48. Characterization of the class A synMuv proteins LIN-56 and LIN-15A
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The receptor tyrosine kinase/Ras pathway essential for vulval induction in C. elegans is negatively regulated by the functionally redundant class A and B synthetic Multivulva (synMuv) pathways. Hermaphrodites mutant in only one of these two pathways appear wild-type for vulval induction. Hermaphrodites mutant in both pathways exhibit the synMuv phenotype: cells that normally adopt a hypodermal fate instead adopt a vulval fate and generate ectopic protrusions of vulval tissue along the ventral side of the animal. Various genetic screens for Multivulva animals have defined four genes in the synMuv class A pathway: lin-8, lin-15A, lin-38, and lin-56. Of these genes, only the lin-15A locus was cloned previously. lin-15A encodes a novel protein with no readily apparent functional or structural motifs. The class B synMuv genes antagonize Ras-mediated vulval development via an Rb/E2F/DP-mediated pathway. This inhibition is thus likely effected by transcriptional repression of genes required for vulval development. The class A synMuv genes function in parallel to this Rb pathway, but the molecular mechanism by which they inhibit vulval development is not known.

We have cloned lin-56 and found it to encode a novel acidic protein. Although no standard motifs are evident in the LIN-56 protein sequence, it does contain a C₃H₂Zn²⁺-finger-like motif of atypical spacing and shares this motif with LIN-15A. Immunohistochemistry using antibodies directed against LIN-56 indicates that this protein is localized to the nuclei of many, if not all, cells throughout development. LIN-15A is also nuclear and broadly expressed. The wild-type LIN-56 expression pattern is maintained in lin-8 and lin-38 mutant animals. By contrast, LIN-56 protein, but not lin-56 mRNA, is greatly reduced in lin-15A mutants, indicating a role for LIN-15A in the translation or stability of LIN-56 protein. Overexpression of a lin-56 cDNA under the control of the heat-shock promoters fails to rescue the lin-15A synMuv phenotype despite production of LIN-56 protein. Preliminary experiments suggest that the level of LIN-15A protein may be reduced in a lin-56, but not in a lin-8 or a lin-38, mutant background. We favor a model wherein LIN-56 and LIN-15A normally coexist in a functional complex, with absence of one of the subunits resulting in the instability of its binding partner(s).