What is claimed is:

1. A retrovirus producing HT1080 cell line that produces a replication competent retrovirus particle, said HT1080 cell line stably expresses a recombinant retroviral genome comprising a *gag* gene, *pol* gene, *env* gene, a heterologous polynucleotide, and retroviral *psi* (Ψ) factor for the assembly of the recombinant retroviral genome, wherein the HT1080 cell line been adapted to being grown and continuously passaged in serum free media and in suspension.

2. The retrovirus producing cell line of claim 1, wherein the replication competent retrovirus comprises:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope;

a retroviral polynucleotide comprising Long-Terminal Repeat (LTR) sequences at the 3' end of the retroviral polynucleotide sequence, a promoter sequence at the 5' end of the retroviral polynucleotide, said promoter being suitable for expression in a mammalian cell, a gag nucleic acid domain, a pol nucleic acid domain and an env nucleic acid domain;

a cassette comprising an internal ribosome entry site (IRES) or regulatory nucleic acid domain operably linked to a heterologous polynucleotide, wherein the cassette is positioned 5' to the 3' LTR and 3' to the env nucleic acid domain encoding the retroviral envelope; and

cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell,

wherein the RCR maintains higher replication competency after 6 passages compared to a pACE vector.

3. The retrovirus producing cell line of claim 2, wherein the retroviral polynucleotide sequence is derived from murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), or Gibbon ape leukemia virus (GALV), murine mammary tumor virus (MuMTV), Rous

Sarcoma Virus (RSV), Gibbon ape leukemia virus (GALV), baboon endogenous virus (BEV), and the feline virus RD114.

4. The retrovirus producing cell line of claim 2 or 3, wherein the MLV is an amphotropic MLV.

5. The retrovirus producing cell line of claim 1, wherein the retrovirus is a gammaretrovirus.

6. The retrovirus producing cell line of claim 2, wherein the promoter sequence is associated with a growth regulatory gene.

7. The retrovirus producing cell line of claim 2, wherein the promoter sequence comprises a tissue-specific promoter sequence.

8. The retrovirus producing cell line of claim 7, wherein the tissue-specific promoter sequence comprises at least one androgen response element (ARE).

9. The retrovirus producing cell line of claim 8, wherein the androgen response element is derived from the probasin promoter.

10. The retrovirus producing cell line of claim 7, wherein the tissue-specific promoter sequence comprises a probasin promoter.

11. The retrovirus producing cell line of claim 2, wherein the promoter comprises a CMV promoter having a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 582 and may include modification to one or more nucleic acid bases and which is capable of directing and initiating transcription.

12. The retrovirus producing cell line of claim 2, wherein the promoter comprises a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 582.

13. The retrovirus producing cell line of claim 2, wherein the promoter comprises a CMV-R-U5 domain polynucleotide.

14. The retrovirus producing cell line of claim 13, wherein the CMV-R-U5 domain comprise the immediately early promoter from human cytomegalovirus linked to an MLV R-U5 region.

15. The retrovirus producing cell line of claim 14, wherein the CMV-R-U5 domain polynucleotide comprises a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 1202 or sequences that are at least 95% identical to a sequence as set forth in SEQ ID NO:19, 20 or 22, wherein the polynucleotide promotes transcription of a nucleic acid molecule operably linked thereto.

16. The retrovirus producing cell line of claim 2, wherein the gag of the polynucleotide is derived from a gammaretrovirus.

17. The retrovirus producing cell line of claim 16, wherein the gag nucleic acid domain comprises a sequence from nucleotide number 1203 to nucleotide 2819 of SEQ ID NO: 19 or 22 or a sequence having at least 95%, 98%, 99% or 99.8% identity thereto.

18. The retrovirus producing cell line of claim 2, wherein the pol domain of the polynucleotide is derived from a gammaretrovirus.

19. The retrovirus producing cell line of claim 18, wherein the pol domain comprises a sequence from nucleotide number 2820 to nucleotide 6358 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, 99% or 99.9% identity thereto.

20. The retrovirus producing cell line of claim 2, wherein the env domain comprises a sequence from nucleotide number 6359 to nucleotide 8323 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, 99% or 99.8% identity thereto.

21. The retrovirus producing cell line of claim 2, wherein the IRES is derived from an encephalomyocarditis virus.

22. The retrovirus producing cell line of claim 21, wherein the IRES comprises a sequence from nucleotide number 8327 to nucleotide 8876 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, or 99% identity thereto.

23. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid comprises a polynucleotide having a sequence as set forth in SEQ ID NO:3, 5, 11, 13, 15 or 17.

24. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid encodes a polypeptide comprising a sequence as set forth in SEQ ID NO:4.

25. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid is human codon optimized and encodes a polypeptide as set forth in SEQ ID NO:4.

26. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid comprises a sequence as set forth in SEQ ID NO: 19 or 22 from nucleotide number 8877 to 9353.

27. The retrovirus producing cell line of claim 26, wherein the 3' LTR is derived from an gammaretrovirus.

28. The retrovirus producing cell line of claim 27, wherein the 3' LTR comprises a U3-R-U5 domain.

29. The retrovirus producing cell line of claim 28, wherein the 3' LTR comprises a sequence as set forth in SEQ ID NO:19 or 22 from nucleotide 9405 to 9998 or a sequence that is at least 95%, 98% or 99.5% identical thereto.

30. The retrovirus producing cell line of claim 2, wherein the retroviral polynucleotide comprises a sequence as set forth in SEQ ID NO:19, 20 or 22.

31. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes a biological response modifier.

32. The retrovirus producing cell line of claim 31, wherein the biological response modifier comprises an immunopotentiating cytokine.

33. The retrovirus producing cell line of claim 32, wherein the immunopotentiating cytokine is selected from the group consisting of interleukins 1 through 15, interferon, tumor necrosis factor (TNF), and granulocyte-macrophage-colony stimulating factor (GM-CSF).

34. The retrovirus producing cell line of claim 32, wherein the immunopotentiating cytokine is interferon.

35. The retrovirus producing cell line of claim 34, wherein the interferon is gamma interferon.

36. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid encodes a polypeptide that converts a nontoxic prodrug in to a toxic drug.

37. The retrovirus producing cell line of claim 36, wherein the polypeptide that converts a nontoxic prodrug in to a toxic drug is thymidine kinase, purine nucleoside phosphorylase (PNP), or cytosine deaminase.

38. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes targeting moiety.

39. The retrovirus producing cell line of claim 38, wherein the targeting moiety comprises a cancer antigen.

40. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes a binding domain.

41. The retrovirus producing cell line of claim 40, wherein the binding domain comprises a receptor domain, an antibody, or antibody fragment.

42. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence comprises an inhibitory polynucleotide.

43. The retrovirus producing cell line of claim 42, wherein the inhibitory polynucleotide comprises an RNAi or siRNA sequence and wherein the regulatory nucleic acid domain is a promoter.

44. A method of producing the retrovirus producing HT1080 cell line of claim 1 comprising:

transforming a 293 cell line with a plasmid encoding a retroviral vector comprising from 5′ to 3′:

a CMV-R-U5 fusion of the immediate early promoter from human cytomegalovirus to an MLV R-U5 region;

a PBS, primer binding site for reverse transcriptase;

a 5′ splice site;

ψ packaging signal;

a gag coding sequence for MLV group specific antigen;

a pol coding sequence for MLV polymerase polyprotein;

a 3′ splice site;

a 4070A env coding sequence for envelope protein of MLV strain 4070A;

an internal ribosome entry site (IRES) from encephalomyocarditis virus or a nucleic acid regulatory domain;

a modified cytosine deaminase coding sequence;

a polypurine tract; and

a U3-R-U5 MLV long terminal repeat;

culturing the 293 cell to produce viral particles;

isolating the viral particles;

infecting an HT1080 cell line with the viral particles thereby affording a retrovirus producing HT1080 cell line that produces replication competent retrovirus particles, wherein the retrovirus

producing HT1080 cell line is grown in serum free media and in suspension.

45. The cell line produced by the method of claim 44.

46. A method for producing a composition for gene therapy comprising culturing the cell line of claim 44 to produce viral particles and substantially purifying the viral particles.

~~What is claimed is:~~

1. A retrovirus producing cell line for the production of a replication competent retrovirus particle, the cell line comprising a fibrosarcoma, an osteosarcoma or a thymoma cell line said cell line stably expressing a recombinant retroviral genome comprising a *gag* gene, *pol* gene, *env* gene, a heterologous polynucleotide, and retroviral *psi* (Ψ) factor for the assembly of the recombinant retroviral genome, wherein the cell line been conditioned to be grown and continuously passaged in serum free media and/or in suspension.

2. The retrovirus producing cell line of claim 1, wherein the replication competent retrovirus comprises:

a retroviral GAG protein;

a retroviral POL protein;

a retroviral envelope;

a retroviral polynucleotide comprising Long-Terminal Repeat (LTR) sequences at the 3' end of the retroviral polynucleotide sequence, a promoter sequence at the 5' end of the retroviral polynucleotide, said promoter being suitable for expression in a mammalian cell, a gag nucleic acid domain, a pol nucleic acid domain and an env nucleic acid domain;

a cassette comprising an internal ribosome entry site (IRES) or regulatory nucleic acid domain operably linked to a

~~heterologous polynucleotide, wherein the cassette is positioned 5'~~ to the 3' LTR and 3' to the env nucleic acid domain encoding the retroviral envelope; and

cis-acting sequences necessary for reverse transcription, packaging and integration in a target cell,

wherein the RCR maintains higher replication competency after 6 passages compared to a pACE vector.

3. The retrovirus producing cell line of claim 2, wherein the retroviral polynucleotide sequence is derived from murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), or Gibbon ape leukemia virus (GALV), murine mammary tumor virus (MuMTV), Rous Sarcoma Virus (RSV), Gibbon ape leukemia virus (GALV), baboon endogenous virus (BEV), and the feline virus RD114.

4. The retrovirus producing cell line of claim 2 or 3, wherein the MLV is an amphotropic MLV.

5. The retrovirus producing cell line of claim 1, wherein the retrovirus is a gammaretrovirus.

6. The retrovirus producing cell line of claim 2, wherein the promoter sequence is associated with a growth regulatory gene.

7. The retrovirus producing cell line of claim 2, wherein the promoter sequence comprises a tissue-specific promoter sequence.

8. The retrovirus producing cell line of claim 7, wherein the tissue-specific promoter sequence comprises at least one androgen response element (ARE).

9. The retrovirus producing cell line of claim 8, wherein the androgen response element is derived from the probasin promoter.

10. The retrovirus producing cell line of claim 7, wherein the tissue-specific promoter sequence comprises a probasin promoter.

~~11. The retrovirus producing cell line of claim 2, wherein the~~ promoter comprises a CMV promoter having a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 582 and may include modification to one or more nucleic acid bases and which is capable of directing and initiating transcription.

12. The retrovirus producing cell line of claim 2, wherein the promoter comprises a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 582.

13. The retrovirus producing cell line of claim 2, wherein the promoter comprises a CMV-R-U5 domain polynucleotide.

14. The retrovirus producing cell line of claim 13, wherein the CMV-R-U5 domain comprise the immediately early promoter from human cytomegalovirus linked to an MLV R-U5 region.

15. The retrovirus producing cell line of claim 14, wherein the CMV-R-U5 domain polynucleotide comprises a sequence as set forth in SEQ ID NO:19, 20 or 22 from nucleotide 1 to nucleotide 1202 or sequences that are at least 95% identical to a sequence as set forth in SEQ ID NO:19, 20 or 22, wherein the polynucleotide promotes transcription of a nucleic acid molecule operably linked thereto.

16. The retrovirus producing cell line of claim 2, wherein the gag of the polynucleotide is derived from a gammaretrovirus.

17. The retrovirus producing cell line of claim 16, wherein the gag nucleic acid domain comprises a sequence from nucleotide number 1203 to nucleotide 2819 of SEQ ID NO: 19 or 22 or a sequence having at least 95%, 98%, 99% or 99.8% identity thereto.

18. The retrovirus producing cell line of claim 2, wherein the pol domain of the polynucleotide is derived from a gammaretrovirus.

19. The retrovirus producing cell line of claim 18, wherein the pol domain comprises a sequence from nucleotide number 2820 to nucleotide 6358 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, 99% or 99.9% identity thereto.

20. The retrovirus producing cell line of claim 2, wherein the env domain comprises a sequence from nucleotide number 6359 to nucleotide 8323 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, 99% or 99.8% identity thereto.

21. The retrovirus producing cell line of claim 2, wherein the IRES is derived from an encephalomyocarditis virus.

22. The retrovirus producing cell line of claim 21, wherein the IRES comprises a sequence from nucleotide number 8327 to nucleotide 8876 of SEQ ID NO:19 or 22 or a sequence having at least 95%, 98%, or 99% identity thereto.

23. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid comprises a polynucleotide having a sequence as set forth in SEQ ID NO:3, 5, 11, 13, 15 or 17.

24. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid encodes a polypeptide comprising a sequence as set forth in SEQ ID NO:4.

25. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid is human codon optimized and encodes a polypeptide as set forth in SEQ ID NO:4.

26. The retrovirus producing cell line of claim 2, wherein the heterologous nuecleic acid comprises a sequence as set forth in SEQ ID NO: 19 or 22 from nucleotide number 8877 to 9353.

27. The retrovirus producing cell line of claim 26, wherein the 3' LTR is derived from an gammaretrovirus.

28. The retrovirus producing cell line of claim 27, wherein the 3' LTR comprises a U3-R-U5 domain.

29. The retrovirus producing cell line of claim 28, wherein the 3' LTR comprises a sequence as set forth in SEQ ID NO:19 or 22 from nucleotide 9405 to 9998 or a sequence that is at least 95%, 98% or 99.5% identical thereto.

30. The retrovirus producing cell line of claim 2, wherein the retroviral polynucleotide comprises a sequence as set forth in SEQ ID NO:19, 20 or 22.

31. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes a biological response modifier.

32. The retrovirus producing cell line of claim 31, wherein the biological response modifier comprises an immunopotentiating cytokine.

33. The retrovirus producing cell line of claim 32, wherein the immunopotentiating cytokine is selected from the group consisting of interleukins 1 through 15, interferon, tumor necrosis factor (TNF), and granulocyte-macrophage-colony stimulating factor (GM-CSF).

34. The retrovirus producing cell line of claim 32, wherein the immunopotentiating cytokine is interferon.

35. The retrovirus producing cell line of claim 34, wherein the interferon is gamma interferon.

36. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid encodes a polypeptide that converts a nontoxic prodrug in to a toxic drug.

37. The retrovirus producing cell line of claim 36, wherein the polypeptide that converts a nontoxic prodrug in to a toxic drug is

~~thymidine kinase, purine nucleoside phosphorylase (PNP), or cytosine~~ deaminase.

38. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes targeting moiety.

39. The retrovirus producing cell line of claim 38, wherein the targeting moiety comprises a cancer antigen.

40. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence encodes a binding domain.

41. The retrovirus producing cell line of claim 40, wherein the binding domain comprises a receptor domain, an antibody, or antibody fragment.

42. The retrovirus producing cell line of claim 2, wherein the heterologous nucleic acid sequence comprises an inhibitory polynucleotide.

43. The retrovirus producing cell line of claim 42, wherein the inhibitory polynucleotide comprises an RNAi or siRNA sequence and wherein the regulatory nucleic acid domain is a promoter.

44. The retrovirus produced by a retrovirus producer cell line of any of claims 1-42 wherein the producing cell line is derived from an HT1080, D17, Cf2 or 293 cell line.

45. A retrovirus produced by the retrovirus producing cell line of any one of claims 1-42.

46. A cell free preparation comprising viral particles obtained from the retrovirus producing cell line of any one of claims 1-42.

47. The cell free preparation of claim 46 comprising ascorbate.

48. A method of producing a vector producing cell line of claim 1 comprising:

transforming a 293 cell line with a plasmid encoding a retroviral vector comprising from 5′ to 3′:

a CMV-R-U5 fusion of the immediate early promoter from human cytomegalovirus to an MLV R-U5 region;

a PBS, primer binding site for reverse transcriptase;

a 5′ splice site;

ψ packaging signal;

a gag coding sequence for MLV group specific antigen;

a pol coding sequence for MLV polymerase polyprotein;

a 3′ splice site;

a 4070A env coding sequence for envelope protein of MLV strain 4070A;

an internal ribosome entry site (IRES) from encephalomyocarditis virus or a nucleic acid regulatory domain;

a modified cytosine deaminase coding sequence;

a polypurine tract; and

a U3-R-U5 MLV long terminal repeat;

culturing the 293 cell to produce viral particles;

isolating the viral particles;

infecting an HT1080 cell line with the viral particles thereby producing the viral particle producing cell line.

49. The cell line produced by the method of claim 48.

50. A method for producing a composition for gene therapy comprising culturing the cell line of claim 48 to produce viral particles and substantially purifying the viral particles.

51. A cell bank comprising the cell line of claim 48.

52. The retroviral producer cell line of claim 1, grown in suspension.

53. The retroviral producer cell line of claim 1 or 52 grown in serum free medium.

54. A pharmaceutical composition comprising a retroviral particle isolated from the culture of a producer cell line of claim 48.