Glioma tumor stem-like cells promote tumor angiogenesis and vasculogenesis via vascular endothelial growth factor and stromal-derived factor 1.


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Cancer stem cells (CSC) are predicted to be critical drivers of tumor progression due to their self-renewal capacity and limitless proliferative potential. An emerging area of research suggests that CSC may also support tumor progression by promoting tumor angiogenesis. To investigate how CSC contribute to tumor vascular development, we used an approach comparing tumor xenografts of the C6 glioma cell line containing either a low or a high fraction of CSC. Compared with CSC-low tumors, CSC-high tumors exhibited increased microvessel density and blood perfusion and induced increased mobilization and tumor recruitment of bone marrow-derived endothelial progenitor cells (EPC). CSC-high C6 cell cultures also induced higher levels of endothelial cell proliferation and tubule organization in vitro compared with CSC-low cultures. CSC-high cultures and tumors expressed increased levels of the proangiogenic factors vascular endothelial growth factor and stromal-derived factor 1, and when signaling by either factor was blocked, all aspects of angiogenesis observed in CSC-high cultures and tumors, including microvessel density, perfusion, EPC mobilization/recruitment, and stimulation of endothelial cell activity, were reduced to levels comparable with those observed in CSC-low cultures/tumors. These results suggest that CSC contribute to tumor angiogenesis by promoting both local endothelial cell activity and systemic angiogenic processes involving bone marrow-derived EPC in a vascular endothelial growth factor-dependent and stromal-derived factor 1-dependent manner.

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