

Claims

1. Use of an adenoviral vector in the manufacture of a medicament for use in *in vivo* gene therapy in a mammalian subject, wherein the adenoviral vector is to be administered to the subject, and wherein the adenoviral vector comprises:
 - (a) a capsid comprising one or more viral polypeptides of an Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, or Ad50 serotype, wherein the one or more viral polypeptides comprise one or more of a:
 - (i) fiber knob;
 - (ii) fiber shaft;
 - (iii) fiber tail;
 - (iv) penton; and
 - (v) hexon; and
 - (b) a double-stranded DNA genome comprising a heterologous nucleic acid payload.
2. The use of claim 1, wherein the genome further comprises:
 - (a) a 3' ITR and a 5' ITR, wherein each of the 3' ITR and the 5' ITR are of the viral polypeptide serotype; and
 - (b) a packaging sequence, wherein the packaging sequence is of the viral polypeptide serotype.
3. The use of claim 1 or 2, wherein:
 - (i) hematopoietic stem cells of the subject are mobilized prior to the administration of the adenoviral vector;
 - (ii) a selecting agent is to be administered to the subject, optionally wherein the selecting agent comprises O⁶BG and/or BCNU;
 - (iii) one or more immunosuppression agents is to be administered to the subject, optionally wherein the administration of the one or more immunosuppression agents is prior to the administration of the adenoviral vector; or
 - (iv) a combination thereof.

4. An adenoviral donor vector comprising:
 - (a) a capsid comprising one or more viral polypeptides of an Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, or Ad50 serotype, wherein the one or more viral polypeptides comprise one or more of a:
 - (i) fiber knob;
 - (ii) fiber shaft;
 - (iii) fiber tail;
 - (iv) penton; and
 - (v) hexon; and
 - (b) a double-stranded DNA genome comprising a heterologous nucleic acid payload.
5. The vector of claim 4, wherein the genome further comprises:
 - (a) a 3' ITR and a 5' ITR, wherein each of the 3' ITR and the 5' ITR are of the viral polypeptide serotype; and
 - (b) a packaging sequence, wherein the packing sequence is of the viral polypeptide serotype.
6. The use or vector of any one of claims 1-5, wherein the one or more viral polypeptides comprise the:
 - (a) fiber knob and fiber shaft;
 - (b) fiber knob and fiber tail;
 - (c) fiber knob and penton;
 - (d) fiber knob and hexon;
 - (e) fiber knob, hexon, and penton;
 - (f) fiber shaft and fiber tail;
 - (g) fiber shaft and penton;
 - (h) fiber shaft and hexon;
 - (i) fiber shaft, hexon, and penton;
 - (j) fiber tail and penton;
 - (k) fiber tail and hexon;
 - (l) fiber tail, hexon, and penton;

- (m) fiber knob, fiber shaft, and fiber tail;
- (n) fiber knob, fiber shaft, and penton;
- (o) fiber knob, fiber shaft, and hexon;
- (p) fiber knob, fiber shaft, hexon, and penton;
- (q) fiber knob, fiber shaft, fiber tail, and penton;
- (r) fiber knob, fiber shaft, fiber tail, penton, and hexon; or
- (s) penton and hexon.

7. The use or vector of any one of claims 1-6, wherein:

- (i) the fiber knob has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 14, 30, 46, 62, 78, 94, 110, 126, and 142;
- (ii) the fiber shaft has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 13, 29, 45, 61, 77, 93, 109, 125, and 141;
- (iii) the fiber tail has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 157, 158, 159, 160, 161, 162, 163, 164, and 165;
- (iv) the penton has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 15, 31, 47, 63, 79, 95, 111, 127, and 143;
- (v) the hexon has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 16, 32, 48, 64, 80, 96, 112, 128, and 144; or
- (vi) a combination thereof.

8. The use or vector of any one of claims 1-7, wherein the adenoviral vector comprises a fiber of the serotype of the viral peptides.

9. The use or vector of any one of claims 1-8, wherein the fiber has a sequence that has at least 80% identity to a sequence selected from SEQ ID NOs: 12, 28, 44, 60, 76, 92, 108, 124, and 140.

10. The use or vector of any one of claims 1-9, wherein the adenoviral vector is a chimeric vector characterized in that the capsid comprises at least one of a fiber knob, fiber shaft, fiber tail, hexon, or penton that is not of the serotype of the viral peptides.

11. The use of any one of claims 1-10, wherein the adenoviral vector is a helper dependent vector.
12. An adenoviral donor vector genome comprising:
- (a) a 3' ITR and a 5' ITR, wherein the 3' ITR and the 5' ITR are each of the same serotype selected from an Ad3, Ad7, Ad11, Ad14, Ad16, Ad21, Ad34, Ad37, or Ad50 serotype;
 - (b) a packaging sequence, wherein the packing sequence is of the ITR serotype; and
 - (c) a heterologous nucleic acid payload.
13. The use, vector, or genome of any one of claims 1-12, wherein the heterologous nucleic acid payload comprises a selectable marker, optionally wherein the selectable marker is MGMT^{P140K}.
14. The use, vector, or genome of any one of claims 1-13, wherein the heterologous nucleic acid payload encodes:
- (i) a protein;
 - (ii) a chimeric antigen receptor (CAR), T cell receptor (TCR), or small RNA, optionally wherein the small RNA is an shRNA;
 - (iii) a gene editing enzyme or system, wherein the gene editing is selected from CRISPR editing, base editing, prime editing, or zinc finger nuclease editing; or
 - (iv) a combination thereof.
15. The use, vector, or genome of any one of claims 1-14, wherein the heterologous nucleic acid payload encodes:
- (i) an agent for treatment of a condition selected from glioblastoma, hemoglobinopathies, platelet disorders, Fanconi anemia, alpha-1 antitrypsin deficiency, sickle cell anemia, thalassemia, thalassemia intermedia, von Willebrand Disease, hemophilia A, hemophilia B, Factor V Deficiency, Factor VII Deficiency, Factor X Deficiency, Factor XI Deficiency, Factor XII Deficiency, Factor XIII Deficiency, Bernard-Soulier Syndrome, Gray

Platelet Syndrome, mucopolysaccharidosis, cystic fibrosis, Tay-Sachs disease, chronic granulomatous disease, Wiskott Aldrich syndrome and phenylketonuria; or

(ii) an agent for treatment of a condition selected from Grave's Disease, rheumatoid arthritis, pernicious anemia, Multiple Sclerosis (MS), inflammatory bowel disease, systemic lupus erythematosus (SLE), adenosine deaminase deficiency (ADA-SCID) or severe combined immunodeficiency disease (SCID), Wiskott-Aldrich syndrome (WAS), chronic granulomatous disease (CGD), , Fanconi anemia (FA), Battens disease, adrenoleukodystrophy (ALD) or metachromatic leukodystrophy (MLD), muscular dystrophy, pulmonary alveolar proteinosis (PAP), pyruvate kinase deficiency, Schwachman-Diamond-Blackfan anemia, dyskeratosis congenita, cystic fibrosis, Parkinson's disease, Alzheimer's disease, and amyotrophic lateral sclerosis (Lou Gehrig's disease).

16. The use, vector, or genome of any one of claims 1-15, wherein the serotype of the viral polypeptides is Ad34.

17. A pharmaceutical composition comprising an adenoviral vector of any one of claims 4-16, wherein the pharmaceutical composition is formulated for injection to a subject in need thereof.

18. The use, vector, genome, or pharmaceutical composition of any one of claims 1-17, wherein the adenoviral vector infects and/or transduces CD34+ cells, CD34+high cells, CD34+/CD90+ cells, and/or CD34+high/CD90+ cells, optionally wherein the cells are hematopoietic cells.