MedicalXpress

'Crosstalk' gives clues to diabetes

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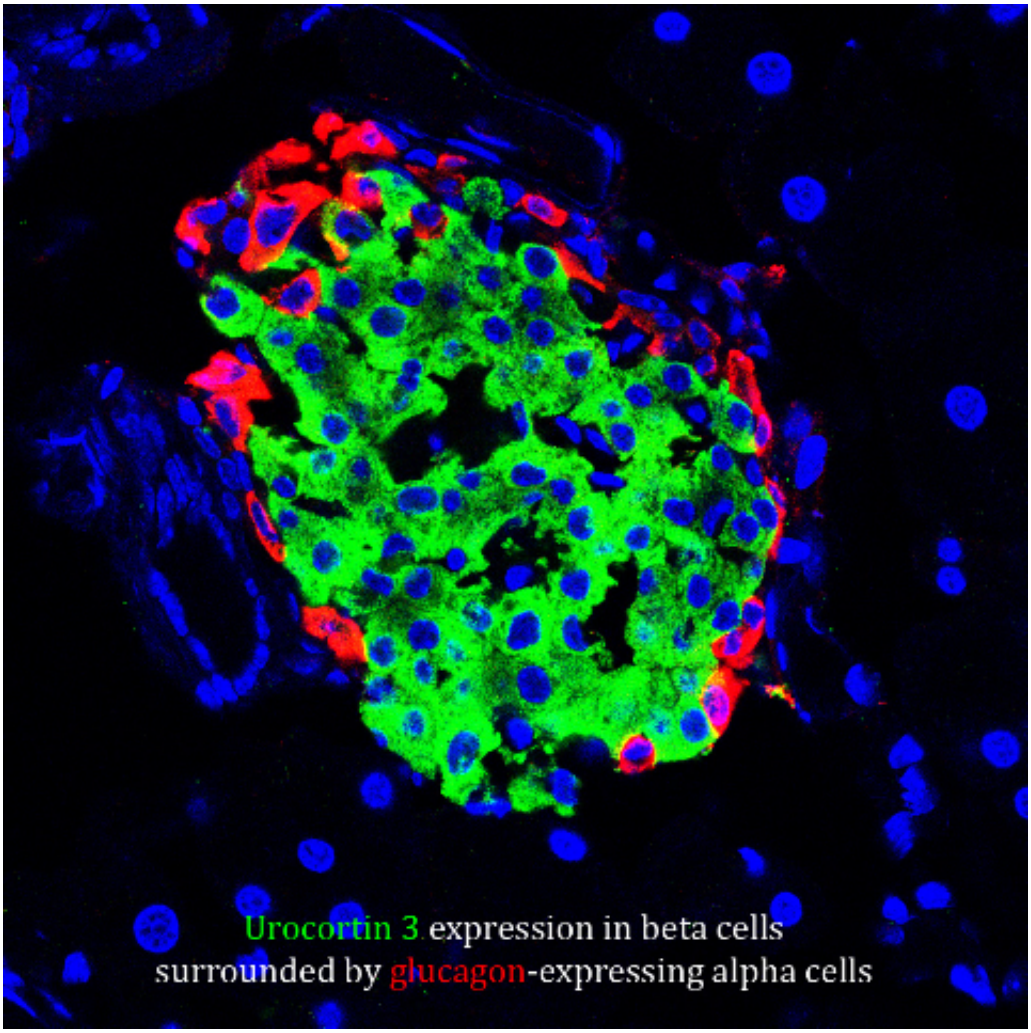

Sugar levels are managed by interactions between cells of the Islets of Langerhans in the pancreas. The hormone urocortin (green) is produced and stored in the same cells as insulin in the islets. Cells that make glucagon, which works to raise blood sugar, are stained red. Credit: Mark Huising, UC Davis

Sometimes, listening in on a conversation can tell you a lot. For Mark Huising, an assistant professor in the Department of Neurobiology, Physiology and Behavior at the UC Davis College of Biological Sciences, that crosstalk is between the cells that control your body's response to sugar, and understanding the conversation can help us understand, and perhaps ultimately treat, diabetes.

Huising's lab has now identified a key part of the conversation going on between cells in the pancreas. A hormone called urocortin 3, they found, is released at the same time as insulin and acts to damp down insulin production. A paper describing the work appears online on June 15 in the journal *Nature Medicine*.

"It's a beautiful system," Huising said. "It turns out that there is a lot of crosstalk going on in the islets to balance insulin and glucagon secretion. The negative feedback that urocortin 3 provides is necessary to tightly control blood sugar levels at all times."

Diabetes affects millions of Americans every year. Both forms of the disease—type 1, "juvenile" or "insulin-dependent" diabetes, and type 2 or "adult-onset" diabetes—occur when the body fails to regulate the level of sugar properly.

Diabetes is tied to structures called the Islets of Langerhans in the pancreas. Within the islets, beta cells make insulin. Increasing blood sugar stimulates insulin production, which causes the body's cells to pull sugar out of circulation.

The islets also house alpha cells, which make another hormone, glucagon, which acts on the liver to release more glucose into the bloodstream.

An islet of Langerhans with urocortin stained green in beta cells.

Glucagon-making cells are stained red. Credit: Mark Huising.

An islet of Langerhans with urocortin stained green in beta cells. Glucagon-making cells are stained red. Credit: Mark Huising.

Urocortin 3 was originally identified as a hormone that is related to the signal in our brain that kick-starts our stress response. Instead, urocortin 3 is produced by islet beta cells and stored and released alongside insulin. In a series of experiments, Huising's group showed that urocortin 3 causes another cell type in the islets, delta cells, to release somatostatin, which turns down insulin production and acts as a natural brake on the release of insulin.

Urocortin 3 is reduced in laboratory animal models of diabetes and in beta cells from diabetic patients. Without urocortin 3, islets produce more insulin, but at the same time lose control over how much insulin they release.

By understanding how different cells and systems communicate to regulate blood sugar, Huising hopes to get a better understanding of what happens when this regulation goes wrong, leading to the different forms diabetes. Eventually this approach could lead to new ways to treat or prevent the disease.

More information: Urocortin3 mediates somatostatin-dependent negative feedback control of insulin secretion, *Nature Medicine* (2015) DOI: 10.1038/nm.3872

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