

62. The *let-7* and *mir-35* Families of MicroRNAs Each Act Redundantly in *C. elegans*

Ezequiel Alvarez-Saavedra¹, Eric A Miska¹, Allison L Abbott², Nelson C Lau³, David P Bartel³, Victor Ambros², Bob Horvitz¹

¹HHMI, Dept Biology, MIT, Cambridge, MA 02139, USA

²Dept. Genetics, Dartmouth Medical School, Hanover, NH 03755, USA

³Whitehead Institute for Biomedical Research and Dept. Biology, MIT, Cambridge, MA 02139, USA

From our efforts to obtain deletion alleles for all microRNA genes in *C. elegans* (see abstract by Miska *et al.*) we have identified and are characterizing two families of microRNAs the members of each of which appear to act redundantly.

The *let-7* microRNA regulates the larval-to-adult transition. *mir-48*, *mir-84*, and *mir-241* encode microRNAs similar in sequence to *let-7*. To study their functions we obtained strains with deletions in these microRNA genes by screening a library of mutagenized worms. Strains with single mutations in *mir-48*, *mir-84* or *mir-241* have a wild-type phenotype. However, *mir-48*; *mir-84* double mutants undergo an additional molt in the adult stage. Worms mutant for both *mir-48* and *mir-241* generate extra seam cells in the third and fourth larval stages, probably as a consequence of reiterations of the second larval stage developmental program. These findings suggest functional redundancy among *let-7* family members and roles for the *let-7* family in the control of the L2-to-L3 transition and the larval-to-adult transition.

The *mir-35* genomic cluster of microRNAs consists of seven genes, *mir-35* through *mir-41*, that share closely related sequences. These microRNAs are expressed only during embryogenesis, as assayed by northern blot and reporter GFP constructs. A deletion that removes all seven of these microRNAs results in a temperature-sensitive late embryonic lethal phenotype, while a deletion that affects only *mir-37* to *mir-41* does not cause lethality. The embryonic lethality can be rescued by expression of *mir-35* and *mir-36*. We are conducting a screen for suppressors of the temperature-sensitive lethality to seek targets of this family of microRNAs.