
# Polymorphisms in the gene encoding the voltage-dependent Ca(2+) channel Ca (V)2.3 (CACNA1E) are associated with type 2 diabetes and impaired insulin secretion.



Author: Holmkvist J.
Tojjar D.
Almgren P.
Lyssenko V.
Lindgren C M
Isomaa B.
Tuomi T.
Berglund G.
Renström E.
Groop L.

Author Affiliation: Department of Clinical Sciences-Diabetes and Endocrinology, CRC, Malmö University Hospital MAS, Lund University, Malmo, Sweden, johan.holmkvist@med.lu.se.

Source: Diabetologia. 2007 Dec;50(12):2467-75

Date: Dec-2007

Language: English

Publication Type: Article

Abstract: AIMS/HYPOTHESIS: Glucose-stimulated insulin secretion is dependent on the electrical activity of beta cells; hence, genes encoding beta cell ion channels are potential candidate genes for type 2 diabetes. The gene encoding the voltage-dependent Ca(2+) channel Ca(V)2.3 (CACNA1E), telomeric to a region that has shown suggestive linkage to type 2 diabetes (1q21-q25), has been ascribed a role for second-phase insulin secretion. METHODS: Based upon the genotyping of 52 haplotype tagging single nucleotide polymorphisms (SNPs) in a type 2 diabetes case-control sample (n = 1,467), we selected five SNPs that were nominally associated with type 2 diabetes and genotyped them in the following groups (1) a new case-control sample of 6,570 individuals from Sweden; (2) 2,293 individuals from the Botnia prospective cohort; and (3) 935 individuals with insulin secretion data from an IVGTT. RESULTS: The rs679931 TT genotype was associated with (1) an increased risk of type 2 diabetes in the Botnia case-control sample [odds ratio (OR) 1.4, 95% CI 1.0-2.0, p = 0.06] and in the replication sample (OR 1.2, 95% CI 1.0-1.5, p = 0.01 one-tailed), with a combined OR of 1.3 (95% CI 1.1-1.5, p = 0.004 two-tailed); (2) reduced insulin secretion [insulinogenic index at 30 min p = 0.02, disposition index (D (I)) p = 0.03] in control participants during an OGTT; (3) reduced second-phase insulin secretion at 30 min (p = 0.04) and 60 min (p = 0.02) during an IVGTT; and (4) reduced D (I) over time in the Botnia prospective cohort (p = 0.05). CONCLUSIONS/INTERPRETATION: We conclude that genetic variation in the CACNA1E gene contributes to an increased risk of the development of type 2 diabetes by reducing insulin secretion.

PubMed ID: 17934712 View in PubMed