2001 International Worm Meeting abstract 178

ORDERING THE synMUV CLASS A PROTEINS: LIN-15A MAY BE IMPORTANT FOR THE NUCLEAR EXPRESSION OF LIN-56

Ewa M. Davison, Bob Horvitz

HHMI, Dept. Biology, MIT, Cambridge, MA 02139 USA

The receptor tyrosine kinase/Ras pathway essential for vulval induction in *C. elegans* is negatively regulated by two redundant pathways, A and B. Hermaphrodites mutant in only one of these two pathways appear wild-type for vulval induction. Hermaphrodites mutant in both pathways exhibit the synthetic Multivulva (synMuv) phenotype: cells that normally adopt a hypodermal fate instead adopt a vulval fate and generate ectopic protrusions of vulval tissue along the ventral side of the animal. Various screens for multivulva animals have defined four genes in the synMuv class A pathway: *lin-8*, *lin-15A*, *lin-38*, and *lin-56*. Of these genes, only the *lin-15A* locus was cloned previously. *lin-15A* encodes a novel protein with no recognizable functional or structural motifs. The class B synMuv genes antagonize Ras-mediated vulval development via an RB/E2F/DP-mediated pathway. This inhibition is thus likely effected by transcriptional repression of genes required for vulval development. The class A synMuv genes function in parallel to this Rb pathway, but the molecular mechanism by which they inhibit vulval development is not known.

To further our understanding of the process by which the class A synMuv genes antagonize the Ras pathway, we have cloned *lin-56* and *lin-8*. Both are predicted to encode novel highly-charged proteins. LIN-8 belongs to a family of highly similar but apparently uncharacterized proteins in *C. elegans*. We have identified molecular lesions associated with both *lin-56* alleles and with 18 *lin-8* alleles. Antibodies directed against LIN-56 indicate the protein is localized to the nuclei of many, if not all, cells throughout development. This wild-type pattern is maintained in *lin-8* and *lin-38* mutant animals. By contrast, preliminary observations suggest that LIN-56 nuclear staining is reduced in *lin-15A* mutants, indicating a potential role for LIN-15A in the expression or nuclear localization of LIN-56. *lin-15A* may therefore function upstream of *lin-56* in the synMuv class A pathway. Antibodies have also been generated against LIN-8, and the expression pattern and subcellular localization of this protein are currently being analyzed.