Epigenetic modifier

Epigenetic modifiers hold promise as adjuvant therapies for gliomas, with synergistic combinations being explored to enhance efficacy and reduce toxicity. A study aimed to evaluate the effects of single or combined treatments with various anticancer drugs (Carboplatin, Paclitaxel, Avastin), natural compounds (Quercetin), and epigenetic modulators (suberoylanilide hydroxamic acid and 5-Azacytidine) on the expression of some long noncoding RNAs and methylation drivers or some functional features in the U87-MG cell line.

Treated and untreated U87-MG cells were used for the evaluation of drug-induced cytotoxicity, apoptotic events, and distribution in cell cycle phases, detection of cytokine release, and assessment of gene expression and global methylation.

Cytotoxicity assays led to the selection of drug concentrations to be used in further experiments. Expression analysis revealed distinct downregulation of nearly all investigated genes and long noncoding RNAs following treatments. All treatments resulted in a higher percentage of global methylation compared to untreated controls. All treatments effectively increased levels of apoptosis, while the epigenetic modulators exhibited a lower proliferation profile, with combined treatments showing elevated values of cell lysis.

The results indicate a link between Carboplatin and Avastin treatments and DNA methylation mechanisms involving EZH2, DNMT3A, and DNMT3B, with Avastin's direct impact on these enzymes warranting further study. This research underscores the promise of platinum-based therapies combined with epigenetic drugs to reactivate silenced tumor suppressor genes and optimize methylation profiles [1)].

1)
Albulescu A, Botezatu A, Fudulu A, Hotnog CM, Bostan M, Mihăilă M, Iancu IV, Plesa A, Brasoveanu L. Combined Effect of Conventional Chemotherapy with Epigenetic Modulators on Glioblastoma. Genes (Basel). 2025 Jan 24;16(2):138. doi: 10.3390/genes16020138. PMID: 40004468; PMCID: PMC11855767.