TRIM9

Tripartite motif containing protein 9 is a protein that in humans is encoded by the TRIM9 gene.

The protein encoded by this gene is a member of the tripartite motif (TRIM) family. The TRIM motif includes three zinc-binding domains, a RING, a B-box type 1 and a B-box type 2, and a coiled-coil region. The protein localizes to cytoplasmic bodies. Its function has not been identified. Alternate splicing of this gene generates two transcript variants encoding different isoforms.

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p38 signaling is broadly involved in controlling inflammation and stress-induced cell death; however, the mechanisms controlling its activity have seldom been studied.

Liu et al. report that TRIM9 short isoform (TRIM9s) potentiates p38 signaling by stabilizing MKK6. Mechanistic studies revealed that TRIM9s promotes the K63-linked ubiquitination of MKK6 at Lys82, thus inhibiting the degradative K48-linked ubiquitination of MKK6 at the same lysine. MKK6 could also stabilize TRIM9s by promoting the phosphorylation of TRIM9s at Ser76/80 via p38, thereby blocking the ubiquitin-proteasome pathway. Further functional analyses showed that p38 signaling plays a critical role in suppressing glioblastoma progression. Co-reduction of MKK6 and TRIM9s is significantly associated with overall poor survival of glioblastoma patients.

Liu et al., identify a positive feedback loop in p38 signaling generated by MKK6-TRIM9s, which suppresses glioblastoma progression, and provide insights into the mechanisms by which TRIM9s and MKK6 potentiate p38 signaling through mutual stabilization [1].

[1]

Liu K, Zhang C, Li B, Xie W, Zhang J, Nie X, Tan P, Zheng L, Wu S, Qin Y, Cui J, Zhi F. Mutual Stabilization between TRIM9 Short Isoform and MKK6 Potentiates p38 Signaling to Synergistically Suppress Glioblastoma Progression. Cell Rep. 2018 Apr 17;23(3):838-851. doi: 10.1016/j.celrep.2018.03.096. PubMed PMID: 29669288.

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