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ANÁLISE DE MUTAÇÕES GENÉTICAS MODIFICADORAS DE HISTONAS EM CARCINOMA SEROSO DE OVÁRIO DE ALTO GRAU

ANALYSIS OF HISTONE-MODIFYING GENETIC MUTATIONS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA

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RESUMO

1. INTRODUCTION

Ovarian cancer (OC) represents the poorest prognosis among gynecological malignancies, and its most frequent subtype is high-grade serous ovarian carcinoma (HGSOC)[1,2]. It is known that abnormal post-translational histone modifications affect gene expression and genomic stability, contributing to tumorigenesis, metastasis, and chemotherapy resistance. Therefore, histone modification has emerged as an epigenetic target in the development of cancer therapies[3]. Considering the

high genomic instability of HGSOC, investigating mutations in genes with molecular functions that impact histone modification contributes to a better understanding of the disease's prognosis and treatment.

2. OBJECTIVE

Thus, this study aims to investigate the mutational profile of genes that impact histone modification in patients with HGSOC.

3. METHODS

For this purpose, blood samples were obtained from four patients with HGSOC from the Tumor Biobank of the Mário Penna Institute (CAAE - 82703418.8.0000.5121). Clinical data were collected from medical records. Cell-free DNA (cfDNA) was extracted, and libraries were prepared for next-generation sequencing. The sequencing was performed on the NextSeq 550 sequencer (Illumina). Variant calling was performed with BCFtools, and clinical annotation and interpretation were conducted using the Variant Effect Predictor algorithm, considering variants classified as pathogenic, likely pathogenic, variants of uncertain significance, and with conflicting classifications.

4. RESULTS

Data analysis revealed that all four patients were affected by alterations in the *PRKDC* gene, while two patients showed one variant in the ATM gene and one patient presented two variants in CHEK2. These genes are associated with the regulation of H2AXS139 phosphorylation, a key marker of DNA repair[4,5]. Additionally, five distinct variants in the BRSK1 gene affected three patients, and one variant in TRIO was found in two patients. Both are associated with the phosphorylation of H3S10 and H4S1, respectively, indicating a broader impact on the epigenetic signalling that regulates malignant transformation and the epithelial-mesenchymal transition[6,7].

5. CONCLUSION

These data support the patients' clinical features, including ovarian capsule involvement, vascular, and peritoneal invasion, which demonstrates the tumor's invasive potential. These findings suggest the dysregulation of histone kinases as a key mechanism in HGSOC tumor progression, highlighting potential prognostic markers.

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NOTAS

CONFLITOS DE INTERESSE

Não há conflitos de interesse.

CONTRIBUIÇÃO DOS AUTORES

Indicar a autoria baseado em contribuições substanciais: (a) Concepção e elaboração do manuscrito, (b) Coleta e Análise de dados, (c) Discussão dos resultados, (d) Revisão e aprovação final do artigo.
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Dissertação

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