OR22 *HLA-G* REGULATORY AND CODING REGION HAPLOTYPES IN PAPILLARY THYROID CARCINOMA

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Aim: To evaluate *HLA-G* coding and regulatory (promoter and 3' untranslated region-3'UTR) haplotypes in papillary thyroid carcinoma (PTC) patients and their associations with clinical and histopathological features.

Methods: We studied 185 PTC patients and polymorphic sites distributed along the three different *HLA-G* gene regions were characterized by Sanger sequencing. *HLA-G* haplotype associations were analyzed using the Fisher exact test, calculating odds ratio (OR), confidence interval (CI) and*P*-values.

Results: More than 90 variation sites were observed along the whole gene. Considering the **promoter region**, i) 010101d haplotype was less frequent in patients presenting classical histological variant of PTC (OR = 0.2789, CI 95% = 0.0755–1.0304, *P* = 0.0499), ii) 0104a haplotype was less frequent in patients presenting tumor multicentricity (OR = 0.3360, CI 95% = 0.1446–0.7810, *P* = 0.0089), and iii) 0103a haplotype was more frequent in patients presenting advanced stage of PTC at diagnosis (TNM staging III and IV) (OR = 0.3541, CI 95% = 0.1360–0.9219, *P* = 0.0370). Regarding the **coding region**, the $G{*}01{:}01{:}12^{(+324G)}$ allele was associated with the presence of tumor multicentricity (OR = 11.2857, CI 95% = 1.3438–94.7784, *P* = 0.0094) and Hashimoto's thyroiditis (OR = 6.4851, CI 95%=1.2383–33.9649, *P* = 0.0224). At **3'UTR**, the UTR-02 haplotype was overrepresented (OR = 1.6759, CI 95% = 1.0616–2.6456, *P* = 0.0328) and UTR-03 haplotype was underrepresented (OR = 0.4106, CI 95% = 0.1912–0.8815, *P* = 0.0200) in patients presenting tumor multicentricity. No association regarding tumor size, local invasion, metastasis at diagnosis and extrathyroidal extension was observed.

Conclusions: Although HLA-G is expressed in more than 80% of PTC specimens, *HLA-G* alleles were primarily associated with tumor morbidity, indicating that local factors may transcriptional and posttranscriptionally modulate *HLA-G* expression.

OR23 HLA CLASS II GENES CORRELATE WITH PROTECTIVE NEUTRALIZING ANTIBODY TITERS IN A DENGUE VACCINE EFFICACY TRIAL

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Aim: A tetravalent, live attenuated dengue vaccine demonstrated efficacy, safety and immunogenicity in several clinical trials in Asia and Latin America. Efficacy differed based on infecting serotypes, presence of pre-existing dengue neutralizing antibody (NAb) titers and age. HLA class II molecules expressed on antigen presenting cells mediate CD4+ T cell stimulation of antibody production by B cells involved in vaccine-induced responses. We hypothesized that the differences in observed vaccine efficacy could be due to variation in NAb immune responses in conjunction with host HLA class II genes.

Methods: Samples were available from a subset of subjects that took part in the first tetravalent dengue vaccine efficacy trial conducted in Thailand. DNA was extracted from 335 saliva samples and HLA genotyping was performed using next-generation sequencing (NGS) of full-length genes. A panel of ancestry informative markers (AIMs) was genotyped to assess population stratification. Serotype-specific NAb titers were measured by plaque-reduction neutralization test 28 days after last injection. The association of NAb titers and HLA class II on dengue infection was tested by logistic regression. Linear regression was used to test association of HLA class II alleles with NAb levels after accounting for sex, age, and serotype as covariates. A minimal false discovery rate to account for multiple comparisons, with a two-sided p-value <0.05 and q-value <0.20 was considered statistically significant.

Results: NGS identified 197 HLA class I and II alleles in the Thai Dengue vaccine trial. AIMs analysis did not identify population stratification comparing cases and controls. Magnitude of NAb levels post vaccination was significantly higher in the presence of HLA-DRB1∗11 (p = 0.002, q = 0.08). HLA-DPB1∗03:01 and ∗05:01 presence correlated with pre-existing NAb titers in the placebos (p = 0.005, q = 0.09; p = 0.001, q = 0.04). We did not observe a direct effect of HLA on dengue infection in either the placebo or treatment arm.

Conclusions: These findings suggest that specific HLA class II alleles modulate protective NAb titers in dengue infection. This is an exploratory study to identify signals to replicate in other dengue vaccine clinical studies. Understanding this HLA class II mechanism will enable improved vaccine design.