

A system genetics approach identifies novel genes and pathways for type II diabetes in human islets

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Impaired insulin secretion from pancreatic islets represents a key pathogenic defect in type 2 diabetes (T2D). To date, More than 48 common genetic variants associated with T2D have been identified which explain only 15% of the diseases heritability. Thereby, there is a need for alternative approaches to identity novel genes for T2D. We have been fortunate to have a large collection of human pancreatic islets from cadaver donors. These islets were systematically characterized by performing cDNA microarray and GWAS in addition to measuring insulin response to glucose and HbA1c.

Using these recourses, we analyzed *cis* and *trans* effect of T2D-associated SNPs on gene expression in human islets. As well, we profiled the expression for all known T2D- genes (48 genes) located near T2D risk variants in pancreatic islets.

In attempt to identify additional T2D genes, we combined data from human islets on genetics, gene expression, protein-protein interaction and function studies to build a global map of genes contributing to islet dysfunction in T2D. We identified gene co-expression and protein-protein interaction networks that were strongly associated with islets insulin secretion and HbA1c. Also, 5 novel T2D genes were identified, of which *CHL1*, *LRFN2*, *RASGRP1* and *PPM1K* were validated in INS-1 clonal beta cells for impact on insulin secretion, whereas *GPR120* affected apoptosis in human islets. In addition, we showed that expression variation of 20 genes in human islets explained 24% of the variance in HbA1c. This study present an alternative route to identification of novel genes involved in T2D pathogenesis.

Biography

Jalal Taneera has completed his Ph.D. at the age of 33 years from Lund University, department of islets patho-physiology and postdoctoral studies from the same university. He is senior scientist at department of Diabetes and endocrinology at Lund University. He has published more than 18 papers in reputed journals on diabetes research.

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