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The Cancer Control Challenge:
Better Understanding It to Better Face It

ASSOCIATION OF INDEL POLYMORPHISMS IN PIRNA CODING REGIONS WITH SUSCEPTIBILITY TO ACUTE LYMPHOBLASTIC LEUKEMIA

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Introduction: Acute Lymphoblastic Leukemia (ALL) is one of the leading main causes of cancer-related death in children. The pathogenesis of ALL can be based on the complex interactions among environmental factors, genetic alterations such as Insertion-Deletion polymorphisms (INDEL), and epigenetic alterations, including the dysregulation of non-coding RNAs (ncRNAs). Investigations have demonstrated that the expression of PIWI-interacting RNA (piRNAs) is deregulated in cancerous tissues. However, the understanding of the impact of variants in piRNA regions and their relationship with the development of ALL is still limited. **Objectives**: This work aimed to investigate the allelic and genotypic distribution of three INDEL variants in piRNAs coding regions: rs10651123 (in pseudogene YWHAEP7, encoding piR-hsa-20788), rs59379238 in the intron of the CYP19A1 gene, encoding the piR-hsa-1856) and rs5856040 (in pseudogene AC093664.1, encoding piR-hsa-8395), and the influence of this variability on the development of LLA, in a case-control study, developed with a population of the Brazilian Amazon. **Methods**: This study was approved by the Research Ethics Committee of the Oncology Research Center, number 37386214.3.0000.5634 and 11433019.5.0000.5634. We collected the blood for DNA extraction from 192 GC patients from the Hospital Universitário João de Barros Barreto and 171 unrelated healthy individuals. The polymorphisms were amplified by PCR multiplex and genotyped in ABI PRISM 3130, and the data were analyzed in the software GeneMapper, followed by statistics analyses performed through the software R v 3.1. We verified whether the genotypic distribution of the variants was in Hardy-Weinberg Equilibrium (HWE) using the chi-squared test corrected by Bonferroni method, and the association between the markers and the susceptibility to GC was assessed by the logistic regression for dominant model. P-value ? 0.05 were considered statistically significant. **Results:** In our analyses, we verified that genotypic distribution of all markers were according to HWE, with exception of the rs5856040 variant in both case and control groups. This imbalance appears to be due to

the increase in heterozygotes in this population ($p < 0.05$). We did not observe significant associations between the investigated variants and the susceptibility to ALL: rs10651123 (DD vs others, P = 0.845; OR = 1.056; 95%CI = 0.607- 1.838), (II vs others, P = 0.427; OR = 0.938; 95%CI = 0.801-1.098); rs5856040 (DD vs others, P = 0.121; OR = 0.912; 95%CI = 0.812-1.024), (II vs others, P = 0.097; OR = 1.140; 95%CI = 0.976-1.331); and rs59379238 (DD vs others, P = 0.711; OR = 0.976; 95%CI = 0.859-1.108), (II vs others, P = 0.441; OR = 0.886; 95%CI = 0.652-1.204). **Conclusion**: In the association analysis, no statistically significant association was observed between the variants and susceptibility to ALL. Nevertheless, this was the first study to analyze INDELs in regions encoding piRNAs and its association with ALL, and the discussion raised here contributes to the understanding of the variants present in piRNAs regions and to future studies that evaluate their impact in the development of cancer.

Keywords: INDEL; piRNA; acute lymphoblastic leukemia.