Book Reviews

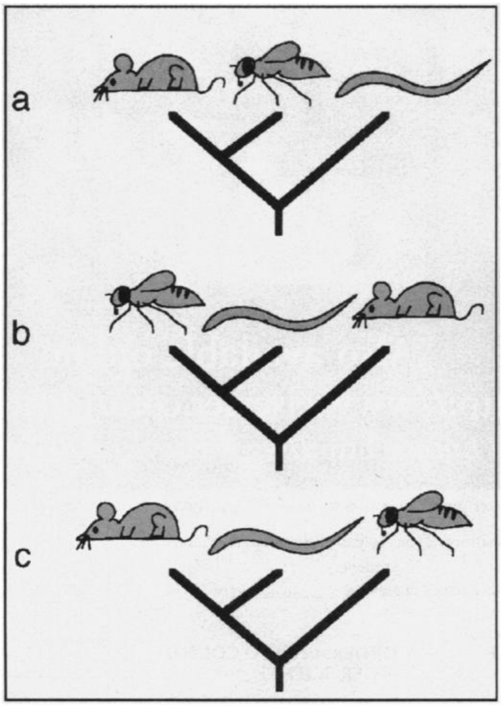
The Worm Returns

***C. elegans* II.** DONALD L. RIDDLE, THOMAS BLUMENTHAL, BARBARA J. MEYER, and JAMES R. PRIESS, Eds. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, 1997. xx, 1222 pp., illus. $175. ISBN 0-87969-488-2. Cold Spring Harbor Monograph 33.

When I began working on the small nematode *Caenorhabditis elegans* in the early '70s, not long after Sydney Brenner had chosen it as a model organism for studying animal development and behavior, one could read most of the essentials then published about the creature in an afternoon. As more people joined the worm community and wrote papers that demanded attention, newcomers and interested spectators faced an ever bigger job trying to familiarize themselves with the field. In 1988, a book, *The Nematode Caenorhabditis elegans*, came to the rescue. "Worm I" reviewed the worm's genome, anatomy, embryology, sex determination, muscle development, and behavior, among other things. Appendixes contained a list of all 959 somatic hermaphrodite cells and their lineages, a list of 774 mapped genes and mutant phenotypes, and a compilation of laboratory methods. "Worm I" has aged gracefully but is irrevocably stuck at 1988. Enter "Worm II."

The new book is about double the size of its predecessor, but its 30 review chapters are manageable chunks, averaging less than 30 pages. Overall, the level of discussion is authoritative yet suitable for those new to the field. Every chapter refers to related discussions in other chapters and avoids unnecessary overlap—a sign of strong editorial control. Worm neurobiology is growing rapidly; and more than seven chapters cover specification of nerve cells, migration of nerve growth cones, formation and modification of synapses, feeding, defecation, chemotaxis, thermotaxis, and learning. (The chapter "The nervous system" in "Worm I" is still a good introduction.) Behavioral effects of mutations or the killing of specific neurons by a laser microbeam are discussed in light of the known wiring of the 302-neuron nervous system. Among many cell lineage mutants discussed are those affected in specification of early embryonic cell fates, timing of developmental events, and programmed cell death.

Some chapters are devoted explicitly to molecular topics, such as RNA processing, regulation of transcription and translation, and extracellular matrix. But the many chapters with developmental or behavioral themes are also rich in molecular detail. For example, the chapter on sex determination and dosage compensation describes molecular switches regulating male versus hermaphrodite development and also describes the hermaphrodite-specific dampening of X chromosome transcription by a protein complex bound to the dampened chromosomes. Fortunately for those of us with limited memories, a few signal transduction pathways turn up repeatedly. For example, the Ras pathway, albeit in varied forms, arises in four chapters; it is required for vulva formation, some cell migrations, oogenesis, and male tail development. We who work on model organisms are pleased that this and other intercellular signaling pathways—such as the *lin-12/glp-1/Notch*, Wnt, G-protein, netrin, and TGF-β pathways (all discussed in "Worm II")—are shared by worms, flies, and humans and must therefore have been invented by a very ancient ancestor; a friend recalling wall charts of common metabolic pathways says we should not be surprised.



"Three possibilities of relationships of *C. elegans* ('the' nematode) to *Drosophila melanogaster* ('the' arthropod) and *Mus musculus* ('the' vertebrate): (*a*) nematodes as an outgroup taxon to vertebrates and arthropods; (*b*) nematodes more closely related to arthropods than to vertebrates; (*c*) nematodes more closely related to vertebrates than to arthropods. Obviously, these hypotheses (like the model systems themselves) are overly simplistic representations for enormously diverse phylogenetic groups. Although present data favor *a* or *b*, robustly distinguishing which hypothesis is most likely depends on the accumulation of much more data." [From D. H. A. Fitch and W. K. Thomas's paper in *C. elegans* II]

Genome sequencing is contributing to the rapid expansion of information about *C. elegans*. Over 60 percent of the 100-Mb genome—1/30 the size of the human genome—is already available, with the rest expected by the end of 1998. The sequencers estimate in their chapter that *C. elegans* has 14,000 genes. This is nine times the number of genetically mapped genes (listed in an appendix). It is also five times the estimated number of essential genes, that is, genes that when knocked out cause inviability. The number of essential functions has probably been underestimated by gene knockouts, however, since examples are accumulating in which two or more genes contribute redundantly, or nearly redundantly, to an essential function. In any case, a large fraction of the worm's genes must provide selective advantages that are not easy to discern in the laboratory by present methods.

How much will we have to learn about *C. elegans* before we can claim to understand how it is made and how it works? Will we, for example, have to identify 1000 transcription factors and all the genes they regulate? I don't know, but we certainly need to know much more about the regulation of cellular differentiation, which I suppose involves lots of middle-management transcription factors and their worker-gene targets—as well as considerable post-transcriptional regulation and protein assembly (see the chapter on muscle). And then topics like evolution, morphogenesis and control of lifespan, also discussed in "Worm II," clearly have a long way to go.

"Worm II" is excellent. It makes one eager for "Worm III."

Robert K. Herman
Department of Genetics and Cell Biology,
University of Minnesota,
St. Paul, MN 55108, USA