Claims

1. A composition comprising recombinant adenovirus particles, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 48, 49 or 50, or a recombinant simian adenovirus, characterized in that the genomes of essentially all adenovirus particles in said composition have as the 5' terminal nucleotides the nucleotide sequence: CTATCTAT.

2. A composition according to claim 1, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

3. A composition according to claim 2, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

4. A composition according to any one of the preceding claims, which is a pharmaceutical composition.

5. A composition according to any one of the preceding claims, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

6. A composition according to any one of the preceding claims, wherein the recombinant adenovirus comprises a transgene.

7. A composition according to any one of the preceding claims, comprising at least 1×10^7, preferably at least 1×10^8, preferably at least 1×10^9, preferably at least 1×10^{10} recombinant adenovirus particles.

8. A method for preparing a batch of recombinant adenovirus particles that have essentially all identical nucleotide sequences in the 5' termini of their genomes comprising:

a) performing a molecular cloning step to exchange the naturally occurring 5' termini of an adenovirus genome with altered 5' termini comprising as the terminal nucleotides the nucleotide sequence: CTATCTAT,

b) propagating in host cells the recombinant adenovirus having the altered 5' termini,

and

c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles that essentially all have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

9. A method for preparing a batch of recombinant adenovirus particles that have essentially all identical nucleotide sequences in the 5' termini of their genomes, comprising:

a) performing a plaque purification of an adenovirus, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 48, 49 or 50, or a recombinant simian adenovirus, to isolate an adenovirus or recombinant adenovirus from a single plaque, wherein said adenovirus or recombinant adenovirus has as the 5' terminal nucleotides of its genome the nucleotide sequence: CTATCTAT,

b) propagating in host cells a recombinant adenovirus obtained from the single plaque of step a), and

c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles that essentially all have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

10. A method according to claim 8 or 9, wherein the batch comprises at least $1x10^7$ recombinant adenovirus particles.

11. A method according to any one of claims 8 to 10, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

12. A method according to any one of claims 8 to 11, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

13. A method according to any one of claims 8 to 12, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

14. A method according to any one of claims 8 to 13, wherein the recombinant adenovirus comprises a transgene.

15. A method according to any one of claims 8 to 14, further comprising purifying the recombinant adenovirus.

16. A method according to claim 15, further comprising formulating the recombinant adenovirus into a pharmaceutical composition.

17. A method according to any one of claims 8-16, wherein step b) is performed in a bioreactor.

Claims

1. A composition comprising recombinant adenovirus particles, wherein the recombinant adenovirus comprises a transgene and is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 49 or 50, or a recombinant simian adenovirus, characterized in that the genomes of at least 99% of the adenovirus particles in said composition have as the 5' terminal nucleotides the nucleotide sequence: CTATCTAT.

2. A composition according to claim 1, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

3. A composition according to claim 2, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

4. A composition according to any one of the preceding claims, which is a pharmaceutical composition.

5. A composition according to any one of the preceding claims, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

6. A composition according to any one of the preceding claims, comprising at least 1×10^7, preferably at least 1×10^8, preferably at least 1×10^9, preferably at least 1×10^{10} recombinant adenovirus particles.

7. A method for preparing a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have identical nucleotide sequences in the 5' termini of their genomes and wherein the adenovirus comprises a transgene, the method comprising:
a) performing a molecular cloning step to exchange the naturally occurring 5' termini that are not CTATCTAT of an adenovirus genome with altered 5' termini comprising as the terminal nucleotides the nucleotide sequence: CTATCTAT,

b) propagating in host cells the recombinant adenovirus having the altered 5' termini, and
c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

8. A method for preparing a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have identical nucleotide sequences in the 5' termini of their genomes and wherein the adenovirus comprises a transgene, the method comprising:
a) performing a plaque purification of an adenovirus, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 49 or 50, or a recombinant simian adenovirus, to isolate an adenovirus or recombinant adenovirus from a single plaque, wherein said adenovirus or recombinant adenovirus has as the 5' terminal nucleotides of its genome the nucleotide sequence: CTATCTAT,
b) propagating in host cells a recombinant adenovirus obtained from the single plaque of step a), and
c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

9. A method according to claim 7 or 8, wherein the batch comprises at least $1x10^7$ recombinant adenovirus particles.

10. A method according to any one of claims 7 to 9, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

11. A method according to any one of claims 7 to 10, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

12. A method according to any one of claims 7 to 11, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

13. A method according to any one of claims 7 to 12, further comprising purifying the recombinant adenovirus.

14. A method according to claim 13, further comprising formulating the recombinant adenovirus into a pharmaceutical composition.

15. A method according to any one of claims 7-14, wherein step b) is performed in a bioreactor.

Claims

1. A composition comprising recombinant adenovirus particles, wherein the recombinant adenovirus comprises a transgene and is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 49 or 50, or a recombinant simian adenovirus, characterized in that the genomes of at least 99% of the adenovirus particles in said composition have as the 5' terminal nucleotides the nucleotide sequence: CTATCTAT.

2. A composition according to claim 1, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

3. A composition according to claim 2, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

4. A composition according to any one of the preceding claims, which is a pharmaceutical composition.

5. A composition according to any one of the preceding claims, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

6. A composition according to any one of the preceding claims, comprising at least 1×10^7, preferably at least 1×10^8, preferably at least 1×10^9, preferably at least 1×10^{10} recombinant adenovirus particles.

7. A method for preparing a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have identical nucleotide sequences in the 5' termini of their genomes and wherein the adenovirus comprises a transgene, the method comprising:
a) performing a molecular cloning step to exchange the naturally occurring 5' termini that are not CTATCTAT of an adenovirus genome with altered 5' termini comprising as the terminal nucleotides the nucleotide sequence: CTATCTAT,

b) propagating in host cells the recombinant adenovirus having the altered 5' termini, and
c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

8. A method for preparing a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have identical nucleotide sequences in the 5' termini of their genomes and wherein the adenovirus comprises a transgene, the method comprising:
a) performing a plaque purification of an adenovirus, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 11a, 26, 34, 35, 49 or 50, or a recombinant simian adenovirus, to isolate an adenovirus or recombinant adenovirus from a single plaque, wherein said adenovirus or recombinant adenovirus has as the 5' terminal nucleotides of its genome the nucleotide sequence: CTATCTAT,
b) propagating in host cells a recombinant adenovirus obtained from the single plaque of step a), and
c) harvesting the recombinant adenovirus to obtain a batch of recombinant adenovirus particles wherein at least 99% of the adenovirus particles in the batch have as the 5' terminal nucleotides of their genomes the nucleotide sequence: CTATCTAT.

9. A method according to claim 7 or 8, wherein the batch comprises at least $1x10^7$ recombinant adenovirus particles.

10. A method according to any one of claims 7 to 9, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 5, 26, 35, 49 or 50.

11. A method according to any one of claims 7 to 10, wherein the recombinant adenovirus is a recombinant human adenovirus of serotype 26 or 35.

12. A method according to any one of claims 7 to 11, wherein the recombinant adenovirus lacks at least a portion of the E1 region.

13. A method according to any one of claims 7 to 12, further comprising purifying the recombinant adenovirus.

14. A method according to claim 13, further comprising formulating the recombinant adenovirus into a pharmaceutical composition.

15. A method according to any one of claims 7-14, wherein step b) is performed in a bioreactor.