

New therapeutic strategies for Glioblastoma Multiforme

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Glioblastoma Multiforme (GBM), the most aggressive type of brain tumor, presents one of the worst prognosis among cancers, and innovative technologies are desperately needed in order to improve patient survival. Traditionally, cancer therapy focused on inducing cancer cell death, but induction of cancer stem cells differentiation as well as senescence and autophagy are new therapeutic strategies for several types of cancers, including GBM. We have studied the effects of new pharmacological agents, such as Resveratrol (Rsv) and Quercetin (Quer), in combination with traditionally used chemotherapeutics, such as Temozolomide (TMZ). This was done in GBM silenced for regulators of apoptosis such as XIAP and Survivin, using stable RNA interference delivered by lentiviral vectors. We found that agents that protect normal neural tissue from cell death, such as Rsv and Quer, cooperate in inducing senescence and Rsv reduces the number of cancer stem cells. Additionally, Rsv and TMZ are strong inducers of autophagy, that may lead to autophagic cell death. Silencing of the caspase inhibitors XIAP and Survivin increases senescence induction and affects the growth of tumor-spheres, an indication of being involved in tumor cell differentiation. Silencing of these caspase inhibitors also makes cells more sensitive to chemotherapeutics used in the clinic. Taken together, there are new fronts in the fight against GBM and the combination of these tools with the ones already in use is a promise for better patient outcome.