

Fly and worm models to teach researchers about human biology and medicine

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In an effort to understand every part of the genome needed for organisms to develop and thrive, the National Human Genome Research Institute, part of the National Institutes of Health, today announced the first grants in a four-year, \$57 million scientific mission to identify all functional elements in the genomes of the fruit fly and round worm.

The effort will build upon the foundation laid by the ENCyclopedia Of DNA Elements (ENCODE) consortium, which is preparing to build a comprehensive catalog, or "parts list," of all elements in the human genome crucial to biological function. In addition to genes that code for proteins, these functional elements include: non-protein-coding genes; regulatory elements involved in the control of gene transcription; and DNA sequences that mediate the structure and dynamics of chromosomes.

"We are making great strides in identifying functional elements in the human genome, but we still don't know much about their biological relevance. This parallel effort in the fruit fly and worm genomes will provide us with information about the functional landscape of two key model organisms, which should aid our efforts to tackle such questions in humans," said NHGRI Director Francis S. Collins, M.D., Ph.D.

Over the past several years, ENCODE researchers have collaborated in a pilot project to develop and use innovative methods and technologies to find functional elements in about 1 percent of the human genome. The new effort, dubbed model organism ENCODE (modENCODE), will

take advantage of many of these methods and technologies. However, rather than using the tools on the large and complex human genome, researchers will apply them to the smaller, and therefore more manageable, genomes of the fruit fly ("Drosophila melanogaster") and the round worm ("Caenorhabditis elegans"). The scientific community relies heavily on these model organisms to identify common genes, proteins and processes that underlie human medical conditions.

"One of the main reasons we were able to complete the Human Genome Project ahead of schedule and under budget was that we learned so much from sequencing the smaller genomes of model organisms, such as the worm and fly. This work enabled us to perfect the high-throughput methods and technologies that would be needed to completely analyze the much larger sequence of the human genome," said Robert H. Waterston, M.D., Ph.D., chair of the Department of Genome Sciences, University of Washington in Seattle, and one of the researchers receiving a modENCODE grant.

The fruit fly and round worm modENCODE projects have been designed so that similar elements in both organisms are being studied and catalogued in parallel. Unlike ENCODE's human-focused effort, modENCODE researchers can also conduct experiments in flies or worms to validate the biological relevance of the functional elements they identify. By combining and comparing data from worm, fly and human, researchers can learn far more about the functional elements than if they analyzed the genome of just one organism.

"Both the fly and worm share many genetic similarities with humans, yet their genomes are far easier to work with in experimental settings. modENCODE will enable us to confirm what we're finding in the human genome by manipulating the fly and worm genomes in a precise and rapid way," said Elise Feingold, Ph.D., the NHGRI program director in charge of the ENCODE and modENCODE projects. "If a DNA

sequence has been conserved throughout evolution -- from worm to fly to human -- it is very likely that the sequence is functionally relevant."

The modENCODE research consortium is made up of teams of experts who bring a great deal of knowledge about the biology of the fruit fly and roundworm. Due to the complexity of the data, the teams will work together to maximize the intellectual discussions and quality of data analysis.

Source: NIH/National Human Genome Research Institute

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