Log of Research Documents

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1. Tumaneng, et al.: YAP mediates crosstalk between the Hippo and PI3K-TOR pathways by suppressing PTEN via miR-29.
    - YAP is main downstream target of mammalian Hippo pathway, promotes organ growth
    - YAP activates mTOR (major regulator of cell growth)
    - YAP is phosphorylated and inhibited by LATS
    - Cell density is known to regulate YAP phosphorylation and activity
    - Yorkie (Drosophila) induces expression of bantam microRNA that serves as a critical mediator of Yorkie's biological functions
    - Establishes a functional link between Hippo and TOR in mammals
2. Kockel, et al.: Dynamic Switch of Negative Feedback Regulation in *Drosophila* Akt-TOR Signaling
    - Three basic concepts of downregulating signaling pathways: control via specific inhibitory ligands/receptors, negative cross-regulation by distinct signaling pathways, auto-regulation by negative feedback mechanisms
    - TORC1 and TORC2 both participate in Akt-TOR signaling but act at different levels in the pathway and integrate distinct stimuli: TORC2 responds to growth factors and might determine substrate specificity of Akt, TORC1 mediates signaling by amino acids and cellular energy stress.
    - dAkt-TOR pathway in Drosophila regulates cell proliferation, developmental timing and sizing of cells, organs, and whole fly
    - Drosophila has only one dAkt gene (mammals have 3)
    - Phosphorylation of dAkt is regulated by negative feedback from Tsc1/Tsc2-TOR-S6K but independent of FoxO
    - Negative feedback regulating dAkt activity is independent of S6K under normal TORC1 activity or dependent on S6K when TORC1 activity is high. Thus, S6K is a sensor of TORC1 that provides additional suppression of the signal when TORC1 is highly active.
3. Zhao, et al.: The Hippo pathway in organ size control, tissue regeneration, and stem cell self-renewal

- Hippo pathway limits organ size by phosphorylating and inhibiting Yki, a key regulator of proliferation and apoptosis
- Hippo pathway is regulated by cell polarity, cell adhesion and cell junction proteins
- Core components of Hippo pathway: warts (wts), hippo (hpo), salvador (sav), all tumor-suppressor genes
- Wts directly phosphorylates and inhibits Yki
- Merlin (Mer) and Expanded (Ex) were found to activate the Hippo pathway
- Fat protocadherin, a cell surface molecule, is an upstream regulator of Hippo pathway. Its activity is regulated by binding to Dachsous (Ds) and is modulated by Dco, Fj, and Lft. Dpp and Wg affect expression of Fj and Ds.
- Yki induces cycE and E2F1 (regulation of cell proliferation), EGFR ligands and Jak-Stat ligands
- An imbalance of Hippo pathway activity in neighboring cells may induce cell competition through differential expression of dMyc in Drosophila
- Mechanism by which upstream regulators of the Hippo pathway are integrated to initiate or terminate signaling is not yet fully understood