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789. IDENTIFICATION AND CHARACTERIZATION OF *lin-35* Rb PATHWAY GENES THAT ANTAGONIZE RAS SIGNALING DURING VULVAL INDUCTION

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The synthetic multivulva (synMuv) class A and class B genes define two functionally redundant pathways that antagonize Ras signaling during vulval induction. Cloned class B synMuv genes encode proteins similar to the mammalian tumor suppressor pRB and the pRB-binding heterodimeric transcription factor DP/E2F. We propose that the class B synMuv proteins act as transcriptional repressors to negatively regulate Ras signaling. Specifically, we propose that a DPL-1 DP/EFL-1 E2F heterodimer binds DNA and recruits LIN-35 Rb and other synMuv proteins involved in chromatin modification, including LET-418 Mi-2, LIN-53 RbAp48 and HDA-1 HDAC, to repress the transcription of genes required for vulval cell-fate specification. To further investigate this RB signaling pathway, we cloned additional known class B synMuv genes and performed a genetic screen to identify new class B synMuv genes.

The class B synMuv genes *lin-52* and *lin-54* were identified by Chip Ferguson and Jeff Thomas, respectively, two former graduate students in our laboratory. We cloned both genes and found that each encodes a protein of unknown function. We obtained candidate null alleles of each gene and are using these alleles to characterize the multivulva, sterile and other abnormalities caused by *lin-52* or *lin-54* loss of function. We are focusing additional functional studies on *lin-54*. We are currently assessing whether a human *lin-54*-like gene can functionally substitute for *lin-54* and are conducting a range of protein-protein interaction studies with LIN-54 and the human LIN-54-like protein.

Together with graduate students Frank Stegmeier and Melissa Harrison we screened for additional class B synMuv genes. Using a *lin-15A* background, we screened 6,500 mutagenized haploid genomes and obtained at least 51 class B synMuv mutations. Our analyses to date have identified at least five new candidate class B synMuv genes. We will describe our genetic and molecular characterizations of these genes.