The claims defining the invention are as follows:

1. A surface modified adeno-associated virus (AAV) capsid, comprising one or more of:
a ligand covalently conjugated to an AAV capsid protein via a linker, the linker comprising:
a crosslinked moiety, wherein the crosslinked moiety is formed by a reaction between first and second members of a crosslinker reactive pair; and
one or more spacers;
wherein the linker is covalently attached to a primary amino group of the capsid protein primary sequence.

2. The surface modified AAV capsid according to claim 0, wherein the first and second members of the crosslinker reactive pair participate in a reaction selected from: a Cu(I)-catalyzed azide-alkyne cycloaddition (CuAAC) reaction, a strain-promoted alkyne-azide cycloaddition (SPAAC) reaction, a strain-promoted alkyne-nitrone cycloaddition (SPANC) reaction, an inverse electron demand Diels–Alder (IEEDD) reaction, and a Staudinger ligation and a [4+1] cycloaddition reaction.

3. The surface modified AAV capsid according to claim 1 or claim 2, wherein the crosslinked moiety comprises at least one of: an eight membered ring and a triazole ring.

4. The surface modified AAV capsid according to claim 0 or claim 3, wherein the reaction is a strain-promoted alkyne-azide cycloaddition (SPAAC) reaction.

5. The surface modified AAV capsid according to any one of claims 1 to 4, wherein the crosslinker reactive pair comprises a cyclooctyne and an azide.

6. The surface modified AAV capsid according to claim 0, wherein the cyclooctyne is selected from dibenzylcyclooctyne (DIBO), dibenzoazacyclooctyne (DBCO), and biarylazacyclooctynone (BARAC), or a derivative thereof.

7. The surface modified AAV capsid according to claim 0, wherein the cyclooctyne is a DBCO.

8. The surface modified AAV capsid according to claim 7, wherein the one or more spacers comprise from 1 to 20 monomers of ethylene glycol.

9. The surface modified AAV capsid according to claim 7, wherein the one or more spacers comprise from 2 to 8 monomers of ethylene glycol.

10. The surface modified AAV capsid according to claim 7, wherein each one of the one or more spacers comprise 4 monomers of ethylene glycol.

11. The surface modified AAV capsid according to any one of claims 1 to 10, wherein the ligand is a cell-type specific ligand.

12. The surface modified AAV capsid according to claim 1, wherein the ligand is selected from cytokines, growth factors, lectins, toxins, single chain antibodies, multiple chain antibodies or antigen binding antibody fragments, peptides and combinations thereof.

13. The surface modified AAV capsid according to any one of claims 1 to 12, wherein the primary amino group is selected from an N-terminal amino group, a lysine epsilon amino group and an arginine amino acid group.

14. The surface modified AAV capsid according to claim 13, wherein the primary amino group is the epsilon amino group of a lysine amino acid residue.

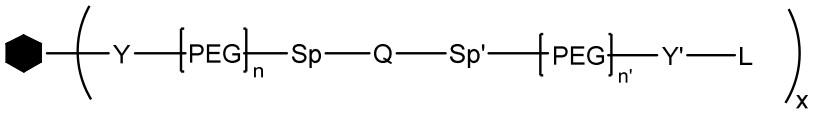
15. The surface modified AAV capsid according to any one of claims 1 to 14, wherein the linker is covalently attached to the ligand via a primary amino group of the ligand.

16. The surface modified AAV capsid according to any one of claims 1 to 15, wherein the protein sequence of the viral capsid has been mutated to attenuate or abrogate binding of the capsid to mammalian cell polysaccharides or proteoglycans.

17. The surface modified viral capsid according to any one of claims 1 to 16, wherein at least one of the arginine residues at 585 and 588 of VP1, or analogous positions in VP2 or VP3, have been mutated.

18. The surface modified viral capsid according to claim 17, wherein the arginine residues at 585 and 588 of VP1, have been mutated to alanine residues.

19. A surface modified AAV capsid according to Formula I:



…(I)

wherein:

 is an AAV capsid;

Y and Y' are independently an attachment moiety;

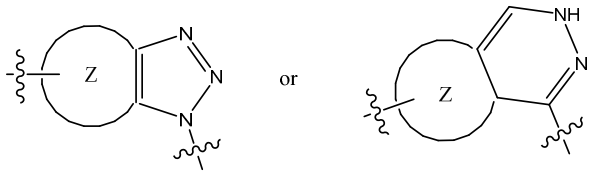
n and n' are independently 0 or an integer from 1 to 50;

Sp and Sp' are independently an optional spacer;

L is a ligand; and

X is a ligand per capsid ratio that is in a range from 1 to 500; and

Q is selected from:



wherein, Z is a 7 or 8 membered cyclic or heterocyclic structure,

wherein the surface modified AAV capsid comprises at least one of Sp or Sp'.

20. The surface modified AAV capsid according to claim 19, wherein x ranges from 100-200.

21. The surface modified AAV capsid according to claim 19, wherein x ranges from 130-170.

22. A surface modified AAV capsid, comprising one or more of:

a ligand covalently conjugated to an AAV capsid protein via a linker, the linker comprising:

a crosslinked moiety, wherein the crosslinked moiety is formed by a strain-promoted alkyne-azide cycloaddition (SPAAC) reaction; and

one or more spacers comprising from 1 to 20 monomers of ethylene glycol;

wherein the linker is covalently attached to a primary amino group of the capsid protein primary sequence.

23. Use of the surface modified AAV capsid according to any one of claims 1 to 22 in the manufacture of a medicament for the treatment of a disease treatable by intracellular delivery of a recombinant polynucleotide cargo.