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NOVEMBER 4, 2009

Change in Regulatory DNA Responsible for Stickleback Evolution

by Julia Galef

CHICAGO, ILLINOIS—The birthplace of modern evolutionary biology can arguably be located at a landmark 1959 conference at the University of Chicago, which synthesized the then-new discoveries of DNA and genetics with Charles Darwin's observations on evolution. Last weekend, the university reprised that famous meeting with a "Darwin 2009" conference (right) that highlighted just how much has changed in the past 50 years: Dizzying genetic and genomic advances are allowing us to answer questions our 1959 counterparts couldn't even have dreamed of asking.

For instance, only recently have scientists begun to suspect that much of evolutionary change might be due not to mutations in the familiar protein-coding DNA but to other, noncoding DNA that regulates how and where the coding DNA expresses itself. The role of noncoding DNA in evolution has been hotly debated by scientists, but even as recently as last year the evidence was still spotty.

That's why one talk at the 29 to 31 October conference set off a particularly excited wave of coffee-break chatter: Stanford University evolutionary biologist David Kingsley revealed new results demonstrating how a change in the regulatory DNA of a single gene can produce a dramatic, adaptive change in an animal's anatomy.

Stickleback fish originated in marine environments, where they evolved a pelvis that protected them against predators by pushing out its spines, turning them into prickly, swimming pincushions (left). Over time, however, many stickleback populations spread to neighboring freshwater regions, where their pelvises were suddenly a disadvantage. In place of their traditional predators, they now faced large carnivorous insects like dragonflies who used the sticklebacks' prominent spines to nab them as they swam in shallow waters. So stickleback populations in freshwater began to lose their pelvises, a classic adaptive trick that Darwin himself could have appreciated; Kingsley's team wanted to know how, exactly, the sticklebacks' genes pulled it off.

Several years ago, Kingsley traced the loss of the pelvis back to a single gene called *Pitx1*. Because the coding DNA in that gene was present in both the marine and freshwater sticklebacks, he reasoned that some part of *Pitx1*'s noncoding DNA must be regulating the gene's expression, producing pelvises in the marine fish and none in the freshwater fish. Although his hypothesis made a big splash upon its publication (and has been widely cited since) it was still just a hypothesis, until this year.

After testing piece after piece of noncoding DNA from the spiny marine sticklebacks, Kingsley's team zeroed in on a sequence that seemed to correspond to pelvic development. So they cloned that sequence from the marine fish and injected it into the embryos of freshwater fish in order to produce the phenotype of a marine fish, a feat rarely attempted, let alone accomplished, in live animals. Sure enough, the resulting sticklebacks developed pelvises.

It's a particularly striking piece of evidence for the regulatory gene hypothesis, in part because the anatomical change is so large. "Losing an entire limb is the kind of dramatic change you usually see between only distantly related species," Kingsley said, so to produce such an effect from a single regulatory sequence of one gene is a bombshell. His results are also remarkable for including multiple, independent lineages of stickleback, addressing another hot topic in evolutionary biology: Do organisms exposed to the same selective pressures use the same genetic mechanism to adapt? Kingsley's results suggest that, at least in some cases, they do.

"The Holy Grail of research on adaptation is to identify adaptive mechanisms, the traits that contributed to adaptation and the genetic basis of adaptive traits," evolutionary biologist Doug Schemske of Michigan State University in East Lansing said after the conference. "Most of us can at best answer one of these questions—Kingsley has done it all."

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