Abstracts

Development of the integument and sensory perception

Program/Abstract # 63
Evidence that a late-emerging population of trunk neural crest cells forms the turtle plastron and nuchal bones
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The origin of the turtle plastron is not known, but these nine bones have been homologized to the exoskeletal components of the clavicles, the interclavicular bone, and gastralia. Earlier evidence from our laboratory showed that the plastron-forming cells were positive for HNK-1 and PDGFR-alpha, two markers of the skeletogenic neural crest. This study looks at the embryonic origin of these plastron-forming cells. We show that the HNK-1+ cells are also positive for p75 and FoxD3, confirming their neural crest identity, and that they originate from the dorsal neural tube of stage 17 turtle embryos, several days after the original wave of neural crest cells have migrated and differentiated. Dil studies show that these are migratory cells, and they can be observed in the lateral regions of the embryo and can be seen forming intramembranous bone in the ventral regions. Before migrating ventrally, these late-emerging neural crest cells reside for over a week in a carapacial staging area above the neural tube and vertebrae. The nuchal bone (the most anterior bone of the carapace) also stains with HNK-1 and stains positively for PDGFR-alpha, suggesting that it, too, has a neural crest origin.

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Program/Abstract # 64
Drosophila Homer is required for retinal apoptosis
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Apoptosis is necessary for the proper development of all organisms. It functions to refine the morphology of developing limbs and tissues, to balance cell proliferation rates, and to eliminate unnecessary or abnormal cells or structures. In Drosophila, the retina provides a sensitive indicator of defects in apoptotic regulation, where misregulation is easily detected at the cellular level. We have previously shown that a transcription factor, klumpfuss (klu), is necessary and sufficient for apoptosis in the retina. Recent microarray data to identify klu-regulated molecules identified homer, which is upregulated in response to klu overexpression. We demonstrate that Homer is required for apoptosis; retina from homer loss-of-function pupae displays a decrease in apoptosis, resulting in extra interommatidial cells. Additionally, we show that Homer is dynamically expressed in these cells, those that will “choose” life or death in the retina, during retinal development. This expression is disrupted in klu mutant backgrounds, supporting a molecular interaction between the two molecules. Previously, Homer has only been suggested to function in an anti-apoptotic capacity through Akt signaling in neuronal cells. Our data indicate a novel role for Homer in apoptosis, and suggest another possible signaling pathway where Homer interacts with klu to affect apoptosis.

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Program/Abstract # 65
Regulation of cell fate and patterning in the mammalian cochlea
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The auditory sensory epithelium in mammals, referred to as the organ of Corti, is a narrow strip of cells, approximately 100 μm wide, that extends along the full length of the cochlear spiral. Within this strip, specialized cell types, including mechano-sensory hair cells and non-sensory supporting cells, are
arranged into highly ordered rows. The organ of Corti develops from a population of placodally derived prosensory cells within the cochlear duct through a series of restrictive and inductive events. Initially, a subset of epithelial cells within the duct become biased towards a prosensory fate through expression of Sox2, leading to induction of the bHLH transcription factor Math1 in a number of these cells. The width of the prosensory domain, and therefore of the organ of Corti, is determined by the extent of expression of Sox2 and Math1, a process that is controlled, at least in part, by the Hedgehog signaling pathway. Expression of Math1 commits all prosensory cells to a hair cell fate, however, subsequent interactions involving both the Id and Notch signaling pathways lead to down-regulation of Math1 and a diversion from the hair cell fate in a subset of prosensory cells. Concurrently, developing hair cells produce inductive signals that recruit the same prosensory cells to develop as supporting cells. In particular, interactions between hair cell-derived Fgf8 and Fgfr3 lead to the development of specific supporting cell types.

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Program/Abstract # 66
Development and regeneration in the zebrafish lateral line
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We have explored some of the molecular mechanisms underlying the development of the mechanosensory lateral line system in the zebrafish. The lateral line sensory organs are the neuromasts, clusters of hair cells surrounded by accessory cells, distributed over the surface of the body. The neuromasts form at the end of embryogenesis through a process of highly stereotyped migration of a primordium and cell deposition. Our study of this system has profited from the availability of several transgenic lines of zebrafish, which express GFP in the different cell types of neuromasts and in the migrating primordium. Previous studies have shown that diverse agents can destroy the lateral line hair cells, but that these can regenerate and become fully functional. We have shown that, as in the vertebrate inner ear, the atonal homolog 1 gene, ath1, is essential for specification of hair cells and that progenitors express the neural stem cell marker sox2. Regeneration of hair cells after damage can occur through two mechanisms. The first involves a postmitotic group of precursors that can quickly replace hair cells when these are damaged. The second requires proliferation of sox2-expressing cells and occurs only when damage is extensive. At present, we are analyzing sox2 function in development of the lateral line and we are carrying its role in cell specification in the migrating primordium.

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Program/Abstract # 67
An insertion mutation in the vesicle traffic vps18 gene produces visual acuity loss in zebrafish embryos
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Oculocutaneous albinism is a characteristic of several diseases associated with vesicle traffic defects, like the Hermansky-Pudlak, Chediak-Higashi, and Griscelli syndromes. Oculocutaneous albinism is also a characteristic of the zebrafish mutant vps18hi2499A, which is affected in the gene vps18, a component of the Homotypic Fusion and Protein Sorting complex (HOPS) that is involved in tethering during vesicular traffic. Vps18, as part of this complex, participates in the formation of early endosomes, late endosomes and lysosomes. Here we show that Vps18 is involved in the formation of melanosomes from the eye. In the zebrafish mutant vps18hi2499A the retroviral insertion located at exon 4 of vps18 leads to the formation of two abnormal splicing variants lacking the coding sequence for the clathrin repeat and the RING finger conserved domains. A deficiency of Vps18 in zebrafish larvae results in hepatomegaly and skin hypopigmentation. We also observed a drastic reduction in the number of melanosomes in the eye’s retinal pigmented epithelium along with the accumulation of immature melanosomes. A significant reduction in the vps18hi2499A larvae visual system capacity was found using the optokinetic response assay. We propose that the insertion mutant vps18hi2499A can be used as a model for studying hypopigmentation diseases in which vesicle traffic problems exist.

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Program/Abstract # 68
The mind of a male worm—Development of the C. elegans male nervous system
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The C. elegans male searches its environment to find a mating partner and copulates when it finds one. Identification of the neural circuits that control male reproductive behavior and the genetic and developmental programs that give rise to them provide the opportunity to study how behavior is encoded in the genome. We are reconstructing the male nervous system from serial section electron micrographs. Results are beginning to reveal the neural pathways through which sensory input guides mate searching and the series of copulatory subbehaviors. Three related Zn-finger DM domain transcription factors are dedicated to male-specific differentiation. Other