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Cell, Tumor, and Stem Cell Biology

Cancer Stem Cells Are Enriched in the Side Population Cells in a Mouse Model of Glioma

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The recent identification of cancer stem cells (CSCs) in multiple human cancers provides a new inroad to understanding tumorigenesis at the cellular level. CSCs are defined by their characteristics of self-renewal, multipotentiality, and tumor initiation upon transplantation. By testing for these defining characteristics, we provide evidence for the existence of CSCs in a transgenic mouse model of glioma, *S100 β -verbB;Trp53*. In this glioma model, CSCs are enriched in the side population (SP) cells. These SP cells have enhanced tumor-initiating capacity, self-renewal, and multipotentiality

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compared with non-SP cells from the same tumors. Furthermore, gene expression analysis comparing fluorescence-activated cell sorting–sorted cancer SP cells to non-SP cancer cells and normal neural SP cells identified 45 candidate genes that are differentially expressed in glioma stem cells. We validated the expression of two genes from this list (*S100a4* and *S100a6*) in primary mouse gliomas and human glioma samples. Analyses of xenografted human glioblastoma multiforme cell lines and primary human glioma tissues show that S100A4 and S100A6 are expressed in a small subset of cancer cells and that their abundance is positively correlated to tumor grade. In conclusion, this study shows that CSCs exist in a mouse glioma model, suggesting that this model can be used to study the molecular and cellular characteristics of CSCs *in vivo* and to further test the CSC hypothesis. [Cancer Res 2008;68(24):10051–9]

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