ITPRIP

Epigenetic gene silencing of the tumor suppressor death-associated protein kinase 1 (DAPK1) is implicated in the progression of malignant gliomas. However, the mechanism underlying the repression of DAPK1 in gliomas remains elusive.

In a study, Cao et al. identified the existence of DAPK1-inositol 1,4,5-trisphosphate receptor (IP3R)-interacting protein (ITPRIP) -myosin regulatory light polypeptide 9 (MYL9) complex in malignant glioma cells. Lentivirus co-infection and coimmunoprecipitation showed that ITPRIP bound with the death domain (DD) of DAPK1 in vitro. Further, dissociating ITPRIP-DAPK1 interaction inhibited glioma tumor growth in vitro but not in vivo. Moreover, knockdown of ITPRIP or DAPK1 impaired the ternary complex formation, whereas MYL9 knockdown did not affect ITPRIP-DAPK1 association. We further found that ITPRIP recruited MYL9 to the kinase domain (KD) of DAPK1, and in turn impeded the phosphorylation of MYL9. Accordingly, interference of ITPRIP enhanced the suppressive effects of DAPK1-KD on glioma progression both in vitro and in vivo. Our results demonstrate that ITPRIP plays a crucial role in the inhibition of DAPK1 and enhancement of tumorigenic properties of malignant glioma cells [1)]

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Cao C, He K, Li S, Ge Q, Liu L, Zhang Z, Zhang H, Wang X, Sun X, Ding L. ITPRIP promotes glioma progression by linking MYL9 to DAPK1 inhibition. Cell Signal. 2021 Jun 7:110062. doi: 10.1016/j.cellsig.2021.110062. Epub ahead of print. PMID: 34111521.