

University of Illinois Ada Doisy Lectures April 2009

Abstracts

Dr. Mark Krasnow

The Branching Program of Lung Development

A central challenge in developmental biology and medicine is understanding how organs form and are maintained, and how aberrations in these processes cause disease. Many organs such as lung, vascular system, kidney, and pancreas are composed of vast branching networks of tubes that transport essential gases or fluids. Although development of such organs has been studied for decades, little was known about the underlying genetic and molecular programs. Krasnow and colleagues established the first tractable genetic system to elucidate an organogenesis program, and their systematic mutant screens in *Drosophila* opened the way to a genetic and molecular understanding of branching morphogenesis. Their characterization of the branching process at single cell resolution, combined with their systematic genetic dissection of the process, parsed the complex branching program into genetically separable steps, and characterization of the identified genes elucidated the molecular pathways that underlie each step. More recently, he and his colleagues have extended their studies to the mammalian lung. This work revealed that lung development is remarkably stereotyped and mathematically elegant: it is generated by three different local modes of branching used in three different sequences throughout the lung. And, although the lung is orders of magnitude more complex than structurally related organs in *Drosophila* and *C. elegans*, this work shows that its developmental program can be genetically dissected in a similar manner. Krasnow and colleagues' work provides the first comprehensive cellular and molecular understanding of an organogenesis program, and it establishes a paradigm for branching morphogenesis, the process by which most organs form. Because current data suggest that the molecular pathways used to build an organ are later reused to maintain, remodel, and repair it, the work has long term implications for understanding how misregulation of the developmental pathways cause disease and how the pathways can be manipulated to regenerate damaged tissue.

Dr. Mario Capecchi

Mouse Models in Human Disease: From Cancer to Neuropsychiatric Disorders

Gene targeting allows the designed modification of any gene in the mouse genome. Since genes impact all biological phenomena this methodology can be used to study any biological phenomena common to mammals in the mouse. We are using it to model human disease in the mouse. The models can be used to analyze the pathology of the disease at a level not feasible in humans and as a platform for the development of new therapeutic protocols. I will discuss modeling two human cancers and one neuropsychiatric disorder in the mouse.