involved, including members of the FGF, ephs, semaphorin, netrin and slit families. Hypothyroid mice appear to have fewer afferent and efferent fibers extending to inner and outer sensory hair cells and fewer synapses with these cells. Moreover, thyroid hormone regulates cochlear expression of genes encoding putative axon guidance cues. The severity of hearing loss is dependent upon the genetic background strain and can be completely rescued by a locus on chromosome 2. Discovery of the identity of such a protective factor could lead to developing treatments that would enhance axonal outgrowth necessary for regenerative therapy in common age-related or environmentally-induced hearing loss, and for the rare cases of congenital hypothyroidism-induced deafness that are not responsive to thyroid hormone supplementation. (March of Dimes)

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Program/Abstract # 12
The role of Hox genes in the specification of neural crest
Stephanie R. Kadison [a], Toshi Iwashita [b], Sean J. Morrison [b], Catherine E. Krull [a]
[a] *Biological and Material Sciences, University of Michigan, Ann Arbor, MI, USA*
[b] *Stem Cell Biology, HHMI/LSI, University of Michigan, Ann Arbor, MI, USA*

The neural crest (NC) is a cell population derived from the dorsal neural tube that gives rise to distinct cell types during embryonic development. Depending upon their anterior–posterior (A/P) level, NC generate cells as disparate as neurons and cartilage. The current model for NC specification suggests that NC fate (with the exception of melanocytes) is determined by environmental cues they encounter during migration, rather than by intrinsic cues prior to leaving the neural tube. To test this model, we performed microarray analyses on post-migratory NC from two distinct cell/tissue types: enteric neurons and sciatic nerve. Notably, we found that Hox genes are differentially expressed between these populations. While it is known that Hox genes play a role in the generation of cephalic NC-derived-structures, little is known about their function in NC derived from other regions of the neural tube. To test whether Hox genes represent an intrinsic cue sufficient to drive NC fate, we misexpressed posteriorly-expressed Hoxb7 in anterior, occipital NC using in ovo electroporation. At levels inconsistent with dorsal root ganglia (DRG) growth, we observed the formation of ectopic DRG, determined by Islet1/2 and Brn3a immunoreactivity, suggesting that Hoxb7 confers a truncal identity to occipital NC. Similar results are observed when other paralogous Hox genes are misexpressed. Collectively, these results provide support for an intrinsic model of NC fate specification. Additional experiments are currently underway which will verify whether Hox genes are required to specify diverse populations of NC.

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Program/Abstract # 13
Extrinsic mechanisms regulate synapse formation
Kang Shen, Vivian Y. Poon, Matthew P. Klassen
Department of Biology, Neuroscience Program, Stanford University, Stanford, CA 94305, USA

Polarity is an essential feature of many cell types, including neurons, the primary building blocks of the brain. These highly polarized cells integrate information from local inputs through their dendrites and propagate nerve impulses to distant targets through a single axon. The formation of this polarized structure can be subdivided into at least two stages: the initial establishment of axons and dendrites, followed by the polarized localization of axonal and dendritic cargo. While intrinsic factors have been shown to regulate the polarized localization of axonal proteins, extracellular cues that coordinate neuronal polarity in vivo have not been explored. Here, we show that axon guidance cue UNC-6/netrin and its receptor UNC-5 exclude presynaptic components from the dendrite of the *C. elegans* motor neuron DA9 which normally reside in a region with high UNC-6 concentration. In unc-6 and unc-5 mutants, synaptic vesicles and active zone proteins are mislocalized to the DA9 dendrite. In addition, ectopically expressed UNC-6/netrin, acting through UNC-5, is sufficient to exclude endogenous synapses from nearby DA9 axon. Interestingly, the antisynaptogenic activity of UNC-6/netrin is interchangeable with that of LIN-44/Wnt despite the different receptors utilized, suggesting that extracellular cues such as Netrin and Wnts not only guide axon navigation but also regulate the polarized accumulation of presynaptic components through local exclusion.

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Program/Abstract # 14
Neuromancer-1 and neuromancer-2 regulate cell fate specification in the embryonic CNS of *Drosophila melanogaster*
Sandra M. Leal [a], Li Qian [c], Rolf Bodmer [d], James B. Skeath [b]
[a] *Department of Biological Sciences, University of Southern MS, Hattiesburg, MS, USA*
[b] *Department of Genetics, Washington University Medical School, St. Louis, MO, USA*
[c] *The Gladstone Institute, San Francisco, CA, USA*
[d] *The Burnham Institute, La Jolla, CA, USA*

T-box genes encode a family of transcription factors that regulate a broad range of developmental processes in vertebrates and invertebrates. In addition to their roles in regulating heart and epidermal development in *Drosophila*, we provide evidence that the T-box genes neuromancer-1 (*nmr-1*) and neuromancer-2 (*nmr-2*) play key roles in embryonic CNS development. We find that *nmr-1* and *nmr-2* function in a partially redundant manner to regulate neuronal cell fate by inhibiting even-skipped (eve) expression in specific post-mitotic neurons in the CNS. Consistent with these observations, we find that Nmr-1 and Nmr-2 transcription factor proteins also exhibit overlapping yet distinct expression profiles within the CNS. Nmr-2 is expressed early in segment polarity stripes (Stage 9), defined subsets of neuroblasts, ganglion mother cells, and discrete sets of post-mitotic neurons. In contrast, Nmr-1 expression is expressed much later (Stages 11/12) and restricted to specific subsets of Nmr-2-expressing post-mitotic neurons. Expression studies identify all Nmr-1- and Nmr-2-positive neurons as interneurons and lineage studies map specific sets of these neurons to neuroblast lineages 2-2, 6-1 and 6-2. Finally, genetic analyses reveal that *nmr-2* collaborates with nkx6 to regulate eve expression in specific neurons. Thus, *nmr-1* and *nmr-2* appear to be members of the eve transcriptional regulatory hierarchy that specifies neuronal subtype identities in the developing CNS.

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Program/Abstract # 15
The zebrafish unplugged/MuSK receptor controls pre- and postsynaptic development
Michael Granato
Department of Cell and Developmental Biology, UPENN, Philadelphia, USA