**Dr. Blandine Laferrere**

The intestinal incretin GLP-1 is a potent glucose-mediated insulin secretagogue. Patients with type 2 diabetes (TDM2) have a blunted incretin effect on insulin secretion. The administration of GLP-1 is able to restore β-cell sensitivity to glucose in T2DM. Patients who experienced TDM2 remission after gastric bypass surgery (GBP) have rapid (within weeks), and sustained (years), exaggerated post-prandial GLP-1 release, with normalization of the incretin effect on insulin secretion. In vitro and/or rodent studies show that GLP-1 can stimulate β-cell growth and differentiation. Whether the sustained enhanced GLP-1 release after GBP results in greater β-cell function is unknown. In this proposal we will examine 1) The role of endogenous GLP-1 in the recovery of β-cell function in response to oral glucose, by using exendin 9-39, a GLP-1 receptor antagonist; 2) The change of maximal β-cell response to glucose infusion and arginine administration after GBP; 3) Insulin sensitivity and body composition, in patients with severe obesity and TDM2, before and up to 2 years after GBP; 4) Determinants of TDM2 remission after GBP. Understanding the mechanisms of TDM2 remission, or lack of, after GBP will help identify predictors of outcome as well as develop medical alternatives for the treatment of severe obesity and TDM2.