C. elegans synMuv Proteins Form At Least Two Putative Chromatin Regulatory Complexes

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Vulval induction is negatively regulated by at least three redundant sets of proteins encoded by the class A, B, and C synthetic Multivulva (synMuv) genes. Double mutants between members of any single class do not result in a Multivulva (Muv) phenotype, but animals with mutations in any two synMuv classes are Muv. Many of the synMuv genes encode proteins with homologs that function in chromatin remodeling and transcriptional regulation.

We have performed immunoprecipitation experiments to identify *in vivo* associations among the class B synMuv proteins. Our initial studies focused on LIN-37, as yeast two-hybrid studies suggested this protein interacts with other class B synMuv proteins (1). We have shown that LIN-37 associates *in vivo* with a subset of synMuv proteins, including LIN-35 Rb, DPL-1 DP, and LIN-53 RbAp48. Gel filtration chromatography suggests that most if not all of these proteins are associated in a large-molecular-weight complex. Using immunoblots to determine protein levels in null mutants for all identified complex members, we have identified a subset of proteins that may be required for the stability of other proteins in the complex.

Previous models have suggested that the class B synMuv proteins function through the recruitment to promoters of a complex similar to the mammalian Nucleosome Remodeling and Deacetylase (NuRD) complex, which includes homologs of the synMuv proteins HDA-1, LET-418, and LIN-53. To test whether the LIN-37-containing complex we identified might act in recruitment of HDA-1 complexes to promoters, we tested for *in vivo* association between *C. elegans* NuRD complex components and LIN-37. We found that HDA-1 HDAC does not co-immunoprecipitate with LIN-37 and that antibodies against HDA-1 fail to co-immunoprecipitate LIN-37. Consistent with these findings, genetic data show that *hda-1* and *lin-37* act redundantly in vulval development. Our results suggest that a large subset of class B synMuv proteins is associated in a complex distinct from a worm NuRD-like complex and that these two complexes may act redundantly during vulval development.

Recently, two groups have identified *Drosophila* dRb-containing complexes that include homologs of a subset of the class B synMuv proteins (2,3). Our results, together with these data, suggest that Rb-like proteins are found in complexes with homologs of the class B synMuv proteins in multiple species and that genetic studies of vulval development in *C. elegans* will help to define how these various chromatin-associated complexes act together to regulate development.

(1) Walhout *et al*. Science **287**:116-122, 2000.
(2) Korenjak *et al*. Cell **119**: 181-193, 2004.
(3) Lewis *et al*. Genes Dev **18**: 2929-2940, 2004.