lst-3 Negatively Regulates the Vulval Cell-fate Decision

Erik Andersen, Scott Clark, Melanie Worley, Bob Horvitz
HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA

The *C. elegans* vulva is formed by the descendants of three of six equipotent hypodermal blast cells. Two distinct vulval cell fates are specified by the actions of at least two conserved antagonistic signaling pathways, Ras and Notch. Mutations affecting these pathways cause the generation of ectopic vulval cells and a multivulva (Muv) phenotype.

To understand more about factors controlling the vulval cell-fate decision, we performed a screen for suppressors of the synthetic multivulva (synMuv) phenotype. The synMuv genes are grouped into at least three functionally redundant classes, A, B and C, that negatively regulate the specification of vulval cell fates. Animals mutant for one or more genes within the same class are non-Muv, whereas animals mutant for genes within any two classes are Muv. We identified *n2070* as a dominant suppressor of the synMuv phenotype of *lin-15AB(n765)* mutants. Our gene dosage experiments suggest that the dominant phenotype conferred by *n2070* is caused by an increase in wild-type function. We mapped *n2070* to a 120-gene interval on LGIV and then used RNAi to inactivate the genes in the interval to eliminate the synMuv suppression phenotype of *n2070*. RNAi of only *lst-3* (lst, lateral signaling target) reverted the synMuv suppression phenotype caused by *n2070*. In a screen for *cis*-dominant suppressors of *n2070*, we identified three independent isolates with nonsense mutations in *lst-3*. *n2070* causes a proline-to-leucine substitution in a putative DNA-binding domain of LST-3.

The Greenwald laboratory identified *lst-3* as a possible transcriptional target of LAG-1, a *lin-12* Notch effector, and suggested that *lst-3* mediates the interplay between the Ras and Notch pathways. *lst-3* encodes a transcription factor similar to mammalian CARP-1, a cell cycle and apoptosis regulator. We isolated a deletion allele of *lst-3*. This allele confers a synMuv phenotype in combination with mutations in class A or C but not with mutations in class B synMuv genes. Through gene expression analysis of gain-of-function and loss-of-function *lst-3* mutants, we have identified candidate LST-3 target genes. We will discuss how the modulation of *lst-3* function might affect the Ras and Notch pathways.

Contact: eca@mit.edu
Lab: Horvitz