

Stefano Piccolo Abstract

Function and regulation of YAP/TAZ by cell mechanics and Wnt signaling

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The transcriptional regulators YAP and TAZ are the focus of intense interest given their remarkable biological properties in development, tissue homeostasis and cancer. YAP and TAZ activity is key for the growth of whole organs, for amplification of tissue-specific progenitor cells during tissue renewal and regeneration, and for cell proliferation. In tumors, YAP/TAZ can reprogram cancer cells into cancer stem cells and incite tumor initiation, progression and metastasis. As such, YAP/TAZ are appealing therapeutic targets in cancer and regenerative medicine. YAP/TAZ are well known for being the effectors of the Hippo signaling cascade, and mouse mutants in Hippo pathway components display remarkable phenotypes of organ overgrowth, enhanced stem cell content and reduced cellular differentiation. YAP/TAZ are primary sensors of the cell's physical nature, as defined by cell structure, shape and polarity. YAP/TAZ activation also reflects the cell "social" behavior, including cell adhesion and the mechanical signals that the cell receives from tissue architecture and surrounding extracellular matrix (ECM). I will also discuss new evidence indicating that YAP/TAZ entertain profound relationships with Wnt signaling. YAP/TAZ thus appear at the centerpiece of a signaling nexus by which cells take control of their behavior according to their own shape, spatial location and growth factor context.

