

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
5 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.
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.
- 10 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
15 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. AAV vector according to any of claims 1 to 4, wherein the hAAT promoter is preceded
20 by an enhancer, such as ApoE enhancer (e.g. SEQ ID NO: 9), preferably the nucleic acid construct comprises SEQ ID NO: 7.
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
25 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 (e.g. SEQ ID NO: 9) ;
- (ii) optionally an intron, such as an intron of the human β globin gene (e.g. SEQ ID NO: 47) ;
- 5 (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.
- 10 **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 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.** A cell transformed with the vector of any one of claims 1 to 10.
- 15 **12.** The cell according to claim 11, which is a liver cell, an intestinal cell or a kidney cell.
- 13.** A composition comprising the vector of any one of claims 1 to 10, or the cell of any one of claims 11 to 12.
- 14.** The vector of any one of claims 1 to 10, the cell according to any one of claims 11 to 12 or the composition according to claim 13, for use as a medicament.
- 20 **15.** The vector of any one of claims 1 to 10, the cell according to any one of claims 11 to 12 or the composition according to claim 13, for use in the treatment of glycogen storage disease (GSD), such as GSD-Ia.