Brain Cancer Stem Cells Display Preferential Sensitivity to Akt Inhibition

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Abstract

Malignant brain tumors are among the most lethal cancers, and conventional therapies are largely limited to palliation. Novel therapies targeted against specific molecular pathways may offer improved efficacy and reduced toxicity compared to conventional therapies, but initial clinical trials of molecular targeted agents in brain cancer therapy have been frequently disappointing. In brain tumors and other cancers, subpopulations of tumor cells have recently been characterized by their ability to self-renew and initiate tumors. Although these cancer stem cells, or tumor initiating cells, are often only present in small numbers in human tumors, mounting evidence suggests that cancer stem cells contribute to tumor maintenance and therapeutic resistance. Thus, the development of therapies that target cancer stem cell signal transduction and biology may improve brain tumor patient survival. We now demonstrate that populations enriched for cancer stem cells are preferentially sensitive to an inhibitor of Akt, a prominent cell survival and invasion signaling node. Treatment with an Akt inhibitor more potently reduced the numbers of viable human glioma xenografts in vivo. Together, these results suggest that Akt inhibitors may function as effective anti-cancer stem cell therapies.

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