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[Instability of cell phenotype and tumor initiating cells in gliomas.]

[Article in French]

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Abstract

Gliomas, the most frequent primitive CNS tumors, have been suggested to originate from astrocytes or from neural progenitors/stem cells. However, the precise identity of the cells at the origin of gliomas remains a matter of debate because no pre-neoplastic state has been yet identified. TGF α , an EGF family member, is frequently over-expressed in the early stages of glioma progression. We questioned whether prolonged TGF α exposure affects the stability of the normal mature astrocyte phenotype and, eventually, their propensity to cancerous transformation. Using mouse astrocyte cultures devoid of residual neural stem cells or progenitors, we demonstrate that several days of TGF α -treatment result in the functional conversion of a population of mature astrocytes into radial glial cells, a population of neural progenitors, without any accompanying sign of cancerous transformation. In contrast, when astrocytes de-differentiated with TGF α were submitted to oncogenic stress using gamma irradiation, they acquired cancerous properties, forming high-grade glioma-like tumors after brain grafting. Gamma irradiation was without effect on astrocytes which were not treated with TGF α . These results suggested that most gliomas should contain tumor cells with stem-like properties (TSCs). Our study of 55 pediatric brain tumors show that tumor cells with stem cell-like or progenitor-like properties can be isolated from a majority of gliomas. Survival analysis showed an association between isolation of TSCs with extended self-renewal capabilities and a patient's higher mortality rate.

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