binding. Using Chick Chorioallantoic Membrane assays, we are investigating the invasive potential of non-metastatic breast cancer cells expressing either wildtype Twist or Twist carrying mutation in the WR domain that prevents binding to other EMT regulatory factors. Our studies lend important insights into the function of a key regulator of developmental and pathological EMTs.

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Program/Abstract # 248
Myosin-X is required for proper behavior of neural crest cells in *Xenopus laevis*
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Non-muscle myosins consist of a N-terminal actin-binding motor domain and multiple C-terminal domains responsible for protein–protein and protein–membrane interactions. One such myosin, Myosin-X (MyoX) has been shown to play important roles in the formation of filopodia and in meiotic spindle organization. *Xenopus* MyoX was identified in a screen for genes expressed in neural crest (NC) under the control of the transcription factor TFAP2. At neurula stage MyoX has the highest level of expression in the NC, but is also abundant in paraxial mesoderm and forebrain. MyoX knockdown using splice-inhibitory morpholinos resulted in retarded migration of cranial NC cells into branchial arches and subsequent reduction of head and jaw cartilage and reduction in the NC-derived trigeminal nerve. These effects could be partially rescued by co-injection of full-length MyoX mRNA. In vitro migration assays on fibronectin using explanted cranial neural crest cells showed significant inhibition of migration resulting from MyoX knockdown. NC cells migrate most efficiently on fibronectin, utilizing integrin alpha5-beta1 as the receptor. It has been reported that the FERM domain of MyoX physically interacts with a conserved NPLY motif present in the cytoplasmic domain of most beta integrins, including beta1. This interaction with integrin beta5 is critical for colocalization of integrin and MyoX at filopodial tips and for cell adhesion, suggesting the hypothesis that MyoX functions in NC cells to regulate β1integrin distribution or activation. This is currently being tested by immunohistochemical and live imaging techniques.

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Program/Abstract # 249
***Xenopus* sonic hedgehog is involved in retinal axon guidance**
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The role of classic morphogens such as Sonic hedgehog as axon guidance cues has recently been examined in a variety of vertebrate organisms. In this work, we have tested whether *Xenopus* sonic hedgehog (Xshh) signaling is involved in guiding retinal axons along the optic tract in the developing midbrain. Xshh is expressed in the brain during retinal axon extension, in close association with these axons, which themselves express the shh co-receptors patched and smoothened. Blocking Xshh appears to disrupt retinal ganglion cell axon guidance — causing abnormal pathfinding along the optic tract and abnormal targeting at the optic tectum. Misexpression of a Shh signal peptide in vivo also causes retinal axon guidance errors. These data suggest that Xshh signaling is required for normal retinal axon pathfinding and target recognition in the developing visual system.

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Program/Abstract # 250
The GSK-3β and α-catenin binding sites of β-catenin exert opposing effects on directional persistence and filopodial protrusions of optic axons in situ
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We overexpressed two deletion mutants of the N-terminal domain of β-catenin in individual optic axons in *Xenopus laevis* tadpoles. One deletion mutant contained both the α-catenin and GSK-3β binding sites of β-catenin (NTERM) whereas the second mutant contained only the GSK-3β binding site (β-cat 107). Epi-fluorescence images showed that NTERM expression in optic axons caused them to follow a more curvy path to the tectum than that of control optic axons and make guidance errors. In contrast, expression of β-cat 107 induced optic axons to follow a straighter path into the tectum. Higher magnification images showed that NTERM also collapsed filopodia in growth cones whereas β-cat107 increased the number of filopodia in growth cones. These data suggest that the GSK-3β and α-catenin binding sites of β-catenin exert opposing effects on the directional persistence and filopodial protrusions of optic axons.

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Program/Abstract # 251
Interactions between [beta]-Catenin and Fgf signaling coordinate directional migration of groups of cells
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The zebrafish lateral line is an excellent model for studying fundamental developmental mechanisms, such as cell migration in vivo. The lateral line consists of sensory organs derived from a cephalic placode/primordium, which undergoes posterior migration towards the tail tip. During migration the primordium deposits sensory organs every 3–5 somites until it reaches the tail tip. The directionality of this collective cell migration is not controlled by a gradient of an extrinsic guidance molecule but is controlled by the polarized expression of two chemokine receptors within the group of cells. Here we report that a feedback mechanism between [beta]-Catenin and Fgf signaling polarizes these clusters of collectively migrating cells by differential regulation of gene expression in the leading versus the trailing edge of the primordium. We also find that these signaling pathways regulate the asymmetric, anteroposterior expression of the two chemokine receptors in the primordium, which is crucial for its directed migration. These findings are important because they uncover an undescribed molecular mechanism capable of locally establishing polarity and directionality in a group of migrating cells. Although [beta]-Catenin, Fgf and chemokine signaling pathways are well known to be involved in cancer progression, we provide with these studies the first in vivo evidence that these pathways are functionally linked.

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