Functional analysis of the microRNA genes of *C. elegans*. *Eric A. Miska[1,2], Ezequiel Alvarez-Saavedra[2], Allison Abbott[3], Andrew Hellman[2], Nelson Lau[4], David Bartel[4], Victor Ambros[3], Bob Horvitz[2].* 1) Gurdon Institute, University of Cambridge, Cambridge, United Kingdom; 2) HHMI, Dept. Biology, MIT, Cambridge, MA 02139, USA; 3) Dept. Genetics, Dartmouth Medical School, Hanover, NH 03755, USA; 4) Whitehead Institute for Biomedical Research and Dept. Biology, MITCambridge, MA 02142, USA.

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.

More 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), 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. We have generated deletion strains corresponding to 92 microRNAs, covering the majority of known microRNA genes. We will present an overview of the classes of mutant phenotypes we have observed. (for information about the *mir-35* and the *let-7* families of microRNAs, see also abstracts by Alvarez-Saavedra *et al.* and Abbott *et al.*). One focus will be the issue of redundancy within families of microRNA genes. This study represents the first comprehensive analysis of microRNA function.