VARIANTS OF THE SLC30A8 GENE ASSOCIATED WITH ANTI-ZNT8 ANTIBODY AND PREDISPOSITION TO TYPE 1 DIABETES

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Introduction: The SLC30A8 gene encodes the zinc transporter protein (ZnT8), present in the membrane of insulin granules and expressed in pancreatic beta cells. The ZnT8 protein was identified as an autoantigen in T1D and the rs2466293 and rs16889462 variants were associated with susceptibility to type 1 diabetes (T1D), but there are few data in Latin-America and in the multi-ethnic Brazilian population.

Objectives: The objective was to evaluate the influence of the variants rs2466293 and rs16889462 in the predisposition to T1D and in the frequency of anti-ZnT8 autoantibody (Ab).

Materials and Methods: We evaluated 623 patients T1D (age: 25 ± 12.7 years; 80% white) and 650 controls (age: 29 ± 11.2 years; 63.4% white). The variants rs2466293 and rs16889462 were genotyped by the Vera Code Golden Gate (Illumina) methodology. Autoantibodies against zinc transporter (anti-ZnT8) were determined by ELISA (Kronus, USA CV of <7%) and against glutamic acid decarboxylase (anti-GAD65) and tyrosine phosphatase (anti-IA2) by radioimmunoassay (RSR Limited, UK, CV <7%). The genotypic associations were analyzed using the Chi-square test or Fisher exact test.

Discussion and results: The frequencies of genotypes of rs2466293 and rs16889462 variants were in Hardy-Weinberg Equilibrium, were similar in patients and controls and were independent of gender. However, in non-whites, the rs2466293 AA genotype conferred protection to T1D, prevailing in controls (57.1%) compared to T1D patients (43.7%); p = 0.0233; OR = 0.5821; CI = 0.3716 to 0.9117. The rs1688946 AG genotype, although rare, was associated with higher frequency of anti-ZnT8 Ab (75%) when compared to GG (48%); p = 0.0415; OR = 3.245; CI = 1.023 to 10.288. None of SLC30A8 variants influenced on age at diagnosis of T1D or on anti-GAD65 and anti-IA2 Abs frequency.

Conclusion: The rs2466293 and the rs16889462 variants in SLC30A8 gene were related to T1D predisposition and to anti-ZnT8 Ab frequency respectively in our population.

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Key Words: Type 1 Diabetes, Anti-ZnT8, SLC30A8