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Molecular therapeutic targets for glioma angiogenesis.

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Abstract

Due to the prominent angiogenesis that occurs in malignant glioma, antiangiogenic therapy has been attempted. There have been several molecular targets that are specific to malignant gliomas, as well as more broadly in systemic cancers. In this review, I will focus on some topics related to molecular therapeutic targets for glioma angiogenesis. First, important angiogenic factors that could be considered molecular targets are VEGF, VEGF-induced proteins on endothelial cells, tissue factor, osteopontin, alpha(v)beta(3) integrin, and thymidine phosphorylase as well as endogenous inhibitors, soluble Flt1, and thrombospondin 1. Second, hypoxic areas are also decreased by metronomic CPT11 treatment as well as temozolomide. Third, glioma-derived endothelial cells that are genetically and functionally distinct from normal endothelial cells should be targeted, for example, with SDF-1 and CXCR7 chemokine. Fourth, endothelial progenitor cells (EPCs) likely contribute towards glioma angiogenesis in the brain and could be useful as a drug delivery tool. Finally, blockade of delta-like 4 (Dll4) results in a nonfunctioning vasculature and could be another important target distinct from VEGF.

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