PTEN

Phosphatase and tensin homolog (PTEN) is a protein that, in humans, is encoded by the PTEN gene.

This gene was identified as a tumor suppressor that is mutated in a large number of cancers at high frequency. The protein encoded by this gene is a phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase. It contains a tensin-like domain as well as a catalytic domain similar to that of the dual specificity protein tyrosine phosphatases. Unlike most of the protein tyrosine phosphatases, this protein preferentially dephosphorylates phosphoinositide substrates. It negatively regulates intracellular levels of phosphatidylinositol-3,4,5-trisphosphate in cells and functions as a tumor suppressor by negatively regulating Akt/PKB signaling pathway.

Phosphatase and tensin homolog (PTEN) regulates cell growth and survival through inhibition of the mammalian target of rapamycin (mTOR) signaling pathway. Germline genetic variation of PTEN is associated with autism, macrocephaly, and PTEN hamartoma tumor syndromes (PHTS). The effect of developmental PTEN somatic mutations on nervous system phenotypes is not well understood, although brain somatic mosaicism of MTOR pathway genes is an emerging cause of cortical dysplasia and epilepsy in the pediatric population.

Koboldt et al. reported two somatic variants of PTEN affecting a single patient presenting with intractable epilepsy and hemimegalencephaly that varied in clinical severity throughout the left cerebral hemisphere. High-throughput sequencing analysis of affected brain tissue identified two somatic variants in PTEN. The first variant was present in multiple cell lineages throughout the entire hemisphere and associated with mild cerebral overgrowth. The second variant was restricted to posterior brain regions and affected the opposite PTEN allele, resulting in a segmental region of more severe malformation, and the only neurons in which it was found by single-nuclei RNA-seq had a unique disease-related expression profile. This study reveals brain mosaicism of PTEN as a disease mechanism of hemimegalencephaly and furthermore demonstrates the varying effects of single- or bi-allelic disruption of PTEN on cortical phenotypes [1)].

The purpose of a investigation was to examine cerebellar levels of several molecular signaling pathways, including PI3K/AKT/mammalian target of rapamycin (mTOR) signaling and markers of neuronal migration, following loss of the phosphatase and tensin homolog (PTEN) gene in a subset of neurons, as well as the accompanying behavior phenotype in mice. Motor coordination and learning were measured by the sticker removal task and the accelerating rotarod. Western blots were conducted on cerebellar tissue samples. We demonstrated that neuron subset-specific deletion of PTEN in mice led to deficits in motor coordination. These changes were accompanied by alterations in many different proteins, including the PI3K/AKT/mTOR signaling pathway, FMRP, glutamate receptors, and neuronal migration markers. These data firstly support a role for hyperactivation of mTOR in the cerebellum following the loss of PTEN, accompanied by behavioral deficits. Moreover, the results of the current study support a broader role for PTEN signaling in early neuronal migration and organization of the cerebellum, and point to a putative role for PTEN in many neuropsychiatric conditions [2)]

The specific roles of PTEN in endothelial cell functions and angiogenesis after cerebral ischemia remain unknown. Therefore, we sought to examine the potential effects of PTEN inhibition on post-ischemic angiogenesis in human blood vessel cells and to determine the underlying mechanism. In this present study, human umbilical vein endothelial cells (HUVECs) were exposed to oxygen-glucose deprivation (OGD), cell proliferation, migration and apoptosis, in vitro tube formation and expression of PTEN/Akt pathway and angiogenic factors were examined in HUVECs after treatment with PTEN inhibitor bisperoxovanadium (bpV) at different doses. The results showed that bpV significantly increased the cell proliferation and reduced cell apoptosis indicating that the drug exerts a cytoprotective effect on HUVECs with OGD exposure. bpV also enhanced cell migration and tube formation in HUVECs following OGD, and upregulated HIF-1α and VEGF expressions, but attenuated endostatin expression. Additionally, western blotting analysis demonstrated that Akt phosphorylation in HUVECs was significantly increased after bpV treatment. These findings suggest that PTEN inhibition promotes post-ischemic angiogenesis in HUVECs after exposure to OGD and this enhancing effect might be achieved through activation of the Akt signal cascade [3].

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2)
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