**CLAIMS**

1. A method for dedifferentiating or reprogramming feeder-free, xeno-free and integration-free mammalian somatic cells to produce induced pluripotent stem cells comprising:

a) seeding the somatic cells in a volume of one ml or less of xeno-free culture medium;

b) transfecting the somatic cells plated at a cell density of 15 000 to 100 000 by contacting the cells with supplemented culture medium of one ml or less, comprising:

1) an effective amount of a fusion product between a synthetic mRNA encoding OCT4 and a N-terminal-linked transactivation domain, and

2) synthetic mRNA reprogramming factors SOX2, KLF4, NANOG, and optionally CMYC or LIN28 until the next daily media change wherein the supplemented culture medium comprises mRNA at a dose up to 800 ng/well in a 6-well plate of mRNA; and

c) culturing said somatic cell in the supplemented culture medium, until the next daily media change, under feeder-free and xeno-free culture conditions whereby the somatic cell is reprogrammed or de-differentiated, producing an induced pluripotent stem cell.

2. The method of claim 1, wherein the synthetic mRNAs are purified to remove any contaminating non-mRNA species from transcription.

3. The method of claim 1, wherein the cells are seeded in density gradient from within a well, and cells grow at varying local densities.

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

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

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

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

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

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

10. The method of claim1, wherein the cells are bovine cells.

11. The method of claim1, wherein the cells are swine cells.

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

13. The method of claim 2, wherein the Oct4 is fused to the N-terminal MyoD transactivation domain in tandem triplicates.

14. The method for reprogramming mammalian cells of claim 4, wherein the method comprises:

1) growing the somatic cells at a density of 15 k to 250 k cells/well of a standard six well tissue culture plate in culture medium and culturing under feeder-free, xeno-free and integration-free conditions; and

2) transfecting the cells with varying doses of about 50 ng to about 800 ng/well in a 6-well plate of mRNA each time during reprogramming/medium change, whereas lower doses are used at earlier time points than later time points; whereby integration-free iPSCs cells are obtained without passaging.

15. The method of claim 4, wherein the method comprises:

1) growing the somatic cells at a density of about 15k, 25k, 50 k, 75 k, 100 k, or 150 k cells/well of a standard six well tissue culture plate in culture medium and culturing under feeder-free, xeno-free and integration-free conditions; and

2) transfecting the cells with varying doses of about 50 ng to about 800 ng/well in a 6-well plate of mRNA each time during reprogramming/medium change, whereas lower doses are used at earlier time points than later time points; whereby integration-free iPSCs cells are obtained without passaging.

16. The method of claim 4, wherein the method comprises:

1) growing the somatic cells at a density of about 15k, 25k, 50 k, 75 k, 100 k, or 150 k cells/well of a standard six well tissue culture plate in culture medium and culturing under feeder-free, xeno-free and integration-free conditions wherein the volume of each well is adjusted to be between 0.5 ml to 5 ml of appropriate medium; and

2) transfecting the cells with varying doses of about 50 ng to about 800 ng/well in a 6-well plate of mRNA each time during reprogramming/medium change, whereas lower doses are used at earlier time points than later time points; whereby integration-free iPSCs cells are obtained without passaging.

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

18. The method of claim 17, wherein the method is Xeno-free.

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

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

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

22. A composition comprising de-differentiated cells produced by *in vitro* transfection using a composition as defined in claim 1.

23. Use of a composition comprising de-differentiated cells produced by *in vitro* transfection using a composition as defined in claim 1in the manufacture of a medicament for the treatment of arthritis, Lupus or autoimmune disease.

24. The method of claim 1, wherein the synthetic mRNAs contain more than 10% 2-thio-uracil of the total uracil.