

CLAIMS

What is claimed is:

1. A method for delivering a transgene to a target cell in a subject, the method comprising intracranially administering to the subject a recombinant adeno-associated virus (rAAV)
5 comprising:
 - (i) an isolated nucleic acid comprising a transgene encoding one or more gene products of interest; and
 - (ii) an adeno-associated acid (AAV) capsid protein having the sequence set forth in SEQ ID NO: 1.
- 10 2. The method of claim 1, wherein the intracranial administration comprises intrahippocampal injection.
3. The method of claim 1 or 2, wherein the target cell is a central nervous system (CNS)
15 cell.
4. The method of any one of claims 1 to 3, wherein the CNS cell is a neuron, oligodendrocyte, astrocyte, or microglial cell.
- 20 5. The method of any one of claims 1 to 4, wherein the subject is a mammal, optionally wherein the mammal is a human.
6. The method of any one of claims 1 to 5, wherein the subject is characterized by production of anti-AAV2 antibodies.
- 25 7. The method of claim 6, wherein after administration of the rAAV, the subject does not elicit a neutralizing immune response against the rAAV.
8. The method of any one of claims 1 to 7, wherein the isolated nucleic acid comprises
30 AAV inverted terminal repeats (ITRs) flanking the transgene.

9. The method of any one of claims 1 to 8, wherein the nucleic acid sequence encoding the one or more gene products is operably linked to a promoter.
10. The method of any one of claims 1 to 9, wherein the one or more gene products comprise
5 a protein or an inhibitory nucleic acid.
11. A method for delivering a transgene to a target cell in a subject, the method comprising intravenously administering to the subject a recombinant adeno-associated virus (rAAV) comprising:
10 (i) an isolated nucleic acid comprising a transgene encoding one or more gene products of interest; and
(ii) an adeno-associated acid (AAV) capsid protein having the sequence set forth in SEQ ID NO: 1,
wherein the administration results in the rAAV crossing the blood brain barrier (BBB) of
15 the subject.
12. The method of claim 11, wherein the target cell is a central nervous system (CNS) cell.
13. The method of claim 12, wherein the CNS cell is a neuron, oligodendrocyte, astrocyte, or
20 microglial cell.
14. The method of any one of claims 11 to 13, wherein the administration results in decreased transduction of liver cells relative to administration of an rAAV having an AAV2 capsid protein
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15. The method of any one of claims 11 to 14, wherein the subject is a mammal, optionally wherein the mammal is a human.
16. The method of any one of claims 11 to 15, wherein the subject is characterized by
30 production of anti-AAV2 antibodies.
17. The method of claim 16, wherein after administration of the rAAV, the subject does not elicit a neutralizing immune response against the rAAV.

18. The method of any one of claims 11 to 17, wherein the isolated nucleic acid comprises AAV inverted terminal repeats (ITRs) flanking the transgene.
- 5 19. The method of any one of claims 11 to 18, wherein the nucleic acid sequence encoding the one or more gene products is operably linked to a promoter.
20. The method of any one of claims 11 to 19, wherein the one or more gene products comprise a protein or an inhibitory nucleic acid.