Title: Making beta cells secrete more insulin by targeting the switch protein ROMO1

Researchers:

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Research area: Prediabetes

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Summary:

Major health concerns for Canadians including obesity, heart disease, cancer, and diabetes, all share a common feature: loss of the normal function of cellular organelles called mitochondria. Often referred to as the “furnace of the cell”, mitochondria are not only essential for our cells to extract energy from food, but they control decisions of life and death: mitochondrial damage is sufficient to trigger cell death. Our previous work has shown that the protein ROMO1 is required to promote mitochondrial health and cell survival, as well as for a specific energy conversion process that is lost in aging and diabetes.

When we generated mice that lack ROMO1 only in the pancreatic beta cell, the cells that produce insulin, we were presented with an unexpected and very intriguing result: male mice lacking ROMO1 in their beta cells become glucose intolerant and even diabetic, while female mice do not. This is of particular interest to us as we observe insulin secretion defects in human as they age, but only in men and not women.

We now want to determine why this function of ROMO1 is unique to male mice to design new strategies to restore this function in men and enhance it even further for women. Given the significant role that diet can play in type 2 diabetes, we also want to study if aging and a western diet makes the glucose intolerance in male mice worse, and possibly makes female mice have a higher blood sugar as well. If this happens, it will identify a new step that we can begin to design drugs to reverse it and improve glucose control.

Taken together, we propose that understanding how ROMO1 works in male mice will identify strategies to treat the loss of beta cell function that happens in humans as they age. We will establish a comprehensive molecular framework for how ROMO1 promotes positive effects in beta cells and how drugs that enhance ROMO1 activity could promote insulin secretion, and in turn, the quality of life of persons living with diabetes.