Human calcium/calmodulin-dependent protein kinase II gamma gene (CAMK2G): cloning, genomic structure and detection of variants in subjects with type II diabetes.

Gloyn,AL; Desai,M; Clark,A; Levy,JC; Holman,RR; Frayling,TM; Hattersley,AT; Ashcroft,SJ

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AIMS/HYPOTHESIS: Ca(2+)/calmodulin-dependent protein kinase II, is expressed in the pancreatic beta cells and is activated by glucose and other secretagogues in a manner correlating with insulin secretion. The activation of Ca(2+)/calmodulin-dependent protein kinase II mediates some of the actions of Ca(2+) on the exocytosis of insulin. We therefore investigated the gene encoding the gamma isoform (CAMK2G) which has been shown to be expressed in human beta cells as a candidate gene for Type II (non-insulin-dependent) diabetes mellitus. METHODS: Human CAMK2G was cloned from a total human P1 artificial chromosome library using a partial Ca(2+)/calmodulin-dependent protein kinase gamma(E) cDNA probe. Positive PAC clones were localised to chromosome 10q22 by fluorescence in situ hybridisation. To obtain structural information and the sequences of the exon-intron boundaries, the published genomic structures of the rat and mouse genes allowed the putative exon-intron boundaries of human CAMK2G to be amplified by vectorette polymerase chain reaction and sequenced. Sequence variants in each exon were identified using single stranded conformational polymorphism analysis. RESULTS: The human CAMK2G gene comprises 22 exons which range in size between 43 to 230 bp. Screening of the exons and exon-intron boundaries identified two single nucleotide polymorphisms. These did not show association with diabetes in 122 patients and 144 control subjects. CONCLUSIONS/INTERPRETATION: We have identified the genomic structure of CAMK2G to enable further study of this potential candidate gene. Variation in this gene is not strongly associated with diabetes in Caucasians in the United Kingdom. We have identified two single nucleotide polymorphisms which, with appropriately large case control studies, can be used to assess the role of CAMK2G in the susceptibility to Type II diabetes.