212. A NOVEL PHENOTYPE OF TRANSGENE MISEXPRESSION YIELDS NEW INSIGHT INTO THE SYNMUV GENES

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In the course of a screen to identify mutants defective in the control of the sex-specific deaths of the CEM neurons using the reporter *pkd-2::gfp* (see abstract by Schwartz and Horvitz), we found 29 independent isolates that had strong GFP expression in the pharynx, a tissue that does not normally express the reporter. Including further clonal and nonclonal screens, we have now identified 68 mutants with this phenotype. This transgene misexpression is not dependent on chromosomal integration, high transgene copy number, or choice of co-injection marker, and the phenotype can be seen with at least one other GFP reporter that contains a different promoter.

We found that mutations in certain synMuv (synthetic Multivulva) genes (see abstracts by Ceol and Horvitz) could produce this phenotype. The synMuv genes act to inhibit vulval development. Animals mutant in both a class A gene and a class B synMuv gene, but not animals mutant in one or more class A genes or in one or more class B genes, display a Multivulva phenotype. Several class B synMuv genes have been cloned and shown to encode genes with homologs implicated in transcriptional silencing and chromatin modification. The synMuv genes able to cause *pkd-2::gfp* expression in the pharynx include one member of the synMuv A pathway and two members of the synMuv B pathway, a result that does not conform to the finding that the two pathways act separately and in parallel to prevent vulval cell fates. None of the 20 other synMuv genes tested caused this phenotype. Of the 68 mutants with this phenotype, 67 appear to be alleles of these three genes. A fourth gene, defined by a single allele, *n3599*, caused an identical phenotype of transgene misexpression. *n3599* mutants are not synMuv A or synMuv B. Interestingly, *n3599* is synthetically nonviable with a subset of synMuv B mutations, including *lin-35 Rb*. This subset does not correspond to other subsets previously shown to be associated with other phenotypes, including the synMuv B mutants shown to be synthetically lethal with the cell cycle regulator *fzr-1* (Fay, Keenan, and Han, Genes and Development 16: 503-517, 2002). It is possible that the synMuv genes synthetically lethal with *n3599* share a normal function distinct from both vulval development and cell cycle regulation, but likely involving transcriptional repression. Further investigation into these transgene-misexpression and synthetic-lethal phenotypes may define new transcriptional silencing complexes that include novel proteins and proteins previously implicated in silencing but acting in novel combinations.