

CLAIMS

What is claimed is:

1. An adeno-associated virus (AAV) vector comprising:
 - (i) a protein capsid comprising a capsid protein subunit comprising the sequence of SEQ ID NO: 180; and
 - (ii) a nucleic acid encapsidated by the protein capsid;
wherein the nucleic acid comprises a transfer cassette;
wherein the transfer cassette comprises, from 5' to 3':
 - a 5' inverted terminal repeat (ITR);
 - a promoter;
 - a transgene that encodes the NPC1 protein;
 - a polyadenylation signal; and
 - a 3' ITR.
2. The AAV vector of claim 1, wherein the transfer cassette comprises an intronic sequence.
3. The AAV vector of claim 2, wherein the intronic sequence comprises the sequence of SEQ ID NO: 10.
4. The AAV vector of claim 1, wherein the 5' ITR comprises the sequence of SEQ ID NO: 3003.
5. The AAV vector of claim 1, wherein the 3' ITR comprises the sequence of SEQ ID NO: 3004.
6. The AAV vector of claim 1, wherein the promoter is the CBA promoter.
7. The AAV vector of claim 1, wherein the promoter comprises the sequence of SEQ ID NO: 3005.

8. The AAV vector of claim 1, wherein the NPC1 protein is the human NPC1 protein.
9. The AAV vector of claim 1, wherein the NPC1 protein comprises the sequence of SEQ ID NO: 3001.
10. The AAV vector of claim 1, wherein the transgene comprises the sequence of SEQ ID NO: 3002.
11. The AAV vector of claim 1, wherein the polyadenylation signal is the SV40 polyadenylation signal.
12. The AAV vector of claim 1, wherein the polyadenylation signal comprises the sequence of SEQ ID NO: 3012.
13. The AAV vector of claim 1, wherein the cassette comprises an enhancer.
14. The AAV vector of claim 1, wherein the AAV transfer cassette comprises the sequence of SEQ ID NO: 3014
15. The AAV vector of claim 1, wherein the AAV transfer cassette comprises the sequence of any one of SEQ ID NO: 3015-3019.
16. An adeno-associated virus (AAV) vector comprising:
 - (i) a protein capsid comprising a capsid protein subunit comprising the sequence of SEQ ID NO: 180, or a sequence comprising about 1 to about 25 amino acid mutations relative to SEQ ID NO: 180; and
 - (ii) a nucleic acid encapsidated by the protein capsid;
wherein the nucleic acid comprises a transfer cassette;
wherein the transfer cassette comprises from 5' to 3':
 - a 5' inverted terminal repeat (ITR);

a promoter;
a transgene which encodes the NPC1 protein;
a polyadenylation signal; and
a 3' ITR.

17. A composition comprising the AAV vector of any one of claims 1-16.
18. A cell comprising the AAV vector of any one of claims 1-16.
19. A method for treating a subject in need thereof comprising administering to the subject an effective amount of the AAV vector of any one of claims 1-16, the composition of claim 17, or the cell of claim 18.
20. The method of claim 19, wherein the subject has Neimann-Pick Disease Type C.
21. The method of claim 19 or 20, wherein the subject is a human subject.