Claims

1. A method for producing a modified AAV capsid, comprising:

a) determining amino acids in capsomere protein of the modified AAV, which are located in the interaction interface region of adjacent pentameric subunits of the capsid;

b) aligning structurally the modified AAV capsid to a template capsid to determine the pairwise correspondence between each amino acid of the modified AAV from the interaction interface region between adjacent pentameric subunits and the amino acid closest thereto of the template capsid, as a structural analogue of the initial amino acid that is considered a potential substitution,

wherein the template capsid is understood to mean a structurally similar capsid of a virus selected from the family Parvoviridae, which is other than AAV;

c) comparing pairwisely amino acid residues, determined in step b), of the modified AAV capsid and the template capsid to identify structural differences between the modified AAV capsid and the template capsid in the interaction interface region of adjacent pentameric subunits of the capsid;

d) selecting positions for mutagenesis, wherein the amino acid residues for mutagenesis are located in the interaction interface region of adjacent pentameric subunits of the modified AAV capsid and have a structural difference between the modified AAV capsid and the template capsid in the interaction interface region of adjacent pentameric subunits of the capsid;

e) selecting an amino acid residue for mutagenesis at position selected in step d) using one of the following principles:

-substitution of the initial amino acid in the capsomere protein of the modified AAV for a corresponding amino acid of the template capsid that has a greater volume, other than cysteine and methionine;

-substitution of the initial amino acid in the capsomere protein of the modified AAV for a corresponding amino acid of the template capsid that has an increased or decreased number of polar contacts between the capsomeres, other than cysteine and methionine;

f) introducing one or more amino acid substitutions selected in steps d)-e) in the interaction interface region of adjacent pentameric subunits of the modified AAV capsid.

2. The method for producing the modified AAV capsid according to claim 1, further comprising checking the modified AAV capsids produced in step f) with one or more amino acid substitutions for the presence of one or more improved properties as compared to AAV capsid free of these modifications, wherein the one or more improved properties are selected from the group:

-increased efficiency of cell transduction,

-increased production of target protein,

-increased efficiency of generation due to highly efficient production (assembly) of encapsidated viral vectors based on recombinant adeno-associated virus (rAAV).

3. The method for producing the modified AAV capsid according to claim 1, further comprising checking the modified AAV capsids produced in step f) for the presence of one or more improved properties as compared to AAV capsid free of these modifications and selecting modified AAV capsids that have one or more improved properties as compared to AAV capsid free of these modifications, wherein the one or more improved properties are selected from the group:

-increased efficiency of cell transduction,

-increased production of target protein,

-increased efficiency of generation due to highly efficient production (assembly) of encapsidated viral vectors based on recombinant adeno-associated virus (rAAV).

4. The method for producing an AAV capsid according to claim 1, wherein the modified AAV capsid is selected from the group comprising: human AAV, simian AAV, or avian AAV.

5. The method for producing an AAV capsid according to claim 1, wherein the modified AAV capsid is selected from the group comprising the following AAV serotypes: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10 AAV11, AAV12, AAV13, AAV14, AAV15, or AAV16.

6. The method for producing an AAV capsid according to claim 1, wherein the structurally similar template capsid is selected from the group comprising: parvovirus B19, human bocavirus 1 (HBoV1), bovine parvovirus (BVP).

7. A modified AAV capsid for producing viral vectors based on recombinant adeno-associated virus, comprising one or more amino acid substitutions located in the interaction interface region of adjacent pentameric subunits of the modified AAV capsid,

wherein one or more amino acid substitutions are in a position of a structural difference between the modified AAV capsid and the template capsid in the interaction interface region of adjacent pentameric subunits of the capsid, and the amino acid residue which substitutes the initial amino acid residue represents:

- a corresponding amino acid of the template capsid that has a greater volume comparing with the initial amino acid residue, other than cysteine and methionine;

- a corresponding amino acid of the template capsid that has an increased or decreased number of polar contacts between the capsomeres comparing with the initial amino acid residue, other than cysteine and methionine;

wherein the template capsid is understood to mean a structurally similar capsid of a virus selected from the family Parvoviridae, which is other than AAV;

the position of structural differences between the modified AAV capsid and the template capsid in the interaction interface region of adjacent pentameric subunits of the capsid is determined as the following:

a) determining amino acids in capsomere protein of the modified AAV, which are located in the interaction interface region of adjacent pentameric subunits of the capsid;

b) aligning structurally the modified AAV capsid with the template capsid to determine the pairwise correspondence between each amino acid of the modified AAV from the interaction interface region between adjacent pentameric subunits and the nearest amino acid of the template capsid, as a structural analogue of the original amino acid that is considered a potential substitution,

c) comparing pairwisely amino acid residues, determined in step b), of the AAV capsid and the template capsid to identify structural differences between the modified AAV capsid and the template capsid in the interaction interface region of adjacent pentameric subunits of the capsid.

8. The modified AAV capsid according to claim 7, wherein the modified AAV capsid is selected from the group comprising: human AAV, simian AAV, or avian AAV.

9. The modified AAV capsid according to claim 7, wherein the modified AAV capsid is selected from the group comprising the following AAV serotypes: AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, AAV10 AAV11, AAV12, AAV13, AAV14, AAV15, or AAV16.

10. A modified AAV capsid for producing viral vectors based on recombinant adeno-associated virus, comprising a modified AAV capsid protein VP1 having an amino acid sequence that is selected from the group: SEQ ID No: 14, 20, 26, 32, 38, 44, 50, 56, 62, 68, 74, 80, 86, 92, 98, 104, 110, 116, 122, 128, 134, 140, 146, 152, 158, 164, 170, 176, 182, 188, 194, 200, 206, 212, 218, 224, 230, 236, 242, 248, 254, 260, 266, 272, 278, 284, 290, 296, 302, 308, 314, 320, 326, 332, 338, 344, 350, 356, 362, or 368.

11. The modified AAV capsid according to claim 10, comprising:

a) a modified AAV capsid protein VP1 having an amino acid sequence that is selected from the group: SEQ ID No: 14, 20, 26, 32, 38, 44, 50, 56, 62, 68, 74, 80, 86, 92, 98, 104, 110, 116, 122, 128, 134, 140, 146, 152, 158, 164, 170, 176, 182, 188, 194, 200, 206, 212, 218, 224, 230, 236, 242, 248, 254, 260, 266, 272, 278, 284, 290, 296, 302, 308, 314, 320, 326, 332, 338, 344, 350, 356, 362, or 368;

b) a modified AAV capsid protein VP2 corresponding to protein VP1 thereof, said modified AAV capsid protein VP2 having an amino acid sequence that is selected from the group: SEQ ID No: 16, 22, 28, 34, 40, 46, 52, 58, 64, 70, 76, 82, 88, 94, 100, 106, 112, 118, 124, 130,

136, 142, 148, 154, 160, 166, 172, 178, 184, 190, 196, 202, 208, 214, 220, 226, 232, 238, 244, 250, 256, 262, 268, 274, 280, 286, 292, 298, 304, 310, 316, 322, 328, 334, 340, 346, 352, 358, 364, or 370;

c) a modified AAV capsid protein VP3 corresponding to protein VP1 thereof, said modified AAV capsid protein VP3 having an amino acid sequence that is selected from the group: SEQ ID No: 18, 24, 30, 36, 42, 48, 54, 60, 66, 72, 78, 84, 90, 96, 102, 108, 114, 120, 126, 132, 138, 144, 150, 156, 162, 168, 174, 180, 186, 192, 198, 204, 210, 216, 222, 228, 234, 240, 246, 252, 258, 264, 270, 276, 282, 288, 294, 300, 306, 312, 318, 324, 330, 336, 342, 348, 354, 360, 366, or 372.

12. An isolated nucleic acid encoding the modified capsid according to claims 7 to 11.

13. A vector based on recombinant adeno-associated virus for delivering to a subject a heterologous nucleic acid sequence, said vector comprising:

1) the modified AAV capsid according to any one of claims 7 to 11, and

2) a heterologous nucleic acid sequence comprising regulatory sequences that promote the expression of the product encoded by the heterologous nucleic acid sequence, in the target cells.

14. The vector based on recombinant adeno-associated virus according to claim 13, wherein the product of expression of the heterologous nucleic acid sequence is a therapeutic polypeptide or reporter polypeptide.