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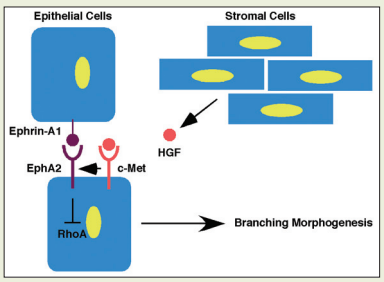
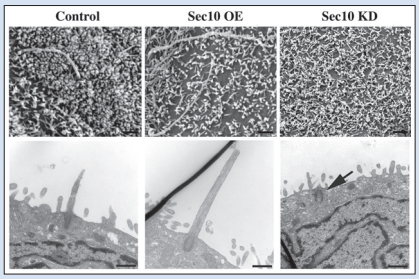
Regulation of Mammary Gland Branching Morphogenesis by Epha2 Receptor Tyrosine Kinase

David Vaught, Jin Chen, and Dana M. Brantley-Sieders



Mammary epithelial morphogenesis is a complex process during which an extensive network of branched ducts forms from a rudimentary epithelial bud. Morphogenesis is regulated by the paracrine interactions of hormones between the developing epithelial ducts and their adjacent mesenchymal stroma, as well as through receptor tyrosine kinases. Through analysis of EphA2-deficient mice, the authors show that this membrane-bound receptor tyrosine kinase plays a critical role in regulating ductal morphogenesis. Loss of EphA2 inhibits proliferation of the mammary epithelium and delays ductal outgrowth in the mammary fat pad independent of the host environment. Previous overexpression analyses had indicated that EphA2 functions as a negative regulator of mammary gland morphogenesis. Thus the new results highlight the importance of knockdown studies. Investigations at the cellular level demonstrated that EphA2-deficient primary mammary epithelial cells are unable to branch and do not respond to hepatocyte growth factor, because of misregulation of the Rho family GTPase. This report shows a positive role for EphA2 receptor function in normal mammary epithelium through inhibition of RhoA GTPase.



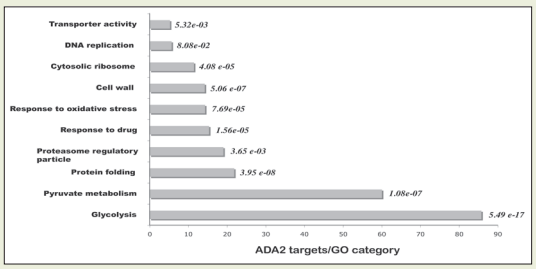
The Exocyst Protein Sec10 Is Necessary for Primary Ciliogenesis and Cystogenesis In Vitro

Xiaofeng Zuo, Wei Guo, and Josh Lipschutz

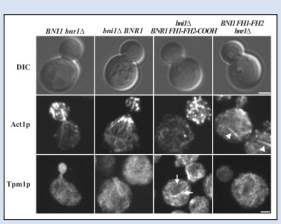
Primary cilia found on renal tubular epithelial cells appear to act as mechanosensors of urinary flow. Defects in primary cilia have been strongly implicated in autosomal dominant polycystic kidney disease, the most common potentially lethal genetic disease. The authors previously showed that the exocyst, a highly conserved eight-protein complex, localizes to both the tight junction and the primary cilium. To investigate the role of the exocyst in ciliogenesis and cystogenesis, the authors performed shRNA knockdown of exocyst component Sec10 in MDCK cells. Sec10 knockdown prevented ciliogenesis, whereas Sec10 overexpression increased ciliogenesis. When placed in collagen, the Sec10 knockdown MDCK cells no longer formed cysts, but the Sec10-overexpressing MDCK cells formed cysts more rapidly and efficiently than untransfected control cells. Furthermore, the exocyst colocalized and coimmunoprecipitated with Par3, another protein that is essential for ciliogenesis. These data support a model in which the exocyst, by trafficking vesicles carrying ciliary proteins, is centrally involved in both ciliogenesis and cystogenesis.

Genome-wide Mapping of the Coactivator ADA2 Yields Insight into the Functional Roles of SAGA/ADA Complex in *Candida albicans*

Adnane Sellam, Christopher Askew, Elias Epp, Hugo Lavoie, Malcolm Whiteway, and André Nantel



The SAGA/ADA transcriptional coactivator complex is widely conserved throughout eukaryotes and regulates numerous cellular processes by coordinating histone acetylation. The authors investigated the genome-wide occupancy of the SAGA/ADA component Ada2p in *Candida albicans* by means of chromatin immunoprecipitation. They demonstrate a key role of Ada2p in many processes related to *C. albicans* pathogenicity, such as drug resistance and oxidative stress tolerance. Importantly, they also demonstrate that transcriptional rewiring requires the recruitment not only of transcription factors, but also of their coactivators. Indeed, sequence-specific transcription factors such as Gal4, Cap1, and Mrr1p, which regulate proteins involved in glycolysis, oxidative stress, and drug resistance, respectively, recruit Ada2p to their respective promoters. Finally, *ada2* deletion causes a clear decrease in histone acetylation in vivo, demonstrating a role for Ada2p in chromatin remodeling through histone acetylation, in addition to its conserved function as a specific transcriptional coactivator.



Polarized Growth in Budding Yeast in the Absence of a Localized Formin

Lina Gao and Anthony Bretscher

Formins are highly conserved proteins containing FH1-FH2 domains that nucleate actin assembly and remain attached to the barbed end of the growing actin filament. Formins also have regions that determine the location, and thus the polarity, of assembled actin structures. In budding yeast, formins localized to the bud cortex and bud neck assemble polarized actin cables that serve an essential role as tracks for the transport of secretory vesicles for cell growth. Thus it was thought that formin localization would be essential for growth. However, the authors show that yeast expressing only the nonlocalized actin nucleating/assembly FH1-FH2 domains of formins grow well. By tracking the movement of secretory vesicles, the authors show that cables were still partially oriented towards the bud neck. Further, they show that myosin II, localized at the bud neck, contributes to actin cable orientation. These results reveal that actin cable orientation can be mediated by systems other than formin localization. ■