GLIOBLASTOMA MULTIFORME: A MULTIDISCIPLINARY APPROACH TO OVERCOME CHEMORESISTANCE AND FIND NEW THERAPEUTIC STRATEGIES

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Objectives: Glioblastoma multiforme is the most frequent malignant brain tumor. Patients die within 15 months after diagnosis. The failure of current therapies is ascribed to a subpopulation of cells with stem-like properties, called glioma stem cells (GSCs). The aim of this study is to develop new effective therapies. Moreover, we want to better characterize the orthotopic xenograft model established by GSCs injection into NOD/SCID mice.
Materials and methods: We tested Temolomide and Valproic acid treatments, alone and in combination, on seven GSC lines by MTT assay and we sequenced p53. Moreover, we characterized our xenograft model investigating the expression of stemness and differentiation markers by immunohistochemistry on FFPE tissues and by immunofluorescence on the correspondent cell line. Finally, we performed aCGH on the DNA extracted from the cell line and from FFPE tissues.
Results: GSCs were resistant to Temozolomide and slightly sensitive to Valproic acid. The two drugs exerted a synergistic effect when combined performing a pre-conditioning with Valproic acid. Furthermore, several cell lines carry p53 mutations. IF and IHC showed a perfect correspondence for stemness markers expression, but discordant data for the others. aCGH analysis evidenced numerous alterations specific for the *ex vivo* sample, suggesting the presence of an *in vivo* clonal selection.
Discussion: This work shows the importance of murine microenvironment in GSCs phenotype *in vivo* and suggests the possibility to use our combined treatment for therapeutic purposes.
Conclusions: Orthotopic models from GSCs and *in vitro* grown cell lines represent good models for the development of GSC-targeted therapies.