Program/Abstract # 115
Axon branching in spiral ganglion neurons
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Proper morphogenesis of neurons during development is important for the assembly of neural circuits, since it regulates what target cells neurons come into contact with. Spiral ganglion neurons are responsible for receiving sound information from hair cells in the cochlea and sending it to the cochlear nucleus. Upon entering the hindbrain, their axons bifurcate to distribute information to different divisions of the cochlear nucleus, where different features of sound are processed. The molecular mechanisms of axon branching are poorly understood, but both intrinsic and extrinsic mechanisms are known to sculpt the final morphology of neurons. Transmembrane proteins are likely to play an important role in intrinsic processes such as branch segregation, but also in extrinsic processes such as response to environmental branching cues. Spiral and vestibular ganglion neurons develop from a common precursor pool in the otic vesicle, and both innervate hair cells in the inner ear and project axons out the eighth nerve that bifurcate in the hindbrain. However, their precise targets are distinct, and vestibular ganglion neurons are born and undergo axon bifurcation first. To identify the molecular mechanisms of axon branching, the expression profiles of spiral ganglion neurons in the process of axon branching were compared to those of spiral and vestibular ganglion neurons that had finished axon branching. Embryonic spiral and vestibular ganglia were isolated by microdissection or FACS sorting of GFP+ neurons. 193 putative transmembrane proteins were identified to be enriched in the spiral ganglion during axon branching. Validation and functional testing of these candidates are under way.

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Program/Abstract # 116
Polarization of retinal amacrine cells by the atypical cadherin Fat3
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Fat cadherin is required in *Drosophila* for developmental events including planar cell polarity (PCP), tissue growth, and dendritic tiling. Comparatively little is known about fat cadherin function during mammalian development. One mouse ortholog, *fat3*, is expressed by amacrine cells (AC) and ganglion cells in the developing retina. ACs modulate synaptic function within the inner plexiform layer (IPL) and function as feed forward elements within the rod circuitry. Although each AC type has a distinct dendritic morphology, one common feature is the unipolar extension of dendrites into the IPL. We have generated *fat3* mutant mice lacking an exon encoding the Fat3 transmembrane domain. Although *fat3* is expressed in the inner ear, mutants lack gross PCP deficits in the organization of hair cell stereocilia bundles (a classic model of vertebrate PCP). In contrast *fat3* mutants have a retina phenotype characterized by the emergence of an ectopic synaptic layer located within the inner nuclear layer (INL). Formation of this layer results from a failure of ACs to develop unipolar dendritic morphologies. Instead *fat3* mutant ACs extend two primary dendrites and develop a bipolar morphology with one dendrite projecting into the IPL and the second towards the INL where it contributes to the ectopic synaptic layer. In addition we see an increase in displaced ACs and a decrease in INL ACs suggesting that *fat3* also directs nuclear layer localization. Finally, the expression of *dachsous* and *four-jointed* orthologs raises the possibility that a conserved Fat/Dachsous/Four-Jointed signaling complex functions during AC development.

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Program/Abstract # 117
Morphogenesis of the mouse node depends on the FERM domain protein Epb4.1l5
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Vertebrate embryos establish asymmetric patterns of gene expression across the left–right (LR) axis, leading to the asymmetric development or placement of internal organs such as the heart and lungs. In the mouse, cilia-driven leftward flow of extracellular fluid across the node is a central event in LR patterning; mutations disrupting the shape of the node or the shape or motility of nodal cilia affect LR patterning. The node also produces the trunk notochord and floor plate, which are required for the formation of a midline barrier to maintain asymmetric gene expression in the lateral plate mesoderm (LPM). Despite this pivotal role for the node in patterning an embryonic body axis, node morphogenesis is poorly understood. We performed detailed imaging of wild type node formation using electron and confocal microscopy. We show that the node and notochordal plate form a contiguous group of ciliated, apically constricted cells that appear to emerge gradually through the endoderm germ layer on the ventral surface of the embryo. Establishment of a single node field is disrupted by the limulus (lulu) mutation; lulu disrupts the Erythrocyte protein band 4.1-like 5 (Epb4.1l5) gene, which encodes a FERM domain protein required for reorganization of the actin cytoskeleton during embryogenesis. Markers of the node and notochord are expressed in lulu mutants, but multiple node-like regions form in lulu embryos, and the notochord becomes discontinuous. Consequently, most lulu embryos display bilateral expression of left-specific LPM markers. We propose that Epb4.1l5 coordinates the cytoskeletal rearrangements required for node morphogenesis.

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Program/Abstract # 118
Bmp2 in the visceral endoderm directs anterior morphogenesis during gastrulation
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Elaboration of the vertebrate body plan requires both specification and morphogenesis as the tissues and organs take shape. Proper development and patterning in the early mouse gastrula depend on reciprocal interactions between the epiblast and two surrounding extra-embryonic tissue layers: extra-embryonic ectoderm and visceral endoderm (VE). While much has been learned about the role of the anterior visceral endoderm (AVE), little is known about the function of the posterior visceral endoderm (PVE). To further investigate the role of the PVE, we undertook studies on Bmp2, a signaling molecule that is expressed in VE overlying the primitive streak at E6.5. The targeted knockout of