Beta cell development
Growth and Maintenance of Beta Cell Mass

Embryo Childhood Adulthood

Rate of Replication

Embryo Childhood Adulthood
Increase in beta-cell number [millions per year]

Age groups [years]

p = 0.044

Increase in beta-cell number [% per year]

Age groups [years]

p = 0.0056
New islet formation?
Potential Sources of new beta cells

- Pancreatic stem cell
- Bone marrow
- Mesenchymal transdifferentiation

Beta Cell Replication
- Beginning of cycle
- Interphase
- G1 phase
- S phase
- G2 phase
- M phase

Beta cell mass

Beta cell apoptosis

Replication independent
- Replication independent
  - G0 phase: nondividing cells
Adaptation to obesity?
p < 0.01

Beta cell mass

Lean Obese

Beta cell mass (g)

Obese

p < 0.01
Beta cell mass

$r = 0.5$
$p < 0.01$
Beta Cell Replication

[Ki67 positive cells/islet]

Lean Obese Lean Obese

HUMAN MOUSE
Gastrin?
Gastrinoma Humans

Meier J Diabetologia 2006
Pregnancy?
Humans
Beta Cell Replication (Ki67)

β cells/100 islets

Infant  Adult  Pregnant
Potential Sources of new beta cells

- Pancreatic stem cell
- Bone marrow
- Mesenchymal transdifferentiation

Beta cell replication

G1 (nondividing cells)

S

G2

M (Beginning of cycle)

Interphase

Beta cell mass

Beta cell apoptosis

G0 (nondividing cells)
Bone Marrow

• Female recipients of male bone marrow.
• FISH and insulin staining of pancreas.
Spleen

FISH to Show X-Chromosome and Y-Chromosome in Human Female Spleen
Boy meets girls!
Endogenous cell formation?
Potential Sources of new beta cells

- Pancreatic stem cell
- Bone marrow
- Mesenchymal transdifferentiation

Beta cell mass

Beta cell apoptosis

Beta Cell Replication

Beginning of cycle

Replication independent

G1 nondividing cells

Interphase

M

G2

S
Beta-cells in the pancreas of patients with long-standing type 1 diabetes

Meier et al. Diabetologia 2005; 48: 2221-2228
Beta-cell apoptosis (cleaved caspase-3)

Type 1 diabetes

Controls

Meier JJ Diabetologia 48, 2005
Beta-cell apoptosis (TUNEL)

Controls

Type 1 diabetes

Meier et al. Diabetologia 2005; 48: 2221-2228
Potential Sources of new beta cells

Replication independent
- Pancreatic stem cell
- Bone marrow
- Mesenchymal transdifferentiation

Replication

Beta cell mass

Beta cell apoptosis

G0 nondividing cells

Beginning of cycle

M

G1

S

Interphase

G2

Beta Cell Replication