Mutant phenotypes of the microRNA genes of C. elegans. Eric A. Miska¹, Ezequiel Alvarez-Saavedra¹, Allison Abbott², Nelson Lau³, David P. Bartel³, Victor Ambros², Bob Horvitz¹. 1) HHMI, Dept. Biology, MIT, Cambridge, MA 02139, USA; 2) Dept. Genetics, Dartmouth Medical School, Hanover, NH 03755, USA; 3) Whitehead Institute for Biomedical Research and Dept. Biology, MIT, Cambridge, MA 02142, USA.

Recently, molecular and bioinformatic approaches have identified many genes encoding 21-25 nt RNAs in C. elegans, Drosophila and mammals. All of these RNAs are derived from longer transcripts that form hairpin loops. These small RNAs, termed microRNAs (miRNAs, mirs), define a large, new class of genes.

To date the only genetically characterized microRNA genes in any organism are the C. elegans genes lin-4 and let-7. Both are heterochronic genes, which regulate the timing of development. To learn more about the biological roles of microRNAs, we have generated 34 deletion strains corresponding to loss-of-function mutations in 40 microRNAs. We have developed an efficient robotics system for the isolation of deletion mutants and are continuing to generate additional microRNA deletion strains. We have examined the 34 deletion strains for general appearance, movement, viability, fertility, egg laying, dauer formation, pumping and defecation. We have also assayed response to body touch, to drugs such as aldicarb, levamisole and ivermectin, and to osmotic barriers. In addition, we are studying genetic interactions of the microRNA genes to uncover synthetic phenotypes. So far we have focused on genes involved in microRNA/RNAi-processing, heterochrony, cell-death, dauer-formation, vulval development and the microRNA genes themselves.

We will present the initial analysis of several mutant phenotypes. We will demonstrate how the microRNAs mir-48 and mir-84 interact with genes of the heterochronic pathway. In addition, we will show that microRNAs are required for embryonic and germline development. Finally, we will present data indicating redundancy between members of several families of microRNAs.

Additional information about both the technology and our phenotypic characterization will be presented by Alvarez-Saavedra et al. (see abstract).