

Angiogenic marker expression in cancer stem cells derived from glioblastoma and peritumor tissue

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Glioblastoma (GBM) is a lethal cancer characterized by florid vascularization and aberrantly elevated VEGF. Antiangiogenic therapy with VEGF antibodies reduces GBM tumor growth. However, the clinical benefits are transient and invariably followed by tumor recurrence. Recently, it has been demonstrated that in GBM cancer stem cells (CSCs) are responsible for either tumorigenesis or neoangiogenesis. In particular, a fraction of CSCs is represented by a population of endothelial progenitors. In our previous studies, we showed the presence of nestin+ cells and nestin+ and endoglin (CD105)+ vasculature, not only in the GBM but also in the tissue surrounding the tumor, suggesting the involvement of CSC endothelial differentiation also in peritumor tissue. In this study, with the aim of understanding CSCs involvement in angiogenesis, we investigated the expression of angiogenesis markers (VEGF, VEGFR1, VEGFR2, HIF1 α and HIF2 α) by immunocytochemistry, western blot or real time PCR analysis, in CSCs derived from GBM (GCSC) and peritumor tissue (PCSC) of 4 patients. Both GCSCs and PCSCs were immunopositive for HIF1 α and HIF2 α , VEGF and its receptors VEGFR1 and VEGFR2, which underlines the presence of autocrine and paracrine growth factor loops. Immunoblotting showed that VEGF is expressed at higher levels in GCSCs than PCSCs, with the exception of a patient who showed an up-regulation in PCSCs. Moreover, real time PCR showed that both VEGFR1 and VEGFR2 were expressed at low level in the two types of CSCs with a down-regulation of VEGFR1 in PCSCs. These results indicate the presence of all angiogenic markers in PCSCs suggesting their involvement in GBM local recurrence. The inhibition of multiple angiogenic pathways may be a new line of attack on this deadly cancer.

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