WHAT IS CLAIMED IS:

1. A human embryonic kidney (HEK) cell which does not express functional endogenous di-hydrofolate reductase (DHFR) and/or glutamine synthetase (GS).

2. A human embryonic kidney (HEK) cell line which does not express functional endogenous di-hydrofolate reductase (DHFR) and/or glutamine synthetase (GS).

3. The HEK cell or cell line of claim 1 or 2, stably or transiently transfected with a first heterologous nucleic acid sequence, and optionally stably or transiently transfected with a second heterologous nucleic acid sequence.

4. The HEK cell or cell line of claim 1 or 2, stably or transiently transfected with a first heterologous nucleic acid sequence and a first selectable marker, and optionally stably or transiently transfected with a second heterologous nucleic acid sequence and a second selectable marker.

5. The HEK cell or cell line of claim 3 or 4, wherein the first heterologous nucleic acid sequence encodes a therapeutic protein or polynucleotide sequence and optional second heterologous nucleic acid sequence encodes a therapeutic protein or polynucleotide sequence.

6. The HEK cell or cell line of claim 4, wherein the therapeutic protein or polynucleotide sequence encoded by the first heterologous nucleic acid sequence and the therapeutic protein or polynucleotide sequence encoded by the optional second heterologous nucleic acid sequence are the same or are different.

7. The HEK cell or cell line of claim 4, wherein the first or second selectable marker does not provide resistance to an antibiotic.

8. The HEK cell or cell line of claim 4, wherein the first or second selectable marker provides a means to amplify the first and/or second heterologous nucleic acid sequence(s).

9. The HEK cell or cell line of claim 4, wherein the first or second selectable marker comprises a nucleic acid encoding a protein having DHFR function.

10. The HEK cell or cell line of claim 4, wherein the first or second selectable marker comprises a nucleic acid encoding a protein having GS function.

11. The HEK cell or cell line of claim 4, wherein the first selectable marker comprises a nucleic acid encoding a protein having DHFR function and the second selectable marker comprises a nucleic acid encoding a protein having GS function.

12. The HEK cell or cell line of claim 3 to 11, wherein the first heterologous nucleic acid sequence comprises a first vector, and the optional second heterologous nucleic acid sequence comprises a second vector.

13. The HEK cell or cell line of claim 11 or 12, wherein the first vector and optional second vector are the same or are different.

14. The HEK cell or cell line of claim 11 or 12, wherein the first vector and optional second vector each comprises a selectable marker comprising a nucleic acid encoding a protein having DHFR function or a nucleic acid encoding a protein having GS function.

15. The HEK cell or cell line of any of claims 12-14, wherein the first vector comprises a first viral vector and optional second vector comprises a second viral vector.

16. The HEK cell or cell line of any of claims 12-14, wherein the first or second viral vector comprises an AAV vector genome.

17. The HEK cell or cell line of any of claims 12-14, comprising first and second viral vectors, wherein the viral vectors each comprise an AAV vector genome

18. The HEK cell or cell line of claim 17, wherein the AAV vector genome(s) comprises one or two AAV ITRs that flank the 5' and/or 3' ends of the heterologous nucleic acid sequence.

19. The HEK cell or cell line of any of claims 4-18, wherein copy number of the heterologous nucleic acid sequence(s) and/or vector(s) and/or viral vector(s) and/or AAV vector genome(s) in the HEK cell or cell line is 1-5 copies per cell, 5-10 copies per cell, 10-50 copies/cell, 50-100 copies per cell, 100-250 copies per

cell, 250-500 copies per cell, 500-1,000 copies per cell, 1,000-2,000 copies per cell, or about or greater than 2,000, 3,000, 4,000 or 5,000 copies per cell, and optionally wherein copy number appears stable over many passages, e.g., at least or greater than 5, 10, 15 or more passages.

20. The HEK cell or cell line of any of claims 16-19, wherein copy number of the AAV vector genome(s) in the HEK cell or cell line is at least 1,000 copies per cell, and the rAAV vector particle yield optionally is at least 1 x 10^8 vg/ml, or at least 1 x 10^9 vg/ml, or at least 1 x 10^{10} vg/ml, or at least 1 x 10^{11} vg/ml or at least 2 x 10^{11} vg/ml from a Roller Bottle of HEK cell or the HEK cell line.

21. The HEK cell or cell line of any of claims 1-20, further comprising AAV rep and/or cap sequences.

22. The HEK cell or cell line of claim 20, wherein the AAV rep and/or cap sequences are provided by a plasmid that either transiently or stably transfected into the HEK cell or cell line.

23. The HEK cell or cell line of any of claims 1-22, further comprising AAV helper function sequences.

24. The HEK cell or cell line of claim of any of claims 1-23, wherein the HEK cells or cell line are HEK 293.

25. The HEK cell or cell line of any of claims 1-24, in a culture or growth medium, or in a medium suitable for long-term storage.

26. The HEK cell or cell line of any of claims 9-25, in a culture medium or growth comprising methotrexate (MTX) and/or methionine sulphoxamine (MSX).

27. The HEK cell or cell line of any of claims 6-26, wherein the HEK cell or cell line produces rAAV vector particles having packaged therein the heterologous nucleic acid sequence(s).

28. The HEK cell or cell line of claim 27, wherein the rAAV vector particles are produced in greater amounts than amounts produced by HEK293 cells that

express functional endogenous DHFR and/or GS and transiently transfected with AAV vector genomes having the heterologous nucleic acid sequence.

29. The HEK cell or cell line of claim 27, wherein the AAV vector particles produced contain less quantities of rAAV empty capsids and/or less quantities of rAAV particles that have packaged contaminating DNA than amounts of AAV empty capsid and/or rAAV particles that have packaged contaminating DNA produced by HEK293 cells that express functional endogenous DHFR and/or GS and transiently transfected with rAAV vector genomes having the heterologous nucleic acid sequence.

30. The HEK cell or cell line of any of claims 3-29, wherein the heterologous nucleic acid sequence(s) encodes a therapeutic protein(s) or an inhibitory nucleic acid sequence(s).

31. The HEK cell or cell line of claim 30, wherein the therapeutic protein(s) comprises an blood clotting factor or immunoglobulin sequence.

32. The HEK cell or cell line of claim 30, wherein the inhibitory nucleic acid sequence comprises a small or short hairpin (sh)RNA, microRNA (miRNA), small or short interfering (si)RNA, trans-splicing RNA, or antisense RNA.

33. The HEK cell or cell line of any of claims 3-32, stably transfected with the first heterologous nucleic acid sequence.

34. The HEK cell or cell line of any of claims 3-32, stably transfected with the first and the second heterologous nucleic acid sequence.

35. Viral or rAAV vector particles isolated or purified from the HEK cell or cell line of any of claims 15-34.

36. Therapeutic protein(s) isolated or purified from the HEK cell or cell line of any of claims 5-34.

37. A method of producing a therapeutic protein(s), viral vector(s) or rAAV vector particles comprising culturing the HEK cell or cell line of any of claims 5-34, under conditions allowing production and/or secretion of the therapeutic

protein(s), viral vector(s) or rAAV vector particles and isolating or purifying the therapeutic protein(s), viral vector(s) or rAAV vector particles from the cell culture, culture medium, or cell culture and culture medium.

38. A method of producing a rAAV vector particles comprising culturing the HEK cell or cell line of any of claims 23-25, under conditions allowing production and/or secretion of the rAAV vector particles and isolating or purifying the rAAV vector particles from the cell culture, culture medium, or cell culture and culture medium, wherein when the HEK cell or cell line has at least 1,000 copies per cell of AAV vector genome the rAAV vector particle yield is at least $2X10^{11}$ vg/Roller Bottle of HEK cell or the HEK cell line.

39. The HEK cell or cell line method according to any of claims 3-38, wherein said first and/or second heterologous nucleic acid sequence encodes a gene product selected from the group consisting of insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF), follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin (hCG), vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor α (TGFα), platelet-derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), TGFβ, activins, inhibins, bone morphogenic protein (BMP), nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and NT4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

40. The HEK cell or cell line or method according to any of claims 23-29, 37 or 38, wherein said rAAV vector particles comprise the first and/or the second heterologous nucleic acid sequence encoding a gene product selected from the group consisting of insulin, glucagon, growth hormone (GH), parathyroid hormone (PTH), growth hormone releasing factor (GRF), follicle stimulating hormone (FSH), luteinizing hormone (LH), human chorionic gonadotropin (hCG),

vascular endothelial growth factor (VEGF), angiopoietins, angiostatin, granulocyte colony stimulating factor (GCSF), erythropoietin (EPO), connective tissue growth factor (CTGF), basic fibroblast growth factor (bFGF), acidic fibroblast growth factor (aFGF), epidermal growth factor (EGF), transforming growth factor α (TGFα), platelet-derived growth factor (PDGF), insulin growth factors I and II (IGF-I and IGF-II), TGFβ, activins, inhibins, bone morphogenic protein (BMP), nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophins NT-3 and NT4/5, ciliary neurotrophic factor (CNTF), glial cell line derived neurotrophic factor (GDNF), neurturin, agrin, netrin-1 and netrin-2, hepatocyte growth factor (HGF), ephrins, noggin, sonic hedgehog and tyrosine hydroxylase.

41. The HEK cell or cell line method according to any of claims 3-38, wherein said first and/or second heterologous nucleic acid sequence encodes a gene product selected from the group consisting of thrombopoietin (TPO), interleukins (IL1 through IL-17), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors α and β, interferons α, β, and γ, stem cell factor, flk-2/flt3 ligand, IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules.

42. The HEK cell or cell line or method according to any of claims 23-29, 37 or 38, wherein said rAAV vector particles comprise the first and/or the second heterologous nucleic acid sequence encoding a gene product selected from the group consisting of thrombopoietin (TPO), interleukins (IL1 through IL-17), monocyte chemoattractant protein, leukemia inhibitory factor, granulocyte-macrophage colony stimulating factor, Fas ligand, tumor necrosis factors α and β, interferons α, β, and γ, stem cell factor, flk-2/flt3 ligand, IgG, IgM, IgA, IgD and IgE, chimeric immunoglobulins, humanized antibodies, single chain antibodies, T cell receptors, chimeric T cell receptors, single chain T cell receptors, class I and class II MHC molecules.

43. The HEK cell or cell line method according to any of claims 3-38, wherein said first and/or second heterologous nucleic acid sequence encodes a protein useful

for correction of in born errors selected from the group consisting of carbamoyl synthetase I, ornithine transcarbamylase, arginosuccinate synthetase, arginosuccinate lyase, arginase, fumarylacetacetate hydrolase, phenylalanine hydroxylase, alpha- 1 antitrypsin, glucose-6-phosphatase, porphobilinogen deaminase, factor V, factor VIII, factor IX, cystathione beta-synthase, branched chain ketoacid decarboxylase, albumin, isovaleryl-coA dehydrogenase, propionyl CoA carboxylase, methyl malonyl CoA mutase, glutaryl CoA dehydrogenase, insulin, beta-glucosidase, pyruvate carboxylate, hepatic phosphorylase, phosphorylase kinase, glycine decarboxylase, RPE65, H-protein, T-protein, a cystic fibrosis transmembrane regulator (CFTR) sequence, and a dystrophin cDNA sequence.

44. The HEK cell or cell line or method according to any of claims 23-29, 37 or 38, wherein said rAAV vector particles comprise the first and/or the second heterologous nucleic acid sequence encoding encodes a protein useful for correction of in born errors selected from the group consisting of carbamoyl synthetase I, ornithine transcarbamylase, arginosuccinate synthetase, arginosuccinate lyase, arginase, fumarylacetacetate hydrolase, phenylalanine hydroxylase, alpha- 1 antitrypsin, glucose-6-phosphatase, porphobilinogen deaminase, factor V, factor VIII, factor IX, cystathione beta-synthase, branched chain ketoacid decarboxylase, albumin, isovaleryl-coA dehydrogenase, propionyl CoA carboxylase, methyl malonyl CoA mutase, glutaryl CoA dehydrogenase, insulin, beta-glucosidase, pyruvate carboxylate, hepatic phosphorylase, phosphorylase kinase, glycine decarboxylase, RPE65, H-protein, T-protein, a cystic fibrosis transmembrane regulator (CFTR) sequence, and a dystrophin cDNA sequence.

45. A method of producing a human embryonic kidney (HEK) cell line which does not express functional endogenous di-hydrofolate reductase (DHFR) comprising mutating or knocking out the endogenous DHFR gene.

46. A method of producing a human embryonic kidney (HEK) cell line which does not express functional endogenous glutamine synthetase (GS), comprising mutating or knocking out the endogenous GS gene.

47. A method of producing a human embryonic kidney (HEK) cell line which does not express functional endogenous di-hydrofolate reductase (DHFR) and glutamine synthetase (GS), comprising mutating or knocking out the endogenous DHFR gene and GS gene.