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Topic: SIGNALING AND EPIGENETICS IN CANCER

Divergence of PI3K and MAPK signaling pathway activities between an adherent cellular model of glioblastoma and their derived neurospheres

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Survival of patients with multiform glioblastoma (GBM) goes from 12 to 18 months after diagnosis, as they have a high rate of relapse and resistance to treatment. Furthermore, we know that GBM is characterized by a heterogeneous set of cancer cells, including glioma-initiating cells (GICs), so therapeutic strategies specifically targeting them could be critical to improve clinical outcomes in GBM patients. After the evaluation of the expression of certain *stem* cell marker proteins in two cell models, adherent GL261 and neurospheres, we concluded that neurospheres acquired *stem* cell characteristics. We also treated these two models with kinase inhibitors of PI3K (Alpelisib and Copanlisib) and MAPK (Trametinib) signaling pathways, which both are deregulated in GBM, and we observed significant differences in their activity: the adherent cells showed higher PI3K pathway activity, while neurospheres had higher MAPK pathway activity. Moreover, we found that co-treatments visibly decreased cell viability, being lower in neurospheres. In conclusion, this study suggests that neurospheres and adherent cells differ in potential therapeutic strategies for tumor treatment and that co-treatments of both pathways are necessary to combat compensatory mechanisms.