

# Cancer Research

2009  
LONDON-AACR PRIZES  
Nomination Deadline: August 25, 2008

Save the Date – February 3-6, 2009  
The Science of Cancer Health Disparities  
in Racial/Ethnic Minorities and the Medically Underserved  
Carefree, AZ  
Abstract Deadline: November 17

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## Priority Reports

### Targeting Cancer Stem Cells through L1CAM Suppresses Glioma Growth

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**Key Words:** Cancer Stem Cell • L1CAM • Olig2

Malignant gliomas are lethal cancers that display striking cellular heterogeneity. A highly tumorigenic glioma tumor subpopulation, termed cancer stem cells or tumor-initiating cells, promotes therapeutic resistance and tumor angiogenesis. Therefore, targeting cancer stem cells may improve patient survival. We interrogated the role of a neuronal cell adhesion molecule, L1CAM, in glioma stem cells as L1CAM regulates brain development and is expressed in gliomas. L1CAM<sup>+</sup> and CD133<sup>+</sup> cells cosegregated in gliomas, and levels of L1CAM were higher in CD133<sup>+</sup> glioma cells than normal neural progenitors. Targeting L1CAM using lentiviral-mediated short hairpin RNA

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(shRNA) interference in CD133<sup>+</sup> glioma cells potently disrupted neurosphere formation, induced apoptosis, and inhibited growth specifically in glioma stem cells. We identified a novel mechanism for L1CAM regulation of cell survival as L1CAM knockdown decreased expression of the basic helix-loop-helix transcription factor Olig2 and up-regulated the p21<sup>WAF1/CIP1</sup> tumor suppressor in CD133<sup>+</sup> glioma cells. To determine if targeting L1CAM was sufficient to reduce glioma stem cell tumor growth *in vivo*, we targeted L1CAM in glioma cells before injection into immunocompromised mice or directly in established tumors. In each glioma xenograft model, shRNA targeting of L1CAM expression *in vivo* suppressed tumor growth and increased the survival of tumor-bearing animals. Together, these data show that L1CAM is required for maintaining the growth and survival of CD133<sup>+</sup> glioma cells both *in vitro* and *in vivo*, and L1CAM may represent a cancer stem cell-specific therapeutic target for improving the treatment of malignant gliomas and other brain tumors. [Cancer Res 2008;68(15):6043–8]

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