Expression of a truncated Sall1 transcriptional repressor is responsible for Townes-Brocks syndrome birth defects

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The multi-zinc finger transcription factors of the Sall family regulate development of multiple organs in flies, worms, fish, and vertebrates. In humans, mutations in SALL1 result in the autosomal dominant syndrome Townes-Brocks (TBS) that causes abnormal ear, kidney, limb, and anal development. TBS was thought to result from haploinsufficiency of SALL1, however a sall1-null allele does not mimic the human syndrome. Since TBS mutations could result in expression of a Sall1 protein that contains the N-terminal transcriptional repression domain and lacks the putative DNA binding domain, we hypothesized that TBS is due to dominant interference from truncated Sall1. To test this hypothesis we created a mutant allele, sall1-Δzn10, that produces truncated Sall1 protein and recapitulates the abnormalities found in TBS. Like sall1-null mice, homozygous sall1-Δzn10 mutants display complete renal agenesis underscoring the critical role for this protein in kidney development. Unlike sall1-null mice, homozygous sall1-Δzn10 mutants display extrarrenal phenotypes including exencephaly, absent carpal bones, oligosyndactyly, and imperforate anus. In addition, heterozygous mice recapitulate the dominant TBS birth defects of hearing loss, renal cystic hyoplasia and wrist bone abnormalities. To investigate the mechanism by which the truncated protein exerts deleterious effects on developing organs, we analyzed the functional domains contained within this N-terminal region. The N-terminus of Sall1 represses transcription via recruitment of an HDAC containing complex and mediates homo- and heterodimer formation with all four vertebrate Sall family members. Expression of the N-terminus in transgenic mice can recapitulate TBS-like phenotypes in limb suggesting these functional domains cause dominant interference during development. We propose a model whereby expression of a truncated Sall1 protein interferes with transcriptional repression of target genes by wild type Sall proteins to alter development of the ear, kidney, limb and anus.

Flower Development of Lycopersicon pimpinellifolium LA1589, a Close Relative of Cultivated Tomato

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Cultivated tomato (Lycopersicon esculentum) display abundant variation in fruit size and shape. To better understand the underlying mechanism of diversity in fruit form, we have undertaken a morphological analysis of tomato flower and fruit development. Understanding ontogeny of the ovary, associated flower parts, and fruit is critical for determining when fruit morphology changes occur. Developing inflorescences and floral buds of L. pimpinellifolium LA1589, a close relative of tomato, were analyzed by dissection, scanning electron, light and confocal microscopy. Transition from vegetative to reproductive development is described. After reproductive development commences, a floral meristem appears to bud off the inflorescence meristem thus giving rise to a raceme inflorescence structure. Floral development stages are described according to the landmarks of floral development as identified by Buzgo et al (2004). Approximately four days after floral meristem formation, initiation of the sepal and petal primordia occurs. Within two days following petal initiation, the stamen and the carpel primordia initiate. Five to six days after carpel primordia initiation, male meiosis takes place, followed by female meiosis one to two days later. Anthesis occurs approximately 19 to 20 days after flower initiation. Buzgo, M., et al. (2004). Trends in Plant Science, 9: 164-173. This work is supported by NSF grant DBI-0227541 to EvdK

Developmental Modeling of the Arabidopsis Shoot Apical Meristem

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The computable plant project is developing an end-to-end research and modeling framework for the Arabidopsis shoot apical meristem (SAM). We observe several cell type specific markers for growth and differentiation in real-time in live plants with a dedicated confocal laser scanning microscope. Using a combination of computational modeling and image processing techniques we then infer specific transduction pathway data and fit mathematical models to produce two- and three- dimensional visualizations of the growing SAM, include phyllotactic and leaf-vein development. In particular, we have developed several green fluorescent protein (GFP) variants that allow us to observe various meristem and floral primordial features including both cell walls and cell nuclei as well as track specific cell lineages over time. Our aim is to determine the spatial and temporal relationships between different genes in an effort to understand how primordial cells are progressively specified. These markers will allow us to correlate gene expression changes with cell growth over time. Thus far the live imaging technique has led to the development of a spatial and temporal map of cell division patterns. We have observed that primordium development is a sequential process linked to distinct cellular behavior, and that the amount of cell division is comparable in regions of the SAM where successive primordia arise. Changes in cell division orientation are associated with initial outgrowth of a flower primordium. These changes are followed by a rapid burst of cell expansion and cell division that transforms a flower primordium into a flower bud. We are developing software to automatically extract cell positions from time-lapse observations; integrating this information with inferred pathways, it should be possible to produce forward simulations that predict and visualize meristem growth. Supported by NSF Grant 0330786.

Analysis of CaM Kinase II in the Early Embryos of Marine Brown Alga, Silvetia compressa

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A transient increase in the concentration of free Ca2+ in the cytosol of a cell is caused by the activation of Ca2+ channels in the plasma membrane or the membranes of the ER. Calcium ions act by binding to calcium-binding proteins, amongst which is calmodulin. A change in protein