potentially correct distant cells too as a result of metabolic cross-correction mechanisms, wherein corrected cells secrete α-galactosidase A that can correct bystander cells. Finally, the inventor's approach entails liver mediated expression of α-galactosidase A following *in-vivo*, AAV mediated gene transfer of hepatocytes, which results in tolerance to the transgenic protein, thereby reducing the risk of developing neutralising antibodies to α-galactosidase A.

Summary

In one aspect, the present invention refers to a nucleic acid molecule comprising a codon optimised nucleotide sequence encoding for a functional α-galactosidase A protein wherein: (a) the nucleotide sequence has at least 95% identity to the sequence of SEQ ID NO. 1, and the codons of the nucleotide sequence have been selected based on the codons used for proteins which are expressed at a high level in the liver; or (b) the nucleotide sequence has at least 98% identity to the sequence of SEQ ID NO. 1. In another aspect, the present invention refers to a vector for expressing α-galactosidase A protein, the vector comprising the nucleic acid molecule of the present invention. In still another aspect, the present invention refers to a host cell comprising the nucleic acid molecule of the present invention or the vector of the present invention. In one aspect, the present invention refers to a pharmaceutical composition comprising the nucleic acid molecule of the present invention or the vector of the present invention, and one or more pharmaceutically acceptable excipients. In a further aspect, the present invention refers to use of the vector of the present invention in the manufacture of a medicament for treating Fabry disease in a patient suffering from Fabry disease. In one other aspect, the present invention refers to the nucleic acid molecule of the present invention or the vector of the present invention for use in therapy. In yet another aspect, the present invention refers to the nucleic acid molecule of the present invention or the vector of the present invention for use in the treatment of Fabry disease. In another aspect, the present invention refers to the use of the nucleic acid molecule of the present invention or the vector of the present invention in the manufacture of a medicament for treating Fabry disease. In one other aspect, the present invention refers to the nucleic acid molecule of the present invention or the vector of the present invention for use in delivery of a nucleotide sequence encoding α-galactosidase A protein to a subject. Also described herein is a nucleic acid molecule comprising a nucleotide sequence

CLAIMS

1. A nucleic acid molecule comprising a codon optimised nucleotide sequence encoding for a functional α-galactosidase A protein wherein:

(a) the nucleotide sequence has at least 95% identity to the sequence of SEQ ID NO. 1, and the codons of the nucleotide sequence have been selected based on the codons used for proteins which are expressed at a high level in the liver; or

(b) the nucleotide sequence has at least 98% identity to the sequence of SEQ ID NO. 1.

2. The nucleic acid molecule of claim 1, wherein the nucleotide sequence has at least 98% or 99% identity to the sequence of SEQ ID NO. 1.

3. The nucleic acid molecule of claim 1 or claim 2, wherein the nucleotide sequence has the sequence of SEQ ID NO. 1.

4. A vector for expressing α-galactosidase A protein, the vector comprising the nucleic acid molecule of any of claims 1 to 3.

5. The vector of claim 4 further comprising a liver specific promoter.

6. The vector of claim 4 or claim 5, wherein the vector is an AAV vector.

7. The vector of any of claims 4-6, wherein the vector is a single stranded vector.

8. The vector of any of claims 4-7, wherein the vector comprises a nucleotide sequence having at least 90% identity to the sequence of SEQ ID NO. 3.

9. The vector of any of claims 4-8, wherein the vector comprises a nucleotide sequence having the sequence of SEQ ID NO. 3.

10. A host cell comprising the nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9.

11. A pharmaceutical composition comprising the nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9, and one or more pharmaceutically acceptable excipients.

12. Use of the vector of any one of claims 4-9 in the manufacture of a medicament for treating Fabry disease in a patient suffering from Fabry disease.

13. The nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9 for use in therapy.

14. The nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9 for use in the treatment of Fabry disease.

15. The use of the nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9 in the manufacture of a medicament for treating Fabry disease.

16. The nucleic acid molecule of any one of claims 1-3 or the vector of any one of claims 4-9 for use in delivery of a nucleotide sequence encoding α-galactosidase A protein to a subject.