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Human leukocyte antigen (HLA)-G gene regulatory region polymorphisms in patients with papillary thyroid carcinoma

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OBJECTIVES: Considering that HLA-G is an immune checkpoint molecule that is expressed in specimens of Papillary Thyroid Carcinoma (PTC), we evaluated the genetic diversity of HLA-G gene regulatory regions in patients with PTC and its association with clinical and pathological features. MATERIALS AND METHODS: Polymorphic sites at HLA-G gene regulatory regions (5' upstream regulatory region - 5'URR and 3' untranslated region - 3'UTR) were characterized by Sanger sequencing analyses in blood samples of 118 patients with PTC and 157 healthy controls and analyzed as haplotypes. RESULTS: Considering HLA-G 5'URR, patients with PTC exhibited higher frequency of the G010101a (p=0.0010) and G010101d (p=0.0403) haplotypes when compared to controls. On the other hand, the G0104a haplotype was underrepresented in PTC (p=0.0007). The G0104a haplotype was more frequent in PTC patients with tumors size ≥ 2cm (p=0.0476) when compared to tumors < 2cm. The G010101d haplotype was significantly more frequent in PTC patients who presented extrathyroidal extension of the tumor (p=0.0302), while G010102a haplotype was less frequent (p=0.0192). The G010101f haplotype was more frequent in PTC patients who presented advanced stage of the disease at diagnosis (p=0.0476). Regarding HLA-G 3'UTR, patients with PTC exhibited higher frequency of UTR-1 (p=0.0137) and UTR-6 (p=0.0172) when compared to controls, while UTR-3 haplotype was less frequent (p=0.0255). Furthermore, UTR-3 haplotype was more frequent in PTC patients with tumors size ≥ 2cm (p=0.0298) when compared to tumors < 2cm. CONCLUSION: Regulatory region polymorphisms associated with increased HLA-G production were also associated with more severe PTC manifestations.