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Role of neural cancer stem cells in angiogenesis

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Growing evidence indicates the existence of small populations of cells endowed with distinctive self-renewal capacity, tumorigenesis and resistance to conventional treatments, defined as cancer stem cells (CSCs) or tumor initiating cells. In addition, it is widely appreciated that the growth of new blood vessel and lymphatic vasculature, which occurs during angiogenesis and lymphangiogenesis, plays a key role in the process of tumor growth. To this regards, an increasing number of studies showed that the employment of angiogenesis inhibitors might have significant therapeutic advantages. Fascinatingly, recent evidence demonstrated that CSCs play a role in angiogenesis, in particular in glioma, which, to date, represents a highly lethal tumor tough to treat. We demonstrated that CSCs isolated from both tumor (GCSCs) and peritumoral tissue (PCSCs) express a number of angiogenesis-related molecules, such as VEGF, HIF1α and HIF2α. In addition, VEGFR1 expression was found significantly reduced in PCSCs vs. GCSCs whereas VEGFR2 appeared to be largely heterogeneous in both stem cell types. With the aim to investigate the aptitude of CSCs-derived neurospheres to regulate the angiogenesis process, we performed in vitro migration analysis by means of Boyden chamber assay. The results of these experiments indicated that ECs migration was stimulated in the presence of PCSCs but remained almost unaffected when endothelial cells were co-cultured with GCSCs. In conclusion, our data suggest that GCSCs and PCSCs contribute differently to tumor angiogenesis by activating distinct molecular mechanisms. PCSCs might, therefore, play a key role in the recruitment as well as activation of ECs in peritumoral tissue.

References

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Key words

Cancer stem cells, angiogenesis, glioblastoma.