

MOLECULAR PROFILE OF CDH1 GENE IN A MIXED-RACE POPULATION FROM THE BRAZILIAN AMAZON WITH GASTRIC CANCER

Patrícia Rodrigues Portugal¹, Ana Clara Araújo dos Santos¹, Marcelo Pio da Silva Tavares¹, Bruna Macedo Lopes¹, Laura de Nazaré Mendes Rodrigues², Marianne Rodrigues Fernandes¹, Juliana Carla Gomes Rodrigues¹, Sidney Emanuel Batista dos Santos¹, Ândrea Ribeiro-dos-Santos⁹, Ney Pereira Carneiro dos Santos¹

¹ Oncology Research Center, Federal University of Pará

² University of the Amazon

³ Human and Medical Genetics Laboratory, Federal University of Pará

Introduction: Gastric cancer (GC) is the fifth most common type of cancer and the fourth leading cause of death related to this disease. In the north of Brazil, this type of cancer is the second most common in men and the fifth in women, which suggests that there may be a genetic influence contributing to this carcinogenesis process. Studies indicate that some genetic factors are important for the development of GC, for example, alterations in important genes such as CDH1, a tumor suppressor gene responsible for producing E-cadherin, a cell adhesion protein that plays an important role in cell growth and differentiation. **Objectives:** To investigate genetic variants in the CDH1 gene in a mixed-race population with gastric cancer, and to compare the allele frequency found with the frequency of the world population. **Methods:** The population consisted of 107 admixed individuals diagnosed with GC, treated at the João de Barros Barreto University Hospital. Genetic material was extracted from peripheral blood using the Biopur Mini Spin Plus 250 Extraction Kit and DNA. DNA quantification was performed using a Nanodrop8000 spectrophotometer (Thermo Fisher Scientific Inc., Wilmington, DE, USA) and quality analysis was performed by 2% agarose gel electrophoresis. The variant library (exome) was prepared using Nextera Rapid Capture Exome (Illumina®, San Diego, CA, USA) and SureSelect Human All Exon V6 (Agilent Technologies, Santa Clara, CA, USA), following the kit protocol provided by the manufacturer. The sequencing reaction was performed by the NextSeq 500® platform (Illumina®, San Diego, CA, USA) using the NextSeq 500 High-output v2 Kit 300 cycle (Illumina®, San Diego, CA, USA). The study was approved by the National Research Ethics Commission (CONEP) and by the Research Ethics Committee of the Institute of Health Sciences of the Federal University of Pará (CAAE: 43199815.9.0000.0018). The frequencies of the variants found were compared with those of other populations using data from the 1000 genomes platform from phase 3. Fisher's Exact Test (statistical program Rstudio v.4.1.2) was used to analyze the results

considering p-value ≤ 0.05 as statistically significant data. **Results:** From the exome analysis and according to SNPeff (which predicts effects of genetic variants, such as amino acid changes), two low-impact variants (rs33964119 and rs1801552) were found in the CDH1 gene. Regarding the rs33964119 variant, it was observed that only the European ($p=0.001$) and South Asian ($p=0.037$) populations were genetically distinct from the mixed-race population evaluated. For the rs1801552 variant, it was also observed that the most genetically distinct population from the mixed-race populations were the Europeans ($p=8.49E-18$), but, in this second analysis, the American population was more distinct than the South Asians ($p=0.008$). **Conclusion:** Only two low-impact variants in one of the genes related to CG susceptibility were found, which raises the possibility that other genes or environmental factors may be contributing to the development of this disease. In addition, it was found that the mixed-race population of the Brazilian Amazon is considerably genetically distinct from the European, South Asian and American populations, based on the allele frequencies of the variants analyzed.

Keywords: CDH1; gastric cancer; brazilian Amazon