Title of Project

The role of RCAN1 in pancreatic islet proliferation and mitochondrial function

Brief outline of project

Type 2 diabetes is a debilitating metabolic disorder characterised by increased fasting blood glucose levels. Obesity has been consistently linked to the onset and the pathogenesis of type 2 diabetes. However the molecular mechanisms leading to diminished function of the insulin producing β-cells of the pancreas are incompletely understood. Interestingly, Down syndrome patients have an increased incidence of diabetes, suggesting that one or more genes on chromosome 21 may be essential for proper β-cell function. We have focussed our research on one chromosome 21 gene, RCAN1. In the brain RCAN1 affects gene expression, mitochondrial function and cell survival, pathways which are also essential in pancreatic β-cells. We have recently shown that RCAN1 is also present in β-cells and increased expression of RCAN1 results in increased blood-glucose levels decreased blood insulin levels, decreased pancreatic islet mass and altered mitochondrial morphology: phenotypes also seen in type 2 diabetic patients.

The focus of this project would be to build on our knowledge of RCAN1 function in β-cells, specifically the molecular mechanisms leading to pancreatic islets shrinkage and mitochondrial function. As the pancreatic islet is the sole source of insulin production understanding the mechanisms controlling proliferation and/or apoptosis would provide a unique understanding of the mechanism leading to diminished insulin secretion and type 2 diabetes.

The methods to be used during the course of this project will include, but are not limited to real-time PCR, confocal microscopy, cell culture and western-blotting.

Key references

Heshan Peiris, Ravinarayan Raghupathi, Claire F. Jessup, Mark P. Zanin, Daisy Mohanasundaram, Kimberly D. Mackenzie, Tim Chataway, Jennifer N. Clarke, John Brealey, P. Toby Coates, Melanie A. Pritchard, Damien J. Keating 2012 Increased expression of the glucose responsive gene, RCAN1, causes hypoinsulinemia, β-cell dysfunction and diabetes. Endocrinology


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