absence of *neurogenin1*-positive nascent DRG cells at 30 h postfertilization (hpf) and by absence of HuC/D-positive DRG neurons at 4 days postfertilization. However, markers that label migrating neural crest cells revealed no obvious defects in the pattern of neural crest migration in *erbB3* mutants at 24 hpf. To learn whether other aspects of neural crest migration are affected in these mutants, we followed neural crest migration in live transgenic embryos in which GFP expression is driven by the zebrafish *sox10* promoter. Treating embryos with the ErbB receptor inhibitor, AG1478, did not appear to affect overall neural crest motility, but did appear to affect the ability of migrating neural crest cells to stop near the position where the DRG normally forms. Although a few neural crest cells are present near where the DRG forms, they do not appear to become DRG neurons. These results suggest that *erbB3* may be involved in the ability of DRG progenitors to recognize their target position during migration and to respond to DRG instructive signals.

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Program/Abstract # 216
Diverse roles of Notch signaling in cardiac cell differentiation, migration and ventricular morphogenesis

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Heart development serves as an excellent model system for studying developmental processes such as tissue patterning, morphogenesis and cell differentiation. We found that a conserved signaling pathway, Notch, plays important and diverse roles in cardiac development, including cell differentiation, migration and ventricular morphogenesis. Expression of a constitutively active form of Notch (NIC) inhibits cardiac muscle differentiation, and promotes the differentiation of conduction cell, a specialized cell typeresponsible for setting and coordinating rhythmic heart beating. Conversely, by using a dominant-negative suppressor-of-hairless construct, we found that reducing Notch signaling resulted in an increasing cardiac muscle marker expression and a decrease of conduction marker expression. In addition, activation of Notch by expression of NIC or addition of soluble Delta1 ligand promoted cardiomyocyte migration ina 3-D migration assay and caused an increase in trabeculae formation in the ventricles in vivo. Interestingly, the effect of Notch on promotion of cardiomyocyte migration can be separated from its effect on cell differentiation, thus representing a novel function of notch during development.

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Program/Abstract # 217
Lipid phosphate phosphatases are necessary for the trans-epithelial migration of germ cells

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Drosophila germ cells form spatially and temporally separate from the somatic cells of the gonad and therefore migrate through the embryo to associate with them. Extracellular lipid phosphates are implicated in this migration because the lipid phosphate phosphatases, wunen and wunen2 are expressed redundantly in somatic tissues to repel germ cells during their migration and also in germ cells to promote their survival. We recently identified a role for Wunens in the process of trans-epithelial migration. In wild-type embryos the germ cells, which initially are tightly clumped, individualize and migrate across the midgut epithelium in order to reach the somatic cells of the gonad. In embryos lacking Wunens in germ cells and somatic cells, the germ cells remain tightly clumped and fail to migrate across the midgut epithelium. We visualized germ cell behavior in this background by live imaging. We see that germ cells inside the midgut are motile. We hypothesize that during trans-epithelial migration Wunens are required either to provide directionality to germ cells or to regulate cell–cell adhesion. We are currently distinguishing between these possibilities by testing for suppression of this phenotype with mutations in cell adhesion molecules.

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Program/Abstract # 218
Identification of genes affecting Drosophila larval somatic muscle patterning

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Cell migration is required for biological processes as diverse as organ formation during embryonic development and metastasis of diseased tissues. During development of the musculature, migrating muscle cells are guided towards specific attachment sites. The *Drosophila* larval muscles provide a simplified system for studying cell migration and guidance during muscle development. *Drosophila* larval somatic muscle fibers are organized into an intricate, repeating pattern during embryonic development. This pattern depends on individual myotubes extending filopodia as they migrate and attach to specialized epidermal cells called tendon cells. These tendon cells release guidance cues to direct muscle fibers to their correct positions. Few molecules have been shown to function in this guidance process. Identification of genes involved in muscle guidance will provide a better understanding of what mechanisms may play a role in this process. We have isolated several *Drosophila* EMS mutations affecting the ability of somatic muscles to correctly select their proper epidermal attachment sites. The phenotypes of

these mutants include muscle fibers that extend past their appropriate attachment sites, as well as muscles with multiple, persistent filopodia. Here we present characterization of the isolated mutant lines and preliminary results implicating a gene known to function in cytoskeletal organization. Further exploration into these muscle mutants will contribute crucial data for understanding muscle guidance and development.

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Program/Abstract # 219
The planar cell polarity pathway regulates parietal endoderm outgrowth
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Parietal extraembryonic endoderm (PE) contributes to the yolk sac and is the first migratory cell type in the developing mammalian embryo. We study this migratory event using the F9 teratocarcinoma cell *in vitro* model system. In suspension culture, F9 cells form embryoid bodies (EBs) consisting of an inner core of undifferentiated stem cells, surrounded by an outer layer of visceral endoderm. When EBs are plated on ECM substrates, PE migrates away from the EB as a sheet of cells that are enriched in migratory and adhesion structures. To determine if PE migration is regulated by the PCP pathway, we first determined if migratory cells were polarized. Based on Golgi localization, more than 70% of the outgrowth cells are polarized in the direction of migration. In the planar cell polarity pathway (PCP), which mediated directed cell migration events, Wnt ligand binds the Frizzled receptor activating Disheveled, which activates Daam1, leading to activation of the Rho/ROCK pathway. Perturbation of the Wnt pathway using the soluble Frizzled Receptor (sFRP) increases outgrowth migration distance and inhibits cell polarity. Our previous data showed that Rho/ROCK inhibited outgrowth migrates further and faster, as observed with Wnt inhibition and we now show that under this condition cells are not polarized. We hypothesize that a Wnt source in the EB repels emerging PE, promoting outgrowth of polarized cells. Candidate Wnts implicated in the PCP pathway are also expressed in F9 EBs. Currently we are investigating the location of Wnts and Frizzled receptors in the outgrowth system and using genetic approaches to perturb the PCP pathway.

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Program/Abstract # 220
Turtle (Tutl)* is required for photoreceptor axon targeting in *Drosophila
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In the *Drosophila* visual system, photoreceptor (R cell) axons innervate the optic ganglia such that R1–R6 project to the superficial lamina layer and R7–R8 target the deeper medulla. The mechanisms regulating this specific innervation pattern remain largely unknown. In this study, we show that the neural-specific immunoglobulin family member, *turtle* (*tutl*), is required for normal lamina targeting. Examination of R2–R5 axons labeled with rough-tau-lacZ revealed a failure of these axons to properly terminate at the lamina layer in *tutl* loss-of-function mutants. This mistargeting phenotype is also observed in flies in which *tutl* has been knocked down by RNA interference. Further, this defect appears to be intrinsic to the photoreceptor cells. R2–R5 misprojections persisted in mosaic flies in which the *tutl* gene was specifically deleted in the eye. The lamina glial layers, which are known to have an important role in terminating R1–R6 axons, were properly generated and organized. Examination of plastic sections of adult eyes and immunochemistry with various R-cell-specific markers did not reveal any defects in photoreceptor cell specification or differentiation or indicate morphological abnormalities. Cell labeling indicates that *tutl* is expressed in at least a subset of R cells. We are presently using a combination of molecular and genetic approaches to identify proteins (i.e. its ligand and downstream effectors) that interact with *tutl* to regulate R-cell axon targeting in the visual system. This work was funded by CIHR.

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Program/Abstract # 221
Nonstop and Rap/Fzr/Cdh1 interact to regulate cell cycle progression and retinal axon targeting
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The *nonstop* (*not*) gene encodes a ubiquitin-specific protease (UBP) which is required for proper glia migration and axon targeting in the developing nervous system. The molecular mechanisms by which Nonstop, a de-ubiquitinating enzyme, regulates glia migration and axon targeting are not well understood. UBPs function to disassemble multi-ubiquitin chains from proteins destined to the 26S proteosome. UBPs have bidirectional control in the rate of protein degradation, accelerating degradation by allowing the recycling of free ubiquitin or inhibiting proteolysis by removing ubiquitin tags from proteins and therefore preventing further degradation. Rap/Fzr is the *Drosophila* homolog of the mammalian Cdh1, an activator of the anaphase promoting complex (APC), a ubiquitin ligase complex. We previously showed that Rap/Fzr regulates mitotic progression by targeting cyclins and promoting cell cycle exit in the developing eye and the embryo. In the following study, we present data that suggest a novel functional role for Rap/Fzr and Nonstop. Nonstop acts as a dominant suppressor of the *rap/fzr* loss-of-function phenotype. Our data