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Effects of the hypomethylating agent 5-aza-2'-deoxycytidine on SMYD2 and SMYD3 expression in MCF7 and BT474 cells

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Introduction: The epigenetic genes SMYD2 and SMYD3, part of the lysine methyltransferase family, play crucial roles in gene expression regulation, cell proliferation, and cancer progression, particularly in breast cancer. Dysregulation of these genes has been linked to aggressive tumor phenotypes, making them promising targets for therapeutic interventions. **Objective:** This study aimed to evaluate the modulatory effects of the hypomethylating agent 5-aza-2'-deoxycytidine (5-aza-dC) on the expression levels of SMYD2 and SMYD3 in luminal A (MCF7) and luminal B (BT474) breast cancer cell lines treated at different concentrations. **Methods:** Cells were cultured in DMEM and RPMI media, respectively, and treated with varying concentrations of 5-aza-dC (10, 20, 30, and 50 μM) for 24, 48, and 72 hours. After each time point, ribonucleic acid (RNA) was extracted, complementary deoxyribonucleic acid (cDNA) synthesized, and gene expression quantified via reverse transcription-quantitative polymerase chain reaction (RT-qPCR), using reference genes for normalization. Data were assessed using analysis of variance (ANOVA) followed by Tukey's post hoc test, with $p < 0.05$ considered significant. **Results:** The experiments revealed dose- and time-dependent modulation. In MCF7, a significant reduction in SMYD3 expression was observed from 30 μM , especially after 48 hours and 72 hours ($p < 0.01$). In BT474, SMYD2 expression showed a significant decrease at 50 μM after 72 hours ($p < 0.05$), while SMYD3 was also repressed at all doses from 48 hours onward, with the most prominent effects at 30 μM and 50 μM ($p < 0.01$). **Conclusion:** Treatment with 5-aza-dC significantly downregulated SMYD2 and SMYD3 expression, suggesting that epigenetic modulation may be an effective pathway for controlling these genes in breast cancer cells. These findings reinforce the potential of epigenetic therapy in antitumor strategies.

Keywords: breast neoplasms; epigenetic.