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## **Mechanisms of Disease: the PI3K-Akt-PTEN signaling node- an intercept point for the control of angiogenesis in brain tumors.**

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The overall prognosis for patients with high-grade glioma remains dismal, despite advances in treatment modalities including neurosurgery, radiation therapy and conventional cytotoxic chemotherapy. In this article, we review literature that provides a rationale for the use of antiangiogenic therapy to improve the treatment of high-grade neoplasms in the CNS. In particular, we focus our discussion on the central role of the phosphatidylinositol 3-kinase-Akt- phosphatase and tensin homolog (PI3K-Akt-PTEN) axis as a potential molecular target for the control of angiogenesis in brain tumors via the coordinated control of cell division, tumor growth, angiogenesis, apoptosis, invasion and cellular metabolism in the tumor and stromal compartments. We suggest that instead of inhibiting a single cell surface receptor, thereby leaving other receptors free to pulse survival, proliferative, angiogenic and invasive signals, a more effective way to approach the design of targeted therapy against brain tumors is to inhibit a nodal point where redundant cell surface receptor signals converge to transmit important, relatively conserved signaling events within the cell. The epigenetic and post-translational regulation of PI3K-Akt-PTEN signaling has a prominent role in brain tumor pathogenesis, and we therefore suggest that PI3K could be an important target for therapies that target brain tumors.

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