CLAIMS

1. A nucleic acid molecule, wherein the nucleotide sequence of the nucleic acid molecule encodes at least one AAV Rep polypeptide, wherein the Rep polypeptide-encoding sequence has two or three of the following features:

(i) it is not operably-associated with a functional AAV p5 promoter;

(ii) it does not comprise a functional AAV p19 promoter and/or it does not encode functional Rep52 and Rep40 polypeptides;

(iii) it does not comprise a functional AAV p40 promoter and/or it does not comprise a functional adenovirus inhibitor sequence.

2. A nucleic acid molecule as claimed in claim 1, wherein the nucleotide sequence encodes functional AAV Rep78 and Rep68 polypeptides.

3. A nucleic acid molecule as claimed in claim 1 or claim 2, wherein the nucleic acid molecule does not comprise a p5 promoter.

4. A nucleic acid molecule as claimed in any one of claims 1-3, wherein the Rep polypeptide-encoding sequence has the features:

(i) it is not operably-associated with a functional AAV p5 promoter; and

(iii) it does not comprise a functional AAV p40 promoter and it does not comprise a functional adenovirus inhibitor sequence.

5. A nucleic acid molecule as claimed in any one of claims 1-4, wherein, in the absence of an operably-associated promoter, the Rep 78 and/or Rep 68 polypeptides are only capable of being expressed at a low, baseline or minimal level.

6. A nucleic acid molecule as claimed in any one of the preceding claims, wherein, in the absence of an operably-associated promoter, the Rep 52 and/or Rep 40 polypeptides are not capable of being expressed.

7. A nucleic acid molecule as claimed in any one of the preceding claims, wherein, in the absence of an operably-associated promoter, the adenovirus inhibitor sequence is not capable of being transcribed.

8. A nucleic acid molecule as claimed in any one of the preceding claims, wherein the adenovirus inhibitor sequence is modified in such a way that the transcription of the adenovirus inhibitor sequence, in a host cell, would not significantly inhibit the replication of a wild-type adenovirus in the host cell.

9. An adenoviral vector comprising a nucleic acid molecule as claimed in any one of the preceding claims.

10. An adenoviral vector as claimed in claim 9, wherein the nucleic acid molecule is inserted into one of the adenoviral Early genes or inserted in a site from which one or more Early genes have been deleted.

11. An adenoviral vector as claimed in claim 9 or claim 10, wherein the nucleic acid molecule is inserted into the E1 region in the same direction of transcription as the E4, E2A and E2B expression cassettes.

12. An adenoviral vector as claimed in any one of claims 9-11, wherein the nucleic acid molecule is not operably-associated with an upstream promoter.

13. An adenoviral vector as claimed in any one of claims 9-12, wherein the adenoviral vector additionally comprises an AAV *cap* gene, preferably wherein the AAV *cap* gene is operably-associated with no promoter or a minimal promoter.

14. An adenoviral vector as claimed in any one of claims 9-13, wherein the adenoviral vector additionally encodes a polypeptide which is capable of transcriptionally-activating a promoter which is not present in the adenoviral vector.

15. An adenoviral vector as claimed in any one of claims 9-14, wherein the adenoviral vector comprises a repressible Major Late Promoter (MLP), preferably wherein the MLP comprises one or more repressor elements which are capable of regulating or controlling transcription of the adenoviral late genes, and wherein one or more of the repressor elements are inserted downstream of the MLP TATA box.

16. A host cell comprising a nucleic acid molecule as claimed in any one of claims 1-8, wherein the nucleic acid molecule is located episomally within the host cell or stably integrated into the host cell genome.

17. A kit comprising:

(A) a first adenoviral vector as claimed in any one of claims 9-15,

and

(B) second adenoviral vector comprising

(i) a nucleic acid molecule encoding an AAV Cap polypeptide, and/or

(ii) a nucleic acid molecule encoding a recombinant AAV genome.

18. A kit as claimed in claim 17, wherein the first adenoviral vector additionally encodes a polypeptide which is capable of transcriptionally-activating a promoter which is present in the second adenoviral vector, preferably wherein the promoter in the second adenoviral vector is one which is operably-associated with an AAV *cap* gene in the second adenoviral vector.

19. A process for producing a modified host cell, the process comprising the step:

(a) introducing a nucleic acid molecule as claimed in any one of claims 1-8 into a host cell, such that the nucleic acid molecule becomes:

(i) stably integrated into the genome of the host cell, or

(ii) present episomally within the host cell.

20. A process for producing a modified adenoviral vector, the process comprising the step of:

(a) introducing a nucleic acid molecule as claimed in any one of claims 1-8 into an adenoviral vector.

21. A process for producing AAV particles, the process comprising the steps:
(a) infecting a mammalian host cell with a first adenoviral vector as claimed in any one of claims 9-15;
(b) infecting the host cell with a second adenoviral vector, wherein the second adenoviral vector comprises a recombinant AAV genome comprising a transgene, wherein at least one of the first and second adenoviral vectors comprise an AAV *cap* gene;
(c) culturing the mammalian host cell in a culture medium under conditions such that AAV particles comprising the transgene are produced; and
(d) isolating or purifying AAV particles from the host cells or from the cell culture medium.

22. A process for producing AAV particles, the process comprising the steps:
(a) infecting a mammalian host cell with an adenoviral vector comprising
(i) a recombinant AAV genome comprising a transgene, and
(ii) an AAV *cap* gene,
wherein the mammalian host cell comprises a nucleic acid molecule as claimed in any one of claims 1-8 located episomally within the host cell or stably integrated into the host cell genome;
(b) culturing the mammalian host cell in a culture medium under conditions such that AAV particles comprising the transgene are produced; and
(c) isolating or purifying AAV particles from the cells or from the cell culture medium.

23. A process for producing AAV particles, the process comprising the steps:
(a) infecting a mammalian host cell with a first adenoviral vector as claimed in any one of claims 9-15, wherein the mammalian host cell comprises a recombinant AAV genome stably integrated into the host cell genome, wherein the recombinant AAV genome comprises a transgene, and wherein:
(i) the adenoviral vector additionally comprises an AAV *cap* gene, or

(ii) an AAV *cap* gene is stably integrated into the mammalian host cell genome, or

(iii) the cell is infected with a second adenoviral vector comprising an AAV *cap* gene;

(b) culturing the mammalian host cell in a culture medium under conditions such that AAV particles comprising the transgene are produced; and

(c) isolating or purifying AAV particles from the cells or from the cell culture medium.

24. A process for producing recombinant AAV particles, the process comprising the steps:

(a) infecting a mammalian host cell with a first adenoviral vector as claimed in any one of claims 9-15, wherein:

(i) the first adenoviral vector additionally comprises an AAV *cap* gene, or

(ii) the cell is infected with a second adenoviral vector comprising an AAV *cap* gene;

(b) infecting the mammalian host cell with a recombinant AAV comprising a transgene;

(c) culturing the mammalian host cell in a culture medium under conditions such that AAV particles comprising the transgene are produced; and

(d) isolating and/or purifying AAV particles from the cells or from the cell culture medium.

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