

GLIOMAL STEM CELLS AS TARGETS AND NORMAL STEM CELLS AS ORIGINS AND VECTORS IN A NEW APPROACH OF CEREBRAL TUMORS

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The discovery of cancer stem cells in solid tumours has changed our view of carcinogenesis and therapy. Among high grade malignant gliomas, we characterized cells able to highly proliferate in non-adherent conditions in a defined medium containing FGF and TGF α . Only malignant glioneuronal tumors (Varlet et al. 2004) raised these cells whereas oligodendrogliomas did not. Cultured for several months (up to 4 years) they exhibit a stable profile of surface antigens typical of neural stem cells including CD56-NCAM, CD15-Lex-SSEA or CXCR4, but no CD133. These cells can differentiate and acquire markers normally observed in neurons (β III-tubulin), astrocytes (GFAP) or oligodendrocytes (olig2). Finally as few as 100 cells grafted in a nude mouse brain give rise to a tumor within a few weeks, that may be further passed. Do cancer stem cells arise from normal stem cells, or do they arise from differentiated cells that acquire self-renewal capacity, or both? Long term treatment of normal mouse mature astrocytes reveals their capacity to dedifferentiate into functional progenitors and even into neural stem cells (Sharif et al. 2006a & 2006b).

Keywords: Cancer stem cells, gliomas, TGF α

References

- Varlet P. et al. *Neurosurgery*. 2004. Dec;55(6):1377-92.
Sharif A, et al *Oncogene*. 2006 Jul 6;25(29):4076-85.
Sharif A. et al. *Oncogene* 2006 in press