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**Program/Abstract # 291**
**PDGF-AA interactions with fibronectin reveal a potential role for heparan sulfate in mediating directed cell migration during *Xenopus laevis* gastrulation**
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Platelet-derived growth factor (PDGF) signaling is essential for processes involving cell motility and differentiation during embryonic development in a wide variety of organisms including the mouse, frog, zebrafish and sea urchin. In early *Xenopus laevis* embryos, PDGF-AA provides guidance cues for the migration of anterior mesendoderm cells as they move across a fibronectin-rich extracellular matrix. The long form of PDGF-A includes a positively charged carboxy-terminal retention motif that can interact with the extracellular matrix and heparan sulfate proteoglycans (HSPG's). In this study we demonstrate that PDGF-AA binds directly to fibronectin and that this association is greatly enhanced by heparin. The PDGF-AA-fibronectin binding occurs across a broad range of pHs (5.5 to 9), which is significant because the PDGF-guided migration of *Xenopus* mesendoderm cells occurs under basic extracellular conditions (pH 8.4). We further demonstrate that endogenous HSPG's are required for the PDGF-AA-guided mesendoderm movement, suggesting an in vivo role for HSPG's in mediating the interaction between PDGF-AA and fibronectin.

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**Program/Abstract # 292**
**BMP signaling is required for both border cell specification and migration**
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Elucidating how cells acquire migratory and invasive properties is important for understanding normal embryonic development, homeostasis and cancer metastasis. Border cell migration in developing egg chambers of the *Drosophila* ovary provides an ideal system to study migration *in vivo*. Border cells are specified at the anterior of the egg chamber due to signals from the JAK–STAT ligand, Unpaired (Upd), expressed in the anterior polar cells. Together, border and polar cells then migrate towards the oocyte. Although *upd* expression is critical for both cell specification and migration, its regulation is poorly understood. We have found that BMP signaling plays important roles in both border cell specification and migration. *glass bottom boat* (*gbb*), encoding a *Drosophila* BMP ligand, is expressed in border cells and acts to control the expression of BMP target genes in both polar and border cells. By manipulating BMP signaling, we were able to reveal that downregulation of BMP signaling specifically in border cells impacts their migration and affects the localization of DE-cadherin, known to affect cell motility. Downregulation of BMP signaling in the polar cells results in a reduction in the number of border cell specified. Based on our findings, we propose a model in which Gbb positively regulates the expression of *upd* in polar cells to maintain JAK–STAT activity critical for both fate specification and cell migration. This study reveals a novel communication between border cells and polar cells which provides a robust system to coordinate border cell specification with migration.

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**Program/Abstract # 293**
**The function of SMN in positioning motor neurons in the ventral neural tube**
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During development, many cells navigate extensively to their final destinations where they form precise connections with their neighbors. We are interested in unraveling the molecules and mechanisms that guide embryonic cells to their targets, using chick embryos as a model system. Here, we focus on the cues that pattern motor neurons and their axons during neural development. Motor neurons extend their axons to innervate specific muscles in the limb. We are examining the role of SMN, the gene responsible for spinal muscular atrophy (SMA), using a loss-of-function approach with specific shRNAs. First, we assessed whether SMN levels were reduced using SMN shRNAs in vitro in HEK293T cells; SMN levels were indeed decreased by SMN shRNAs but not by missense shRNAs. In vivo, at early stages when SMN levels are reduced, motor axons are growth-impaired and exhibit fasciculation defects. Surprisingly, when SMN levels are reduced in vivo and embryos are grown to later stages, Islet-1-positive motorneurons appear to migrate aberrantly out of the neural tube, along the spinal nerve; this was never observed in control electroporations. Boundary cap cells were in place, as shown by various markers including cadherin7 and lingo-1 antibodies. Moreover, the architecture of the neural tube appeared impaired, as indicated by laminin antibody staining. Collectively, these results suggest that other molecular mechanisms regulate the positioning of motor neurons in the ventral neural tube.

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**Program/Abstract # 294**
**The role of Smads IN BMP-mediated commissural axon guidance**
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Bone Morphogenetic Proteins (BMPs) have distinct functions in the establishment of the elaborate, yet precise circuitry of the spinal cord. BMPs first specify the fate of dorsal neural populations and subsequently direct the axonal trajectory of the dorsal-most commissural (C) neurons. BMPs mediate cell fate by binding to a BMP receptor (Bmpr) complex, thus activating the Smad second messenger system, which alters gene transcription. Our studies suggest that Bmprs not only mediate the morphogenetic activities of the BMPs, but also guide C axons towards their intermediate target in the developing spinal cord. However, the intracellular effectors of the BMP guidance cue remain unclear. To elucidate whether the canonical signaling pathway downstream of the Bmpr complex also regulates C axon pathfinding, we have examined the potential role of the Smad complex. Using inhibitory (I) Smads, Smad6 and 7 to disrupt normal Smad signaling, we found that overexpression of each of the I-Smads differentially affect C cell fate and axonal outgrowth suggesting that different Smads regulate distinct phases of C neuron development. Supporting this hypothesis, the BMP specific receptor-activated (R) Smads, Smad1, 5 and 8, have spatially divergent patterns in the spinal cord during C axiogenesis. Our preliminary results suggest that knocking down Smad1 protein by RNA interference during C axiogenesis results in C outgrowth defects. Taken together, these findings suggest that Smads function as a second messenger intermediate for the BMP guidance cue and that