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RESEARCH NEWS

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Same Genetic Machinery Generates Skin Color Evolution in Fish and Humans

When humans began to migrate out of Africa about 100,000 years ago, their skin color gradually changed to adapt to their new environments. And when the last Ice Age ended about 10,000 years ago, marine ancestors of ocean-dwelling stickleback fish experienced dramatic changes in skin coloring as they colonized newly formed lakes and streams. New research shows that despite the vast evolutionary gulf between humans and the three-spined stickleback fish, the two species have adopted a common genetic strategy to acquire the skin pigmentation that would help each species thrive in their new environments.

The researchers, led by Howard Hughes Medical Institute investigator David Kingsley, published their findings in the December 14, 2007, issue of the journal *Cell*. Kingsley and first author Craig Miller are at the Stanford University School of Medicine, and other co-authors are from the University of Porto in Portugal, the University of British Columbia, the University of Chicago, and the Pennsylvania State University. Further studies of stickleback, they say, may reveal other malleable pieces of genetic machinery both fish and humans have used for adaptation.

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— David M. Kingsley

The stickleback has become a premier model organism for studying evolution because of its extraordinary evolutionary history, said Kingsley. Sticklebacks have undergone one of the most recent and dramatic evolutionary radiations on earth, he said. When the last Ice Age ended, giant glaciers melted and created thousands of lakes and streams in North America, Europe, and Asia. These waters were colonized by the stickleback's marine ancestors, which subsequently adapted to life in freshwater. This created a multitude of little evolutionary experiments, in which these isolated populations of fish adapted to the new food sources, predators, water color, and water temperature that they found in these new environments, Kingsley explained.

Among those adaptations were new colorations that helped the fish camouflage themselves, distinguish species, and attract mates in their new environments. Until now, however, scientists had not understood what genetic factors drove the changes in skin pigmentation.

Human populations have also undergone pigmentation changes as they have adapted to life in new environments. The ecological reasons for those changes may be quite different from the forces driving the evolution of pigmentation in sticklebacks, said Kingsley. As human populations migrated out of Africa into northern climates, the need for darker pigmentation necessary to protect against the intense tropical sun diminished. With skin that was more transparent to sunlight, humans were better able to produce sufficient vitamin D in their new climate.

To begin to understand the genetic basis of skin pigmentation changes in fish, Kingsley and his colleagues crossed stickleback species that had different pigmentation patterns and used genetic markers and the recently completed sequence map of the fish's genome to search for the mechanism regulating stickleback pigmentation. They searched for chromosome segments in the offspring that were always associated with inheritance of dark or light gills and skin. Through detailed mapping of one such segment, Kingsley and his colleagues found that a gene called *Kitlg* (short for Kit ligand) was associated with pigmentation inheritance. *Kitlg* was an excellent candidate for regulating pigmentation because mutant forms of the corresponding gene in mice produce changes in fur color, said Kingsley.

The *Kitlg* gene is involved in a variety of biological processes, including germ cell development, pigment cell development, and hematopoiesis. Light-colored fish have regulatory mutations that reduce expression of the *Kitlg* gene in gills and skin, but that do not reduce the gene's function in other tissues. By altering expression of this gene in one particular place in the body, the fish can fine tune the level of expression of that factor in some tissues but not others, said Kingsley. That lets evolution produce a big local effect on a trait like color while preserving the other functions of the gene.

Humans also have a *Kitlg* gene, and Kingsley and his colleagues wondered if it played a role in regulating the pigmentation of human skin. One clue they had came from previous research by other groups that had revealed that the human *Kitlg* gene has undergone different changes among different human populations, suggesting that it is evolutionarily significant.

Kingsley and his colleagues tested whether the different human versions of the *Kitlg* gene are associated with changes in skin color. Humans with two copies of the African form of the *Kitlg* gene had darker skin color than people with one or two copies of the new *Kitlg* variant that is common in Europe and Asia.

Although multiple chromosomal regions contribute to the complex trait of pigmentation in both fish and humans, we have identified one gene that plays a central role in color changes in both species, said Kingsley.

Since fish and humans look so different, people are often surprised that common mechanisms may extend across both organisms, he said. But there are real parallels between the evolutionary history of sticklebacks and humans. Sticklebacks migrated out of the ocean into new environments about ten thousand years ago. And they breed about once every one or two years, giving them five thousand to ten thousand generations to adapt to new environments.

Although modern humans arose in Africa, they are thought to have migrated out of Africa in the last 100,000 years. Humans breed about once every 20 years, giving them about 5,000 generations or so to emerge from an ancestral environment and colonize and adapt to new environments around the world, Kingsley added. So despite the difference in total years, the underlying process is actually quite similar. Whether it be fish or humans, there were small migrating populations encountering new environments and evolving significant changes in some traits in a relatively short time. And the genetic mechanisms that can produce these changes may be so constrained that evolution will tend to use the same sorts of genes in different organisms.

Kingsley and his colleagues are now exploring the genetic basis of other evolved traits in the stickleback that could find a parallel in humans. And given the degree to which evolutionary mechanisms appear to be shared between populations and organisms, we're optimistic about finding the particular genes that underlie other recent adaptations to changing environments in both fish and humans, he said.