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DIABETES

SFRP4—a biomarker for islet dysfunction?

Secreted frizzled-related protein 4 (SFRP4) reduces insulin secretion and is a potential biomarker for islet dysfunction in type 2 diabetes mellitus (T2DM), report researchers.

Mahdi *et al.* discovered these insights into the pathophysiology of T2DM by the analysis of global gene expression in human pancreatic islets. The researchers identified a group of co-expressed genes (also called a gene co-expression module) associated with T2DM, reduced insulin secretion and elevated HbA_{1c} levels after analysing global microarray expression data from human islets of 48 individuals, including 10 with T2DM. This module was enriched for IL-1-related genes.

The investigators identified *SFRP4* as a gene highly expressed in islets from patients with T2DM. The protein encoded by *SFRP4* is an extracellular regulator of the Wnt pathway, and has roles in tissue development, cancer and phosphate metabolism. Further study revealed that the expression and release of SFRP4 from islets was stimulated by IL-1β. Furthermore, elevated systemic SFRP4 levels led to reduced glucose tolerance as a result of decreased islet expression of voltage-gated Ca^{2+} channels and supressed insulin exocytosis.

Interestingly, levels of SFRP4 were elevated in serum of patients a few years before they developed T2DM, which indicates that this protein has potential to be used as a biomarker for T2DM. The researchers also point out that their data suggest that SFRP4 could be a therapeutic target for the treatment of islet dysfunction.

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Original article Mahdi, T. *et al.* Secreted frizzled-related protein 4 reduces insulin secretion and is overexpressed in type 2 diabetes. *Cell Metab.* doi:10.1016/j.cmet.2012.10.009