CLAIMS

The invention claimed is:

1. A method of producing viral vectors or particles, the method comprising:

providing a starter population of cultured cells;

forming cell hybrids from the starter population, each comprising two or more cells;

identifying and selecting cell hybrids that have higher amounts of mitochondria and/or reactive oxygen species (ROS) per cell and produce viral vectors or particles at a higher functional titer, compared with cells in the starter population;

genetically altering the selected cell hybrids to express elements of a virus and a payload,

culturing the genetically altered cells to produce the viral vectors or particles containing said elements and encapsulating said payload.

2. A process for establishing a producer cell line for high efficiency production of viral vectors or particles, the process comprising:

(a) providing a starter population of cultured cells;

(b) forming cell hybrids from the starter population, each comprising two or more cells;

(c) dividing the cell hybrids into a plurality of aliquots;

(d) taking a sample of cells from each of the aliquots;

(e) genetically altering cells in each of the samples to express elements of a virus and a reporter gene;

(f) measuring production of viral vectors or particles containing a product of the reporter gene by each of the samples, thereby identifying which aliquots contain cell hybrids produce a higher functional titer of viral vectors or particles than cell hybrids in other aliquots;

(g) growing cells from one or more of the aliquots identified in step (f) to establish said producer cell line.

3. The process of claim 2, wherein the cell hybrids formed in step (b) are cloned in step (c), or wherein the cells measured in step (f) are cloned during or following step (g).

4. The process of claim 2 or claim 3, wherein step (c) comprises sorting or separating cell hybrids according to cell phenotype,

    wherein the cell phenotype includes high or low intracellular content of one or more organelles such as mitochondria, peroxisomes, endoplasmic reticulum, Golgi apparatus, or nucleoli, and/or one or more cytoplasmic or transcellular features such as reactive oxygen species (ROS), cellular redox, or pH.

5. The process of any one of claims 2 to 4, wherein step (f) comprises identifying which aliquots contain cell hybrids produce more viral capsids per cell and/or which aliquots produce a greater proportion of capsids that are filled with a product of the reporter gene.

6. The process of any one of claims 2 to 5, wherein the starter population are cells from a single cell line selected from CHO cells, human embryonic kidney 293 (HEK 293) cells, and HeLa cells.

7. A process for establishing a producer cell line for high efficiency production of viral vectors or particles, the process comprising:

    (a) providing a starter population of cultured cells;

    (b) forming cell hybrids from the starter population, each comprising two or more cells;

    (c) dividing the cell hybrids into a plurality of aliquots;

    (d) testing the aliquots or a subpopulation thereof to identify which aliquots have higher amounts of mitochondria and/or reactive oxygen species (ROS) per cell;

    (e) growing cells from one or more of the aliquots identified in step (d) to establish said producer cell line.

8. The process of any one of claims 2 to 7, further comprising genetically altering cells from the producer cell line to express a transgene encoding one or more elements of a virus, thereby adapting the cells to produce a viral vector or particle containing said elements.

9. The process of claim 8, further comprising genetically altering said cells to express a transgene encoding a payload, thereby adapting the cells to produce a viral vector or particle encapsulating said payload.

10. A producer cell line adapted for high efficiency production of viral vectors or particles, established according to the process of any of claims 2 to 9.

11. A line of producer cells, wherein each cell is a hybrid of two or more parental cells from a starter cell line, and have higher amounts of mitochondria and/or reactive oxygen species (ROS) per cell, compared with the starter cell line;

wherein the producer cells comprise an expressible transgene that encodes one or more elements of a virus, whereby the cells are configured to produce a viral vector or particle containing said elements.

12. The producer cell line of claim 11, wherein the cells further comprise a transgene constituting or encoding a payload, thereby adapting the cells to produce a viral vector or particle encapsulating said payload,

wherein said payload includes:

- a nucleic acid configured for expression in a human subject *in vivo* upon administration to the subject,
- a protein configured for delivery into cells of the subject upon administration of the particle to the subject, or
- a nucleic acid or a protein configured for transfection of cells *ex vivo*.

13. The producer cell line of any one of claims 10 to 12, which compared with cells from the starter cell population that have been genetically altered with the same transgenes, produces more viral vectors or particles, produces viral vectors or particles with higher functional titer, or produces viral vectors or particles with a higher proportion containing said payload.

14. Use of a producer cell line obtained according to the process of any one of claims 2 to 9 in the manufacture of a viral vector or particle for treatment of a human disease or condition.

15. Use of a producer cell line according to any one of claims 10 to 13 in the manufacture of a viral vector or particle for treatment of a human disease or condition.

16. The use according to claim 14, wherein the viral vector or particle contains either:

    a polynucleotide encoding a gene product for genetic therapy of a human subject in need thereof, or a target antigen of a pathogenic microbe, or

    a nucleic acid encoding said target antigen for eliciting an immune response in a subject in need thereof against said microbe.

17. A method of manufacture, comprising culturing cells from the producer cell line obtained according to the process of claim 9 to produce viral vectors or particles encapsulating said payload.

18. A method of manufacture, comprising culturing cells from the producer cell line according to claim 12 to produce viral vectors or particles encapsulating said payload.

19. The method of claim 1, claim 17, or claim 18, further comprising purifying the vectors or particles from the cell culture, and compounding the vectors or particles to produce the pharmaceutical product in a manner such that the product is suitable for human administration.

20. A pharmaceutical product for administration to a human subject or for *ex vivo* therapy, obtained according to the method of claim 19.