IDENTIFICATION OF A2B5+CD133- TUMOR-INITIATING CELLS IN ADULT HUMAN GLIOMAS.

EXPERIMENTAL STUDIES

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Abstract:
OBJECTIVE: Several studies have shown that human gliomas contain a small population of cells with stem cell-like features. It has been proposed that these "cancer stem cells" may be uniquely responsible for glioma formation and recurrence. However, human gliomas also contain an abundance of cells that closely resemble more differentiated glial progenitors. Animal model studies have shown that these cells also possess the capacity to form malignant gliomas.

METHODS: To investigate the contributions of stem-like and progenitor-like cells in human gliomas, we used flow cytometry to characterize the expression of a cancer stem cell marker (CD133) and a glial progenitor marker (A2B5) in 25 tumors. We found that human gliomas consistently express A2B5 in a large percentage of cells (61.7 +/- 3.8%, standard error of the mean). In contrast, CD133 expression was less abundant and less consistent (14.8 +/- 3.6%, standard error of the mean), with several glioblastomas containing very few or no detectable CD133+ cells. When present, the CD133+ population was almost entirely contained within the A2B5+ population. Thus, most gliomas could be divided into three distinct populations on the basis of these markers (A2B5+/CD133+, A2B5+/CD133-, and A2B5-/CD133-). To test the tumorigenic potential of these populations, we separated cells from six tumors by fluorescence-activated cell sorting and reinjected them into nude rats.

RESULTS: We found that the capacity for these different populations to form tumors varied depending on the human tumor specimen from which they were isolated. Of the six human gliomas tested, four contained A2B5+/CD133- cells that formed tumors when transplanted into nude rats, three contained A2B5+/CD133+ cells that formed tumors, and only one glioma contained A2B5-/CD133- cells with the capacity to form tumors.

CONCLUSION: Together, these results demonstrate that human gliomas contain multiple populations of cells with the capacity to form tumors and specifically identify a population of tumorigenic A2B5+ cells that are phenotypically distinct from CD133+ cells.