Claims

[Claim 1]

Insulin-producing cells comprising: insulin-positive and NKX6.1-positive cells at a proportion of 30% or more; and insulin-positive and NKX6.1-negative cells at a proportion of more than 15%; and Ki67-positive cells at a proportion of less than 3%.

[Claim 2]

The insulin-producing cells according to claim 1, wherein an expression level of a MafA gene or a gene product thereof is lower than an expression level of a MafA gene or a gene product thereof in a pancreatic islet isolated from a healthy individual.

[Claim 3]

The insulin-producing cells according to any one of claims 1 to 2, comprising glucagon-positive and insulin-negative cells at a proportion of less than 3%.

[Claim 4]

The insulin-producing cells according to any one of claims 1 to 3, wherein the insulin-producing cells exhibit glucose-stimulated insulin secretion (GSIS) response.

[Claim 5]

The insulin-producing cells according to any one of claims 1 to 4, comprising chromogranin A-positive cells at a proportion of more than 45%.

[Claim 6]

The insulin-producing cells according to any one of claims 1 to 5, comprising alkaline phosphatase-positive pluripotent stem cells at a proportion of less than 0.01%.

[Claim 7]

A medicament comprising the insulin-producing cells according to any one of claims 1 to 6.

[Claim 8]

The medicament according to claim 7, wherein the insulin-producing cells are accommodated in a device.

[Claim 9]

The medicament according to claims 7 or 8, wherein the insulin-producing cells are dispersed in a hydrogel.

[Claim 10]

The medicament according to any one of claims 7 to 9, to be used for transplantation into a living body.

[Claim 11]

The medicament according to any one of claims 7 to 10, to be used for subcutaneous transplantation.

[Claim 12]

The medicament according to any one of claims 7 to 11, for use in treatment of diabetes mellitus.

[Claim 13]

The medicament according to any one of claims 7 to 11, for use in improvement and/or retention of control of fasting and postprandial glucose levels in a patient.

[Claim 14]

The medicament according to any one of claims 7 to 11, to be used to reduce risk of hypoglycemia in a patient with diabetes mellitus.

[Claim 15]

The medicament according to any one of claims 7 to 11, for use in a method for inducing differentiation into pancreatic islet-like cells in a living body.

[Claim 16]

The medicament according to claim 15, wherein pancreatic islet-like cells differentiated in a living body comprise chromogranin A-positive cells at a proportion of 50% or more.

[Claim 17]

The medicament according to claim 15 or 16, wherein pancreatic islet-like cells differentiated in a living body comprise Ki67-positive cells at a proportion of less than 3%.

[Claim 18]

The medicament according to any one of claims 15 to 17, wherein pancreatic islet-like cells differentiated in a living body comprise glucagon-positive and insulin-negative cells at a proportion of 10% or more.

[Claim 19]

The medicament according to any one of claims 15 to 18, wherein pancreatic islet-like cells differentiated in

a living body exhibit insulin-secreting action in response to hypoglycemia.

[Claim 20]

A method for producing insulin-producing cells comprising: insulin-positive and NKX6.1-positive cells at a proportion of 30% or more; insulin-positive and NKX6.1-negative cells at a proportion of more than 15%; and Ki67-positive cells at a proportion of less than 3%, the method comprising the steps of:

culturing pluripotent stem cells in the presence of 5 to 50 ng/mL of activin A to produce definitive endoderm cells; and

culturing endocrine progenitor cells in a medium containing an FGFR1 inhibitor to produce the insulin-producing cells.

[Claim 21]

Use of insulin-producing cells according to claim 1 in the manufacture of a medicament for treating diabetes mellitus, wherein the insulin-producing cells are to be transplanted into a living body to induce differentiation into pancreatic islet-like cells.

[Claim 22]

Use of insulin-producing cells according to claim 1 in the manufacture of a medicament for improving and/or retaining control of fasting and postprandial glucose levels in a patient, wherein the insulin-producing cells

are to be transplanted into a living body to induce differentiation into pancreatic islet-like cells.

[Claim 23]

Use of insulin-producing cells according to claim 1 in the manufacture of a medicament for reducing risk of hypoglycemia in a patient with diabetes mellitus, wherein the insulin-producing cells are to be transplanted into a living body to induce differentiation into pancreatic islet-like cells.

[Claim 24]

The insulin-producing cells according to claim 1 for use in medicine.