

Claims

- 1.** An adeno-associated virus (AAV) vector comprising a nucleic acid construct for the expression of a glucose-6-phosphatase-a (G6Pase-a) in a cell, the construct comprising a nucleic acid sequence encoding the G6Pase-a, wherein the nucleic acid sequence encoding the G6Pase-a is operably linked to a human alpha-1 antitrypsin (hAAT) promoter, wherein the AAV vector delivers the nucleic acid construct to liver cells.
- 2.** The AAV vector according to claim 1, wherein the G6Pase-a has an amino acid sequence at least 90% identical to SEQ ID NO: 1.
- 3.** The AAV vector according to any of claims 1 or 2, wherein the nucleic acid sequence encoding the G6Pase-a comprises a nucleotide sequence having at least 90% identity with SEQ ID NO: 2.
- 4.** The AAV vector according to any of claims 1 to 3, wherein the nucleic acid sequence encoding the G6Pase-a is codon optimized, preferably the nucleic acid sequence encoding the G6Pase-a is codon optimized by decreasing the content of GC and decreasing GC dimers in said nucleic acid sequence encoding the G6Pase-a.
- 5.** The AAV vector according to any of claims 1 to 4, wherein the hAAT promoter comprises a nucleotide sequence having at least 90% identity with SEQ ID NO: 8.
- 6.** The AAV vector according to any of claims 1 to 4, wherein the hAAT promoter is preceded by an enhancer, such as ApoE enhancer.
- 7.** The AAV vector according to any of claims 1 to 6, wherein the nucleic acid construct comprises a nucleotide sequence having at least 90% identity with with SEQ ID NO: 11, with SEQ ID NO: 48, with SEQ ID NO: 49, with SEQ ID NO: 50, with SEQ ID NO: 51, with SEQ ID NO: 53, or with SEQ ID NO: 55, or with SEQ ID NO: 56, preferably having at least 90% identity with SEQ ID NO: 48.
- 8.** The AAV vector according to any of claims 1 to 7, wherein the nucleic acid construct comprises, in the 5' to 3' orientation:
 - (i) the hAAT promoter preceded by an enhancer, such as ApoE enhancer;

- (ii) optionally an intron, such as an intron of the human β globin gene;
 - (iii) the nucleic acid sequence encoding the G6Pase-a; and
 - (iv) a polyadenylation signal, such as the bovine growth hormone polyadenylation signal, the HBB2 polyadenylation signal, the SV40 polyadenylation signal, or another naturally occurring or artificial polyadenylation signal.
- 9.** The AAV vector according to any of claims 1 to 8, wherein the cell is a liver cell, a kidney cell or an intestine cell.
- 10.** The AAV vector of any of claims 1 to 9, which is an AAV serotype 8 (AAV8) vector, an AAV9 vector, AAVrh74 vector, an AAV2i8 vector or an AAVmut5 vector, preferably an AAV8 vector.
- 11.** The AAV vector according to any of claims 6 to 10, wherein the ApoE enhancer has the sequence SEQ ID NO: 9.
- 12.** The AAV vector according to any of claims 1 to 4 and 6 to 11, wherein the nucleic acid construct comprises SEQ ID NO: 7.
- 13.** The AAV vector according to any of claims 8 to 12, wherein the intron of the human β globin gene has the sequence SEQ ID NO: 47.
- 14.** A cell transformed with the vector of any one of claims 1 to 13.
- 15.** The cell according to claim 14, which is a liver cell, an intestinal cell or a kidney cell.
- 16.** A composition comprising the vector of any one of claims 1 to 10, or the cell of any one of claims 14 to 15.
- 17.** The vector of any one of claims 1 to 13, the cell according to any one of claims 14 to 15 or the composition according to claim 16, for use as a medicament.
- 18.** Use of the vector of any one of claims 1 to 13, the cell according to any one of claims 14 to 15 or the composition according to claim 16, in the manufacture of a medicament for the treatment of GSD-Ia.