Screening assay for agents that induce Langerhans islet neogenesis in vitro

Overview:

The present invention relates to an in vitro method to identify agents capable of inducing islet cell neogenesis or duct-to-islet cell transdifferentiation. Besides subcutaneous insulin injection, total endocrine replacement therapy in the form of whole pancreas or Langerhans islets transplantation has been considered a treatment option for diabetes. Besides a limited access to organs, the risk of long term immunosuppression is substantial. A new approach would be to induce pancreatic neogenesis in the diabetic patient. The current assay allows testing compounds for their capacity to induce islet neogenesis and new islet formation (Figure 1).

Characteristics:

Existing assays utilize non-human cell lines to test for beta-cell differentiation. The current assay tests the neogenesis of fully functional islets, including various cell types and secretion products and their glucose responsiveness. Controls and up to 50 compounds can be analysed in triplicate after pre-screens in a pancreatic cell line. The assay was instrumental for identifying a peptide (INGAP) as an agent that induces islet regeneration in vivo.

Figure 1 DUCT-ISLET TRANSFORMATION: Islet cell hormones, insulin, glucagon and somatostatin were all undetectable in all of the cells in the control group after 4 days whereas in the DRUG A group, the presence of these islet cell hormones was detected using immunohistochemistry and were found to be expressed in the same proportion as in normal adult human islets.

Figure 2: Insulin secretion (measured by ELISA) increases significantly after Drug A treatment. The control group does not secrete any insulin as the amount measured corresponded to the amount of insulin added to the basal media. Therefore new islets formed from the ducts can store insulin but can also secrete it.
**The originator:** Dr. Lawrence Rosenberg

**Profile:**

**Dr. Lawrence Rosenberg M.D., Ph.D.**

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Dr. Lawrence Rosenberg received his M.D. from McGill University and completed surgical training in general surgery at the Montreal General Hospital. During his residency, Dr. Rosenberg earned a Ph.D. in experimental surgery at McGill.

After completing post-doctoral studies, which included a transplant surgery fellowship at the University of Michigan, he was appointed Assistant Professor of Surgery and Medicine at McGill in 1987. His current studies address the creation of new insulin-producing cells. He is the co-discoverer of INGAP, a novel pancreatic growth factor, currently in clinical trial as a novel therapy to re-grow new insulin-producing cells in those with diabetes.

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Opportunity: research collaboration