WNK1

WNK lysine deficient protein kinase 1, also known as WNK1, is an enzyme that in humans is encoded by the WNK1 gene.

The human gene is located on short arm of chromosome 12 (12p13.3).

WNK1 is also known as Human Accelerated Region 5. WNK1 may have played a key role in differentiating Humans from Apes.

The WNK1 protein is composed of 2382 amino acids (molecular weight 230 kDa). The protein contains a small N-terminal domain followed by the kinase domain and a long C-terminal tail. The kinase domain has some similarity to the MEKK protein kinase family.

The WNK1 gene encodes a cytoplasmic serine-threonine kinase expressed in the distal nephron.

The protein appears to be part of the ERK5 MAP kinase pathway upstream of MEKK2 / MEKK3 and to function as a tetramer. It selectively binds to and phosphorylates synaptotagmin 2 (SYT2) within its calcium-binding C2 domains. It activates the serum- and glucocorticoid-inducible protein kinase SGK1, leading to activation of the epithelial sodium channel. It along with WNK4 stimulates clathrin-dependent endocytosis of renal outer medullar potassium 1 (ROMK1). It (and WNK4) interactes with intersectin (ITSN1, ITSN2).

In a study, the novel regulatory role of NgR in a serine-threonine kinase WNK1 was identified. NgR's transcriptional regulation of WNK1 was identified by RT-qPCR and semiquantitative western blot after the overexpression or knockdown of NgR, and the regulation is specific to WNK1, which is not the same for its family members, WNK2, WNK3 and WNK4. Furthermore, NgR inhibition by NEP fails to affect WNK1, which indicates that WNK1 functions outside of the Nogo-A/NgR pathway. By performing a proliferation, migration and axonal extension assay, we also identified that overexpressed NgR critically regulated these processes and impairment by overexpressing NgR was rescued with coexpression of WNK1, indicating the partial role of WNK1 in NgR-mediated morphological regulation. The study identifies a separation of functions for the NgR-regulated WNK1 in mediating proliferation, migration and axonal extension in PC12 cells as well as a specific regulatory role between NgR and WNK1 that is important for recovery from central nervous system injury [1)].

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Yang T, Zhao K, Shu H, Chen X, Cheng J, Li S, Zhao Z, Kuang Y, Yu S. The Nogo receptor inhibits proliferation, migration and axonal extension by transcriptionally regulating WNK1 in PC12 cells. Neuroreport. 2017 May 6. doi: 10.1097/WNR.0000000000000800. [Epub ahead of print] PubMed PMID: 28489665.