PTEN signaling in brain: neuropathology and tumorigenesis

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Abstract

Phosphatase and tensin homolog deleted on chromosome 10 (PTEN) is a tumor suppressor that antagonizes the phosphatidylinositol-3-kinase (PI3K)/Akt/mTOR pathway by functioning as a lipid phosphatase. This ubiquitous and evolutionarily conserved signaling cascade influences numerous functions including cell growth, survival, proliferation, migration and metabolism. Inherited mutations in PTEN cause pleiotropic effects including cancer predisposition as well as a range of neurological abnormalities revealing specialized roles for PTEN in nervous system development and maintenance. Somatic mutations in PTEN occur frequently as late events in sporadic brain tumors. Mouse models based on Pten deletion in the brain have provided insights into the normal functions of Pten in the nervous system as well as the initiation and progression of gliomas. Compromised PTEN function may contribute to gliomagenesis through disrupted regulation of proliferation, migration, invasion, angiogenesis, stem cell self-renewal and regulation of other tumor suppressor pathways such as p53. Clinical findings in high-grade glioma suggest that PTEN gene alterations are associated with poor prognosis and may influence response to specific therapies. Emerging research using specific pharmacological inhibitors of the PI3K pathway may provide novel therapeutic options for the treatment of PTEN-deficient tumors.

Keywords: PTEN, PI3 kinase, tumor suppressor, brain, glioblastoma