348B Genetic Control of the Maintenance of the AIA Cell Fate. *Josh Saul*[1,2], Takashi Hirose[1,2], Bob Horvitz[1,2] 1) HHMI; 2) Dept. Biology, MIT, Cambridge, MA 02139.

Cell fate can be considered to involve two steps: establishment, in which an undifferentiated cell commits to and expresses a final differentiated fate, and maintenance, in which a differentiated cell preserves the expression of its fate while precluding the expression of other fates. Cell-fate establishment has been well studied and is characterized by changes in gene expression, cell morphology and cellular function. Cell-fate maintenance has received comparatively little attention, and while several examples of defects in cell-fate maintenance exist, the mechanisms by which cell fate is maintained are poorly understood.

We have identified a gene, *ctbp-1*, that appears to be involved in maintaining one or more cell fates in *C. elegans*. *ctbp-1* encodes the only worm member of the C-terminal Binding Protein (CtBP) family of proteins, which in mice and *Drosophila* have been shown to act as transcriptional corepressors that regulate gene expression during embryonic development[1–3]. *ctbp-1* mutant adult worms show ectopic expression of an M4 neuron-specific reporter in the two embryonically-born AIA neurons, whereas L1 *ctbp-1* animals do not display this abnormality. Furthermore, adult but not L1 *ctbp-1* animals are defective in an AIA-mediated turning behavior. These observations suggest that AIA gene expression and function are normal in L1 *ctbp-1* animals but abnormal in *ctbp-1* adults, consistent with the hypothesis that *ctbp-1* mutants properly establish the AIA cell fate but fail to maintain this fate.

We are further testing this hypothesis and investigating the mechanism by which *ctbp-1* might regulate cell-fate maintenance. We performed an EMS mutagenesis screen for suppressors of the M4-specific reporter misexpression phenotype of *ctbp-1* mutants to identify genetic interacting partners of *ctbp-1* and have identified 21 independent isolates that we are currently mapping. We are also attempting to determine if any cells besides the AIAs are defective in cell-fate maintenance in *ctbp-1* mutants.

We hope to better understand the genetic control of cell-fate maintenance by determining how *ctbp-1* promotes the maintenance of the AIA cell fate. This work might provide insight into diseases, such as cancer, in which perturbation of the maintenance of tumor cell fate might intervene with the oncogenic process.

1. Nibu, Y., Zhang, H. & Levine, M. Interaction of short-range repressors with *Drosophila* CtBP in the embryo. *Science* **280,** 101–104 (1998). 2. Fang, M. *et al.* C-terminal-binding protein directly activates and represses Wnt transcriptional targets in *Drosophila*. *EMBO J.* **25,** 2735–2745 (2006). 3. Hildebrand, J. D. & Soriano, P. Overlapping and unique roles for C-Terminal Binding Protein 1 (CtBP1) and CtBP2 during mouse development. *Mol. Cell. Biol.* **22,** 5296–5307 (2002).