P013 HLA HOMOZYGOSITY IS SIGNIFICANTLY MORE ASSOCIATED WITH LYMPHOMA THAN ACUTE MYELOGENOUS LEUKEMIA

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Aim: The aim of this study was to investigate a possible association of HLA homozygosity in lymphoma and AML.

Methods: In this study, we examined 655 lymphoma and 1002 AML patients. These patients were typed for possible stem cell transplants between 2006 and 2016. All of the patients were typed at high resolution for HLA-A, B, C, DRB1 and DQB1. The control data set consisted of 1,014,848 high resolution HLA typings from an NMDP database. Homozygosity also included two alleles belonging to the same P-group.

Results: Homozygosity at one or more loci was observed in 39.4% of lymphoma patients ($p = 0.0002$) as compared with 32.0% of AML patients (p = n.s.) and 32.3% of the control population. Lymphoma patients had a significantly higher percentage of homozygosity at every loci with the exception of HLA-C.

Conclusions: Lymphoma is associated with a significantly higher degree of HLA homozygosity at HLA-A, B, DRB1 and DQB1 but AML is not.

Homozygosity at Individual Loci is Increased in Lymphoma Patients

	Lymphoma (%)	Controls (%)	p-value
HLA-A	17.2	13.1	0.0023
HLA-B	9.0	6.0	0.0014
HLA-C	11.0	9.6	0.2626
HLA-DRB1	10.5	8.1	0.026
HLA-DQB1	17.2	13.8	0.013

P014 HLA-C, HLA-E AND HLA-G REGULATORY AND CODING REGION POLYMORPHISMS IN PATIENTS EXHIBITING GESTATIONAL DIABETES MELLITUS

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Aim: Studies on gestational diabetes (GDM) have highlighted the induction of genes involved in the immune response, particularly those associated with inflammation. *HLA-C*, *HLA-E* and *HLA-G* are the only *HLA* genes expressed on trophoblast cells, playing an important role in the modulation of the maternal immune response against the fetus. Considering that: (i) there is a similar transcriptional profile between GDM and the autoimmune type 1 diabetes mellitus; and (ii) some allelic combinations between *KIR* and *HLA* genes, mainly *HLA-C,* are strongly associated with pre-eclampsia and recurrent miscarriage, we investigated the possible role of *HLA-C*, *-E* and *-G* variability in GDM.

Methods: We evaluated 102 GDM and 150 non-GDM women to detect *HLA-C, -E* and *-G* polymorphisms and haplotypes considering the entire gene segment, including the promoter, coding sequence and 3'untranslated region (3'UTR), by using next generation sequencing and a local bioinformatics strategy to get reliable genotypes and haplotypes.

Results: We observed 14 allelic groups when the *HLA-C* gene was evaluated, and two of them (*HLA-C*05,* mainly represented by the C*05:01:01, and *HLA-C*08*, mainly represented by the allele C*08:02:01) were associated with protection against GDM ($P = 0.0376$, OR = 0.3450 and $P = 0.0184$, OR = 0.2894 respectively). An *HLA-C* promoter region here named P09 and a 3'UTR here named U09 are strongly associated with protection against GDM ($P = 0.0376$ OR = 0.3450). These regulatory haplotypes are in fact shared by all C*05 and C*08 alleles here detected, suggesting that the protective feature against GDM could be associated with some trait of these specific regulatory regions or associated with the C*05 or C*08 allele groups or both. The *HLA-E*01:03:05 allele, originally described in a Brazilian population, was observed only in controls, indicating a protection role for GDM ($P = 0.033$ and OR = 0.1343). No associations were observed for the *HLA-G*, considering allele, coding region, promoter, 3'UTR or extended haplotype.

Conclusions: Only *HLA-C* and *HLA-E* were associated with GDM, by mechanisms yet to be understood and explored. The study of other HLA genes, as well as the transcription profiles observed in GDM patients, may increase the understanding of the role of these genes in the pathogenesis of GDM.