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Targeting pancreatic beta cell-derived isletokines to improve islet cell transplantation

Michael Lawrence
Baylor Scott & White Research Institute, USA

Pancreatic islets are central to the regulation of glucose metabolism and homeostasis. The loss or impairment of islet beta cells results in diabetes and high risk of cardiovascular disease with detrimental health consequences. Islet cell transplantation represents a cell replacement therapy to prevent or reverse diabetes. One major hurdle to the success of islet transplantation is the early loss of islet cells due to an acute innate inflammatory response within the first 24 hours of islet cell infusion. We have identified cytokines and chemokines produced by beta cells that evoke acute islet inflammation. These "isletokines" are upregulated in stressed beta cells by calcineurin/NFAT and MAPK signaling and contribute to early islet cell graft loss. Here, we discuss our latest findings of key cellular events that induce beta cell isletokine expression and islet inflammation. We also identify molecular targets to prevent beta cell-induced islet inflammation and develop therapeutic strategies to improve islet cell transplantation.

Biography

Michael Lawrence, PhD, is currently investigating mechanisms that regulate and affect pancreatic islet endocrine function in health and disease. Impairment or dysfunction of beta cells of the pancreatic islets leads to hyperglycemia and diabetes. He is identifying methods and approaches to prevent loss of pancreatic beta-cell function from metabolic and inflammatory stress to reverse and prevent diabetes. His current focus is on 1) protecting pancreatic beta cells from inflammatory and immune destruction in the pathogenesis of diabetes and in islet transplantation; 2) cell-mediated repair and restoration of islet function via pancreatic-derived mesenchymal stem cells; and 3) engineering islet endocrine tissue from islet precursor cells for islet cell transplantation. He also is actively involved in clinical islet cell isolation procedures for the islet cell transplant program at Baylor University Medical Center at Dallas and Baylor All Saints Medical Center at Fort Worth.

Michael.Lawrence@BaylorHealth.edu

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