71. FUNCTIONAL ANALYSIS OF THE MICRORNA GENES OF *C elegans*

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The heterochronic genes *lin-4*and *let-7* encode unusually small (21-22 nt) non-protein coding regulatory RNAs[1,2]. Strains carrying a mutation in either of these genes are heterochronic, displaying retarded development with some cell lineages having an altered temporal pattern of cell division and differentiation. *lin-4*and *let-7* normally inhibit translation of target genes that when mutated lead to an opposing phenotype: precocious development and early expression of certain paths of cell division and differentiation.

Recently, molecular and bioinformatic approaches have identified many genes encoding small RNAs in *C. elegans*,*Drosophila* and mammalian cell lines[3,4,5,6]. All of these genes encode 21-25 nt RNAs derived from longer transcripts that contain partially double-stranded RNAs. These small RNAs, termed microRNAs (miRNAs, *mirs*), define a large, new class of genes.

We have identified over 100 miRNAs in *C. elegans* to date, some of which are conserved in *Drosophila* and mammals. To understand the biological functions of miRNAs, we are attempting to generate mutations in all of these genes. Using a library of *C. elegans* mutants and automated liquid handling, we are screening for deletion strains. In parallel, we hope to establish the temporal and spatial expression patterns of these genes.

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