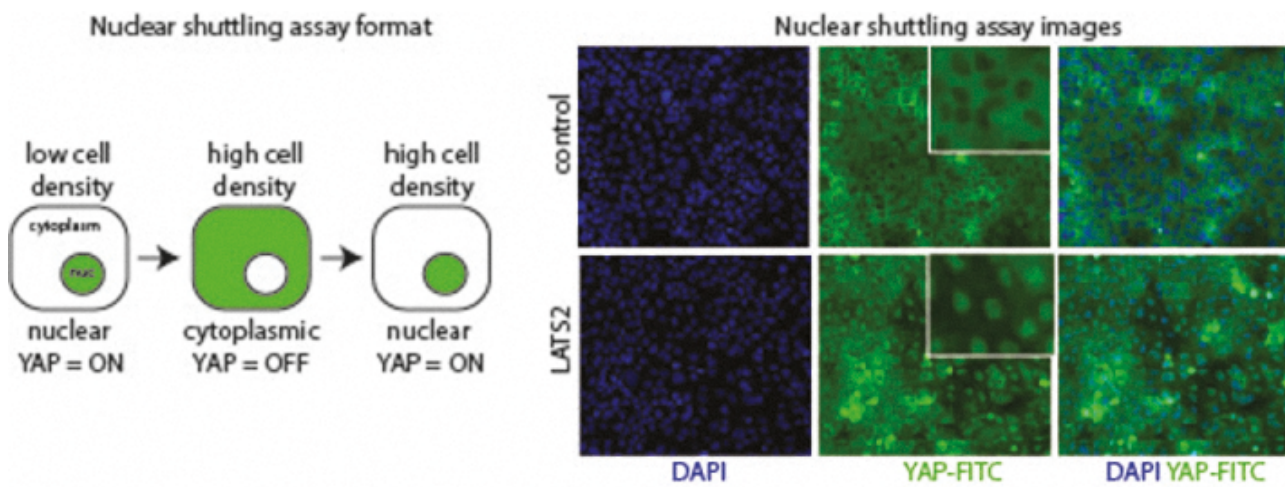


Essential biological pathways modulate many different aspects of cell biology

High throughput screening is the most common way to discover novel drugs as well as new ways in which drugs could act. Screening chemicals for drug discovery has identified a group of molecules which are able to inhibit many different biochemical assays these have been called “promiscuous compounds”. Compounds have also been identified that influence many different cell based assays, these compounds were found to act not by inhibiting multiple targets, as promiscuous compounds do, but by effecting multiple biological processes. Our recent paper: 'Activation of Yap-Directed Transcription by Knockdown of Conserved Cellular Functions' describes how genetic reagents that remove conserved cellular functions can appear to have a specific effect; even though they will impact on many aspects of cell biology. This observation came about from a screen for genes that might serve to activate a cell signalling pathway, which is essential for liver regeneration.



This figure gives an outline of the screen used in this study as well as pictures showing the effect on YAP localization comparing the effect of control siRNAs as well as siRNAs against LATS2

The article describes how genetic tools were used to inhibit the function of 7000 possible genes in a cell based assay that monitors the location of the YAP protein in the cell. Normally for cells which are touching each other YAP is mostly present in the cell cytoplasm, the goal of this screen was to identify genes that when reduced would allow YAP to move into the cell nucleus where it would direct the expression of genes required for cell division and growth.

The article shows how almost a quarter the genes identified in this screen are part of essential, cell pathways such as processes required for the movement of proteins within the cell or the degradation of proteins. These targets could all be validated by showing that they lead to increased

activation of the YAP-Hippo pathway and that these effects could be reproduced using chemical tools that inhibited these gene targets. This observation will help researchers to deprioritize similar observations in screens for gene targets in other cell responses. Hopefully this report will be useful for others to prioritize the genes that show activity in their assays so as to identify those most specific for drug discovery efforts.

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Publication

[Activation of Yap-Directed Transcription by Knockdown of Conserved Cellular Functions.](#)

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