SIBBM Lecture

Control of Organ Size by the Hippo Pathway

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Abstract

The Hippo pathway is a complex signalling network that controls developmental tissue growth and is frequently deregulated in different human cancers. Discovered by us and others using genetic screens in Drosophila in 2002, the Hippo pathway is now the subject of intense investigation. Despite this, the mechanism of signal transduction within this pathway is incompletely understood. We have used targeted approaches as well as large-scale genetic and proteomic screens to address these knowledge deficiencies.

We have been involved in the discovery of 15 Hippo pathway proteins, including the three founding members (Salvador, Warts and Hippo) and the first transmembrane receptor (Fat cadherin). Using genetic screens, we identified Tao-1 as a kinase that regulates activity of the Hippo kinase, and Hipk as a kinase that promotes activity of the Yorkie transcription co-activator. Using proteomic screens, we identified a new branch of the Hippo pathway, from transmembrane receptor to the nucleus, that operates downstream of the Dachsous cadherin. We also discovered the GTPase regulatory proteins Pix and Git as proteins that activate the Hippo kinase. These studies have provided important insights into the signalling logic that operates in the Hippo pathway in the context of tissue growth. More recently, we have begun to explore Hippo-like signaling networks, which are used iteratively throughout metazoans to regulate diverse cellular functions.