

CLAIMS

1. An expression cassette, comprising a polynucleotide sequence encoding GLUT1 or a functional variant thereof, operatively linked to a promoter.
2. The expression cassette of claim 1, wherein the promoter is an endothelial promoter, optionally a Tie-1 promoter, Tie-2 (TEK) promoter, FLT-1 promoter, FLK-1(KDR) promoter, ICAM-2 promoter, VE-Cadherin (CDH5) promoter, VWF promoter, ENG promoter, PDGFB promoter, ESM1 promoter, APLN promoter, or Claudin-5 (Ple261) promoter, provided the endothelial promoter is not a Glut1 promoter.
3. The expression cassette of claim 1 or claim 2, wherein the promoter is a FLT-1 promoter.
4. The expression cassette of claim 3, wherein the FLT-1 promoter is a human FLT-1 (hFLT-1) promoter.
5. The expression cassette of claim 4, wherein the hFLT-1 promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 1.
6. The expression cassette of claim 1 or claim 2, wherein the promoter is a Tie-1 promoter.
7. The expression cassette of claim 6, wherein the Tie-1 promoter is a human Tie-1 (hTie-1) promoter.
8. The expression cassette of claim 7, wherein the hTie-1 promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 2.
9. The expression cassette of claim 1 or claim 2, wherein the promoter is a vascular endothelial-cadherin (VE-cadherin) promoter.
10. The expression cassette of claim 9, wherein the VE-cadherin promoter is a human VE-cadherin (hVE-cadherin) promoter.
11. The expression cassette of claim 10, wherein the hVE-cadherin promoter shares at least 75%, 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% or 100% identity with SEQ ID NO: 3.

12. The expression cassette of claim 1, wherein the promoter is a ubiquitous promoter.
13. The expression cassette of claim 1 or claim 12, wherein the promoter is a CMV promoter.
14. The expression cassette of claim 1 or claim 12, wherein the promoter is a CAG promoter.
15. The expression cassette of any one of claims 1 to 14, wherein the expression cassette comprises a polyA signal, optionally a human growth hormone (hGH) polyA.
16. The expression cassette of any one of claims 1 to 15, wherein the expression cassette comprises a Woodchuck Hepatitis Virus Posttranscriptional Regulatory Element (WPRE), optionally a WPRE(x).
17. The expression cassette of any one of claims 1 to 16, 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.
18. The expression cassette of any one of claims 1 to 17, wherein the polynucleotide sequence encoding GLUT1 is a *SLC2A1* polynucleotide.
19. The expression cassette of claim 18, wherein the *SLC2A1* polynucleotide is a human *SLC2A1* polynucleotide.
20. The expression cassette of any one of claim 17 to 19, 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.
21. The expression cassette of any one of claims 1 to 20, 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.
22. The expression cassette of any one of claim 1 to 21, 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.

23. A gene therapy vector, comprising the expression cassette of any one of claim 1 to 21.
24. The vector of claim 23, wherein the gene therapy vector is a recombinant adeno-associated virus (rAAV) vector.
25. The vector of claim 24, wherein the rAAV vector is an AAV6, AAV8, AAV9, AAVrh.74, or AAVrh.10 vector, or a functional variant thereof.
26. The vector of claim 24 or claim 25, wherein the rAAV vector is not an AAV2 vector.
27. The vector of any one of claim 24 to 26, 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.
28. A method of treating and/or preventing a disease or disorder in a subject in need thereof, comprising administering the vector of any one of claims 23 to 27 to the subject.
29. The method of claim 28, wherein the disease or disorder is a neurological disorder.
30. The method of claim 28 or claim 29, wherein the disease or disorder is Glucose transporter 1 deficiency syndrome (GLUT1DS) or De Vivo Disease.
31. The method of any one of claim 28 to 30, wherein the vector is administered by intracerebroventricular (ICV) injection.
32. The method of any one of claims 28 to 31, 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.
33. The method of any one of claims 28 to 32, 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 the CSF, optionally at increased levels compared to a reference rAAV vector, wherein optionally the increases is an increase of at least about 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 100% or higher.
34. The method of any one of claims 28 to 33, wherein the vector is administered at a dose of 1E12 vector genomes (vg), 1E13 vg, 1E14 vg, or 3E14 vg.

35. The method of any one of claims 28 to 34, wherein the method causes increased glucose uptake by cerebral microvasculature endothelial cells compared to a method performed using an endogenous Glut1 promoter or a ubiquitous promoter.
36. A method of expressing GLUT1 in a cell, comprising contacting the cells with the vector of any one of claims 23 to 27.
37. The method of claim 36, wherein the cell is an endothelial cell.
38. The method of claim 37, wherein the endothelial cell is a cerebral microvasculature endothelial cell.
39. The method of claim 37 or claim 38, wherein the endothelial cell is an *in vivo* endothelial cell.
40. The method of claim 36, wherein the cell is a neuron.
41. The method of claim 40, wherein the neuron is an *in vivo* neuron.
42. The method of any one of claims 36 to 40, wherein the method comprises *in vivo* administration of the vector to a subject.
43. The method of any one of claims 36 to 41, 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.
44. A pharmaceutical composition comprising the vector of any one of claims 23 to 27.
45. A kit comprising the vector of any one of claims 23 to 27 or the pharmaceutical composition of claim 43 and optionally instructions for use.