

EVALUATION OF COPY NUMBER CHANGES (CNAs) IN THYROID NEOPLASMS

Authors: Joseane Pereira Honorato¹; Patricia da Costa Moda Celso¹; Edivaldo Herculano Correa de Oliveira^{1,2}

¹ Laboratory of Cytogenomics and Environmental Mutagenesis, Environment Section (SAMAM), Evandro Chagas Institute (ECI), Ananindeua, Brazil.

² Institute of Exact and Natural Sciences, Faculty of Natural Sciences, Federal University of Pará (UFPA), Brazil.

Introduction: The incidence of thyroid cancer (TC) has been increasing globally, yet the proper identification of malignant tumors remains challenging. Copy number alterations (CNAs) are common genomic events in cancer and play a significant role in identifying relevant markers and classifying tumor types, contributing to the understanding of the genetic mechanisms underlying cancer, since the analysis of genes present in these regions helps in the evaluation of the genomic profile, in addition to providing potential biomarkers. **Objectives:** identify patterns in CNAs of neoplastic thyroid tissue samples. **Methods:** The study was approved by the ethics committee IEC/SVS/MS (ID 3.317.960), involved 38 patients with TC admitted to the Ophyr Loyola Hospital in the state of Pará, Brazil. Samples corresponded to 7 benign and 31 malignant tumors, from 34 female and 4 male patients. Tumor sample DNA was extracted and integrity number (DIN) >7. CNAs were detected by aCGH, using Aberration Detection Method 2 (ADM-2) algorithm. $\text{Log}_2\text{Ratio} > 0.25$ and < -0.25 were defined as copy gains and losses, respectively. CNAs were described based on frequency of genomic alterations, considering factors such as tumor classification (benign or malignant), chromosomal regions and frequently altered genes. The biological significance of CNAs was explored through functional enrichment using the Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) databases. Statistical analyses were conducted to evaluate the association between patient health data and CNAs findings, using Mann-Whitney and Pearson test. In our data analysis, we used Python and R programming languages. For statistical tests, values of $p \leq 0.05$ were considered significant. **Results:** CNAs were more frequent in malignant tumors and in female patient samples. The chromosomal region 14q32.33 was frequently in benign and malignant tumors, the chromosomal region 14q11.2 was frequently altered malignant tumors. Non-coding RNA (ncRNA) genes are prominent in terms of the frequency in tumor samples. Genes frequently altered in malignant tumors of female and male patients were associated with different biological processes, highlighting the possible sex bias of TC. CNAs can interfere in a complex manner in the modulation of the tumor microenvironment in TC. **Conclusion:** the results suggest that age, sex and altered chromosomal regions are associated with tumor types. Our results reinforce the role of CNAs in the progression of TC and highlight the importance of clinical and CNAs data for the classification of thyroid tumors, contributing to new approaches for classification, diagnosis and

treatment of this neoplasm. Although the incidence of thyroid cancer (TC) has been increasing globally, the proper identification of malignant tumors remains challenging. CNAs play an important role in the identification of relevant markers and in the classification of tumor types.

Keywords: Thyroid; Neoplasms; CNAs; aCGH; Benign tumors; Malignant tumors.