11, or
- (c) a composition according to any one of claims 12-27

in the manufacture of a medicament for treating a subject suffering from overexpression of a peripheral myelin protein-22 (*PMP22*) gene.

30. The use of claim 29 wherein the subject suffers from Charcot-Marie-Tooth Disease Type 1A (CMT1A).

31. The use of claim 29 or 30, wherein the subject is a human subject.