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relating to the specification and determination of sensory cell fates. Yet, other insect species that are of ecological and economic importance such as Heliothine moths provide alternative systems for investigation. This research project aimed to characterize key phases of antennal imaginal disc development in *Heliothis virescens*, commonly known as the tobacco budworm. *Heliothis virescens* is a major agricultural pest species; in recent years much work has been focused on understanding pheromone processing in mating behaviors of *H. virescens* and related species. Our objective was to investigate the development of antennae in *Heliothis virescens*. The approach was to use sequence information from known regulators such as *atonal* (*ato*), *daschund* (*dac*) and *distal-less* (*dll*) to identify moth homologues. Identified sequences and other reagents were used to characterize developmental transitions during larval and pupal stages of antennal disc development. This study provides key insights into the complex events that shape the formation of a sensory organ involved in pheromone detection.

doi:10.1016/j.ydbio.2009.05.383

Program/Abstract # 354
Epithelial Hedgehog signals direct mesenchymal villus patterning through BMP

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The intestine is an essential organ, acting as the main absorptive tissue for liquids and nutrients. The highly organized and specialized structure of the intestine provides increased surface area to allow maximum absorptive function. Finger-like projections called villi increase the surface area of the intestine by ten-fold. Nutrient deficiency is prevalent among patients affected by diseases, such as celiac disease, that compromise villus structure. Villus development is coordinated through crosstalk between the two layers, endoderm and mesoderm, of the embryonic intestine. Paracrine Hedgehog (Hh) signaling from the endoderm to the mesoderm plays a key role in villus development and reduced Hh signaling compromises villus development. Using Hh pathway reporter mice, we observed that clusters of mesenchyme cells which are associated with emerging villi are Hh responsive. The clusters also express a multitude of Bmps and Bmp modulators. Clusters are regularly spaced in an apparent field pattern and likely function to provide a signaling center to initiate villus emergence and mark the site of vascular development for the villus core blood supply. Through the employment of a novel organ culture system, we found that manipulation of Bmp signaling can alter the formation and spacing of mesenchymal clusters and in turn alter villus development.

doi:10.1016/j.ydbio.2009.05.384

Program/Abstract # 355
Cloning and characterization of the mouse Hol mutation that mimics human DiGeorge syndrome

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Our laboratory uses genetic and developmental approaches, exploiting the mouse as a model system, to study organ morphogenesis and its perturbations during embryonic development. Phenotype-based forward genetic screens by ENU mutagenesis are being performed to uncover novel genes required for mammalian skeletal development. The Hol mutant line was selected based on striking limb and craniofacial developmental defects. Hol mutant embryos die in utero at E15 and display defects of the face (hypoplastic jaw and ear, mimicking DiGeorge syndrome) and limbs (shorter bones and polydactyly). We hypothesize that Hol is a critical gene required for early skeletal development. We are establishing the onset and nature of the skeletal defects in Hol mutants. Also, we are examining the embryonic expression of genes critical for skeletal development. We have linked the Hol-critical interval to a 500kb of DNA on mouse chr11. To identify the mutation responsible for the Hol phenotype, we will sequence all the genes in the interval (25), starting with the most promising candidates. Finally, we will confirm that the identified molecular lesion is responsible for the Hol phenotype by analyzing the mutated protein and performing genetic complementation in the mouse. Completion of these studies will significantly advance our understanding of the genetic control of skeleton morphogenesis and homeostasis. Our ultimate goal is to discover a new gene critical for skeletal development and likely involved in human DiGeorge syndrome.

doi:10.1016/j.ydbio.2009.05.385

Program/Abstract # 356
The effect of gene dosage imbalance and NFATc1 localization on endocardial cushion development in the Ts65Dn mouse model for Down syndrome

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Down syndrome (DS) is a genetic disorder caused by triplication of chromosome 21. The Ts65Dn mouse model for trisomy 21, which inherits 50 of the orthologous genes triplicated in DS, often displays phenotypes comparable to those observed in DS patients, including cardiovascular abnormalities. Therefore, this organism provides a useful model for studying the development of congenital heart defects that affect nearly one half of all DS individuals. In this study, we examined the role of gene dosage imbalance, and in particular, that of the nuclear factor of activated T-cell (NFATc) signaling pathway, during cardiac development. The NFATc signaling pathway is crucial for proper cardiac cushion development and is also necessary for normal septal and valvular formation between embryonic days 9.5 (E9.5) and E14.5 of mouse development. Using primary monoclonal antibody to NFATc1 on sectioned heart tissue at E10.5 through E12.5, we employed fluorescence immunohistological techniques to detect altered protein expression. We detected little NFATc1 at E10.5, protein localization to the cardiac cushion endocardium at E11.5, and reduced NFATc1 expression in the endocardium of E12.5 trisomic and euploid embryos. Furthermore, we showed that there was a differential level of NFATc1 expression in the cardiac cushion mesenchyme of trisomic embryos at E12.5 as compared to their euploid siblings. Using these assays and future studies, we hope to show that dysregulation of the NFATc signaling pathway plays a critical role in the disruption of early cardiac valve development in our mouse model and DS.

doi:10.1016/j.ydbio.2009.05.386