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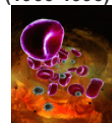
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Cancer Cell Biology

CD133 negative glioma cells form tumors in nude rats and give rise to CD133 positive cells

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KEYWORDS
CD133 • brain cancer • angiogenesis • cancer stem cell • xenograft

ABSTRACT

CD133 is a cell surface marker expressed on progenitors of haematopoietic and endothelial cell lineages. Moreover, several studies have identified CD133 as a marker of brain tumor-initiating cells. In this study, human glioblastoma multiforme biopsies were engrafted intracerebrally into nude rats. The resulting tumors were serially passaged *in vivo*, and monitored by magnetic resonance imaging. CD133 expression was analyzed at various passages. Tumors initiated directly from the biopsies expressed little or no CD133, and showed no contrast enhancement suggesting an intact blood-brain barrier. During passaging, the tumors gradually displayed more contrast enhancement, increased angiogenesis and a shorter survival. Real-time qPCR and immunoblots showed that this was accompanied by increased CD133 expression. Primary biopsy spheroids and xenograft tumors were subsequently dissociated and flow sorted into CD133 negative and CD133 positive cell populations. Both populations incorporated BrdU in cell culture, and expressed the neural precursor marker nestin. Notably, CD133 negative cells derived from 6 different patients were tumorigenic when implanted into the rat brains. For 3 of these patients, analysis showed that the resulting tumors contained CD133 positive cells. In conclusion, we show that CD133 negative glioma cells are tumorigenic in nude rats, and that CD133 positive cells can be obtained from these tumors. Upon passaging of the tumors *in vivo*, CD133 expression is upregulated, coinciding with the onset of angiogenesis and a shorter survival. Thus, our findings do not suggest that CD133 expression is required for brain tumor initiation, but that it may be involved during brain tumor progression. © 2007 Wiley-Liss, Inc.

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