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Islet microexons as potential therapeutic targets in Type 2 diabetes

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Diabetes is a metabolic disorder that results from dysfunction or loss of insulin-secreting pancreatic beta cells. Its prevalence is increasing worldwide and has severe clinical complications. Therefore, a deep understanding of all regulatory layers important for beta cell function and dysfunction is a major biomedical need. We uncovered a program of microexons that are expressed only in endocrine cells of the islets of Langerhans and in neurons. Microexons are tiny pieces of DNA that are part of some genes and that can change how proteins work in those cells by adding just a few aminoacids to their sequences. We showed that these microexons, termed IsletMICs, are usually in genes important for insulin secretion and associated with type 2 diabetes risk. Moreover, their manipulation in beta cells led to defects in the regulation of insulin secretion and in the glucose levels of mouse models. Importantly, our work also revealed that the manipulation of individual IsletMICs can modulate insulin secretion. Our current efforts are focused on exploring these effects of IsletMICs as potential therapies for diabetes through functional screens and manipulation in mouse models.