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Transcriptional modulation of SMYD2 and SMYD3 genes by ozone therapy in breast tumor cells

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Introduction: Breast cancer is one of the leading causes of mortality among women worldwide, which drives the search for new therapeutic approaches. In this context, the SMYD2 and SMYD3 genes, which belong to the lysine methyltransferase family, have been associated with tumor progression and epigenetic regulation in cancer. **Objective:** This study aimed to evaluate the gene expression levels of SMYD2 and SMYD3 in luminal breast carcinoma cells (MCF7) and triple-negative carcinoma cells (DU4475) after treatment with different concentrations of ozone. **Methods:** Cells were cultured under standard conditions (37°C, 5% CO_2) and subjected to in vitro ozone therapy with doses of 5, 10, 15, 20, 30, and 40 µg/mL for 40 minutes. After 24, 48, and 72 hours of incubation, total ribonucleic acid (RNA) was extracted, and complementary deoxyribonucleic acid (cDNA) was synthesized. Gene expression was quantified by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) using housekeeping genes for normalization. Statistical evaluation was performed using analysis of variance (ANOVA) followed by Tukey's post hoc test, with significance set at $p<0.05$. **Results:** A dose- and time-dependent response was observed for both genes. In DU4475 cells, there was a significant reduction in SMYD3 expression from 20 µg/mL, particularly at 48 hours and 72 hours ($p<0.01$). For SMYD2, a progressive decrease in expression was noted in MCF7 cells at concentrations above 15 µg/mL after 72 hours ($p<0.05$). In DU4475, SMYD2 expression showed a slight reduction, though not statistically significant at lower doses. **Conclusion:** Ozone demonstrated the ability to modulate SMYD2 and SMYD3 gene expression in a dose- and time-dependent manner, suggesting a possible differential epigenetic effect between the cell subtypes. These findings support the potential of ozone therapy as an adjuvant strategy in breast cancer treatment.

Keywords: breast neoplasms; ozone; genomic instability.