1052A Regulation of neurogenesis by stress. *S. Luo*[1,2], B. Horvitz[1,2] 1) HHMI; 2) Dept. Biology, Massachusetts Institute of Technology, Cambridge, MA.

Unlike most neurons, which are derived from ectoderm, the *C. elegans* pharyngeal I4 neuron is generated from a mesodermal cell lineage. We found that efficient generation of I4 is dependent on HLH-3, the *C. elegans* homolog of the mammalian proneural protein Mash1, and the Mediator CDK-8 kinase complex (DPY-22, LET-19, CDK-8, CIC-1), which is conserved throughout evolution. HLH-3 and the CDK-8 Mediator function synergistically to promote efficient I4 neurogenesis. Recently we discovered that I4 neurogenesis is also modulated by environmental stresses, such as DMSO or ethanol. We found that DMSO and ethanol induce endoplasmic reticulum (ER) stress, as they elicit expression of *hsp-4p::gfp*, an ER stress reporter, but not of the mitochondria stress reporter *hsp-6p::gfp* or the cytosolic stress reporter *hsp-16.2p::gfp*. DMSO and ethanol each enhance I4 loss in *hlh-3* but not in Mediator mutants, suggesting that DMSO and ethanol-induced stresses might function by suppressing CDK-8 Mediator function. Interestingly, we found that the p38 MAPK innate immunity pathway is required for DMSO and ethanol to suppress I4 neurogenesis. We hypothesize that DMSO or ethanol activates the p38 MAPK pathway, which suppresses I4 neurogenesis by inhibiting the CDK-8 Mediator function. Since in mammals the p38 MAPK pathway has been implicated in inflammation and neurodegeneration, by identifying the molecular mechanisms by which the p38 MAPK pathway regulates I4 neurogenesis, we hope to generate novel insights into the mechanisms of stress-induced neurogenesis defects and neuropathology.