WHAT IS CLAIMED IS:

1. A recombinant adenovirus (Ad), wherein:

a capsid hexon polypeptides of an Ad strain Ad5 comprises at least one capsid hexon hypervariable region (HVR) polypeptide from Ad strain Ad57, or

a capsid hexon polypeptides of the Ad strain Ad5 comprises a variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, wherein the variant comprises:

i) an amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, or SEQ ID NO: 16, or any combination thereof;

ii) one or more insertions of:

a polypeptide of EQ (Glu-Gln) between positions 156 and 157 of SEQ ID NO:1,

a polypeptide comprising amino acid sequence SEQ ID NO: 5 between positions 187 and 188 of SEQ ID NO: 1,

a polypeptide of TT (Thr-Thr) between positions 438 and 439 of SEQ ID NO: 1, or

a polypeptide of GATT (Gly-Ala-Thr-Thr; SEQ ID NO: 6) between positions 438 and 439 of SEQ ID NO: 1;

iii) one or more deletions of:

K252 of SEQ ID NO: 1,

polypeptide Q435E436 of SEQ ID NO: 1, or

E445 of SEQ ID NO: 1; or

any combination of replacements, insertions, and deletions of the foregoing.

2. The recombinant Ad of claim 1, wherein:

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of AATALEINLE (SEQ ID NO: 3) has SEQ ID NO: 3 replaced by an amino acid sequence of DDTQVQVAAE (SEQ ID NO: 4);

the hexon polypeptide of Ad strain Ad5 comprises the polypeptide of EQ between residue E (Glu) at position 156 and residue V (Val) at position 157 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 does not comprise an insertion, deletion, or substitution at, or between, residue T (Thr) at position 166 and residue F (Phe) at position 169 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises an insertion of a polypeptide

comprising the amino acid sequence of TNGAA (SEQ ID NO: 5) between residue G (Gly) at position 187 and residue V (Val) at position 188 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 does not comprise an insertion, deletion, or substitution at or between residue H (His) at position 218 and residue A (Ala) at position 220 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises a deletion of residue K (Lys) at position 252 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 does not comprise an insertion, deletion, or substitution at or between residue F (Phe) at position 267 and residue S (Ser) at position 268 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 does not comprise an insertion, deletion, or substitution at or between residue G (Gly) at position 434 and residue Q (Gln) at position 435 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises a deletion of residues QE at positions 435 and 436 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises an insertion of a polypeptide comprising the sequence of TT between residue G at position 438 and residue W (Trp) at position 439 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises an insertion of a polypeptide comprising the amino acid sequence of GATT (SEQ ID NO: 6) between residue G at position 438 and residue W at position 439 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprises a deletion of residue E at position 445 of SEQ ID NO: 1;

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of SEQ ID NO: 7 has the amino acid sequence of SEQ ID NO: 7 replaced by the amino acid sequence of SEQ ID NO: 8;

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of SEQ ID NO: 9 has the amino acid sequence of SEQ ID NO: 9 replaced by the amino acid sequence of SEQ ID NO: 10;

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of SEQ ID NO: 11 has the amino acid sequence of SEQ ID NO: 11 replaced by the amino acid sequence of SEQ ID NO: 12;

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of SEQ ID NO: 13 has the amino acid sequence of SEQ ID NO: 13 replaced by the amino acid

sequence of SEQ ID NO: 14;

the hexon polypeptide of Ad strain Ad5 comprising the amino acid sequence of SEQ ID NO: 15 has the amino acid sequence of SEQ ID NO: 15 replaced by the amino acid sequence of SEQ ID NO: 16; or

the hexon polypeptide of Ad strain Ad5 comprises a variant of the amino acid sequence of SEQ ID NO: 2 or SEQ ID NO: 18, wherein the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937 as compared to SEQ ID NO: 2 or SEQ ID NO: 18.

3. The recombinant Ad of claim 1 or 2, wherein the hexon polypeptide comprises:

an amino acid sequence of SEQ ID NO: 18;

a variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 18; or

an amino acid sequence that is at least 75, 80, 85, 90, 91, 92, 93, 94, 95, 98, 97, 98, or 99% identical to the amino acid sequence of SEQ ID NO: 18.

4. The recombinant Ad of claim 3, wherein the variant hexon polypeptide comprises:

an amino acid sequence that is at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937; or

1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutations (e.g., substitutions, insertions, or deletions), as compared to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937.

5. The recombinant Ad of claim 3 or 4, wherein:

the variant hexon polypeptide has increased in transduction in the spleen as compared to the liver;

the variant hexon polypeptide has increased in transduction in the spleen as compared to the liver as compared to a recombinant Ad comprising the hexon polypeptide having the amino acid sequence of SEQ ID NO: 1; or

the variant hexon polypeptide does not increase liver enzymes when administered to a subject as compared to a recombinant Ad comprising the hexon polypeptide having the amino acid sequence of SEQ ID NO: 1

6. A recombinant Ad of any one of claims 1-5 further comprising a polynucleotide encoding a heterologous protein, optionally wherein the heterologous protein is a cytokine, an immunoglobulin, an immunomodulatory protein, a viral protein, a patient specific neoepitope, or any combination thereof, and optionally further comprising a targeting moiety.

7. The recombinant Ad of claim 6, wherein:

the viral protein is from HBV, HPV, EBV, CMV, HTLV, Polyoma, or any combination thereof;

the immunomodulatory protein is from the B7 family;

the immunomodulatory protein is B7.1 or B7.2;

the immunomodulatory protein from the B7 family is fused to a domain from an immunoglobulin protein;

the patient specific neoepitope is a tumor-specific antigen derived from somatic tumor mutation from a patient;

the targeting moiety is a moiety that targets the Ad to carbohydrates, cell membranes and cells selected from muscle cells, tumors, cancer cells, kidney cells, liver cells, or mucosal cells.

8. A nucleic acid molecule encoding capsid hexon polypeptides of an Ad strain Ad5 comprising:

at least one capsid hexon HVR polypeptide from Ad strain Ad57; or

a variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, wherein the variant comprises:

i) an amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, or SEQ ID NO: 16, or any combination thereof;

ii) one or more insertions of:

a polypeptide of EQ (Glu-Gln) between positions 156 and 157 of SEQ ID NO:1,

a polypeptide comprising amino acid sequence SEQ ID NO: 5 between positions 187 and 188 of SEQ ID NO: 1,

a polypeptide of TT (Thr-Thr) between positions 438 and 439 of SEQ ID NO: 1, or

a polypeptide of GATT (Gly-Ala-Thr-Thr; SEQ ID NO: 6) between positions 438 and 439 of SEQ ID NO: 1;

iii) one or more deletions of:

K252 of SEQ ID NO: 1,

polypeptide Q435E436 of SEQ ID NO: 1, or

E445 of SEQ ID NO: 1; or

any combination of replacements, insertions, and deletions of the foregoing.

9. The nucleic acid molecule of claim 8, wherein the nucleic acid molecule comprises a sequence of SEQ ID NO: 17, and optionally wherein the nucleic acid molecule encodes for a variant of a hexon polypeptide comprising:

the amino acid sequence of SEQ ID NO: 18;

an amino acid sequence that is at least 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to the amino acid sequence of SEQ ID NO: 18;

an amino acid sequence that is at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937;

1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutations (e.g., substitutions, insertions, or deletions), as compared to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937.

10. The nucleic acid molecule of claim 8 or 9, wherein:

the variant hexon polypeptide has increased in transduction in the spleen as compared to the liver;

the variant hexon polypeptide has increased in transduction in the spleen as compared to the liver as compared to a recombinant Ad comprising the hexon polypeptide having the amino acid sequence of SEQ ID NO: 1; or

the variant hexon polypeptide does not increase liver enzymes when administered to a subject as compared to a recombinant Ad comprising the hexon polypeptide having the amino acid sequence of SEQ ID NO: 1.

11. A vector comprising the nucleic acid molecule of any one of any one of claims 8-10, optionally wherein:

the vector is an Ad vector comprising a transgene encoding, for example, a heterologous polypeptide; or

the Ad vector further comprises at least one of an E1 deletion and an E3 deletion.

12. An immunogenic composition comprising the vector of claim 11.

13. The immunogenic composition of claim 11 for use in inducing an immune response in a subject in need thereof, the use comprising administering to the subject the immunogenic composition, optionally wherein:

the immune response is induced without significantly increasing liver enzymes in the subject;

the immune response is induced without significantly increasing liver enzymes in the subject as compared to a vector comprising a hexon polypeptide having the amino acid sequence of SEQ ID NO: 1; and/or

the immunogenic composition is administered subcutaneously or intravenously.

14. A recombinant Ad strain Ad5 hexon polypeptide comprising at least one capsid hexon hypervariable region (HVR) polypeptide from Ad strain Ad57; optionally wherein the capsid hexon polypeptides of the Ad strain Ad5 comprises a variant of a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, wherein the variant comprises:

i) an amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, or SEQ ID NO: 16, or any combination thereof;

ii) one or more insertions of:

a polypeptide of EQ (Glu-Gln) between positions 156 and 157 of SEQ ID NO:1,

a polypeptide comprising amino acid sequence SEQ ID NO: 5 between positions 187 and 188 of SEQ ID NO: 1,

a polypeptide of TT (Thr-Thr) between positions 438 and 439 of SEQ ID NO: 1, or

a polypeptide of GATT (Gly-Ala-Thr-Thr; SEQ ID NO: 6) between positions 438 and 439 of SEQ ID NO: 1;

iii) one or more deletions of:

K252 of SEQ ID NO: 1,

polypeptide Q435E436 of SEQ ID NO: 1, or

E445 of SEQ ID NO: 1; or

any combination of replacements, insertions, and deletions of the foregoing.

15. The recombinant hexon polypeptide of claim 14, wherein the hexon polypeptide comprises:

an amino acid sequence of SEQ ID NO: 18;

a variant of a hexon polypeptide comprising the amino acid sequence of SEQ ID NO: 18; optionally wherein:

the variant hexon polypeptide comprises an amino acid sequence that is at least 75, 80, 85, 90, 91, 92, 93, 94, 95, 95, 96, 98, or 99% identical to the amino acid sequence of SEQ ID NO: 18; or

the variant hexon polypeptide comprises a variant of a polypeptide comprising an amino acid sequence that is at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937;

the variant hexon polypeptide comprises 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 mutations (e.g., substitutions, insertions, or deletions), as compared to the amino acid sequence of SEQ ID NO: 18, provided that the variant comprises: the amino acid sequence of SEQ ID NO: 4, SEQ ID NO: 8, SEQ ID NO: 10, SEQ ID NO: 12, SEQ ID NO: 14, and SEQ ID NO: 16; or the variant comprises an aspartic acid (D) residue at position 864 and/or an arginine (R) residue at position 937.