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Studies on the role of immunomodulatory *HLA-G* molecule/gene in diabetes

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HLA-G has well-recognized tolerogenic properties and the constitutive expression of *HLA-G* has been reported in few organs, including pancreas. Since little attention has been devoted to the role of *HLA-G* in diabetes, we evaluated: *HLA-G* expression in pancreas of type 1 (T1D), type 2 (T2D) diabetes patients and in non-diabetic pancreatitis; differential gene and microRNA expression in T1D, T2D, and gestational diabetes (GDM) and; *HLA-G* regulatory gene variability in T1D. *HLA-G* immunohistochemical staining was observed in islet and acini cells in histologically normal pancreas. *HLA-G* was weakly observed in the few remaining acinar cells and in lympho-mononuclear cell infiltration in T1D. In T2D, *HLA-G* expression was closely similar to normal pancreas. *HLA-G* expression in non-specific chronic pancreatitis was similar to T1D. The transcriptional profiles of peripheral blood lympho-mononuclear cell mRNA and microRNA obtained from T1D, T2D and GDM patients showed that the transcriptional profiles of GDM patients was closer to T1DM than to T2D. Major gene clusters shared between T1DM and GDM that differed from T2DM were associated with inflammation, chemokine/cytokine, toll-like receptor and nod-like receptor signaling and with natural killer cell genes which modulated *HLA-G* expression. Compared to controls, several *HLA-G* polymorphic sites at promoter (increased PROMOG0103f, decreased PROMOG0104a haplotypes) and 3'untranslated region (increased+3001 T allele, decreased+3010 CC genotype) were associated with T1D. The decreased pancreas expression of the immunoregulatory *HLA-G* molecule, together with the presence of modulated genes associated with inflammation in a genetic susceptible host may contribute to diabetes development.

Biography

Eduardo Antônio Donadi has completed his PhD at University of São Paulo, Brazil, and Post-doctoral studies at Virginia Mason Research Center, Washington University, Seattle. He is the Director of Laboratory of Immuno-genetics at the Faculty of Medicine of Ribeirão Preto, Brazil. He has published more than 260 papers in reputed journals and has a long-standing collaboration with the group of Philippe Moreau in Paris to study the regulation of the *HLA-G* gene.

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