Cell Fate Specification

Program/Abstract # 288
Regulation of neural stem cell differentiation by Lin28 and let-7
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Normal development of multicellular organisms requires accurate timing of cell division and differentiation. In the nervous system, coordinate differentiation of neurons and glia is pertinent to its function. Lin28 and let-7 are attractive candidates for temporal control of neural differentiation. Lin28 is present throughout the neural tube early on and its expression overlaps with neural stem cell markers. As development progresses, Lin28 diminishes, consistent with a role in coordinating events prior to differentiation. We hypothesize that Lin28 and let-7 can regulate timing of differentiation. We are testing the role of let-7 and found that misexpression of let-7 causes a significant decrease in cell proliferation. This effect may be mediated by suppressing Lin28 expression as we observe a decrease in LIN28. Work is underway to knockdown Lin28 and to examine if neuronal differentiation can be controlled by this micro-RNA. We are also testing the loss of Lin28; our preliminary data show that depleting Lin28 leads to a decrease in cell proliferation in the neural tube, suggesting that it may normally be required for stem cell maintenance.

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Program/Abstract # 289
Characterization and mapping of mutants that affect sex-specific neurons in C. elegans
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Programmed cell death of sex-specific neurons plays an important role in the development of sexual dimorphism in C. elegans. Hermaphrodite-specific neurons (HSNs) and cephalic male neurons (CEMs) are born in the embryos of both sexes but are selectively eliminated by programmed cell death in a sex-specific manner during embryogenesis. HSNs, which innervate vulval muscles and regulate egg laying, die during male embryogenesis since they are unnecessary in males. CEMs are involved in the chemotaxis of males to hermaphrodites during mating and die during hermaphrodite embryogenesis since they are not needed. An EMS screen, using GFP reporter transgenes expressed in sex-specific neurons, produced mutants that have defects in the death and/or differentiation of CEMs and HSNs. We are studying these mutants in order to better understand the genetic regulation of sex-specific cell death and differentiation. sm129 males have fewer GFP expressing CEMs and have defects in the position of the cell body and in axon projections. sm138 hermaphrodites are normal but have similar defects when CEM cell death is blocked by a mutation in ced-3, which is required for programmed cell death. The recessive sm138 mutation maps to linkage group III. sm129 mutant males have a significant reduction in CEMs as judged by GFP expression. In addition, sm129 mutant males have male tail defects and mate at a very low frequency. The recessive sm129 mutation maps to linkage group II and complements a null mutation in mab-3, which has a similar phenotype. We will present updates on the characterization and mapping of these interesting new mutants.

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Program/Abstract # 291
Zebrafish kuririn is a crucial factor for the telencephalic neurogenesis through the regulation of Hes-related gene
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The inferior olivary nucleus (ION) is involved in coordinating balance and movement by relaying inputs from the cortex and the spinal cord to the Purkinje cells in the cerebellum. The progenitors that generate the neurons of the ION have been localized to the caudal extent of the dorsal embryonic hindbrain neural tube inclusive of an anatomical region known as the lower rhombic lip (LRL). Progenitors within the LRL are arranged along the dorsoventral (D/V) axis into distinct domains predictive of future cell fate. The relative location of ION progenitors has been mapped to ventral regions of the caudal LRL that express Ptf1a, Olig3, and Wnt1. We have data that suggests that posterior regions of the ION might arise from more dorsal pools of progenitors that express either Ngn1 or Mash1, suggesting a much larger territory of progenitors responsible for ION production. We wished to determine if over- or misexpression of either of these transcription factors in the mouse by electroporation would predispose progenitors to developing an ION fate. In utero electroporation during the birthdates of ION neurons (E9.5–11.5) leads to high levels of embryonic lethality. To circumvent this issue we developed an in vitro electroporation assay where E11.5 embryos are electroporated and then cultured for up to 48h. We found that we can successfully overexpress green fluorescent protein while retaining normal endogenous gene expression.

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