

WHAT IS CLAIMED IS:

1. A viral capsid protein comprising a sequence selected from the group
5 consisting of xxDxTKx (SEQ ID NO:1) and xDxTKxx (SEQ ID NO:2).

2. The viral capsid protein of claim 1, wherein the viral capsid protein has at
least 95% sequence identity to an amino acid sequence selected from the group consisting of
10 SEQ ID NO: 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46,
48, 50, 52, 54, 56, 58, 60, 62, 64, 66, 68, 70, 72, 74, 76, and 78.

3. The viral capsid protein of claim 1, wherein the viral capsid protein has an
amino acid sequence selected from the group consisting of SEQ ID NO: 4, 6, 8, 10, 12, 14,
16, 18, 20, 22, 24, 26, 28, 30, 32, 34, 36, 38, 40, 42, 44, 46, 48, 50, 52, 54, 56, 58, 60, 62, 64,
15 66, 68, 70, 72, 74, 76, and 78.

4. The viral capsid protein of claim 1, wherein the viral capsid protein is encoded
by a nucleic acid having at least 95% sequence identity to a nucleic acid sequence selected
from the group consisting of SEQ ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23,
20 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49, 51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73,
75, and 77.

5. The viral capsid protein of claim 1, wherein the viral capsid protein is encoded
by a nucleic acid having a sequence selected from the group consisting of SEQ ID NO: SEQ
25 ID NO: 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 33, 35, 37, 39, 41, 43, 45, 47, 49,
51, 53, 55, 57, 59, 61, 63, 65, 67, 69, 71, 73, 75, and 77.

6. A viral particle comprising the viral capsid protein of any of claims 1-5.

7. The viral particle of claim 6, wherein the viral particle exhibits a preference
30 for retrograde movement.

8. The viral particle of claim 6, wherein the viral particle possesses retrograde transport capability.

5 9. The viral particle of any of claims 6-8, further comprising a nucleic acid encoding a payload.

10 10. The viral particle of claim 9, wherein the nucleic acid encoding a payload comprises a promoter sequence operably linked to a coding sequence that encodes the payload.

11. The viral particle of claim 10, wherein the promoter is selected from the group consisting of synapsin-1, CMV, GFAP, CAG, CaMKII, MBP, EF1alpha, TRE and mDlx.

15 12. The viral particle of claim 10 or 11, wherein the coding sequence encoding the payload is selected from the group consisting of a protein-coding gene and an inhibitory RNA nucleic acid.

20 13. The viral particle of claim 12, wherein the inhibitory RNA nucleic acid is an antisense oligonucleotide, an siRNA, or an RNAi.

14. The viral particle of claim 9, wherein the payload is an effector protein.

25 15. The viral particle of claim 14, wherein the effector protein is selected from the group consisting of a recombinase (e.g., Cre or Flp), a gene editing system (e.g., CRISPR/Cas9, TALEN, zinc finger nuclease), optogenetic reagents (activators (e.g., channelrhodopsin or variants thereof) or inhibitors (e.g., halorhodopsin or Arch)), chemogenetic reagents (e.g., activator/inhibitor versions of the DREADD or PSAM/PSEM systems), activators and/or inhibitors of cell system pathways, and enzymes for control of
30 epigenetics.

16. The viral particle of claim 9, wherein the payload is an optical reporter construct.

17. The viral particle of claim 16, wherein the optical reporter construct is selected from the group consisting of GCaMP6 (s, m, or f), a fluorophore (e.g., green fluorescent protein (GFP), enhanced GFP (EGFP), red fluorescent protein (RFP), yellow fluorescent protein (YFP), tdTomato), a color-flipping construct (e.g., a payload that expresses one reporter in one cell population and a different reporter in another population), Glucose Sensors, jRCaMP, jRGECO, and CaMPARI, voltage indicators, secondary messengers, receptor signalers, transcription reporters, epigenetic reporters, and neuromodulator reporters.

18. The viral particle of claim 9, wherein the payload is a viral protein.

19. The viral particle of claim 18, wherein the viral protein is the rabies G protein, or is a protein that complements the function of a virus other than the AAV or a protein that relates to cellular and transcellular transport.

20. The viral particle of claim 9, wherein the coding sequence encoding the payload is a therapeutic gene.

21. The viral particle of claim 20, wherein the therapeutic gene is for treatment of a neurodegenerative disorder.

22. The viral particle of claim 21, wherein the therapeutic gene is HSP104 for treatment of Alzheimer's disease or other diseases with toxic protein aggregates, or is frataxin for treatment of Friedreich's ataxia, or is lysosomal glucocerebrosidase (GBA) for treatment of Parkinson's disease, or is polyQ-binding protein for treatment of Huntington's disease.

23. The viral particle of claim 21, wherein the therapeutic gene is survival motor neuron 1 for treatment of Spinal muscular atrophy, amyotrophic lateral sclerosis (ALS), autism, dementia, peripheral neuropathy, schizophrenia, or retinal degeneration.

5 24. The viral particle of claim 9, wherein the payload is a therapeutic moiety.

25. The viral particle of claim 24, wherein the therapeutic moiety is an antibody or fragment thereof, or is an immunomodulatory protein, or is a RNA interference molecule.

10 26. The viral particle of any of claims 6-25, wherein the viral particle exhibits up to two orders of magnitude greater retrograde access to cortico-pontine projection neurons than canine adenovirus-2 (CAV-2).

15 27. The viral particle of any of claims 6-25, wherein the retrograde access to cortico-pontine projection neurons or afferents to the dorsomedial striatum (DMS) is comparable to the synthetic tracer, Fluoro-Gold fluorescent beads.

28. An in-vitro method of delivering a payload to one or more neurons, the method comprising:

20 contacting one or more neurons with a variant adeno-associated virus (AAV) comprising a payload packaged therein, wherein the variant AAV comprises a capsid protein comprising a sequence selected from the group consisting of xxDxTKx (SEQ ID NO:1) and xDxTKxx (SEQ ID NO:2).

25 29. The method of claim 28, wherein the variant AAV exhibits retrograde movement in the neurons.

30. The method of claim 28, wherein the neurons are projection neurons.

30 31. The method of any of claims 28-30, wherein the contacting step is in cell culture.