YAP1

YAP1 (Yes-associated protein 1), also known as YAP or YAP65, was first identified by virtue of its ability to associate with the SH3 domain of Yes and Src protein-tyrosine kinases.

YAP1 is a potent oncogene, which is amplified in various human cancers, and it is one of the two main effectors of the Hippo signaling pathway.

The activation of proline-rich phosphoprotein Yes-associated protein 1 (YAP1) possesses a possible link between stem/progenitor cells, organ size, and cancer. YAP1 has been indicated as an oncoprotein, and overexpression of YAP1 is reported in many human brain tumors, including infiltrating gliomas. During normal brain development, the neurofibromatosis 2 (NF2) protein suppresses YAP1 activity in neural progenitor cells to promote guidepost cell differentiation, but loss of NF2 causes elevating YAP1 activity in midline neural progenitors, which disrupts guidepost formation. Overexpression of endogenous CD44 (cancer stem cell marker) promotes phosphorylation/inactivation of NF2, and upregulates YAP1 expression and leads to cancer cell resistance in glioblastoma. The hippo pathway is also related to the YAP1 action. However, the mechanism of YAP1 action in glioma is still far from clear understanding. Advances in clinical management based on an improved understanding of the function of YAP1 may help to serve as a molecular target in glioma therapeutics. Knockdown of YAP1 by shRNA technology has been shown to reduce glioma in vitro; however, clinical implications are still under investigation. YAP1 can be used as a diagnostic marker for gliomas to monitor the disease status and may help to evaluate its treatment effects. More functional experiments are needed to support the direct roles of YAP1 on gliomas at molecular and cellular levels [1)].

Results showed the overexpression of YAP1 and Survivin as well as a decreased activity of large tumor suppressor 1 (LATS1) in high-grade glioblastoma versus anaplastic astrocytoma and low-grade glioma. Furthermore, Aguennouz et al. also demonstrated that miR-221 and miR-10b are specifically involved in Hippo signaling pathway via LATS1 regulation and that their knockdown significantly decreased glioma cell proliferation. This preliminary data confirmed the crucial role of the Hippo signaling pathway in cancer and suggested that miR 221 and miR 10b could be potential therapeutic targets for glioma treatment [2)].

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Liu YC, Wang YZ. Role of Yes-associated protein 1 in gliomas: pathologic and therapeutic aspects. Tumour Biol. 2015 Apr;36(4):2223-7. doi: 10.1007/s13277-015-3297-2. Epub 2015 Mar 7. Review. PubMed PMID: 25750037.
2)
Aguennouz M, Polito F, Visalli M, et al. microRNA-10 and -221 modulate differential expression of Hippo signaling pathway in human astroglial tumors [published online ahead of print, 2020 Aug 5]. Cancer Treat Res Commun. 2020;24:100203. doi:10.1016/j.ctarc.2020.100203