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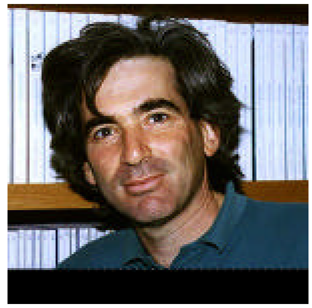

Professor of Genetics and Development

Research Interests

My group is pursuing three lines of research: the transcriptional control of Drosophila embryogenesis, notochord differentiation in the tunicate, Ciona intestinalis, and a critical test of classical models for the evolutionary origins of the chordate body plan.

Current Projects

Our studies on the Drosophila embryo center on understanding how crude regulatory gradients direct sharp, on/off patterns of transcription, such as segmentation stripes of gene expression. Many of these studies focus on Dorsal, which is a Rel-containing regulatory factor that is distributed in a broad nuclear gradient in the early embryo. Dorsal specifies the embryonic mesoderm, neurogenic ectoderm, and dorsal ectoderm through the differential regulation of varous target genes in a concentration-dependent manner.

We are also using the early Drosophila embryo to study transcriptional repression. These studies suggest that there are two basic modes of repression, short-range and long-range. Short-range repressors work over distances of less than 100 bp to inhibit (or quench) nearby upstream activators. In contrast, long-range repressors can function over distances of 1 kb or more to silence the transcription complex.

Another focus of our studies on the Drosophila embryo concerns the regulation of enhancer-promoter interactions in complex genetic loci. We have obtained evidence that proper enhancer-promoter interactions depend on insulator DNAs and functionally diverse core promoters.

The Drosophila embryo has been used with considerable success to unravel complex networks of gene activity. However, it has been difficult to link these networks to cellular morphogenesis. For this purpose we have recently begun to study Ciona embryogenesis. Ciona is a simple chordate with a small genome and well-defined embryonic lineages (e.g., the notochord is composed of just 40 cells). It is possible to introduce transgenic DNA into developing Ciona embryos using simple electroporation methods. These studies have led to the detailed characterization of a notochord-specific enhancer from the promoter region of the

Ciona Brachyury gene. In addition, it has been possible to identify putative Brachyury "target genes" that are responsible for notochord differentiation.

We are just beginning a new project on the evolutionary origins of the chordate body plan. Ciona represents the most primitive and basic type of chordate; the tadpole contains a notochord and dorsal, hollow neural tube. However, other protochordates, the hemichordates and echinoderms, lack these features and possess radically divergent body plans. Over 100 years ago Garstang proposed that the chordate tadpole arose from a simple reorganization of the larvae of certain echinoderms (sea cucumbers and starfish) and hemichordates (enteropneusts). We intend to use a variety of molecular methods to test this hypothesis.