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1: Oncogene. 2004 Sep 20;23(43):7267-73.

Cancer stem cells in nervous system tumors.

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Most current research on human brain tumors is focused on the molecular and cellular analysis of the bulk tumor mass. However, evidence in leukemia and more recently in solid tumors such as breast cancer suggests that the tumor cell population is heterogeneous with respect to proliferation and differentiation. Recently, several groups have described the existence of a cancer stem cell population in human brain tumors of different phenotypes from both children and adults. The finding of brain tumor stem cells (BTSCs) has been made by applying the principles for cell culture and analysis of normal neural stem cells (NSCs) to brain tumor cell populations and by identification of cell surface markers that allow for isolation of distinct tumor cell populations that can then be studied in vitro and in vivo. A population of brain tumor cells can be enriched for BTSCs by cell sorting of dissociated suspensions of tumor cells for the NSC marker CD133. These CD133+ cells, which also expressed the NSC marker nestin, but not differentiated neural lineage markers, represent a minority fraction of the entire brain tumor cell population, and exclusively generate clonal tumor spheres in suspension culture and exhibit increased self-renewal capacity. BTSCs can be induced to differentiate in vitro into tumor cells that phenotypically resembled the tumor from the patient. Here, we discuss the evidence for and implications of the discovery of a cancer stem cell in human brain tumors. The identification of a BTSC provides a powerful tool to investigate the tumorigenic process in the central nervous system and to develop therapies targeted to the BTSC. Specific genetic and molecular analyses of the BTSC will further our understanding of the mechanisms of brain tumor growth, reinforcing parallels between normal neurogenesis and brain tumorigenesis.

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