Regulation of Hippo-YAP/TAZ Pathway in Cancer Biology

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The Hippo-YAP/TAZ Signaling Pathway have emerged as key regulator of organ size and tissue homeostasis, and their dysregulation contributes to human cancer. Here I will present an overview of various upstream regulators of Hippo-YAP/TAZ and TEAD including Mechanotransduction, GPCR ligands, Cell Polarity, and Energy stress as potential targets for anticancer therapies. I will also focus on our recent findings on YAP/TAZ as bona fide effectors of the alternative Wnt signaling pathway. Wnt5a/b and Wnt3a induce YAP/TAZ activation via the alternative Wnt pathway that is independent of Wnt/b-catenin signaling. In addition, we recently identified TAZ expression in leukemia and macrophage cells in several pathologic contexts, which suggest a novel function of Hippo signaling in leukemogenesis and immunity. Unlike YAP/TAZ, the transcription factor TEAD are constantly nuclear. However, our recent findings revealed that specific stress promotes cytoplasmic translocation of TEAD via protein-protein interaction with p38 MAPK. Importantly, inhibition of TEAD by p38-induced cytoplasmic translocation suppresses YAP/TAZ-driven cancer cell growth. Therefore, the Hippo pathway is an attractive target for anticancer drug development.