New discovery a step towards better diabetes treatment

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In today's issue of the prestigious journal *Cell Metabolism* Uppsala scientists are presenting new findings that shed light on the processes that determine the release of the blood sugar-lowering hormone insulin. The discovery is based on the development of image analysis methods that make possible the detailed study of events immediately inside the plasma membrane of the insulin-secreting cells.

Cyclic AMP (cAMP) is a universal messenger molecule that controls a number of different
functions inside the cell. For example, it plays a role in the release of insulin from the beta
cells in the pancreas (see Facts). It is well-known that the production of cAMP explains how certain hormones can amplify insulin secretion. On the other hand, it has been unclear to what extent cAMP also contributes to the major release of insulin triggered by an increase in blood sugar (glucose).

Anders Tengholms research team at Uppsala University has developed methods that make it
possible for the first time to measure both the secretion of insulin and the cAMP concentration
in individual beta cells. The results show that ATP, the energy-rich molecule that is produced
when glucose is metabolized, causes an increase in cAMP concentration right at the cell
membrane where the release of insulin takes place. This increase varies

rhythmically and
coincides with similarly regular variations in another stimulant messenger, the calcium ion,
resulting in pulsatile secretion of insulin.

Optimal glucose-induced insulin secretion requires that the varying cAMP
and calcium signals are coordinated in time. The study sheds new light on the cellular
mechanisms that underlie the pulsatile release of insulin in healthy individuals, says Anders Tengholm.

The discovery that the cell metabolism directly stimulates the production of cAMP
illustrates a new principle for the regulation of this messenger molecule. The connection between metabolism and cAMP is not only important for the secretion of insulin; it also
plays a role in gene regulation, cell growth, and cell survival. The observations thereby pave the way for understanding of the disturbed beta cell function in type 2 diabetes and for the
development of new drugs for the disease.

Source: Uppsala University