

GENOMICS

Ecological Genomics Gets Down to Genes—and Function

The promise of genomics lures ecologists into the once-alien world of molecular biology

KANSAS CITY, MISSOURI—A decade ago, many ecologists and molecular biologists were barely on speaking terms. As universities devoted ever more space and resources to molecular biology, ecologists felt they got the short end of the stick. And those who wanted to incorporate new molecular techniques into their studies were hamstrung by grants too small to pay for the new technologies.

But in recent years, ecologists and molecular biologists have been finding common ground—to the benefit of both disciplines. “Ecology needs better grounding in mechanisms, particularly molecular mechanisms. And those [researchers] who focus on the molecular level often do so at the expense of reality,” says Jack Schultz, an ecologist at the University of Missouri, Columbia. “These two areas really need each other.” Now, says Schultz, “when you walk around, you see people [doing] genomic studies on all kinds of organisms.”

Some of the results of this detente were on display last month, when about 90 researchers and students gathered* to discuss progress in ecological genomics—the application of genomic techniques and resources to the study of ecology. Some are applying tools such as microarrays or RNA

*The Ecological Genomics Symposium was held 13 to 15 November in Kansas City, Missouri.



Go light. In White Sands, New Mexico (above), mutations have lightened the eastern fence lizard (right, top) and little striped whiptail lizard (far right, top) to help them blend in better.



interference to their favorite study animal or plant. Others are developing genetic maps and databases of gene fragments for non-model organisms, with the goal of eventually sequencing those genomes. These efforts are pinpointing genes involved in ecologically relevant traits, and researchers are beginning to figure out the roles those genes play in an organism's function and evolution. “It's not enough to identify a list of candidate genes for adaptation; you now need to integrate a functional approach,” says Jay Storz, an evolutionary biologist at the University of Nebraska, Lincoln.

How bees are like us

May Berenbaum, an entomologist at the University of Illinois, Urbana-Champaign, has long been interested in innovations in the arms race between insect herbivores and their hosts. Her work has focused on genes for cytochrome P450, a family of enzymes that break down toxins. (One particular P450 enables a black swallowtail caterpillar, for example, to feast on the normally toxic wild parsnip and its relatives.) For many years, Berenbaum tracked down P450 genes one at a time, but now that several genomes have been sequenced, she can use computer programs to search for typical P450 sequences across an organism's entire genome and verify them with more detailed studies. More than 7000 P450 genes are now listed in public databases; insects generally have scores of them, and some plants have hundreds.

As she described at the meeting, Berenbaum noticed something strange when she looked



Food safety. Honey bees usually don't eat raw nectar but convert it into honey.

over the P450 counts for the honey bee, mosquito, fruit fly, and red flour beetle genomes. Honey bees had a mere 48, compared with 87 in the fruit fly, 112 in the mosquito, and 144 in the beetle. “How could they function with so few [toxin] metabolism genes?” she wondered.

She ruled out the possibility that the small number was attributable to the fact that female worker bees have just one set of chromosomes instead of the usual two: *Nasonia vitripennis*, a small parasitoid wasp, has the same unusual genetic system, yet it has 90 different P450 genes. Berenbaum next tried activating the honey bee's detoxification genes by exposing the insects to a chemical that usually triggers P450 gene activity. She got no response. It was as if honey bees didn't often encounter toxins.

At first this finding didn't make sense. Honey bees gather nectar from a wide range of plants, and nectar contains a variety of toxins, so Berenbaum expected that the bees would have a robust, readily activated detoxification program. But as she thought about it more, Berenbaum hit on a possible explanation: Honey bees rarely eat “raw” food. Instead, they collect nectar and pollen and process it into honey and bee bread in the hive. Sitting in the warm hive, nectar's toxins break down, nectar is dewatered, and its sugar profile and pH change as it is transformed into honey. The transformation likely renders the food less harmful. The honey bee “is the only other organism [besides humans] that prepares its food,” says Berenbaum. “They use social behavior, as do we, to deal with toxic foods.”

The work “is an exciting example of genome-enabled research—particularly the poten-

tial for comparisons between genomes of different species that have different lifestyles,” says Erica Bree Rosenblum, an evolutionary biologist at the University of Idaho, Moscow.

How deer mice live the high life

Several talks at the meeting indicated how evolutionary biologists are coming to depend on genome sequence data to provide important insights into the evolution of specific traits. “Genomic technology [has] provided us with the means of identifying the genetic basis of adaptation and speciation,” says Storz. “The future lies in obtaining a more mechanistic understanding of those processes.”

Storz’s group has already begun to go down that path. They have characterized changes in genes for hemoglobin—a component of blood that transports oxygen—that enable deer mice, *Peromyscus maniculatus*, to thrive at oxygen-poor high altitudes. A survey of the sequenced genomes of the lab mouse, human, and lab rat revealed that the organization of the hemoglobin genes was conserved and “showed where in the genome these genes were located,” says Storz. Two copies of the gene for the alpha globin subunit appeared together in one location; two copies of the beta globin subunit appeared together in another spot. He used the sequences and their locations to track down those same genes in the deer mouse.

At the meeting, Storz and his colleagues described how hemoglobin genes were quite different in mice living at high altitudes compared with those at low altitudes. These genes were more different than were other genes from the two locations, indicating that they experienced selection pressures in high- and low-altitude environments that other genes did not.

Based on the sequences of these subunit genes, Storz and his colleagues pinpointed five amino acid changes in the alpha globin subunits and four in the beta globin subunits associated with altitude. They purified hemoglobin from deer mice of known genetic makeups and tested how well each version of hemoglobin grabbed onto oxygen. The versions from mice living on the peaks had high oxygen affinity—which made taking in oxygen in the rarefied mountain air more efficient. Now Storz and his colleagues are making artificial hemoglobins with different combinations of the changes they see in the high-altitude mice to see which changes are most important.

“What [Storz] is doing is really at the cutting edge, the foreground, of ecological, evolutionary and functional genomics,” says



Mountain high. Researchers studying high-altitude deer mice (above) find special hemoglobin genes help these mice breathe easy.

lizard’s defective protein does not integrate well into the cell membrane, where it normally sits. The whiptail lizard’s defective protein settles into the membrane just fine, however, but it doesn’t pass signals along very well. “Even though we have the same gene, we have different [ways] the function is compromised,” she reported at the meeting.

The lightened skin also changes other skin-color patterns—in particular, the yellow, orange, blue, and green that lizards rely on for social

cues. So Rosenblum wondered how these changes have affected courtship and territorial behavior. She and her colleagues tested whether White Sands males react differently to each other compared with males from the surrounding desert. They also looked at the White Sands males’ preferences for females of like or different color. White males were more aggressive toward other white males and more attentive to the white females, Rosenblum found: “The lizards, in a couple of thousand generations, can tell the difference.” But the color changes also had an unexpected effect: White males tended to court the desert scrub males—most likely because the desert scrub males’ blue belly patches were about the same size as the White Sands females’ belly patches, which made them look like White Sands females. “We have a link between natural and sexual selection,” she adds. “Therefore, a single mutation can have important effects for both adaptation and the early stages of speciation.”

How lizards lighten their skin

Rosenblum has also used genomics to probe mechanisms that underlie the adaptations organisms make to their environment. Her animals of choice are three species of lizard in White Sands, New Mexico—a large patch of white gypsum surrounded by dark desert scrub. Over the past 10 years, Rosenblum and her colleagues have determined that the three species have different mutations of the *Mclr* pigment gene that cause normally brown skin to be quite pale. When mutated, *Mclr* causes less brown pigment to be produced, helping the lizards blend in with the white sand.

She was puzzled that the mutations have different effects in two of the lizards. In the eastern fence lizard (*Sceloporus undulatus*), the blanched color was passed on as a dominant trait, whereas in the little striped whiptail lizard (*Aspidoscelis inornata*), it was a recessive trait. This difference probably affected how quickly the mutation spread in the White Sands populations of each species. When she tested the effect of each mutation on the function of the *Mclr* protein in cell cultures, she discovered that the fence

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As the work with lizards, deer mice, and honey bees shows, ecologists have converged on genomics from very different perspectives. Yet once genomics has helped them find specific genes and identify selective pressures, their interests broaden to include physiology, cell biology, and interactions with the environment. As Michael Herman of Kansas State University points out, those in this field “are spanning all levels of biological organization.”

—ELIZABETH PENNISI