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GENOMIC AND CLINICAL DATA ANALYSIS OF APE1 PROTEIN, BREAST CANCER STEM CELL PHENOTYPE, AND HYPOXIC TUMOR MICROENVIRONMENT

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Introduction: Breast cancer (BC) is a heterogeneous disease at cellular and molecular levels. BC tumors present a cellular subpopulation of breast cancer stem cells (BCSCs) linked with tumor initiation and progression, recurrence, and therapeutic failure. The BCSC is preferentially found in hypoxic areas of the tumor, which are common features of BC and are significantly associated with worse prognosis. Although hypoxia activates an aggressive BCSC phenotype, the proteins that perform this molecular crossroad are still unknown. Therefore, finding proteins that performed this crossing would help define new promisors' clinical strategies. Apurine/Apyrimidine Endonuclease 1 (APE1) protein has emerged as a new therapeutic target in cancer treatment and is overexpressed in more aggressive BC tumors. However, the relationship of APE1 with BCSC considering the hypoxia microenvironment does not exist. **Objectives:** This study aimed to analyze the genomic/transcriptomic and clinical data of the APE1, BCSC phenotype, and hypoxic tumors. **Methods:** Genomic/transcription data and clinical attributes were collected and clustered on the Xena UCSC platform from The Cancer Genome Atlas (TCGA) BRCA database. Clinical molecular signatures from BCSC and hypoxia-related genes were used to separate BC patients in high or low expression groups for these genes and they evaluated their clinical data, including survival and APE1 expressions. **Results:** Patients with high expression of BCSC-related genes exhibited worse prognosis and overexpression of APE1. Additionally, high expression of hypoxia-related genes was also associated with worse prognosis and exhibited high levels of APE1. Patients with high expression of BCSC genes also exhibited high levels of hypoxia-related genes. APE1, BCSC, and hypoxia-related genes were more expressed in BC compared to adjacent normal samples. **Conclusion:** Data suggest that APE1 is overexpressed in hypoxia and BCSC phenotype, which are associated with worse prognosis for BC.

Keywords: Apyrimidine endonuclease. Breast cancer. Stem cell. Hypoxia. Breast cancer. Prognosis.