Claims

1. An rAAV particle comprising a modified capsid protein that comprises any one of the following combinations of non-native amino acid substitutions:

(a) Y701F and Y705F, but not Y731F;

(b) T492V and S663V, but not Y444F, Y500F or Y730F; or

(c) Y705F, Y731F, and T492V;

of the wild-type AAV3 capsid protein as set forth in SEQ ID NO:3, or at the equivalent surface-exposed amino acid residues in any one of wild-type AAV1, AAV2, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, or AAV10 capsid proteins, as set forth in SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, respectively, or in any combination thereof;

or wherein the one or more amino acid substitutions are chosen from:

(d) Y444F and T550V;

(e) Y730F and T491V, but not Y444F, Y500F or S662V;

(f) S458F and S492V, but not S662V;

of the wild-type AAV2 capsid protein as set forth in SEQ ID NO:2, or at the equivalent surface-exposed amino acid residues in any one of wild-type AAV1, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, or AAV10 capsid proteins, as set forth in SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, respectively, or in any combination thereof.

2. The rAAV particle in accordance with claim 1, wherein the transduction efficiency of the particle is 2- to 50-fold, 6- to 40-fold, or 8- to 30-fold higher in a selected mammalian host cell than that of a particle that comprises a corresponding, unmodified, rAAV capsid protein; or

wherein the particle is less susceptible to ubiquitination when introduced into a mammalian cell than that of a particle that comprises a corresponding, unmodified, rAAV capsid protein.

3. The rAAV particle in accordance with claim 1, wherein the particle further comprises a nucleic acid segment that encodes a diagnostic, therapeutic, or chemotherapeutic agent operably linked to a promoter capable of expressing the nucleic acid segment in a suitable host cell comprising the rAAV particle.

4. The rAAV particle in accordance with claim 3, further comprising at least a first mammalian intron sequence operably linked to the nucleic acid segment.

5. The rAAV particle in accordance with claim 3, wherein the promoter is a heterologous promoter, a tissue-specific promoter, a cell-specific promoter, a constitutive promoter, an inducible promoter, or any combination thereof.

6. The rAAV particle in accordance with claim 3, wherein the nucleic acid segment expresses or encodes a polypeptide, a peptide, a ribozyme, a peptide nucleic acid, an siRNA, an RNAi, an antisense oligonucleotide, an antisense polynucleotide, an antibody, an antigen binding fragment, or any combination thereof.

7. The rAAV particle in accordance with claim 3, wherein the nucleic acid segment encodes a chemotherapeutic agent.

8. The rAAV particle in accordance with claim 3, wherein the diagnostic, therapeutic or chemotherapeutic agent is an agonist, an antagonist, an anti-apoptosis factor, an inhibitor, a receptor, a cytokine, a cytotoxin, an erythropoietic agent, a glycoprotein, a growth factor, a growth factor receptor, a hormone, a hormone receptor, an interferon, an interleukin, an interleukin receptor, a nerve growth factor, a neuroactive peptide, a neuroactive peptide receptor, a protease, a protease inhibitor, a protein decarboxylase, a protein kinase, a protein kinsase inhibitor, an enzyme, a receptor binding protein, a transport protein or an inhibitor thereof, a serotonin receptor, or an uptake inhibitor thereof, a serpin, a serpin receptor, a tumor suppressor, a cytotoxic agent, a cytostatic agent, an anti-inflammatory agent, or any combination thereof.

9. An isolated nucleic acid segment that encodes the modified capsid protein in accordance with any one of claims 1-8.

10. An isolated mammalian host cell comprising the rAAV particle in accordance with any one of claims 1-8.

11. A composition comprising:

(I) (a) the rAAV particle in accordance with any one of claims 1-8; or

(b) a nucleic acid segment that encodes the modified capsid protein of the rAAV particle of (a); and

(II) a pharmaceutically-acceptable buffer, diluent, or excipient.

12. The composition in accordance with claim 11, further comprising a lipid, a liposome, a lipid complex, an ethosome, a niosome, a nanoparticle, a microparticle, a liposphere, a nanocapsule, or any combination thereof.

13. The composition in accordance with claim 11, for use in therapy or prophylaxis.

14. A kit comprising:

(1) the rAAV particle in accordance with any one of claims 1-8; and

(2) instructions for using the rAAV particle in the diagnosis, prevention, treatment, or amelioration of one or more symptoms of liver cancer in a human.

15. A medicament for diagnosing, preventing, treating or ameliorating one or more symptoms of mammalian cancer, comprising a composition in accordance with claim 11.

16. A pharmaceutical composition for providing a mammal in need thereof with a diagnostically- or therapeutically-effective amount of a selected biological molecule, comprising the rAAV particle in accordance with any one of claims 1-8, which is provided to a cell, tissue or organ of a mammal in need thereof in an amount and for a

time effective to provide the mammal with a diagnostically- or a therapeutically-effective amount of the selected biological molecule.

17. A pharmaceutical composition for diagnosing, preventing, treating, or ameliorating at least one or more symptoms of liver cancer, including HCC, in a mammal, comprising the rAAV particle in accordance with any one of claims 1-8, which is to be administered to a mammal in need thereof in an amount and for a time sufficient to diagnose, prevent, treat or ameliorate the one or more symptoms of the liver cancer in the mammal.

18. A pharmaceutical composition for transducing a population of liver cells or liver tumor cells in a human comprising an effective amount of the rAAV particle in accordance with any one of claims 1-8, which is to be administered to the human for a time effective to transduce the population of liver cells or liver tumor cells.

19. The rAAV particle in accordance with claim 3, wherein the nucleic acid segment further comprises an enhancer, a post-transcriptional regulatory sequence, a polyadenylation signal, or any combination thereof, operably linked to the nucleic acid segment.

20. The rAAV particle in accordance with claim 5, wherein the tissue-specific promoter is a liver-specific promoter, a tumor cell-specific promoter, or a combination thereof.

21. The isolated mammalian host cell in accordance with claim 10, wherein the host cell is a stem cell, a hematopoietic cell, a blood cell, a neural cell, a retinal cell, an epithelial cell, an endothelial cell, a pancreatic cell, a cancer cell, a muscle cell, a vascular cell, a diaphragm cell, a stomach cell, a liver cell, a tumor cell, or a CD34+ cell.

22. The composition in accordance with claim 11, wherein the composition is comprised within a kit for diagnosing, preventing, treating or ameliorating one or more

symptoms of a mammalian disease, injury, disorder, trauma or dysfunction, including, but not limited to liver cancer.

23. The composition in accordance with claim 22, wherein the liver cancer is HCC.

24. The composition in accordance with claim 13, wherein the therapy or prophylaxis is for a human cancer.

25. The medicament in accordance with claim 15, wherein the mammalian cancer is human liver cancer.

26. The pharmaceutical composition in accordance with claim 17, wherein the mammal is human.

27. The pharmaceutical composition in accordance with claim 18, wherein the human is diagnosed with, having, or suspected of having HCC.