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Growth of cancer cell lines under stem cell-like conditions has the potential to unveil therapeutic targets

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Abstract

Malignant tumors comprise a small proportion of cancer-initiating cells (CIC), capable of sustaining tumor formation and growth. CIC are the main potential target for anticancer therapy. However, the identification of molecular therapeutic targets in CIC isolated from primary tumors is an extremely difficult task. Here, we show that after years of passaging under differentiating conditions, glioblastoma, mammary carcinoma, and melanoma cell lines contained a fraction of cells capable of forming spheroids upon *in vitro* growth under stem cell-like conditions. We found an increased expression of surface markers associated with the stem cell phenotype and of oncogenes in cell lines and clones cultured as spheroids vs. adherent cultures. Also, spheroid-forming cells displayed increased tumorigenicity and an altered pattern of chemosensitivity. Interestingly, also from single retrovirally marked clones, it was possible to isolate cells able to grow as spheroids and associated with increased tumorigenicity. Our findings indicate that short-term selection and propagation of CIC as spheroid cultures from established cancer cell lines, coupled with gene expression profiling, represents a suitable tool to study and therapeutically target CIC: the notion of which genes have been down-regulated during growth under differentiating conditions will help find CIC-associated

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Keywords: Cancer stem cells; Cancer cell lines; Glioblastoma; Mammary carcinoma; Melanoma

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