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Glioblastoma and stem cells.

Altaner C.

Cancer Research Institute SAS Bratislava, Slovakia. exonalt@savba.sk

This review presents compelling evidence that human glioblastoma is a heterogenous tumor composed from tumor cells and small portion of cancer stem cells -- tumor-initiating cells, which have a high tumorigenic potential and a low proliferation rate. Glioma cancer stem cells are phenotypically similar to the normal stem cells, they express CD133 gene and other genes characteristic of neural stem cells and posses the self-renewal potential. Cancer stem cells derived from glioblastoma are capable recapitulate original polyclonal tumors when xenografted to nude mice. They are chemoresistant and radioresistant and therefore responsible for tumor progression and recurrence after conventional glioblastoma therapy. Cancer stem cells contribute to glioma radioresistance by an increase of DNA repair capacity through preferential activation of the DNA damage response checkpoints. Potential therapies that modulate or target cancer stem cells are also reviewed. Mesenchymal stem cells and/or neural stem cells were shown to target brain tumors therefore these cells are considered as an effective delivery system to target and disseminate therapeutic agents to brain tumors. Stem cell-based gene therapies for glioblastoma were shown in experiments to be effective way to target brain tumors. Effects of bone morphogenetic protein (BMP4) on glioma cancer stem cells are also reviewed. BMP4 reduces effectively proliferation of CD133 positive cells in vitro and the tumor growth in vivo. BMP4 may act as a key inhibitory regulator of cancer initiation and therefore may be used in combined stem cell-based therapy as a non-cytotoxic therapeutic agent.

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