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Clinical Relevance of Tumor Cells with Stem-Like Properties in Pediatric Brain Tumors

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Abstract

Background

Primitive brain tumors are the leading cause of cancer-related death in children. Tumor cells with stem-like properties (TSCs), thought to account for tumorigenesis and therapeutic resistance, have been isolated from high-grade gliomas in adults. Whether TSCs are a common component of pediatric brain tumors and are of clinical relevance remains to be determined.

Methodology/Principal Findings

Tumor cells with self-renewal properties were isolated with cell biology techniques from a majority of 55 pediatric brain tumors samples, regardless of their histopathologies and grades of malignancy (57% of embryonal tumors, 57% of low-grade gliomas and neuro-glial tumors, 70% of ependymomas, 91% of high-grade gliomas). Most high-grade glioma-derived oncospheres (10/12) sustained long-term self-renewal akin to neural stem cells (>7 self-renewals), whereas cells with limited renewing abilities akin to neural progenitors dominated in all other tumors. Regardless of tumor entities, the young age group was associated with self-renewal properties akin to neural stem cells ($P = 0.05$, chi-square test). Survival analysis of the cohort showed an association between isolation of cells with long-term self-renewal abilities and a higher patient mortality rate ($P = 0.013$, log-rank test). Sampling of low- and high-grade glioma cultures showed that self-renewing cells forming oncospheres shared a molecular profile comprising embryonic and

neural stem cell markers. Further characterization performed on subsets of high-grade gliomas and one low-grade glioma culture showed combination of this profile with mesenchymal markers, the radio-chemoresistance of the cells and the formation of aggressive tumors after intracerebral grafting.

Conclusions/Significance

In brain tumors affecting adult patients, TSCs have been isolated only from high-grade gliomas. In contrast, our data show that tumor cells with stem cell-like or progenitor-like properties can be isolated from a wide range of histological sub-types and grades of pediatric brain tumors. They suggest that cellular mechanisms fueling tumor development differ between adult and pediatric brain tumors.

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