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An Evolution Saga: Beach Mice Mutate and Survive

It's a pitiless lesson—adapt or die—but the sand-colored mice that scurry around the beaches of Florida's Gulf Coast seem to have learned the lesson well. Now researchers have identified a genetic mutation that underlies natural selection for the sand-matching coat color of the beach mice, an adaptive trait that camouflages them from aerial predators.

In the July 7, 2006, issue of the journal *Science*, evolutionary geneticist Hopi Hoekstra and colleagues at the University of California, San Diego, report that a single mutation causes the lifesaving color variation in beach mice (*Peromyscus polionotus*) and provides evidence that evolution can occur in big leaps.

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— **Hopi Hoekstra**

The Gulf Coast barrier islands of Florida and Alabama where the beach mice are found are less than 6,000 years old—quite young from an evolutionary standpoint. Hoekstra said that the identification of a single mutation that contributes to the color change that has arisen in these animals argues for a model of evolution in which populations diverge in big steps. This model, in which change is driven by large effects produced by individual mutations, contrasts with a popular model that sees populations diverging via small changes accumulated over long periods of time.

Recent genomic studies have revealed that the regions of chimpanzee and human DNA that encode proteins are 99 percent similar. This finding led scientists to believe that most adaptive mutations would be found in the regulatory regions—the one percent of the genomes that differ substantially between the species.

The new findings reported in *Science*, however, indicate otherwise. We've identified a single nucleotide in the coding region of a gene that has an effect

on which animals survive in natural populations, said Hoekstra. This is a striking example of how protein-coding changes can play a role in adaptation and divergence in populations, and ultimately species.

Hoekstra, who now mentors a Howard Hughes Medical Institute (HHMI) predoctoral fellow at UCSD, did her own graduate work on a predoctoral fellowship from HHMI's graduate science education program. The program helps prepare some of the most promising young scientists and physicians for research careers.

The mutation that Hoekstra and her colleagues found alters the melanocortin-1 receptor (*Mclr*). This hormone receptor has been associated with color variation in several mammalian species. The mutation, which appears in mice that live on the coast, is absent in mainland mice. By mating the beach mouse and the mainland subspecies, the researchers found that mutations in *Mclr* explain as much as one-third of the coat-color variation of the animals.

Hoekstra and colleagues are the first to prove that the mutation causes coat-color variation. When they grew cells in the laboratory with the "light" and "dark" versions of *Mclr*, they found that the receptor's function is diminished in cells expressing the lighter form of *Mclr*. Specifically, they observed lower levels of the signaling molecule cyclic AMP (cAMP), which is associated with dark pigment. Therefore, the researchers suggested, the lack of dark pigment in mice expressing the light *Mclr* may be due to reduced cAMP production.

An accompanying article in the same issue of *Science* reports that the permafrost-buried bones of woolly mammoths also contained variations in *Mclr*. Our work in mice raises the exciting possibility that woolly mammoths may have had similar variations in coat color, Hoekstra remarked, although she said it is unclear whether this would have had adaptive significance for mammoths. It's hard to imagine, but you never know, she said.

For evolutionary geneticists, who often restrict their studies to model organisms such as *Caenorhabditis elegans*, a miniscule worm, the beach mouse offers a promising model with an extensively studied ecology. An added advantage is that, unlike most wild animals, it can be bred in captivity. We're just now starting to build genetic tools in emerging model systems to address interesting questions about how adaptation proceeds at the molecular level," Hoekstra said.

Hoekstra noted that although Florida's Atlantic Coast beach mice have a light coloration similar to that of the Gulf Coast mice, the team did not find the light version of *Mclr* in those animals. This indicates that other genetic mechanisms also play a role in beach mouse color, Hoekstra said, and she plans to continue searching for new genes and mechanisms that contribute to these adaptive color patterns.