

## **Dr. Benjamin Bikman Research**

### **Introduction**

Diabetes is an epidemic. The disease affects roughly 400 million people worldwide and is likely to increase by over 50% in the next 20 years. A large part of the increased disease risk of diabetes is the worldwide trend of weight gain—almost all obese individuals have or will develop diabetes.

The Bikman Lab (Laboratory of Obesity and Metabolism) has a twofold mission. First, we aim to identify the molecular mechanisms that explain the increased risk of disease that accompanies weight gain. We particularly focus on the factors involved in the onset of insulin resistance (the key factor of type 2 diabetes), excess insulin production, and disrupted mitochondrial function. Second, we hope to reveal novel cellular processes that are responsible for fat growth in the course of weight gain.

Our recent work suggests that exposure to various chemical and biological toxins alters cellular metabolic function and leads to fat gain in the body. This is largely the result of the lipotoxic accumulation of a molecule called ceramide. Ceramide has been shown to selectively accumulate in tissues with high metabolic rates (e.g. skeletal muscle, liver, brain, etc.), suggesting a potential role in modulating tissue and whole-body metabolism. Moreover, ceramide may be partly responsible for the changes in pancreatic function that typify type 1 and type 2 diabetes.

We employ numerous pharmacological and genetic tools to better understand the origins and consequences of ceramide accumulation on various factors related to metabolic function, including signal transduction, substrate utilization, and energy expenditure.

### **1) Current Research Efforts**

- a) Determine the factors that increase ceramide accumulation in body tissues, such as skeletal muscle
- b) Elucidate how ceramide negatively alters mitochondrial function
- c) Determine how insulin increases fat gain in the body
- d) Discover new methods/therapies to reduce ceramide synthesis in muscle
- e) Quantify the ability of common toxins (e.g., vehicle exhaust, cigarette smoke) to increase ceramide production
- f) Explore the ‘fattening’ effects of commonly used medications (e.g., anti-inflammatory steroids)

### **2) Anticipated Research Results**

- a) Prevention of Type 1 diabetes
- b) Prevention/reversal of Type 2 diabetes

- c) Determine the impact of ceramide accumulation on mitochondrial function and whole-body metabolism
- d) Identify factors critical to maintaining/restoring healthy mitochondrial function
- e) Reveal method to improve insulin sensitivity (decreasing reliance on insulin-sensitizing medications, including insulin injections)
- f) Find improved methods of obesity prevention through novel regulation of recently revealed important metabolic pathways