"Long before it's in the papers"

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New gene “encyclopedias” delve deeper into life’s mechanics

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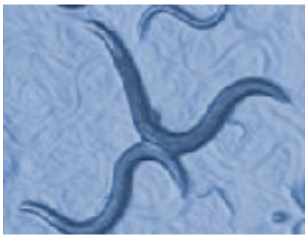
Courtesy of the National Human Genome Research Institute
and World Science staff

Eight years ago, the massive Human Genome Project identified most of the roughly 20,000-25,000 genes in human DNA.

Now, a newly published pair of catalogs seeks to dig deeper into the mechanics of life, though using only fruit flies and roundworms as simpler, more convenient models. The listings are intended to work as “encyclopedias” that explain how each gene actually works to develop and maintain cells and organs.



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Researchers say the work should lead to a better understanding of humans, since the studies of these simpler organisms have revealed many overlapping features with our genome.

“What we learn from these model organisms will contribute greatly to our understanding about the genomic basis of health and disease in humans,” said Eric D. Green, who directs the U.S. National Human Genome Research Institute in Bethesda, Md. The two catalogues are the fruit of projects the institute launched in 2007, called modENCODE for model organism Encyclopedia of DNA Elements.

The chemical codes of the genes of the fruit fly, *Drosophila melanogaster*, and the roundworm, *Caenorhabditis elegans*, were initially sequenced, or “written out” by researchers as part of the Human Genome Project.

The new results, by contrast, “allow scientists to begin reading the genome sequences, moving from a list of letters to delineating words and punctuation marks,” said Elise Feingold, program director overseeing the projects at the institute. The new findings are reported in the Dec. 24 issue of the journal *Science*, with companion studies published in the journal *Nature*’s advance online edition and in the journals *Genome Research* and *Genome Biology*.

The projects are meant to complement work being done by the affiliated ENCODE (for ENCycloped Of DNA Elements Consortium) Project, which is building a comprehensive catalog of “functional genomic elements” in the human genome.

The modENCODE projects apply to the smaller – and therefore easier to understand – genomes of the fruit fly and the roundworm. Unlike the researchers in the human effort, modENCODE researchers can conduct genetic experiments on flies or worms to follow up on and validate the current work.

The researchers studied many different cell types and developmental stages to produce the catalogs of genes and other important DNA sequences. The genes studied include ones that — unlike most better-studied genes — don’t harbor code for the production of proteins, complex molecules that carry out most of the body’s functions. These non-protein coding genes may instead govern how active other genes, or sets of genes, are. Other non-protein coding DNA sequences under

investigation influence the shapes and dynamics of chromosomes, the greater structures that package the genetic code.

“We now know when these genes are used in the life cycle and increasingly what cells the genes are used in,” said Robert H. Waterston, senior author of the roundworm paper in *Science* and chair of the University of Washington’s Department of Genome Sciences. “Putting the pieces together has begun to reveal how genes may work in concert to produce the marvelous biology of the roundworm and fruit fly.”

“Identification of thousands of new gene transcripts has significantly increased our knowledge of the protein repertoire used in fruit flies,” said Susan Celniker, who co-authored the fruit fly paper and heads the Department of Genome Dynamics at Lawrence Berkeley National Laboratory in California. “Our work provides new resources for studying development, sex determination and aging.”

The researchers also examined the organization and structure of chromatin in the cells throughout the life stages of each organism. Chromatin is the protein superstructure that packages DNA and modulates which sections of the genome are accessible to regulatory molecules that convert the genetic code into cellular action. Both groups discovered specific chromatin signatures associated with the regulation of protein-coding genes. Unique chromatin signatures were associated with distinct regions of the genome that either turn genes on or off.

“Chromatin signatures are emerging as a powerful lens into the structure and function of the regulatory portion of the genome that controls cell activity,” said Manolis Kellis, senior author of the fruit fly paper and a computer scientist at the Massachusetts Institute of Technology.