Claims

1. A composition comprising a non-native pancreatic β cell, wherein:

   (a) the non-native pancreatic β cell comprises one or more crystalline insulin granules;

   (b) the non-native pancreatic β cell expresses the following genes: INS, PDX1, NKX6-1, and ZNT8;

   (c) the non-native pancreatic β cell exhibits an *in vitro* glucose-stimulated insulin secretion response to a first glucose challenge; and

   (d) the non-native pancreatic β cell does not express one or both of somatostatin and glucagon.

2. The composition of claim 1, wherein the non-native pancreatic β cell exhibits an *in vitro* glucose-stimulated insulin secretion response to a first glucose challenge, a second glucose challenge, and a third glucose challenge, when the first glucose challenge, the second glucose challenge and the third glucose challenge are applied sequentially.

3. The composition of claim 1, wherein the non-native pancreatic β cell further expresses at least one gene selected from the group consisting of MAFA, PAX6, NEUROD1, GCK, SLC2A1, PCSK1, KCNJ11, ABCC8, SNAP25, RAB3A, GAD2, PTPRN, NKX2-2, and PAX4.

4. The composition of claim 1, wherein the non-native pancreatic β cell secretes insulin in response to a first glucose concentration compared to a second glucose concentration in a ratio of at least 1.1 wherein the first glucose concentration is higher than the second glucose concentration.

5. The composition of claim 1, wherein the non-native pancreatic β cell is monohormonal.

6. The composition of claim 1, wherein the insulin secreted by the non-native pancreatic β cell is at least 0.5μIU per 1000 cells per 30 minute incubation when the non-native pancreatic β cell is exposed to at least 20 mM of glucose.

7. The composition of claim 1, wherein insulin secretion from the non-native pancreatic β cell is enhanced in response to an anti-diabetic agent.

8. The composition of claim 1, wherein the non-native pancreatic β cell exhibits cytokine-induced apoptosis in response to a cytokine.

9. The composition of claim 1, wherein the non-native pancreatic β cell has a gene expression profile that is different from the gene expression profile of a native β cell.

10. A population of cells comprising one or more non-native pancreatic β cells of claim 1, wherein at least 10% of the cells in the population of cells are the non-native pancreatic β cells.

11. The population of cells of claim 12, further comprising insulin-positive endocrine cells.

12. The population of cells of claim 12, wherein the population of cells comprises one of the following:
    a. a C-peptide-negative/glucagon-positive cell;
    b. a C-peptide-negative/somatostatin-positive cell;
    c. a glucagon-positive/somatostatin-negative cell;
    d. a glucagon-negative/somatostatin-positive cell; or
    e. any combination thereof.

13. The population of cells of claim 12, wherein at least 3% of the population of cells are C-peptide-negative/glucagon-positive cells or glucagon-positive/somatostatin-negative cells.

14. An artificial islet or pancreas comprising the population of cells of claim 12.

15. A method of differentiating progenitor cells into pancreatic β cells *in vitro*, the method comprising culturing a cluster of the progenitor cells in suspension in

a culture medium comprising a thyroid hormone signaling pathway activator and a transforming growth factor β (TGF-β) signaling pathway inhibitor, thereby differentiating the progenitor cells into pancreatic β cells, wherein the pancreatic β cells exhibit an *in vitro* glucose-stimulated insulin secretion response to at least a first glucose challenge.

16. The method of claim 15, wherein the progenitor cells comprise an insulin-positive endocrine cell.

17. The method of claim 15, wherein the progenitor cells comprise a PDX1-positive progenitor cell.

18. The method of claim 15, wherein the thyroid hormone signalling pathway activator is triiodothyronine.

19. The method of claim 18, wherein the concentration of the triiodothyronine is at least 0.1 μM.

20. The method of claim 15, wherein the TGF-β signaling pathway inhibitor is Alk5 inhibitor II.

21. The method of claim 20, wherein the concentration of the Alk5 inhibitor II is at least 100 nM.

22. The method of claim 20, wherein the concentration of the Alk5 inhibitor II is 100 μM or less.

23. The method of claim 15, wherein the culturing comprises changing the culture medium at least every other day.

24. The method of claim 15, wherein the culturing lasts for at least seven days.

25. The method of claim 15, wherein the culture medium is a serum-free culture medium.

26. The method of claim 15, wherein the progenitor cells are cultured in the presence of a low-adherent substrate.

27. The method of claim 15, wherein the progenitor cells are human progenitor cells.

28. The method of claim 15, wherein the pancreatic β cells exhibit an *in vitro* glucose-stimulated insulin secretion response to a first glucose challenge and a second glucose challenge when the first glucose challenge and the second glucose challenge are applied sequentially.

29. The method of claim 15, wherein the pancreatic β cells exhibit an *in vitro* glucose-stimulated insulin secretion response to a first glucose challenge, a second glucose challenge, and a third glucose challenge, when the first glucose challenge, the second glucose challenge, and the third glucose challenge are applied sequentially.