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 claim 1 or 2, comprising Ki67-positive cells at a proportion of less than 3%.~~

[Claim 34]

The insulin-producing cells according to any one of claims 1 to 23, comprising glucagon-positive and insulin-negative cells at a proportion of less than 3%.

[Claim 45]

The insulin-producing cells according to any one of claims 1 to 34, wherein the insulin-producing cells exhibit glucose-stimulated insulin secretion (GSIS) response.

[Claim 5~~6~~]

The insulin-producing cells according to any one of claims 1 to 4~~5~~, comprising chromogranin A-positive cells at a proportion of more than 45%.

[Claim 6~~7~~]

The insulin-producing cells according to any one of claims 1 to 5~~6~~, comprising alkaline phosphatase-positive pluripotent stem cells at a proportion of less than 0.01%.

[Claim 7~~8~~]

A medicament comprising the insulin-producing cells according to any one of claims 1 to 6~~7~~.

[Claim 8~~9~~]

The medicament according to claim 7~~8~~, wherein the insulin-producing cells are accommodated in a device.

[Claim 9~~10~~]

The medicament according to claim 7~~8~~ or 8~~9~~, wherein the insulin-producing cells are dispersed in a hydrogel.

[Claim 10~~11~~]

The medicament according to any one of claims 7~~8~~ to 9~~10~~, to be used for transplantation into a living body.

[Claim 11~~12~~]

The medicament according to any one of claims 7~~8~~ to 10~~11~~, to be used for subcutaneous transplantation.

[Claim 12~~13~~]

The medicament according to any one of claims 7~~8~~ to 11~~12~~, for use in treatment of diabetes mellitus.

[Claim 13~~14~~]

The medicament according to any one of claims 7~~8~~ to 11~~12~~, for use in improvement and/or retention of control of fasting and postprandial glucose levels in a patient.

[Claim 14~~15~~]

The medicament according to any one of claims 7~~8~~ to 11~~12~~, to be used to reduce risk of hypoglycemia in a patient with diabetes mellitus.

[Claim 15~~16~~]

The medicament according to any one of claims 7~~8~~ to 11~~12~~, for use in a method for inducing differentiation into pancreatic islet-like cells in a living body.

[Claim 16~~17~~]

The medicament according to claim 15~~16~~, wherein pancreatic islet-like cells differentiated in a living body comprise chromogranin A-positive cells at a proportion of 50% or more.

[Claim 17~~18~~]

The medicament according to claim 15~~16~~ or 16~~17~~, wherein pancreatic islet-like cells differentiated in a living body comprise Ki67-positive cells at a proportion of less than 3%.

[Claim 18~~19~~]

The medicament according to any one of claims 15~~16~~ to 17~~18~~, 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~~20~~]

The medicament according to any one of claims 15~~16~~ to 18~~19~~, wherein pancreatic islet-like cells differentiated in a living body exhibit insulin-secreting action in response to hypoglycemia.

[Claim 20~~21~~]

A method for producing 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%, the method comprising the steps of:

culturing pluripotent stem cells in the presence of 5 to 50 ng/mL ~~a low dose~~ 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 22]~~

~~A method for generating pancreatic islet-like cells, the method comprising~~

~~transplanting insulin-producing cells into a living body to induce differentiation into pancreatic islet-like cells, wherein the insulin-producing cells comprise: insulin-positive and NKX6.1-positive cells in a~~

~~proportion of 30% or more; and insulin-positive and NKX6.1-negative cells in a proportion of more than 15%.~~

[Claim 21~~23~~]

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~~24~~]

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~~25~~]

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~~26~~]

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