MAP2K7

Dual specificity mitogen-activated protein kinase kinase 7, also known as MAP kinase kinase 7 or MKK7, is an enzyme that in humans is encoded by the MAP2K7 gene.

This protein is a member of the mitogen-activated protein kinase kinase family. The MKK7 protein exists as six different isoforms with three possible N-termini (α, β, and γ isoforms) and two possible C-termini (1 and 2 isoforms).

Histone deacetylase 6 (HDAC6) activity contributes to the malignant proliferation, invasion and migration of glioma cells (GCs), but the molecular mechanisms underlying the processes remains elusive. Huang et al. reported that HDAC6 inhibition by Ricolinostat (ACY-1215) or CAY10603 led to a remarkable decrease in the phosphorylation of JNK and c-Jun, which preceded its suppressive effects on glioma cell growth. Further investigation showed that these effects resulted from HDAC6 inhibitor-induced suppression of MKK7, which was identified to be critical for JNK activation and exerts the oncogenic roles in GCs. Selectively silencing HDAC6 by siRNAs had the same responses while transient transfections expressing HDAC6 promoted MKK7 expression. Interestingly, by performing Q-PCR, HDAC6 inhibition did not cause downregulation of MKK7 mRNA level, whereas the suppressive effects on MKK7 protein can be efficiently blocked by the proteasomal inhibitor MG132. As a further test, elevating MKK7-JNK activity was sufficient to rescue HDAC6 inhibitor-mediated-suppressive effects on c-Jun activation and the malignant features. The suppression of both MKK7 expression and JNK/c-Jun activities was involved in the tumour-growth inhibitory effects induced by CAY10603 in U87-xenograft mice. Collectively, our findings provide new insights into the molecular mechanism of glioma malignancy regarding HDAC6 in the selective regulation of MKK7 expression and JNK/c-Jun activity. MKK7 protein stability critically depends on HDAC6 activity, and inhibition of HDAC6 probably presents a potential strategy for suppressing the oncogenic roles of MKK7/JNK/c-Jun axis in GCs [1].

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Huang Z, Xia Y, Hu K, Zeng S, Wu L, Liu S, Zhi C, Lai M, Chen D, Xie L, Yuan Z. Histone deacetylase 6 promotes growth of glioblastoma through the MKK7/JNK/c-Jun signaling pathway. J Neurochem. 2019 Aug 7. doi: 10.1111/jnc.14849. [Epub ahead of print] PubMed PMID: 31390677.