Glioblastoma cancer stem cells: Role of the microenvironment and therapeutic targeting.

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Abstract
It has been recently suggested that many types of cancer, including glioblastoma (GBM), contain functionally subsets of cells with stem-like properties named "cancer stem cells" (CSCs). These are characterized by chemotherapy resistance and considered one of the key determinants driving tumor relapse. Many studies demonstrated that Glioma stem cells (GSCs) reside in particular tumor niches, that are necessary to support their behavior. A hypoxic microenvironment has been reported to play a crucial role in controlling GSC molecular and phenotypic profile and in promoting the recruitment of vascular and stromal cells in order to sustain tumor growth. Recent advances in the field allow researches to generate models able to recapitulate, at least in part, the extreme heterogeneity found within GBM tumors. These models try to account for the presence of GSCs and more differentiated cells, the influence of different microenvironments enclosed within the mass, heterotypic interactions between GBM and stromal cells and genetic aberrations. Understanding the mechanism of action of the microenvironmental signals and the interplay between different cell types within the tumor mass, open new questions on how GSCs modulate GBM aggressiveness and response to therapy. The definition of these tumor features will allow to setup innovative multimodal therapies able to target GBM cells at multiple levels. Here, we will discuss the major advances in the study of GSC role in GBM and the therapeutic implications resulting from them, thus reporting the latest strategies applied to counteract and overcome GBM intrinsic resistance to therapy for a better management of patients.

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