The Essential Class A synMuv Gene *lin-38* Encodes a Novel Zinc-finger Protein

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C. elegans vulval induction requires an RTK/Ras signaling pathway and is antagonized by the synthetic multivulva (synMuv) genes. synMuv genes can be grouped into at least three redundant classes: A, B, and C. Animals with one or more mutations in any one class are non-Muv, whereas animals with mutations in genes in any two classes have a Muv phenotype. Many class B and C genes encode proteins predicted to act in chromatin remodeling and transcriptional regulation. Four of the five known class A synMuv genes have been cloned and encode novel proteins. We have cloned the fifth class A synMuv gene, *lin-38*, and performed screens to seek new class A synMuv genes.

lin-38 was mapped between *rol-1* and *unc-52* on chromosome II. Using SNP mapping, rescue experiments and cDNA sequencing, we found that the predicted genes *Y48E1B.6* and *Y48E1B.7* are in fact a single gene that is *lin-38*. LIN-38 has a single zinc-finger domain, a repeated VEEE motif, and no homologs outside of nematodes. We determined the sequence of the entire coding region of *lin-38* in the four *lin-38* mutants and found coding missense mutations in two of the four. All four mutants are viable, but both a deletion allele and RNAi of *lin-38* cause early larval arrest. Currently, we are characterizing the *lin-38* lethal phenotype and attempting to isolate suppressors of that phenotype.

To identify new class A synMuv genes, we performed F_1 clonal screens in the class B synMuv mutant backgrounds *lin-15B(n744)* and *lin-52(n771)*. We screened 19,500 haploid genomes and isolated 27 independent mutations that cause a Muv phenotype. Twenty-six of the mutations affect genes known to cause a Muv phenotype in a class B synMuv background. One of the 26 isolates, *n4418*, is a missense mutation in the class A synMuv gene *mcd-1*. Previously identified synMuv alleles of *mcd-1* are weakly synMuv and cause synthetic lethality when combined with mutations in certain class B synMuv genes. *n4418* does not cause such synthetic lethality, despite exhibiting a stronger synMuv phenotype than other *mcd-1* alleles. We suggest that there are other class A synMuv genes remaining to be identified that have separable roles in vulval development and viability.

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