Dr. Tessem Research

Introduction

There are two major iterations of diabetes. Type 1 diabetes (T1D) is caused by autoimmune destruction of an individuals β-cells. An individual with T1D has severe insulin deficiency, and today is treated with multiple daily insulin injections. Type 2 diabetes (T2D) is associated with obesity and a sedentary lifestyle, and is characterized by insulin insensitivity in the muscle and adipose tissue. These patients are initially treated with insulin sensitizing compounds. While β-cell mass is originally maintained in T2D individuals, ultimately these patients loose β-cells and eventually also receive daily insulin injections. Therefore, T1D and T2D are ultimately characterized by decreased functional β-cell mass. Functional β-cell mass refers to the β-cell insulin secretion rate, the β-cell proliferation rate and the β-cell death rate. An increase in the β-cell secretion rate or proliferation, or a decrease in the cell death rate would all increase the functional β-cell mass. The ability to increase functional β-cell mass could be used as a tool to cure individuals with Type 1 and Type 2 diabetes.

The Tessem lab (Diabetes research group: tessemlab.byu.edu) is interested in delineating the molecular pathways that control functional β-cell mass with the ultimate application of increasing β-cells *ex vivo* for islet transplantation or *in situ* for enhancement of a patient's own residual β-cells. Our studies are focused on identifying the molecular accelerators and brakes that control β-cell replication, determining how these factors regulate functional β-cell mass, develop small molecule activators of the β-cell proliferation pathways and apply these findings to two state models of β-cell function such as obese vs. lean or aged vs. young models. Finally, our studies focus on discovering unique regulators of integrative metabolism.

Our experimental models use tissue culture β-cell lines, primary rodent islets and primary human islets. We use microarray expression analysis to determine genes involved in the particular pathways, followed by a variety of molecular and pharmacological techniques to manipulate pathways in order to understand how they effect functional β-cell mass. We measure changes in proliferation rate, glucose stimulated insulin secretion and protection against apoptosis as metrics of β-cell function.

Major Emphasis: Type I; Minor Emphasis: Type II

1) ***Current research efforts***
    a) Map molecular pathways that control β-cell proliferation, insulin secretion and protection from cellular death.
    b) Determine genes upstream of Nkx6.1 critical for functional β-cell mass
    c) Verify genes downstream of Nkx6.1 that are necessary and sufficient for functional β-cell mass

d) Using small molecule chemistry find agonist that manipulate key players in the functional β-cell mass pathway (i.e. Nr4a1, Nr4a3)
e) Explore the idea of β-cell subtypes in terms of proliferation, insulin secretion and protection from cell death

2) ***Anticipated Research Results***
   a) Rescue Type 1 and Type 2 diabetic patients through increased islet mass
      i) Ex vivo expansion of β-cell mass for transplantation
      ii) In situ expansion of endogenous β-cells
   b) Classify subgroups of β-cells
   c) Explore function of Nr4a family on mitochondrial function
   d) Characterize the genes essential for the Nkx6.1 β-cell proliferation and function pathway
      i) Nkx6.1— β-cell specific transcription factor
      ii) NKX6.1 activates VGF that protects against apoptosis and increases glucose stimulated insulin secretion
      iii) Nkx6.1 activates Nr4a1 and Nr4a3 which stimulate beta cell proliferation

**See full profile and publications here