

# Unraveling the Genomic Code for Development

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Scientists at the California Institute of Technology have produced the first complete description of the complex network of genes that create a particular type of cell in an organism.

Scientists have known for decades that the program for development is encoded in the genome, the total genetic complement of any living thing. "Cats beget cats and frogs beget frogs, so how you develop depends on what genome you've inherited," says Eric H. Davidson, the Norman Chandler Professor of Cell Biology at Caltech.

Just knowing the sequence of the genome, however, won't get you far. To actually make a cat or a frog, you need to understand the relationships between genes--what genes control other genes, turning them on or off at specific times during the development of the organism to produce an organism's skeletal system, or leaves, or skin. Biologists call the complex network of gene interactions involved in this process a gene regulatory network.

In 2006, the Baylor College of Medicine Human Genome Sequencing Center, along with Davidson and Andy Cameron of Caltech, and an international team of researchers from more than 70 institutions, revealed the entire 814 million base-pair sequence of the genome of the California purple sea urchin (*Strongylocentrotus purpuratus*). The genome is about one-fourth the size of the human genome, and contains some 23,300 genes.

Using these data and other techniques to determine the regulatory genes expressed at each point during embryonic development and how their interrelationships influence the architecture of the sea urchin's skeletal system, Davidson and his colleagues created a complete blueprint for the development of a lineage of cells whose particular function is to build a series of biomineral skeletal rods inside the embryo.

The work, coauthored by Qiang Tu, a postdoctoral research fellow at Caltech, and Paola Oliveri, now of University College London, appears in the April 22 issue of the *Proceedings of the National Academy of Sciences*.

Unlike a regular blueprint, which describes how to simultaneously construct all of the various parts of a structure, the gene regulatory network represents a dynamically changing plan, with the relationships between genes at one stage providing the program for the next stage of development.

According to Davidson, the research marks the first time that all of the "moving parts"--the regulatory genes specifically expressed in a particular developmental process that recognize target DNA sequences, bind them, and control the expression of other genes--have been included in a gene regulatory network.

"We've reached the point where all of the biology that you see in a microscope for this cell lineage can be interpreted in terms of what we know about this control program. The network concerns only one day in the life cycle of an animal that lives for 50 or a hundred years, and only one cell lineage of the embryo, but it is a step forward to be able to relate the biology to the regulatory DNA sequence in this way."

In a commentary accompanying the published paper, biologist Leroy Hood of the Institute for Systems Biology describes the study as a "tour

de force." The research, he says, "represents a brilliant integration of biology, technology, computational approaches, and powerful logic." The paper, he adds, "will be the model for many more that will undoubtedly follow, transforming the landscape of developmental biology and ultimately elucidating the molecular systems that drive development."

The major effort in the Davidson lab is to decipher the gene regulatory networks that control the rest of the embryonic development of the California purple sea urchin.

That information will reveal for the first time the code for a whole embryo, a small but complex creature. At that point, scientists can begin to tinker with and re-engineer the network--a process that simulates the genetic changes that accompany the evolution of organisms in real life. "The evolution of animals is due to changes in the structure of these gene regulatory networks, so this work provides us with an opportunity to study evolution in a new and decisive way," he says.

Indeed, in a second paper in the same issue of the journal, Davidson and his colleague Feng Gao report that the gene regulatory network for the sea urchin's embryonic skeletal development evolved from another network present in adult animals, and probably was co-opted into the embryonic network by hijacking a big piece of the regulatory apparatus that controls the construction of the adult skeletal system.

Source: Caltech

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