Association of *TNF-α*, *CTLA4*, and *PTPN22* polymorphisms with type 1 diabetes and other autoimmune diseases in Brazil

N.A.C. Tavares¹, M.M.S. Santos¹,³, R. Moura¹,³, J. Araújo², R.L. Guimarães¹,³, S. Crovella¹,³ and L.A.C. Brandão¹,⁴

¹Laboratório de Imunopatologia Keiso Asami, Universidade Federal de Pernambuco, Recife, PE, Brasil
²Unidade de Endocrinologia Pediátrica do Hospital das Clínicas, Universidade Federal de Pernambuco, Recife, PE, Brasil
³Departamento de Genética, Universidade Federal de Pernambuco, Recife, PE, Brasil
⁴Departamento de Patologia, Universidade Federal de Pernambuco, Recife, PE, Brasil

Corresponding author: N.A.C. Tavares
E-mail: nathaliadealencar@gmail.com

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ABSTRACT. Type 1 diabetes mellitus (T1D) is a complex disorder characterized by an autoimmune response against human pancreatic beta-cells. Patients with T1D can also develop a response toward one or more other factors, such as in autoimmune thyroiditis (AITD) and celiac disease (CD). In the presence of T1D + AITD, the patient is diagnosed with autoimmune polyglandular syndrome type III (APSIII); patients with APSIII may also present with CD. These diseases have a strong genetic component and share many susceptibility genes, suggesting potentially overlapping pathogenic pathways. Polymorphisms in the *TNF-α* (rs1800629), *CTLA-4* (rs231775), and *PTPN22* (rs2476601) genes have been previous associated with T1D; however, there is no consensus regarding their role in...
T1D and scarce literature focusing on AIDT and/or CD. Thus, we analyzed these genetic variants in 205 Northeast Brazilian patients with T1D and with/without AITD and/or CD, and in 308 healthy controls. The \textit{PTPN22} gene variants were associated with T1D susceptibility and APSIII [odds ratio (OR) = 2.57 and 2.77, respectively]. \textit{CTLA4} rs231775 and \textit{TNF-\alpha} rs1800629 were not associated with T1D onset in the Brazilian population. However, when comparing APSIII individuals in the T1D only group, we observed an association of the \textit{TNF-\alpha} SNP in the allelic (\(P = 0.0442\); OR = 0.44) and dominant models (\(P = 0.0387\); OR = 0.40). This study reinforces the importance of \textit{CTLA-4} and other variants in unraveling the pathogenic mechanisms of T1D in different populations and in understanding their relationships with the development of other T1D-related autoimmune diseases.

\textbf{Key words:} Type 1 diabetes mellitus; Autoimmune disease; \textit{CTLA-4}; \textit{PTPN22}; \textit{TNF-\alpha}