

Original Article

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Glioblastoma-derived stem cell-enriched cultures form distinct subgroups according to molecular and phenotypic criteria

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Abstract

Tumor cells with stem cell-like properties can be cultured from human glioblastomas by using conditions that select for the expansion of neural stem cells. We generated cell lines from glioblastoma specimens with the goal to obtain model systems for glioma stem cell biology. Unsupervised analysis of the expression profiles of nine cell lines established under neural stem cell conditions yielded two distinct clusters. Four cell lines were characterized by the expression of neurodevelopmental genes. They showed a multipotent differentiation profile along neuronal, astroglial and oligodendroglial lineages, grew spherically *in vitro*, expressed CD133 and formed highly invasive tumors *in vivo*. The other five cell lines shared expression signatures enriched for extracellular matrix-related genes, had a more restricted differentiation capacity, contained no or fewer CD133^[plus] cells, grew semiadherent or adherent *in vitro* and displayed reduced tumorigenicity and invasion *in vivo*. Our findings show that stable, multipotent glioblastoma cell lines with a full stem-like phenotype express neurodevelopmental genes as a distinctive feature, which may offer therapeutic targeting opportunities. The generation of another distinct cluster of cell lines showing similarly homogeneous profiling but restricted stem cell properties suggests that different phenotypes exist, each of which may lead to the typical appearance of glioblastoma.

Keywords: glioma, neural stem cell, neurosphere, microarray, pathway