Involvement of cancer stem cells in glioblastoma angiogenesis

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It is widely accepted that glioblastoma (GBM) develops from cancer stem cells (CSCs), a subset of stem-like cells displaying high resistance to treatment. In fact, despite aggressive therapy, 90% of patients relapse within 2 cm from tumor edge. Our recent findings showed the existence of a CSC type, residing in GBM peritumor tissue (PCSCs), that bears distinct characteristics from CSCs of the tumor mass (GCSCs). It should be considered the possibility that, after surgical resection, PCSCs might represent a reservoir of cells able to recapitulate the tumor. In this setting, characterization of PCSCs appears to be crucial in order to identify novel effective therapeutic targets. Thus, our aim was to investigate GCSCs and PCSCs role in angiogenesis, a key event in both GBM and peritumor tissue, whose vasculature shows features similar to those found in the tumor mass.

In particular, we analyzed, by immunocytochemistry (ICC), Western blotting or real-time PCR, the expression of molecules involved in hypoxia and angiogenesis, such as HIF1α, HIF2α, and VEGF along with its receptors (VEGFR1, VEGFR2). ICC has highlighted the presence and the specific localization of these molecules in both GCSCs and PCSCs. The two cell populations showed comparable levels of VEGF. The transcript of VEGFR1 was in general expressed at higher levels in GCSCs than in PCSCs, while VEGFR2 mRNA and protein did not show a unique trend of expression.

The expression of VEGF and its receptors in both GCSCs and PCSCs suggests that, besides well-known paracrine loops, autocrine signalings are also involved in tumor angiogenesis. Moreover, the expression of angiogenesis markers in PCSCs suggests these cells to have a direct role in peritumor tissue new vessel formation. In this regard, PCSCs should be considered a promising therapeutic target to counteract the angiogenesis-supported tumor progression.