



Original article

## HLA non-class II genes may confer type I diabetes susceptibility in a mapuche (Amerindian) affected family

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### Abstract

A rare case of type I diabetes is studied in an Amerindian (Mapuche) family from Chile, analyzing glutamic acid decarboxylase, islet-cell autoantibodies and human leukocyte antigen (HLA) genes. The affected sib is the only one that has one specific HLA haplotype combination that differs from the other sibs only in the HLA class I genes. It is concluded that HLA diabetes susceptibility factors may be placed outside the class II region or even that susceptibility factors do not exist in the HLA region in this Amerindian family.

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### 1. Introduction

Insulin-dependent diabetes mellitus or type I diabetes (IDDM-1) is one of the most common diseases of childhood with an incidence rate that appears to be increasing in all studied countries [2]. Between 1986–1993, a low incidence of type I diabetes

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(2.5/100.000 inhabitants/year) was found in Santiago de Chile [8], but during the 1994–1998 period the incidence rose to 4.1/100.000 inhabitants/year [8]. Type I diabetes is thought to be in part an autoimmune process that destroys insulin-producing beta cells of the pancreas. In this disease several autoantibodies can be found, including, insulin antibodies (IAA), cytoplasmic islet cell antibodies (ICA) and glutamic acid decarboxylase antibodies (GAD) [4]. Human leukocyte antigen (HLA) genes bear most of the genetic susceptibility in Spanish or Mediterranean-descent Caucasoids [5,10] (<http://www.ncbi.nlm.nih.gov/omim>), and studies carried out revealed that the major histocompatibility complex (MHC), also designated IDDM-1, is the major, but not the exclusive, type 1 diabetes susceptibility locus. Genes outside the MHC have also been implicated in diabetes susceptibility, such as those of the insulin, the insulin receptor or cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4) genes. On the other hand, not all carriers of the “susceptible genes” and autoantibodies develop the disease, which suggests that environmental factors also play a role in triggering the autoimmune process. Evidence of a protective influence of breast feeding was first derived from studies which reported a negative correlation between incidence rates of breast feeding and type I diabetes [5,6]. The Chilean population is formed by an admixture of Amerindian native groups and descendants of several European countries migrants [9]. Mapuche subjects are the largest native group in the country, and they might or might be not descendants of Asian migrations that settled in the southern part of Chile up to Patagonia [1]. The total Mapuche population is about 900,000 inhabitants distributed throughout the country, mainly living in rural areas. Data about the low incidence of diabetes (<0.001/100.000 inhabitants/year in type II and <0.4/100.000 inhabitants/year in type I diabetes) was published in the rural population of Mapuche Indians in 1985 [3].

In the present work, we have analyzed a rare case of type I diabetes that appeared for the first time in a rural Mapuche Amerindian family (Fig. 1) with at least four generations of Mapuche ancestors; both of the sib’s parents showed a normal glucose tolerance test. It is shown that HLA factors other than HLA class II genes may be involved in the development of Amerindian type I diabetes [7] (<http://www.ncbi.nlm.nih.gov/omim/>) or even that not HLA factors may be involved.

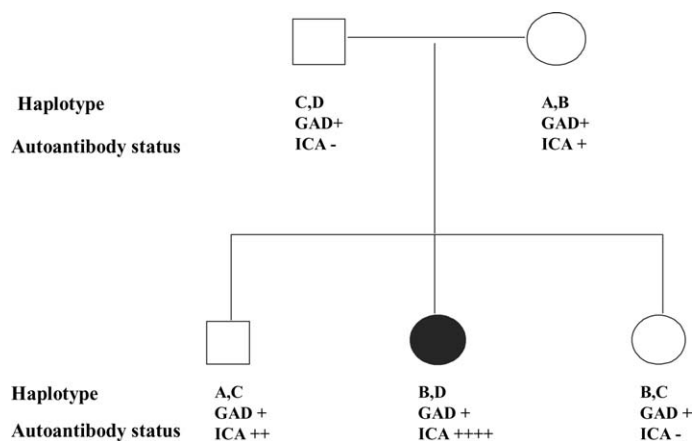


Fig. 1. Family tree indicating the haplotype composition of parents and children, along with the autoantibody status.

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