The heterochronic genes *lin-4* and *let-7* encode small (21-22 nt) non-protein coding regulatory RNAs. 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 a phenotype opposite that of *lin-4* and *let-7* mutants: 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 mammals. 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, *mir*), define a large, new class.

To understand the biology of the *C. elegans* microRNA genes, we decided to combine the generation of loss-of-function mutants with GFP expression studies and target prediction using bioinformatics. To date we have generated deletion strains corresponding to 51 microRNAs. We will present the initial characterization of mutant phenotypes (for information about the *mir-35* and the *let-7* families of microRNAs, see poster by Alvarez-Saavedra *et al.*). One focus will be the issue of redundancy within families of microRNA genes.

In a complementary approach we are generating knockout strains for the *argonaute* family of genes. The *argonaute* genes have been implicated both in RNAi and microRNA function. We will present the initial characterization of the knockout phenotypes of two *argonaute* genes, *prg-1* and *prg-2*. We will present the defects of these mutants in germline development and the relationship of these genes to the microRNAs and to RNAi pathways.