

Abstract

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Association of the vitamin D metabolism gene CYP27B1 with type 1 diabetes.

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OBJECTIVE: Epidemiological studies have linked vitamin D deficiency with the susceptibility to type 1 diabetes. Higher levels of the active metabolite, 1alpha,25-dihydroxyvitamin D, could protect from immune destruction of the pancreatic beta cells. 1alpha,25-dihydroxyvitamin D is derived from its precursor 25-hydroxyvitamin D by the enzyme 1alpha-hydroxylase encoded by the CYP27B1 gene, and is inactivated by 24-hydroxylase encoded by the CYP24A1 gene. Our aim was to study the association between the CYP27B1 and CYP24A1 gene polymorphisms and type 1 diabetes.

METHODS: We studied 7,854 patients with type 1 diabetes and 8,758 controls from Great Britain and 2,774 affected families. We studied four CYP27B1 variants, including common polymorphisms -1260C>A (rs10877012) and +2838T>C (rs4646536), and 16 tag polymorphisms in the CYP24A1 gene.

RESULTS: We found evidence of association with type 1 diabetes for CYP27B1 -1260 and +2838 polymorphisms, which are in perfect linkage disequilibrium. The common C allele of CYP27B1 -1260 was associated with an increased disease risk in the case-control analysis (OR = 1.07, P = 2.9 x 10⁻³), and in the fully independent collection of families (RR = 1.11, P = 6.4 x 10⁻³). The combined support of an association for CYP27B1 -1260 is P = 3.8 x 10⁻⁶. For the CYP24A1 gene we found no evidence of association with type 1 diabetes (multilocus test P = 0.23).

CONCLUSIONS: The present data provides evidence that common inherited variation in the vitamin D metabolism affects susceptibility to type 1 diabetes.

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