CLAIMS

1. A method for de-differentiating or reprogramming a human somatic cell comprising: transfecting the human somatic cell with a composition comprising:

(i) an effective amount of a purified synthetic mRNA encoding reprogramming factor Oct4 fused to an N-terminal MyoD transactivation domain, and

(ii) purifiedone or more synthetic mRNAs encoding a reprogramming factorsfactor selected from Oct4, Sox2, Klf4, cMycMyc, Nanog, and Lin28;

wherein the synthetic mRNAs are purified through size-exclusion chromatography;

and a transactivation domain, whereby the somatic cell is reprogrammed or de-differentiated.

22. The method of claim 1, which comprises purifying the synthetic mRNAs to remove any contaminating non-mRNA species from transcription.

3. The method of claim 1, which comprises purifying the synthetic mRNAs through size-exclusion chromatography.

4. The method of claim 1, wherein the transactivation domain comprises a MyoD, VP16, GAL4, GATA1 or P53 transactivation domain.

5. The method of claim 1, wherein the cells are seeded in a density gradient within a well.

36. The method of claim 1, wherein the cells are human cells.

7. The method of claim 1, wherein the cells are non-human primate cells.

8. The method of claim 1, wherein the cells are cynomolgus monkey cells.

9. The method of claim 1, wherein the cells are rhesus monkey cells.

10. The method of claim 1, wherein the cells are baboon cells.

11. The method of claim 1, wherein the cells are canine cells.

~~12. The method of claim 1, wherein the cells are equine cells.~~

~~13. The method of claim 1, wherein the cells are bovine cells.~~

~~14. The method of claim 1, wherein the cells are swine cells.~~

~~15. The method of claim 1, wherein the cells are ovine cells.~~

~~16. The method of claim 1, wherein the synthetic mRNA encodes Oct4 fused to an N-terminal MyoD transactivation domain.~~

~~17. The method of claim 1, which comprises transfecting the somatic cell with a composition comprising:~~

~~(1) an effective amount of a synthetic mRNA encoding reprogramming factor Oct4 fused to an N-terminal MyoD transactivation domain, and~~

~~(2) synthetic mRNAs encoding reprogramming factor Sox2, Klf4, Myc, Nanog, and Lin28.~~

~~18~~. The method of claim 1, wherein Oct4 is fused to an N-terminal MyoD transactivation domain in tandem triplicates.

4~~19~~. The method of claim 1, wherein the composition further comprises Rarg and LrH-1~~synthetic mRNA encodes Oct4 fused to a VP16~~ transactivation domains~~domain~~.

5~~20~~. The method of claim 1, wherein the purified synthetic mRNA comprises~~contains~~ 2-thio-uracil.

6~~21~~. The method of claim 1, wherein the purified synthetic mRNA comprises 5m-CTP and Pseudo-UTP.

7. The method of claim 1, wherein the purified synthetic mRNA comprises an ARCA cap.

8. The method of claim 7, which comprises generating the synthetic mRNA by *in vitro* transcription reactions using a 4:1 ratio of ARCA cap analog to GTP~~, and the nucleotide triphosphate mix has a full substitution of 5m-CTP for CTP and Pseudo-UTP for UTP~~.

9~~22. The method of claim 1, wherein the somatic cells are grown at a density of 2.6 k cells/cm^2 to 26 k cells/cm^2.~~

~~23. The method of claim 1, which comprises:~~

~~a) growing somatic cells on a feeder-free, xeno-free surface; and~~

~~b) transfecting the somatic cells with the synthetic mRNAs, wherein the mRNAs are added to the mammalian fibroblast cells with once daily media changes, using xeno-free media; and thereby producing feeder-free, xeno-free and integration-free induced pluripotent stem cells (iPSCs).~~

~~24~~. A method for reprogramming human somatic~~mammalian~~ cells, wherein the method comprises:

growing target cells at a density of 25 k to 250 k cells/well in a standard 6-well plate on a feeder-free surface; and transfecting the cells with any one or more of the purified synthetic mRNA of reprogramming factor of claim 1 in doses ranging from about 50 ng to about 800 ng/ml.

10~~transfecting the cells with any one or more of the synthetic mRNAs of claim 1 in doses ranging from about 50 ng to about 800 ng/ml.~~

~~25~~. The method of claim 1, wherein the method comprises:

growing target cells at a density of 50 k, 75 k, 100 k, or 150 k cells/well in a standard 6-well plate on a feeder-free surface; and

transfecting the cells with any one or more of the purified synthetic mRNA of reprogramming factor~~mRNAs~~ of claim 1 in doses ranging from about 50 ng to about 800 ng/ml of mRNA, wherein lower doses are used at earlier time points than later time points; and attaining iPSCs without passaging.

11~~26. The method of claim 1, which comprises:~~

~~a) growing somatic cells on a feeder-free, xeno-free surface; and~~

~~b) transfecting the somatic cells with the synthetic mRNAs, wherein the mRNAs are added to the mammalian fibroblast cells with once daily media changes, using xeno-free media; and thereby producing feeder-free, xeno-free and integration-free induced pluripotent stem cells (iPSCs).~~

~~27~~. The method of claim 1, wherein the method comprises:

growing target cells at a density selected any one of the following: 15K, 30K~~15 k, 30 k~~, 50 k, 75 k, 100 k, 150 k, 250 K~~k~~, 500 K~~k~~ cells/well in a standard 6-well plate in~~on~~ a feeder-free surface; wherein the volume of each well is adjusted to be between 0.5 ml to 5 ml of appropriate medium; and

transfecting cells with any one or more of the purified synthetic mRNA of reprogramming factor~~mRNAs~~ of claim 1 in doses ranging from about 50 ng to 800 ng/ml of mRNA wherein lower doses are used at earlier time points than later time points; and attaining iPSCs without passaging the cells.

12~~attaining iPSCs without passaging the cells.~~

~~28~~. The method of claim 1, wherein the method is Xeno-free.

13~~29~~. The method of claim 1, wherein the human~~one or more factors are selected from the group consisting of mRNAs, regulatory RNAs, siRNA, miRNA, and combinations thereof.~~

~~30. The method of claim 1, wherein the somatic cells are transfected with at least two different RNAs.~~

~~31. The method of claim 1, wherein the~~ somatic cells are selected from the group consisting of unipotent, multipotent, pluripotent, and differentiated cells.

14~~32~~. The method of claim 1, wherein the synthetic mRNAs~~one or more RNAs~~ induces de-differentiation of the somatic cells to unipotent, multipotent, or pluripotent cells.

15~~33. The method of claim 1, wherein at least one of the factors is selected from the group consisting of OCT4, SOX2, NANOG, LIN28, KLF4 and MYC mRNA.~~

~~34. The method of claim 1, wherein OCT4, SOX2, NANOG, and LIN28 mRNA are administered in combination.~~

~~35. The method of claim 1, wherein OCT4, SOX2, KLF4 and MYC mRNA are administered in combination.~~

~~36~~. The method of claim 1, wherein the transfected cells are maintained in culture as induced pluripotent stem (iPS) cells.

16~~37~~. The method of claim 1, wherein the transfected cells form induced pluripotent stem cells, further comprising inducing the iPS cells to form differentiated cells.

17~~38~~. A composition for treating or inhibiting one or more symptoms of a disease or disorder in a patient comprising de-differentiated cells according to the method of claim 1, and wherein the cells are to be administered to the patient.~~.~~

~~39. The method of claim 1, wherein the composition further comprises Rarg and LrH-1 transactivation domains.~~