Master regulators of embryonic development: Humans and fruit flies have similar Hox genes

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Hox genes are the master regulators of embryonic development for all animals, including humans, flies and worms. They decide what body parts go where. Not surprisingly, if something goes wrong with these genes, the results can be disastrous.

In Drosophila, the fruit fly, a Hox mutation can produce profound changes—an extra pair of wings, for example, or a set of legs, instead of antennae, growing from the fly's head.

"The job of the Hox genes is to tell cells early on in embryonic development what to become—whether to make an eye, an antenna or wings," says Robert Drewell, associate professor of biology at Harvey Mudd College in Claremont, Calif. "Just a single mutation in the Hox gene can produce these dramatic anomalies."

Humans have Hox genes too. For this reason, Drewell is trying to understand the molecular function of Hox genes in the fruit fly, including what happens when they work properly and what happens when they don't, in order to learn more about their behavior in humans.

Genetically, humans and fruit flies are very much alike; in fact, many known human disease genes have a recognizable match in the genetic code of the fruit fly. Thus, the information researchers gain from studying flies could provide insights into certain birth defects, such as extra ribs and extra digits, and potentially serious diseases.

"We have exactly the same genes, and use them in exactly the same way," he says. "By understanding them in Drosophila, we can understand them in humans."

Drewell is conducting his research under a National Science Foundation Faculty Early Career Development (CAREER) award, which he received in 2009. The award supports junior faculty who exemplify the role of teacher-scholars through outstanding research, excellent education and the integration of education, and research within the context of the mission of their organization. He is receiving about $600,000 over five years.

Hox genes have been entirely conserved throughout animal evolution, meaning "since around 530 million years ago, when many complex animal life forms appeared, they had Hox genes," Drewell says.

Fruit flies are model organisms for studying genetics since they have a short lifespan—several generations can be studied in a matter of weeks—and are small and easy to grow. More importantly, they can provide a wealth of information for computational analysis because scientists have deciphered their entire genetic blueprint.

"We live in this post-genomic era, so we can do comparisons across species to look at exactly how the regulatory regions at Hox genes are changing over time," Drewell says.

Drewell's lab uses several different approaches, applying biology, genetics and computational methods to learn more about the behavior of Hox genes.

"We make what are called 'reporter' genes," he says. "We construct these artificial genes in the lab, then reintroduce them back into Drosophila. This allows us to measure what is happening to those genes. The genes we are putting in are combinations of fragments from Hox genes—different DNA regions—and we are testing if these different regions are responsible for regulating when and where the Hox gene is turned on and off."

Through their experiments, "We can look at what genes are turned on and off, and can detect exactly which DNA elements regulate the process, and how they regulate it."

Because the fruit fly's genome is available, "we are able to do comparisons across species to look at exactly how these regulatory regions are changing over time," using computational biology methods, he says. Moreover, "through that process, we can essentially start to get a handle on the role that Hox genes play in controlling cell identify in the developing embryo. We can do this in all animals, including humans."

The educational component of his CAREER grant has allowed Drewell to incorporate new elements to the curriculum, including mathematical and computational approaches, and provides undergraduate students the opportunity to conduct research that typically would not be available to them.

"Harvey Mudd doesn't have a graduate program, so all the research, essentially, is done by undergraduates," Drewell says. "They get an opportunity to do something they might not otherwise get to do. Each student is fully encouraged to take ownership of his or her own project. In this way, this often exposes them to a research field for the very first time and establishes a great foundation for their future endeavors in research."

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