Urocortin 2 (Ucn2) and Urocortin 3 (Ucn3) are hormone peptides that were originally identified by Clayton researcher, the late Dr. Wylie Vale and characterized for their role in the brain during stress. More recently, Drs. Vale and Huising discovered that Ucn3 is present in the pancreas of healthy individuals and is decreased or absent in diabetic patients. In healthy individuals, Ucn3 is released from beta cells alongside insulin and is also released from alpha cells along with glucagon. Glucagon and insulin have opposite roles: insulin decreases liver production of glucose while glucagon stimulates the production and release of glucose from the liver. The loss of Ucn3 correlates with hyperglycemia and increased glycemic volatility in diabetic patients.

It turns out that the Ucn3 receptor, CRHR2 is expressed only on delta cells. Delta cells produce somatostatin, which tells beta cells to stop producing insulin and tells alpha cells to stop producing glucagon. Ucn3, by binding to CRHR2 on delta cells, provides the signal for these delta cells to produce somatostatin. Ucn3 thereby plays a key role in regulating the timely release of two key hormones, insulin and glucagon.

Type 1 Diabetes (TDM1) is characterized by the loss of beta cell function. While the disease can be controlled with insulin injections, serious therapeutic issues arise due to the high glycemic volatility in these diabetic patients. Glucagon levels cannot be appropriately regulated and instead of decreasing at mealtime, levels increase. The loss of Ucn3 further substantiates increased glycemic volatility and the lack of Ucn3 is correlated with hyperglycemia in these patients. Restoring Ucn3 is expected to re-engage somatostatin-mediated negative feedback on alpha cells. We propose urocortin 3 or its analogue urocortin 2 as a therapeutic in order to control the levels of glucagon release in TDM1 patients.