Identification of novel genes for glucose metabolism based upon expression pattern in human islets and effect on insulin secretion and glycemia

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Supplementary note

A brief description of the top correlated genes

**MCF2L2** (MCF.2 cell line derived transforming sequence-like 2) is a protein-coding gene. A genetic variation within MCF2L2 was reported to be associated with T2D in a Japanese study [1]. Also, there is evidence that genetic polymorphisms within MCF2L2 have effects on the resistance of diabetic nephropathy (DN) in female T1D patients [2].

**WSCD2** (WSC domain containing 2) is a protein-coding gene. WSCD2 was reported for association with hypertension in a Japanese study [3]. No reports for association with T2D.

**TAGLN3** (transgelin 3) is a protein-coding gene. TAGLN3 has been previously associated with brain alterations due to chronic exposure to alcohol [4]. No reports for association with T2D.

**B3GALNT2** (beta-1,3-N-acetylgalactosaminyltransferase 2) is a protein-coding gene. GO annotations related to this gene include galactosyltransferase activity. Mutations in B3GALNT2 can cause congenital muscular dystrophy and hypoglycosylation of α-dystroglycan [5]. Overexpression of B3GALNT2 showed to be involved in the cell growth of breast cancer [6].

**KCNH8** (potassium voltage-gated channel, subfamily H (eag-related), member 8) is a protein-coding gene. The gene is associated with neuronitis. GO annotations for KCNH8 include phosphorelay sensor kinase activity and voltage-gated potassium channel activity. KCNH8 has previously been linked to T2D through regulation of LXRβ gens promoter activity, mutation of KCNH8 significantly reduced the promoter activity and impaired the glucose response [7].

**MYC** (v-myc avian myelocytomatosis viral oncogene homolog) is a protein-coding gene. The gene is associated with Burkitt's lymphoma and uterine corpus cancer. GO annotations related to this gene include protein dimerization activity and sequence-specific DNA binding transcription factor activity. Myc was reported as a principal upstream driver of beta-cell proliferation in rat insulinoma cell lines and is an effective mediator of human beta-cell replication [8]. It has been shown that Myc is a mediator of glucotoxicity and can directly induce impaired insulin secretion and loss of beta cell mass in vivo [9,10].

**IL1R2** (interleukin 1 receptor, type II), is involved in cell proliferation, differentiation, survival/apoptosis, viral infection and autoimmune diseases. The gene located in IDD locus which reported to provide a significant amount of protection from diabetes in NOD mice. Higher expression of IL1R2 was reported in human diabetic but with no influence on insulin secretion after siRNA silencing [11].

**RPGR** (retinitis pigmentosa GTPase regulator) is a protein-coding gene. GO annotations related to this gene include protein binding and guanyl-nucleotide exchange factor activity. The gene is primarily associated to retinitis pigmentosa [12] and reduced orientation of respiratory cilia [13]. No reports for association with T2D.
KLF6 (Krumpel-like factor 6) is a protein-coding gene, and is affiliated with the lncRNA class. KLF6 associated with prostate cancer, progression and metastasis and transient global amnesia. GO annotation related the gene to DNA binding and zinc ion binding. KLF6 was reported to regulate the liver GCK promoter-reporter and contribute to the development of hepatic insulin resistance [14].

CC13 (chemokine (C-C motif) ligand 13) is a protein-coding gene. The gene associated with far eastern spotted fever and gastric adenocarcinoma diseases. CCL13 functions as chemotactic factor that attracts monocytes, lymphocytes, basophils and eosinophils, but not neutrophils and plays a role in the accumulation of leukocytes at both sides of allergic and non-allergic inflammation. CCL13 has been reported as critical molecules that linked obesity and chronic inflammation in Japanese subjects [15].

SLC16A7 (solute carrier family 16 (monocarboxylate transporter), member 7) is a protein-coding gene. The gene associated with embryonal rhabdomyosarcoma, colorectal and prostate cancer. It encodes a metabolite transporting protein with highest affinity for pyruvate and lactate. SLC16A7 has been shown for being directly regulated by HNF1A [16].

ATP4A (ATPase, H+/K+ exchanging, alpha polypeptide) is a protein-coding gene. The gene is associated with dyskinesia of esophagus, and gastric outlet obstruction. GO annotations related to this gene include protein heterodimerization activity and hydrogen:potassium-exchanging ATPase activity. ATP4A is a key function in gastric secretion and a major antigen in autoimmune atrophic body gastritis. No reports for linked with diabetes [17].

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References


