

Claims

1. A method for the selection of a stable producer cell line expressing one or more protein(s) of interest (POIs), comprising the steps of:
 - 5 (a) providing a cell line,
 - (b) concurrently stably transfecting said cell line with
 - 10 (i) a gene encoding a constitutively active variant of a growth factor receptor, wherein growth of said cell line in the absence of expression of said constitutively active variant of a growth factor receptor is dependent on the growth factor that is recognized by said growth factor receptor, and
 - (ii) one or more gene(s) of interest (GOIs) encoding said POIs, and
 - 15 (c) cultivating said cell line in a cell culture medium either not containing the growth factor that is recognized by said growth factor receptor or containing said growth factor at concentrations which are too low to support growth of the cells in the absence of expression of said constitutively active variant of a growth factor receptor, and wherein the constitutively active variant of a growth factor receptor is a human CD8-IGF-1R fusion protein.
- 20 2. The method of claim 1, wherein the cell line is selected from the group consisting of CHO cells, HEK293 cells, CAP cells, Per.C6 cells, BHK cells, Vero cells, MDCK cells, hybridoma cells, and fibroblasts.
- 25 3. The method of claim 1 or claim 2, wherein the POIs are selected from the group consisting of extracellular matrix proteins, growth factors, peptide hormones, cytokines, enzymes, antibodies, antibody fragments, blood clotting factors, protease inhibitors, and viral protein products.
- 30 4. The method of any one of claims 1 to 3, wherein the POIs are selected from the group consisting of human recombinant alpha-1-antitrypsin (rhAAT), fibrinogen, laminins (LAM), interferons (IFN), interleukins (IL), Immunglobulin G (IgG), Immunglobulin M (IgM), bispecific monoclonal antibodies (BsAb),

erythropoietin (EPO), Factor VII (FVII), Factor VIII (FVIII), Factor IX (FIX), von-Willebrand-Factor (vWF), C1 esterase inhibitor (C1-inhibitor; C1 Inh), gag-pol from HIV-1, HIV-2, EIAV, SIV, or other retroviridae (gag-pol), rep protein from Adeno-Associated Virus (REP), cap protein from Adeno-Associated Virus (CAP) and variants thereof.

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5. The method of any one of claims 1 to 4, wherein the gene encoding a constitutively active variant of a growth factor receptor and the GOIs are present on the same vector.

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6. The method of claim 1, wherein said human CD8-IGF-1R fusion protein comprises or consists of the amino acid sequence of SEQ ID NO: 1.

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7. The method of claim 1 or claim 6, wherein said human CD8-IGF-1R fusion protein is encoded by a nucleic acid comprising or consisting of the nucleotide sequence of SEQ ID NO: 2.

8. The method according to any one of claims 1 to 7, wherein step (c) is performed for a duration that allows selection to occur.

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9. A method for the expression of one or more protein(s) of interest (POIs) in a stable producer cell line, comprising the steps of:

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- (a) performing the method according to any one of claims 1 to 8,
- (b) expressing said POIs in said stable producer cell line, and
- (c) recovering said POIs from the cells or the cell culture medium.

10. Use of a constitutively active variant of a growth factor receptor as selection marker in the cultivation of cells, wherein the constitutively active variant of a growth factor receptor is a human CD8-IGF-1R fusion protein.

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11. The use of claim 10, wherein the cells are a cell line as defined in claim 2.

12. The use of claims 10 or 11, wherein the constitutively active variant of a growth factor receptor is as defined in any one of claims 6 to 7.