MOLECULAR ALTERATIONS IN MT-*ND5* GENE IN BREAST CANCER PATIENTS FROM AN AMAZONIAN POPULATION

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Introduction: Mitochondrial DNA (mtDNA) encodes proteins involved in the regulation and homeostasis of cellular metabolism. Alterations in mtDNA regions may lead to metabolic changes and promote tumor growth in various types of malignant neoplasms, including breast cancer. In this context, variants in the *ND5* region, which encodes proteins of Complex I of the respiratory chain, can impair mitochondrial function, contributing to cell proliferation and resistance to apoptosis. **Objectives**: To investigate single nucleotide variations (SNVs) in the *ND5* region in breast tumor samples and associate them with the clinical characteristics of patients from the Pará population. **Methods**: A total of 33 breast tumor samples and 21 control samples were analyzed. This study was approved by the Ethics Committee of the involved institutions. DNA was extracted using a commercial kit, amplified by conventional PCR, and sequenced using the Sanger method. The sequences were aligned with the GenBank reference using BioEdit, and the identified SNVs were analyzed using the MITOMAP, mtDB, and ClinVar databases. Associations between SNVs and clinical data were assessed using statistical tests in BioEstat 5.0 software, with statistical significance set at $p \leq 0.05$. Putative structural alterations in the protein were analyzed using NPS@ and ProtParam, and STRING software was used to predict ND5 protein interactions. **Results**: We identified 25 SNVs in the tumor group and 14 SNVs in the control samples. None of the variants showed a statistically significant association with molecular subtypes or clinical data. Among the identified SNVs, C12705T (I123M) was the most frequent in both tumor (36.7%) and control samples (34.8%). Although this alteration is not listed in ClinVar, previous studies have reported its presence in various pathological conditions, including neurological disorders, respiratory diseases, and cardiac conditions. Additionally, other relevant variants were observed: A12437W (H34R – 5.8%) and G12454A (V40I – 4.4%), considered likely benign and benign, respectively, but previously associated with kidney diseases, liver aging, and tumors such as breast and prostate cancer. These three SNVs result in subtle alterations to the protein structure and may also affect its function. It was also noted that the ND5 protein is part of a broad interaction network, including other proteins of the mitochondrial respiratory chain, such as CO1 and ND1. **Conclusion**: The results indicate that alterations in the *ND5* region are frequent in breast cancer and can lead to structural modifications in the resulting protein. Although no correlations between the SNVs and clinicopathological data were observed, possibly due to the small sample size, the fact that alterations in Complex I of the respiratory chain may lead to mitochondrial dysfunction and cellular oxidative stress underscores the importance of further studies focused on mtDNA. Considering the above, further studies are essential to better understand the functional role of the observed SNVs in the deregulation of cellular energy metabolism.

Keywords: Mitochondrial DNA; Complex I; ND5