Shb-deficiency impairs glucose –stimulated insulin secretion by increasing secretion of insulin in the absence of glucose

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Diabetes is a serious disease with unknown cause. There are two kinds of diabetes. Type 1 diabetes which is an autoimmune disease and happens because of the pancreatic beta cells' destruction and results in deficiency in insulin production and type 2 diabetes which happens because the muscle and other tissues normally do not react to insulin and do not take up glucose from the blood stream.

Impaired glucose homeostasis due to insufficient insulin secretion is observed in the absence of Shb. In addition, the beta-cells exhibit reduced stress sensitivity. This adaptor protein has introduced as a flexible component in different intracellular signaling pathways which results in different cellular responses like proliferation, differentiation, cell migration and cell death based on the situation. There is an interaction between Shb with insulin receptor substrate 1 and 2 after insulin stimulation and this promotes FAK-association and PI3Kinase and ERK activation and finally results in pro-proliferative and anti-apoptotic signaling. The general rationale for this project is to survey for gene expression changes that explain reduced insulin secretion in Shb knockout islets of Langerhans.

The islets cell were isolated from the chosen mice pancreatic tissue and picked under a stereo microscope and after RNA isolation, the RNA yield was determined with a spectrophotometer at 260 nm. After real-time RT-PCR, the CT values were calculated and standardized against Beta-actin. All results of this study suggested that the expression changes of genes used in this experiment do not explain reduced insulin secretion in Shb knockout islets of Langerhans. To understand the signaling pathways responsible for the reduced insulin secretion in Shb deficient islets, western blot for ERK, Akt, IRS1 was done. Strong expression of pAkt and pIRS1 in knockout mice was observed which could suggest that knockout islets release insulin in the absence of glucose thus explaining the aberrant insulin secretory profile.

Degree project in biology, Master of science (2 years), 2012
Examensarbete i biologi 30 hp till masterexamen, 2012
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