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Role of YAP/TAZ in mechanotransduction

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Cells perceive their microenvironment not only through soluble signals but also in term of physical and mechanical cues, such as extracellular matrix (ECM) stiffness or confined adhesiveness. By mechanotransduction systems, cells translate these stimuli into biochemical signals controlling multiple aspects of cell behavior, including growth, differentiation and cancer malignant progression; but how rigidity mechanosensing is ultimately linked to activity of nuclear transcription factors remains poorly understood. Here we report the identification of the Yorkie-homologues YAP and TAZ as nuclear relays of mechanical signals exerted by ECM rigidity and cell-shape. This regulation requires Rho activity and tension of the acto-myosin cytoskeleton but is independent from the Hippo/LATS cascade. Crucially, YAP/TAZ are functionally required for differentiation of mesenchymal stem cells induced by ECM stiffness and for survival of endothelial cells regulated by cell geometry; conversely, expression of constitutive active YAP overrules physical constraints in dictating cell behavior. These findings identify YAP/TAZ as sensors and mediators of mechanical cues instructed by the cellular microenvironment.