Research In Progress Seminar

Tuesday, March 7, 2017
2:00PM

Location: The Fishbowl, 2120 Biological Sciences 3

Speaker:
Mike Drummond, Developmental & Cell Biology

Talk Title:
Cdc42 restricts primary cilia by fine-tuning ciliary actin

Abstract:
Primary cilia are polarized organelles that assemble during interphase and allow the cell to detect extracellular signals such as Hedgehog, yet how the cilium generates and maintains a structure that finely tunes cellular response remains unclear. Previously, we identified the polarity protein atypical Protein Kinase C iota/lambda (aPKC) as a critical regulator of ciliogenesis and Hedgehog signaling in basal cell carcinoma. Here we find that aPKC is in one of three actin regulatory complexes that Cdc42 recruits to the basal body of mesenchymal cells to restrict cilia number and length. Par6a-aPKC, MIM, and Toca1-N-WASp are recruited by Cdc42 to the basal body to maintain homeostatic levels of polymerized actin and restrict primary cilia. aPKC activity is necessary to restrict cilia and transcriptome analysis of aPKC inhibitor-treated cells indicate the Src pathway as a major effector. aPKC promotes Src-mediated restriction of cilia whereas MIM antagonizes Src activity. As actin regulation is a function of Src through activation of Cortactin-N-WASp, we also find that loss of N-WASp-Arp2/3 and the Cdc42 mediator Toca1 increase cilia number and length. Finally, the increase in primary cilia amplifies Hedgehog signaling except when aPKC is lost through knockdown of aPKC or Cdc42. Our data suggests Cdc42 serves as a master regulator of ciliogenesis by recruiting three distinct actin regulatory complexes to the basal body to restrict primary cilia and promote Hedgehog signaling.

Questions:
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