Claims

1. A method for producing an adenovirus comprising (a) culturing PER.C6® cells in a serum-free suspension culture containing Ex-cell® VPRO media and (b) infecting the suspended cells with an adenovirus at a multiplicity of infection (MOI) of 5, wherein the adenovirus comprises a pre-proendothelin promoter, whereby adenoviruses are produced and exhibit a viral potency of at least 3×10^{10} plaque forming units/mL and a virus particle/plaque forming unit (VP/PFU) ratio of less than or equal to 30.

2. The method of claim 1, wherein said adenovirus is selected from the group consisting of a non-replicating adenovirus and a conditionally replicating adenovirus.

3. The method of claim 2, wherein said non-replicating adenovirus comprises a polynucleotide which comprises: (i) a fas-chimera transgene transcriptionally linked to said pre-proendothelin promoter, (ii) an anti-angiogenic transgene transcriptionally linked to said pre-proendothellin promoter, (iii) a pro-angiogenic transgene transcriptionally linked to said pre-proendothelin promoter, or (iv) a suicide transgene transcriptionally linked to said pre-proendothelin promoter.

4. The method of claim 2, wherein said conditionally replicating adenovirus is transcriptionally linked to said pre-proendothelin promoter.

5. The method of claim 2 or 3, wherein said non-replicating adenovirus comprises a polynucleotide which comprises an anti-angiogenic transgene transcriptionally linked to said pre-proendothelin promoter.

6. The method of claim 2 or 3, wherein said non-replicating adenovirus comprises a polynucleotide which comprises a pro-angiogenic transgene transcriptionally linked to said pre-proendothelin promoter.

7. The method of claim 2 or 4, wherein said adenovirus is a conditionally replicating adenovirus transcriptionally linked to said pre-proendothelin promoter, and wherein said adenovirus is devoid of non-viral heterologous sequences encoding pro- or anti-angiogenic agents.

8. The method of claim 1 or 2, wherein said adenovirus further comprises a heterologous nucleic acid sequence encoding a therapeutic agent operably linked to said pre-proendothelin promoter.

9. The method of claim 8, wherein said heterologous nucleic acid sequence comprises an apoptotic gene.

10. The method of any one of claims 1 to 9, further comprising recovering the adenovirus from said cells following said culturing and infecting.

11. The method of claim 3, wherein said fas-chimera transgene comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3 and SEQ ID NO: 4.

12. The method of any one of claims 1 to 11, wherein said pre-pro endothelin promoter further comprises a nucleotide sequence selected from the group consisting of SEQ ID NO: 6 or the antisense sequence thereof, SEQ ID NO: 7 or the antisense sequence thereof, SEQ ID NO: 8 or the antisense sequence thereof, and any combinations thereof.

13. The method of any one of claims 1 to 11, wherein said pre-pro endothelin promoter comprises a nucleotide sequence as set forth in SEQ ID NO: 12.

14. The method of any one of claims 1 to 11, wherein said adenovirus is adenovirus serotype 5.

15. The method of claim 14, wherein said adenovirus serotype 5 comprises a nucleic acid sequence as set forth in SEQ ID NO: 9 or 10.

16. The method of any one of claims 1 to 15, wherein said method of producing is a large scale method.

17. The method of any one of claims 1 to 15, wherein said method is effected in a culture volume of 5-200L.

18. The method of any one of claims 1 to 15, wherein the PER.C6® cells are cultured in a serum-free suspension culture containing HEPES and glutamine.