

# New potential target for treatment of diabetes

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Researchers at Karolinska Institutet have discovered that one of the building blocks in the calcium channels in the pancreatic beta cells play an important role in regulating our blood glucose values. Treatments

aimed at this building block may be a new way to combat primarily type 2 diabetes the researchers suggest in an article in the scientific journal *Cell Reports*.

Beta cells in the pancreas produce the hormone [insulin](#), which regulates the [blood glucose](#) level in our bodies. In diabetes, the beta cells have lost part or all of their function. Calcium ions ( $\text{Ca}^{2+}$ ) act as an important signal for the release of insulin. When blood [glucose](#) increases, this causes the levels of  $\text{Ca}^{2+}$  in the beta cells to increase, triggering the release of insulin. Under normal conditions the  $\text{Ca}^{2+}$  signal displays a specific regular pattern when the cells are stimulated by glucose. When, on the other hand, the beta cells are not able to release normal amounts of insulin, as in diabetes, this pattern changes.

## **Identified cause of reduced release of insulin**

The level of  $\text{Ca}^{2+}$  increases in the beta cell when a specific calcium channel, made up of several different building blocks, opens in the beta cell's wall. Per-Olof Berggren's research group at Karolinska Institutet has previously shown that one of the building blocks in the channel, the so-called  $\beta 3$  subunit, plays an important regulatory role.

"In our new study, we are able to show that beta cells from diabetic mice have an increased amount of the  $\beta 3$  subunit and that this causes an altered  $\text{Ca}^{2+}$  pattern, a reduced release of insulin, and thereby impaired blood glucose regulation," says Per-Olof Berggren, Professor at the Rolf Luft Research Centre for Diabetes and Endocrinology at the Department of Molecular Medicine and Surgery at Karolinska Institutet, who led the study.

## **Better regulation of the blood glucose levels**

When the researchers reduced the amount of the  $\beta 3$  subunit in the beta cells in the diabetic mice, the  $\text{Ca}^{2+}$  signal normalised and thereby the release of insulin, resulting in better regulation of the [blood glucose levels](#). They also saw that mice that totally lacked the  $\beta 3$  subunit demonstrated a better beta cell function and blood glucose regulation when they were given a diabetogenic diet. When the researchers tried transplanting beta cells without the  $\beta 3$  subunit into mice with diabetes, the [blood](#) glucose regulation of the mice improved.

Experiments with human beta [cells](#) showed that the release of insulin deteriorates with increased amounts of the  $\beta 3$  subunit.

"Our findings indicate that just this building block in the calcium channel can be a new target for treating type 2 diabetes. However, even in type 1 diabetes manipulation of the beta 3 subunit may be beneficial in order to establish better functioning insulin secreting [beta cells](#) for transplantation," says Per-Olof Berggren.

**More information:** Kayoung Lee et al. Blocking  $\text{Ca}^{2+}$  Channel  $\beta 3$  Subunit Reverses Diabetes, *Cell Reports* (2018). [DOI: 10.1016/j.celrep.2018.06.086](#)

Provided by Karolinska Institutet

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