EPO - DG 2
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REVISED CLAIMS:

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1. A composition comprising non-pluripotent progenitors of surrogate pancreatic cells that are suitable for treating insulin-dependent diabetes, wherein the progenitors (i) have a stem cell morphology and proliferate in culture without change in said morphology, (ii) are reprogrammed but have no reprogramming genes integrated into their genomes, (iii) differentiate to the pancreatic lineage pursuant to a protocol that employs only defined reagents, and (iv) are substantially unable to differentiate to the mesodermal lineage.

2. A method for generating a composition comprising non-pluripotent progenitors of surrogate pancreatic cells that are suitable for treating insulin-dependent diabetes, comprising:

a. culturing primary human cells, harvested from viable human pancreatic tissue in minimal, defined culture conditions, wherein the culturing is for a period of days that is fewer than about 9 days; then
b. using reprogramming genes to reprogram primary human cells from (b) such that reprogrammed cells are obtained that have no reprogramming genes integrated genomically but that do have a stem cell morphology;
c. firstly selecting among the reprogrammed cells obtained in (c) for an ability to proliferate, without losing said morphology, in minimal, defined culture conditions whereby proliferating reprogrammed cells are obtained; and then
d. secondly selecting from among the proliferating reprogrammed cells for a cell population characterized by (i) an ability to survive and differentiate to the pancreatic lineage in the course of a protocol that employs only defined reagents, and (ii) a substantial inability of differentiate to the mesodermal lineage,

whereby said non-pluripotent progenitors are obtained.

3. A composition comprising surrogate pancreatic cells that are suitable for treating insulin-dependent diabetes, wherein (A) the surrogate pancreatic cells are derived from the non-pluripotent progenitors of claim 1 and (B) more than about 90% of cells comprising the composition express the markers Pdx1, Nkx6.1, and NeuroD1.

4. A method for generating surrogate pancreatic cells that are suitable for treating insulin-dependent diabetes, comprising:

a. exposing non-pluripotent progenitors of claim 1 to a first combination of components that drive differentiation to the endodermal lineage, whereby endodermal cells are obtained, said first combination excluding serum and any wnt family member; and then

b. exposing said endodermal cells to a combination of components that drive differentiation to the pancreatic endocrine lineage,

whereby said surrogate pancreatic cells are obtained.

5. The method of claim 1, wherein the progenitors manifest expression of Oct4 and Nanog.

6. The method of claim 2, wherein the reprogramming genes are selected from the group consisting of Oct4, Sox2, Klf4, and Myc.

What is claimed is:

1. A method for generating a composition comprising non-pluripotent progenitors of surrogate pancreatic cells that are suitable for treating insulin-dependent diabetes, comprising:

a. harvesting human cells from viable human pancreatic tissue in minimal, defined culture conditions;

b. culturing the primary human cells for a period of days that is fewer than about 9 days; then

c. delivering reprogramming genes into the primary human cells from (b) to reprogram the primary human cells to obtain reprogrammed cells such that no reprogramming genes are integrated into the genome of the reprogrammed cells, wherein the reprogrammed cells have a stem cell morphology;

d. firstly selecting among the reprogrammed cells obtained in (c) for an ability to proliferate, without losing said stem cell morphology, in minimal, defined culture conditions whereby proliferating reprogrammed cells are obtained; and then

e. secondly selecting from among the proliferating reprogrammed cells for a cell population characterized by (i) an ability to survive and differentiate to a pancreatic lineage in the course of a protocol that employs only defined reagents, and (ii) a substantial inability to differentiate to a mesodermal lineage, whereby said non-pluripotent progenitors are obtained.