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 markers (AIMs) was genotyped to assess population stratification. Magnitude of NAb levels post vaccination was assessed by plaque-reduction neutralization test 28 days after last injection. The association of 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.

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.