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GSK343 and EZH2: epigenetic modulation in breast tumor cells

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Introduction: The enzyme enhancer of zeste homolog 2 (EZH2), a catalytic component of the polycomb repressive complex 2 (PRC2), is associated with transcriptional repression of tumor suppressor genes and the progression of various cancer types, including breast cancer. **Objective:** This study aimed to evaluate the expression levels of the EZH2 gene in two breast cancer cell lines—MDA-MB-134 (luminal) and HTB-123 (triple negative)—treated with different concentrations of the selective EZH2 inhibitor, GSK343. **Methods:** Cells were cultured under standardized conditions (37°C, 5% CO_2) and treated with GSK343 at established concentrations (1, 5, 15, 30, and 60 μM) for 24, 48, and 72 hours. After the exposure periods, total ribonucleic acid (RNA) was extracted and complementary deoxyribonucleic acid (cDNA) synthesized. EZH2 gene expression was quantified by reverse transcription-quantitative polymerase chain reaction (RT-qPCR), using housekeeping genes for data normalization. Statistical evaluation was performed using analysis of variance (ANOVA) with Tukey's post hoc test, with $p<0.05$ considered statistically significant. **Results:** The results revealed a dose-dependent reduction in EZH2 expression, particularly at concentrations of 15 μM and above. In the HTB-123 cell line, inhibition was more pronounced starting at 30 μM, with a significant decrease after 48 hours and more marked after 72 hours ($p<0.01$). In MDA-MB-134, the response occurred earlier, with significant reductions already observed at 15 μM after 24 hours ($p<0.05$), indicating greater sensitivity to the inhibitor. **Conclusion:** GSK343 is effective in negatively modulating EZH2 expression in breast cancer cells of different subtypes, with effects dependent on dose and exposure time, reinforcing its potential as an epigenetic agent in antitumor therapeutic strategies.

Keywords: breast neoplasms; genomic instability.