

1026. ISOLATION AND CHARACTERIZATION OF NEW SYNMUV GENES, INCLUDING *lin-61*, A CLASS B GENE WITH ROLES IN CELL DIVISION AND MULTIPLE POSTEMBRYONIC DEVELOPMENTAL PROCESSES

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The regulation of vulval induction in *C. elegans* provides a useful model system for the study of genetic and molecular mechanisms involved in signal transduction and cell-fate determination. Previous work has defined two classes of genes (A and B) that act redundantly to negatively regulate the adoption of vulval cell fates by vulval precursor cells. The simultaneous elimination of the function of a member of both gene classes results in a synthetic multivulva (synMuv) phenotype. The class B synMuv genes include genes similar to members of the mammalian RB signaling pathway. By contrast, the determination of the molecular nature of the known class A synMuv genes has thus far yielded relatively little insight into the mechanism of their function.

We have cloned a new class B synMuv gene. *lin-61* is located on LG I and encodes a protein weakly similar to members of the *Drosophila* polycomb family and strongly similar to predicted human and *C. elegans* proteins of unknown function. *lin-61* reduction-of-function mutations produce a synMuv B phenotype in a variety of class A synMuv backgrounds. By contrast, elimination of both maternal and zygotic *lin-61* activity via RNAi results in early embryonic lethality as a result of a failure to complete cytokinesis beginning at the first embryonic cell division. We further examined the developmental functions of *lin-61* by injecting *lin-61* dsRNA into RNAi defective *rde-1* hermaphrodites and then mating these animals with N2 males (a technique described by Herman, 2001; *Development* 128, 581-90). Cross progeny were then observed in an effort to gain an understanding of the phenotype produced after the reduction of zygotic *lin-61* activity while maintaining at least some maternal *lin-61* function. Unlike *lin-61*(RNAi), this approach yields animals that reach

adulthood but display a host of developmental abnormalities. Based on these results we conclude that *lin-61* functions in a variety of embryonic and post-embryonic developmental processes in addition to its role in vulval development.

We are also attempting to identify new class A synMuv genes. Previous screens to isolate class A genes would not have recovered synMuv mutations that also cause sterility or maternal-effect lethality. For this reason, we are now conducting a clonal screen to seek alleles of new class A synMuv genes. Beginning with a strain containing a strong *lin-15B* allele, *n744*, we have screened approximately 30,000 haploid genomes and isolated more than 40 mutants that display a Muv phenotype. These isolates include at least two homozygous viable mutations in new candidate class A synMuv genes and over 15 Muv and synMuv mutations that cause sterility or maternal-effect lethality as homozygotes. Complementation testing and mapping of these mutations is currently underway.