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# Rapid Screening Technique Advances Efforts to Determine Gene Function

**Image Title:** Gerald M. Rubin and colleagues can now probe the expression patterns of 96 *Drosophila* genes at a time. Their technique should speed the identification of novel genes involved in fruit fly development. - Paul Fetters

A rapid technique for tracking the expression of genes in the fruit fly *Drosophila* has identified hundreds of previously unknown genes that are likely to play a role in the orderly growth and development of animals ranging in complexity from insects to humans.

Researchers have long studied gene expression by examining one gene at a time. But developmental biologists led by Gerald M. Rubin and Corey S. Goodman of the Howard Hughes Medical Institute at the University of California, Berkeley, developed a technique that speeds the process by probing the expression patterns of 96 genes at a time. "We can very rapidly screen large numbers of genes for a particular expression pattern," Rubin says. Expression patterns indicate when a gene is turned on and thus directing the production of a specific protein.

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**— Gerald M. Rubin**

In an article in the August 18, 1998, issue of *Proceedings of the National Academy of Sciences,* the HHMI research team mapped gene expression for 2,518 segments of DNA from fruit fly embryos. The genes included 917 whose pattern of expression changes as the embryo grows, indicating that the genes may play a role in directing fruit fly development. When the researchers sequenced 1,001 of the gene segments and compared the sequences with those of known genes, they found that 811 represented new genes. The rapid identification of so many genes in a long-studied organism reflects the strength of the new approach.

The researchers identified so many previously missed developmental genes in part because the new method overcomes some of the disadvantages of older techniques that relied on introducing mutations into an animal's genome to "knock out" one of its genes and then see what changes occur in the organism. Rubin has estimated that for about two-thirds of *Drosophila* genes, defects resulting from such experiments yield no apparent changes in the fly, often because other genes can fulfill that same function as the altered gene. Other genetic manipulations are lethal early in development, eliminating the possibility of observing any changes at all.

The HHMI team designed their experiments to favor discovering genes that play a role in signaling that occurs between cells. Such signaling is the guiding force in stimulating processes that shape the development of an organism from a single fertilized egg to an adult. Although the researchers focused on developmental genes, the lab protocol can be adapted for rapid screening of all kinds of genes, Rubin explains.

The data from this study can be viewed on the World Wide Web as part of the Berkeley *Drosophila* Genome Project, sponsored by the Department of Energy and the National Institutes of Health. "Part of what we are doing is creating a resource for all who study *Drosophila* worldwide," Rubin says.

*Drosophila* studies have a history stretching back nine decades to Thomas Hunt Morgan's seminal experiments mapping genes to specific chromosomes in the cell nucleus. As was the case in Morgan's day, fundamental principles observed in *Drosophila* operate in other, less easily studied organisms. In recent decades, developmental biologists have identified sets of genes that trigger production of signaling proteins that guide the orderly development of body segments and establish the organism's central axis.

"One of the big surprises over the last five years is how well conserved these signaling pathways are," Rubin says. "Pathways discovered in *Drosophila* are doing the same things in vertebrates."

Norbert Perrimon , an HHMI investigator at Harvard Medical School, says that "studying the fly is a way to dissect signaling pathways that have been conserved through evolution and that are relevant to human physiology and disease." He adds that genes that play a role in normal growth in the fly also have been shown to be abnormal in some human birth defects and cancers. Perrimon's commentary on Rubin's and Goodman's research also appears in the August 18, 1998, issue of *Proceedings of the National Academy of Science.*