## CLAIMS

What is claimed is:

1. A method of producing a population of producer cells expressing a target polypeptide, the method comprising the steps of:

(a) transfecting host cells with one or more vectors that encode one or more mRNAs, wherein the one or more mRNAs encode a selectable polypeptide and a target polypeptide;

(b) isolating from the transfected host cells, within 2 to 15 days of transfection, a sub-population of early-expressing transfected host cells which express the selectable polypeptide; and

(c) expanding the sub-population of transfected host cells, thereby producing a population of producer cells expressing the target polypeptide.

2. The method of claim 1, wherein steps (b) and (c) are each performed in drug-selection-free medium.

3. The method of claim 1 or 2, further comprising isolating the target polypeptide from the population of producer cells.

4. The method of claim 1 or 2, further comprising isolating one or more single transfected host cells from the expanded sub-population and culturing the one or more single transfected host cells to produce clonal populations of the one or more single transfected host cells.

5. The method of claim 4, wherein at least one of the clonal populations of the one or more single transfected host cells yields a 2- to 30-fold improvement in production of the target polypeptide compared to that of a stable pool of transfected but uncloned host cells obtained in step (c).

6. The method of any one of claims 1 to 5, wherein the transfected host cells subject to selection in step (b) contains at least 80-120 x $10^6$ cells.

7. The method of any one of claims 1 to 6, wherein the isolating in step (b) is performed less than 6 days after transfection.

8. The method of claim 7, wherein the isolating in step (b) is performed between two and four days after transfection.

9. The method of any one of claims 1 to 8, wherein the sub-population of transfected host cells contains 0.5-6.0 x $10^6$ cells prior to expansion in step (c).

10. The method of any one of claims 1 to 9, wherein the expanding in step (c) is for between 4-31 days.

11. The method of any one of claims 1 to 10, wherein the mRNA encoding the target polypeptide and the mRNA encoding the selectable polypeptide are both encoded on one vector.

12. The method of any one of claims 1 to 11, wherein the isolating in step (b) employs magnetic activated cell sorting (MACS), fluorescence activated cell sorting (FACS), or ClonePix.

13. The method of any one of claims 1 to 12, wherein the selectable polypeptide is a FACS selectable polypeptide and the isolating in step (b) employs FACS.

14. The method of claim any of claims 1 to 13, wherein the target polypeptide and the selectable polypeptide form a fusion polypeptide.

15. The method of any of claims 1 to 14, wherein the target polypeptide and the selectable polypeptide are encoded by a single multicistronic mRNA.

16. The method of claim 15, wherein the multicistronic mRNA comprises a first open reading frame (ORF) that encodes the selectable polypeptide and a second ORF that encodes the target polypeptide, wherein the first ORF is 5' to the second ORF.

17. The method of claim 16, wherein the first ORF has a non-AUG start codon.

18. The method of claim 16 or 17, wherein the second ORF has an AUG start codon.

19. The method of claim 16, wherein the first ORF is devoid of any AUG sequences.

20. The method of any one of claims 1 to 19, wherein the target polypeptide is a therapeutic agent.

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