

A Robust Approach for *In Vitro* Generation of Functional Beta Cells

INVENTION: The generation and production of insulin-secreting cells, typically found in the pancreas and termed beta cells, has long been a major goal in regenerative medicine to cure Type 1 and certain types of Type 2 diabetes. To date, no method exists for the production of fully “functional” pancreatic beta cells; i.e. in vitro generated cells that can secrete insulin properly in response to physiological levels of glucose. The production of such cells represents the best hope of curing diabetes. Accordingly, methods for obtaining fully functional beta cells and using such cells for the treatment of diabetes are urgently required.

Salk investigators have now discovered a way to create functional pancreatic beta cells. They expressed a protein called estrogen-related receptor (ERR)gamma in a beta-like cell derived from induced pluripotent stem cells (iPSCs) in vitro, which activates a transcriptional network that promotes mitochondrial oxidative metabolism. This metabolic reprogramming of the beta-like cells is both necessary and sufficient to generate mature beta cells capable of insulin secretion in response to glucose. Importantly, these mature beta cells are able to restore glucose homeostasis in a Type 1 diabetic mouse model, indicating that they are indeed fully functional and have strong therapeutic potential that could be applied to human therapies.

APPLICATIONS:

- In vitro generation of functional human beta cell therapeutics
- Cell-based therapy for Type 1 and certain types of Type 2 diabetes
- Replacement of missing or non-functional pancreatic beta cells
- Generation of mature and functional pancreatic beta cells in vitro for research applications

ADVANTAGES:

- Generation of functional, transplantable beta cells in vitro without the need for kidney capsule maturation
- Potential for derivation from a patient’s own cells to minimize rejection upon transplant
- A powerful tool to dissect pancreatic beta cell maturation

STAGE OF DEVELOPMENT:

Mature beta cells resulting from ERR-gamma induction were transplanted into the kidney of a Type 1 diabetic mouse model and successfully restored glucose-sensitive insulin secretion.

BACKGROUND: In healthy individuals, beta cells in the pancreas secrete insulin in response to nutrients, such as glucose, amino acids, and free fatty acids to regulate blood glucose levels and lipid metabolism. Beta cell failure or impaired function is associated with both Type 1 and Type 2 diabetes, therefore development of transplantable beta cells is one of the central goals of stem cell therapy.

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<http://www.salk.edu/news-release/salk-scientists-find-secret-sauce-for-personalized-functional-insulin-producing-cells/>

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