CLAIMS

1. A method of amplifying a DNA molecule in a host cell, wherein the DNA molecule is operably-linked to a CARE element, the method comprising the step of culturing a host cell which comprises:

(a) a first nucleic acid molecule comprising the DNA molecule operably-linked to a CARE element;

(b) a second nucleic acid molecule comprising a heterologous promoter operably-associated with a nucleotide sequence encoding a L4 22K polypeptide or a variant thereof;

(c) a third nucleic acid molecule comprising a nucleotide sequence encoding an AAV Rep polypeptide or a variant thereof;

and optionally additionally,

(d) one or more further nucleic acid molecules comprising one or more promoters operably-associated with one or more adenovirus Early gene products,

under conditions such that the second and third, and optionally additionally one or more of the further nucleic acid molecules, are expressed, thus promoting the amplification of the DNA molecule.

2. A method as claimed in claim 1, wherein the first, second, third and further (when present) nucleic acid molecules are independently present in the host cell:

(i) in an adenoviral vector;

(ii) stably integrated into the host cell genome; or

(iii) in an episomal vector or plasmid.

3. A method as claimed in claim 1 or claim 2, wherein the DNA molecule encodes a therapeutic polypeptide or a viral polypeptide.

4. A method as claimed in claim 3, wherein the DNA molecule encodes a *rep* gene sequence and/or a *cap* gene sequence and/or a viral Transfer Vector comprising flanking AAV inverted Terminal Repeats (ITRs), or a fragment thereof.

5. A process for producing virus particles, the process comprising the steps:

(a) introducing, into a host cell,

an adenoviral vector comprising:

(i) a nucleic acid molecule comprising a heterologous promoter operably-associated with a nucleotide sequence which encodes the L4 22K polypeptide or a variant thereof;

(ii) a Transfer Plasmid comprising 5'- and 3'-viral ITRs flanking a transgene;

(iii) sufficient helper genes for packaging a viral Transfer Plasmid,

the host cell comprising:

a CARE element, operably-linked to

(i) an AAV *cap* gene; and

(ii) a nucleic acid molecule comprising a nucleotide sequence encoding a viral Rep polypeptide,

(b) culturing the host cell under conditions such that virus particles are assembled within the host cell; and

(c) harvesting packaged virus particles from the host cell or from the culture medium.

6. A process for producing virus particles, the process comprising the steps:

(a) introducing, into a host cell,

an adenoviral vector comprising:

(i) a nucleic acid molecule comprising a heterologous promoter operably-associated with a nucleotide sequence which encodes the L4 22K polypeptide or a variant thereof;

(ii) a nucleic acid molecule comprising a nucleotide sequence encoding an viral Rep polypeptide,

(iii) sufficient helper genes for packaging a viral Transfer Plasmid,

the host cell comprising:

(i) a CARE element, operably-linked to an AAV *cap* gene; and

(ii) a Transfer Plasmid comprising 5'- and 3'-viral ITRs flanking a transgene, wherein the Transfer Plasmid may or may not be operably-linked to the CARE element,

stably integrated into the host cell genome;

(b) culturing the host cell under conditions such that virus particles are assembled within the host cell; and

(c) harvesting packaged virus particles from the host cell or from the culture medium.

7. A process for producing virus particles as claimed in claim 5 or claim 6, wherein in Step (a), the nucleotide sequence encoding a viral Rep polypeptide is not operably-associated with a functional promoter

8. A process as claimed in any one of claims 5-7, wherein the AAV *cap* gene is integrated into the host cell genome under the control of a promoter that is activated by a polypeptide that is encoded within the adenoviral vector.

9. A process as claimed in any one of claims 5-8, wherein the adenoviral vector comprises a repressible Major Late Promoter (MLP).

10. A process as claimed in claim 9, 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.

11. A process as claimed in any one of claims 5-10, wherein the nucleotide sequence encoding the viral Rep polypeptide is inserted into the E1 region of an E1/E3-deleted adenoviral vector.

12. A process as claimed in any one of claims 5-11, wherein the nucleic acid molecule comprising the nucleotide sequence encoding a viral Rep polypeptide does not comprise a functional p5 or a functional p19 promoter, and the nucleic acid molecule is not operably-associated with any other functional promoter, such that only baseline or minimal transcription of the Rep polypeptide-encoding sequence is obtained.

13. A process for producing a modified host cell, the process comprising Step (a) and Step (b):

(a) introducing a first nucleic acid molecule into a host cell, wherein the first nucleic acid molecule comprises a DNA molecule which encodes an AAV *cap* gene operably-linked to a CARE element; and

(b) introducing a second nucleic acid molecule comprising a heterologous promoter operably-associated with a nucleotide sequence encoding a L4 22K polypeptide or a variant thereof into the host cell;

and optionally:

(c) introducing a third nucleic acid molecule comprising a nucleotide sequence encoding an AAV Rep polypeptide or a variant thereof into the host cell;

such that the first, second and (when present) third nucleic acid molecules independently become:

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

(ii) present episomally within the host cell.

14. A kit comprising:

(A) a host cell comprising:

(a) a first nucleic acid molecule comprising a DNA molecule operably-linked to a CARE element, wherein the DNA molecule encodes one or more of

(i) an AAV Cap polypeptide, and

(ii) an AAV Rep polypeptide,

wherein the first nucleic acid molecule is stably integrated into the host cell's genome or is present in an episomal plasmid;

and

(B) an adenoviral vector comprising:

(i) a nucleic acid molecule which encodes an adenoviral L4 22K polypeptide or a variant thereof, wherein L4 22K polypeptide or a variant thereof coding sequence is not operably-associated with the adenoviral MLP, and

(ii) a nucleic acid molecule which encodes an AAV Transfer Vector.

15. A kit comprising:

(A) a host cell comprising:

(a) a first nucleic acid molecule comprising a DNA molecule operably-linked to a CARE element,

wherein the DNA molecule encodes

(i) an AAV Cap polypeptide, and optionally

(ii) an AAV Transfer Vector

wherein the first nucleic acid molecule is stably integrated into the host cell's genome or is present in an episomal plasmid;

and

(B) an adenoviral vector comprising:

(i) a nucleic acid molecule which encodes an adenoviral L4 22K polypeptide or a variant thereof, wherein L4 22K polypeptide or a variant thereof coding sequence is not operably-associated with the adenoviral MLP, and

(ii) a nucleic acid molecule which encodes an AAV Rep polypeptide.

16. A kit as claimed in claim 15, wherein the nucleic acid molecule is not operably-associated with a functional promoter.