TAZ

The transcriptional coactivator with PDZ-binding motif (TAZ) is one of the important downstream effectors of Hippo signaling pathway.

Yes-associated protein (YAP) and transcriptional coactivator with PDZ-binding motif (TAZ) (hereafter YAP/TAZ) are the downstream effectors of the Hippo signaling pathway. YAP/TAZ overexpression or activation is sufficient to induce tumor initiation and progression, as well as recurrence and therapeutic resistance. However, there is growing evidence that YAP/TAZ also exert a tumor-suppressive function in a context-dependent manner. Therefore, caution should be taken when targeting Hippo signaling in clinical trials in the future. In a review article, Luo et al will first give an overview of YAP/TAZ and their oncogenic roles in various cancers and then systematically summarize the tumor-suppressive functions of YAP/TAZ in different contexts. Based on these findings, they will further discuss the clinical implications of YAP/TAZ-based tumor targeted therapy and potential future directions [1)]

The highly conserved and ubiquitously expressed 14-3-3 proteins regulate differentiation, cell cycle progression and apoptosis by binding intracellular phosphoproteins involved in signal transduction. By screening in vitro translated cDNA pools for the ability to bind 14-3-3, Li et al., identified a novel transcriptional co-activator, TAZ (transcriptional co-activator with PDZ-binding motif) as a 14-3-3-binding molecule. TAZ shares homology with Yes-associated protein (YAP), contains a WW domain and functions as a transcriptional co-activator by binding to the PPXY motif present on transcription factors. 14-3-3 binding requires TAZ phosphorylation on a single serine residue, resulting in the inhibition of TAZ transcriptional co-activation through 14-3-3-mediated nuclear export. The C-terminus of TAZ contains a highly conserved PDZ-binding motif that localizes TAZ into discrete nuclear foci and is essential for TAZ-stimulated gene transcription. TAZ uses this same motif to bind the PDZ domain-containing protein NHERF-2, a molecule that tethers plasma membrane ion channels and receptors to cytoskeletal actin. TAZ may link events at the plasma membrane and cytoskeleton to nuclear transcription in a manner that can be regulated by 14-3-3 [2)].

TAZ expression was identified to be upregulated in glioma specimens and positively correlated with tumor grade. Meanwhile, its expression in nucleus was increased more significantly with the ascending order of tumor grade. Knocking down TAZ inhibited glioma cell proliferation, invasion and promoted apoptosis. Conversely, enforced upregulation of TAZ promoted proliferation, invasion of glioma cells, and suppressed apoptosis in vitro. When orthotopic glioblastoma mouse model implanted with TAZ knocked down cells, glioma growth was inhibited and survival period was prolonged. Expression of Ki67, MMP-9, Cyclin D1, Bcl-2 and C-myc was varied in accordance with the level of TAZ in glioma cell. The biomarkers of EMT (epithelial-mesenchymal transition), vimentin and N-cadherin, were downregulated when TAZ was suppressed. Using Co-immunoprecipitation TAZ was identified to bind to TEAD4. Therefore, this findings indicate that TAZ is overexpressed in glioma and translocated more into nucleus in high grade glioma. TAZ is involved in gliomagenesis by promoting glioma growth and may benefit to EMT progression. This result suggests that TAZ serves as a potential target for the treatment of glioma [3)].

1)
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2)
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3)
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