

CLAIMS

1. An expression cassette, comprising a polynucleotide sequence encoding GLUT1 operatively linked to a promoter, wherein the promoter is a human FLT-1 (hFLT-1) promoter sharing at least 75% identity with SEQ ID NO: 1.
2. The expression cassette of claim 1, wherein the hFLT-1 promoter shares at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 1.
3. The expression cassette of claim 1 or claim 2, wherein the expression cassette comprises a polyA signal, optionally a human growth hormone (hGH) polyA.
4. The expression cassette of any one of claims 1 to 3, wherein the expression cassette comprises a Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE), optionally a WPRE(x).
5. The expression cassette of any one of claims 1 to 4, wherein the expression cassette comprises a 3' untranslated region (3' UTR) comprising a sequence that shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 4.
6. The expression cassette of any one of claims 1 to 5, wherein the polynucleotide sequence encoding GLUT1 is a *SLC2A1* polynucleotide.
7. The expression cassette of claim 6, wherein the *SLC2A1* polynucleotide is a human *SLC2A1* polynucleotide.
8. The expression cassette of claim 6 or claim 7, wherein the polynucleotide sequence encoding GLUT1 shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 5.
9. The expression cassette of any one of claims 1 to 8, wherein the expression cassette is flanked by 5' and 3' inverted terminal repeats (ITRs), optionally AAV2 ITRs, optionally an ITR that shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 6 or SEQ ID NO: 7.

10. The expression cassette of any one of claim 1 to 9, wherein the expression cassette shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with any one of SEQ ID NOs: 8-16, SEQ ID NO: 97, SEQ ID NO: 99, and SEQ ID NO: 101.
11. A gene therapy vector, comprising the expression cassette of any one of claim 1 to 10.
12. The vector of claim 11, wherein the gene therapy vector is a recombinant adeno-associated virus (rAAV) vector.
13. The vector of claim 12, wherein the rAAV vector is an AAV6, AAV8, AAV9, AAVrh.74, or AAVrh.10 vector, or a functional variant thereof.
14. The vector of claim 12 or claim 13, wherein the rAAV vector is not an AAV2 vector.
15. The vector of any one of claims 12 to 14, wherein the rAAV vector comprises a capsid protein that shares 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% identity to any one of SEQ ID NOs: 15-17.
16. Use of the vector of any one of claims 11-15 in the manufacture of a medicament for treating or preventing Glucose transporter 1 deficiency syndrome (GLUT1 DS) or De Vivo Disease.
17. The use of claim 16, wherein the vector is to be administered by intracerebroventricular (ICV) injection.
18. The use of claim 17, wherein the administration results in expression of the polynucleotide sequence encoding GLUT1 in the brain, optionally at increased levels compared to a reference rAAV vector.
19. The use of claim 17 or claim 18, wherein the administration results in an increase in expression of GLUT1 protein in the brain and/or an increase in glucose levels and/or lactate levels in cerebrospinal fluid (CSF), optionally at increased levels compared to a reference rAAV vector, wherein optionally the increases is an increase of at least 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or higher.
20. The use of any one of claims 17-19, wherein the vector is to be administered at a dose of 1E12 vector genomes (vg), 1E13 vg, 1E14 vg, or 3E14 vg.

21. The use of any one of claims 17 to 20, wherein the administration causes increased glucose uptake by cerebral microvasculature endothelial cells compared to a method performed using an endogenous Glut1 promoter or a ubiquitous promoter.
22. An *in-vitro* method of expressing GLUT1 in a cell, comprising contacting cells with the vector of any one of claims 11-15.
23. The *in-vitro* method of claim 22, wherein the cell is an endothelial cell.
24. The *in-vitro* method of claim 23, wherein the endothelial cell is a cerebral microvasculature endothelial cell.
25. The *in-vitro* method of claim 22, wherein the cell is a neuron.
26. The *in-vitro* method of any one of claims 22-25, wherein the vector causes increased glucose uptake by the cell compared to a cell contacted with a vector comprising an endogenous Glut1 promoter or a ubiquitous promoter.
27. A pharmaceutical composition comprising the vector of any one of claims 11 to 15.
28. A kit comprising the vector of any one of claims 11 to 15 or the pharmaceutical composition of claim 27 and optionally instructions for use.