IDENTIFICATION AND CHARACTERIZATION OF GENES THAT ACT WITH *LIN-35* RB TO NEGATIVELY REGULATE VULVAL INDUCTION

Craig Ceol, Frank Stegmeier, Melissa Harrison, Bob Horvitz

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

The synthetic multivulva (synMuv) class A and class B genes define two functionally redundant pathways that antagonize Ras signaling during vulval induction. Molecular analyses of the class B synMuv genes have defined a *C. elegans* pathway that includes a counterpart of the mammalian retinoblastoma, or Rb, tumor suppressor gene. Members of this pathway include *lin-35* Rb, genes encoding the presumed heterodimeric transcription factor DPL-1 DP / EFL-1 E2F, and genes, such as *lin-53* RbAp48 and *hda-1* HDAC, predicted to modulate chromatin structure.

The class B synMuv gene *lin-54* was originally identified in screens conducted by Jeff Thomas, a former graduate student in our laboratory. We cloned *lin-54* and found that it encodes a novel protein with cysteine-rich motifs. These motifs have cysteine signatures unlike those found in proteins with known functions; however, these motifs are conserved in proteins predicted from mammalian, plant and fly ESTs. A rescuing *lin-54::gfp* transgene is expressed broadly and is localized to nuclei, an expression pattern like that of all synMuv genes thus far assayed. We obtained two deletion alleles of *lin-54* and found that, in addition to a Muv phenotype in a *synmuvA* background, they cause sterility in a wild-type background. We are currently characterizing this sterile phenotype.

We are also identifying new class B genes. Using a *lin-15A* background, we screened 6,500 mutagenized haploid genomes and obtained 95 Muv mutant strains. A partial analysis of these mutants has identified at least three previously unknown class B synMuv genes. We will describe our further characterization of these mutants.