



# Investigating the Mechanism of Leptin Therapy in Type 1 Diabetes

Michelle M. Kwon, Nelly Saber, Mitchell Braam, Min Feng, Gal Av-Gay

The hormone leptin regulates body weight; leptin deficient humans and mice are obese. Leptin is also emerging as an important regulator of glucose metabolism. Underlining this, leptin administration to mice rendered diabetic with streptozotocin (STZ, a beta-cell toxin) can normalize blood glucose levels, without increasing plasma insulin levels. Yet, the mechanism for these profound effects on glucose metabolism are unclear. Leptin-treated STZ-mice cannot maintain stable blood glucose levels during prolonged fasting and fall into life threatening hypoglycemia, suggesting that leptin-treated STZ-mice may be unable to sustain endogenous glucose production (gluconeogenesis) and this may be the mechanism by which leptin lowers blood glucose levels. The liver is the major site for gluconeogenesis. We have sequenced the hepatic transcriptome of leptin-treated STZ-mice and controls, and have completed four complementary analyses to elucidate the mechanism of leptin-therapy in diabetic rodents.

