**Project Title:**
Consequences of high cholesterol diet on ‘insulin producing’ pancreatic islets

**Code:** WMI6

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**Project Type:**  Laboratory based

**Project Category:**  Endocrinology & Metabolism

**Project Keywords:**
1. Diabetes
2. Cholesterol
3. Macrophage
4. Pancreatic islets
5. Beta cells

**Project Description:**

We have a long track record of studying the effects of diet on the liver. Currently, we have been investigating the effect of the western “atherosclerotic” diet, in the development of liver inflammation. In this study normal healthy mice are fed either regular chow, high sucrose, or with “arthrosclerosis” diet containing high sucrose, cholesterol and cholate (bile acid). Interestingly, we noticed that a side effect of this diet is that the pancreatic islets of the mice fed high cholate diets were double in size compared to islets of the mice fed with other diets; and these islets also appeared to have the presence of immune cell infiltrates.

Excess bile acids have been shown to induce the farnesoid X receptor (FXR) pathway, which may be associated with the secretion of the incretin hormone “glucagon-like peptide 1” (GLP1), a major drug target for type-2 diabetes treatment. GLP-1 is associated with an increase in insulin release a decreased glucagon secretion and to potentially increase the islet beta-cell mass. Additionally, GLP-1 has been shown to induce an M2 macrophage phenotype, which has recently been associated with beta-cell hypertrophy. We hypothesize therefore, that bile acids can induce morphological changes on pancreatic islet cells through the direct effect of GLP-1 on the islets and/or indirectly by inducing an M2 macrophage phenotype.

This study will utilize high-throughput imaging technology and data analysis to investigate the morphology of resident macrophage in the pancreas, and determine the mechanisms associated with increased of beta-cell mass. This project will also be suitable for an Honors or PhD candidacy.