upstream of Hindsight (Hnt), a Notch target gene that coordinates responses in the follicle cells. Genetic interactions between CoREST and components of the Notch repressor complex, CtBP and Gro, as well as changes in chromatin modifications in CoREST mutant cells, indicate that CoREST is a nuclear modulator of the Notch pathway.

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Program/Abstract #69
Establishment of transgenic lines that report nervous system specific Notch activity based on nort gene regulatory sequence
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Notch signaling is important in development of the vertebrate retina. During zebrafish retinal neurogenesis Notch activity is polarized as demonstrated by the Tg(−3.4 kb her4.3:dRFP)knu2 transgenic line (Del Bene, 2008). Destabilized fluorescent protein (FP) expression driven by the her4 regulatory sequence was elevated in retinal progenitors with apical nuclei. We are interested in determining if her4.3 FP expression is unique to this transgene or general to other Notch target genes. To investigate this phenomenon we generated additional Notch reporter lines using the previously characterized Tp1 promoter, which consists of 12 Notch responsive RBP-Jκ binding sites driving FP (Parsons, 2009). In addition, we established other Notch reporter transgenic lines based on regulatory sequence for the notch-regulated transcript (nort) gene. Expression of nort is augmented by Notch and enriched in neural progenitors, including those of the retina (Tsutsmi and Itoh, 2007). We generated a construct in which FP was expressed from 3.5 kb of genomic sequence directly upstream of nort. Expression of FP from the nort transgene overlapped with endogenous nort expression. Like endogenous nort, we found that FP from the −3.5 kb nort transgene was partially dependent on Notch activity, as demonstrated by morpholino knockdown of Notch receptors or RBP-Jκ. Similar to the her4.3:FP transgene, nort:FP and Tp1bglob:FP were elevated in a subset of retinal cells with apical nuclei. Interestingly, while each transgene showed overlapping expression, distinct temporal patterns were noted. We are currently assessing how each expression pattern relates to cell fate within the retina.

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Program/Abstract #70
Neuropeptide signaling in planarian sexual development and regeneration
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Sexual free-living planarians can dynamically develop or dismantle their reproductive tissues in response to external conditions. We recently showed that a Neuropeptide Y-like peptide secreted by planarian nerve cells is essential for proper sexual development. Specifically, planarians without this hormone fail to develop or maintain reproductive organs. To identify receptors for this peptide, we analyzed spatial expression and RNA interference phenotype of a number of genes predicted to encode G-protein coupled receptors (GPCRs) with similarity to neuropeptide Y receptors from other organisms. This analysis found one gene, referred to as gpcr-b01, RNAi knockdown of which resulted in a block in germ cell differentiation within the testes and failure in the development of accessory reproductive organs. NPY-like hormones are implicated in diverse functions such as feeding behavior, energy homeostasis, and alcohol sensitivity, in species ranging from flies to humans. Our study suggests a role for NPY signaling in the regulation of reproductive physiology in flatworms.

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Program/Abstract #71
Lefty activity is regulated by prodomain-mature lefty interaction
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Members of the transforming growth factor beta (TGFβ) superfamily of secreted ligands play an integral role in vertebrate embryonic development. One member of this superfamily, Nodal, regulates mesendoderm induction and left-right axial development. Lefty, an atypical member of the TGFβ superfamily, inhibits Nodal signaling by interaction with EGF-CFC Nodal co-receptors and Nodal itself. Without Lefty function, unregulated Nodal signaling severely disrupts embryonic development, yet little is known about how Lefty activity is regulated. Many members of the TGFβ superfamily, including Lefty, are inactive prior to proteolytic cleavage of the prodomain from the mature portion of the protein, as shown by mutants incapable of being cleaved. Based on three results, we propose that in Lefty this inhibition is mediated by interaction between the prodomain and mature Lefty. First, the Xenopus Lefty (Xlefty) prodomain can co-immunoprecipitate mature Xlefty, but not uncleaved Xlefty. Second, the co-expression of the prodomain with full-length Xlefty in the Xenopus embryo antagonizes the effects of Xlefty overexpression. Third, the expression of the Xlefty prodomain in the Xenopus embryo results in exogastrulation, a phenotype which we have previously observed with knockdown of Xlefty. Additionally, we propose that prodomain-mature Xlefty interaction prevents mature Xlefty from interacting with Nodal co-receptors. Consistent with this proposal, preliminary results suggest that Xenopus Cripto-related 1, an EGF-CFC co-receptor, co-immunoprecipitates mature Xlefty, but not uncleaved Xlefty. Future studies will be aimed at determining if a post-cleavage prodomain-mature Xlefty interaction mediates a latent Xlefty complex.

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Program/Abstract #72
Poster Board #B15

Program/Abstract #72 will be presented as scheduled, but the abstract cannot be published due to lack of license agreement between authors and publisher.

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Program/Abstract #73
Notum 1a is a specific inhibitor in Wnt/Beta-Catenin signalling
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Wnts are a large family of secreted proteins crucial for numerous processes in the developing embryo. Proper development requires tight regulation of Wnt signalling both intracellularly and extracellularly. Glypicans are a class of heparan-sulfate proteoglycans