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How Did Humans Evolve? Ask a Mouse

by Elizabeth Pennisi on 14 February 2013, 12:00 PM | 0 Comments

Mice carrying human disease genes have proved valuable for learning what goes awry in people. Now, researchers have tapped the rodents to understand human evolution. Mice with a human version of a gene called *EDAR* have more sweat glands than normal, providing clues to how East Asians adapted to a humid environment 30,000 years ago.

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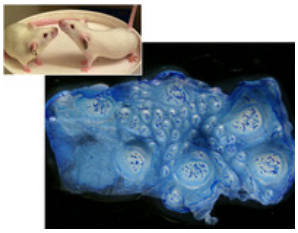

Altered trait. Mice (*inset*) carrying a human version of the EDAR gene have footpads with more sweat glands (blue tubes).

Credit: Yana G. Kamberov

Harvard University evolutionary geneticist Pardis Sabeti first began looking at *EDAR* in 2007. Through statistical analyses of genome data, she and her colleagues discovered that although most people had the same version of the *EDAR* gene as mice and other mammals, a variant of *EDAR* called 370A was very common in East Asians and Native Americans. The EDAR protein is involved in hair formation, and these groups of people have thicker hair, but the researchers didn't know if the genetic change in *EDAR* caused the change in hair texture.

So one of Sabeti's Harvard colleagues, postdoctoral fellow Yana Kamberov, inserted *EDAR* 370A into mouse embryonic stem cells. By breeding the resulting mice for several generations, she made a strain carrying 370A. Although the 370A protein differed from the mouse EDAR protein by just one amino acid, it led to several important changes in the mouse, Kamberov, Sabeti and their colleagues report today in *Cell*. The mice had thicker hairs in their fur, as expected. But they also had more sweat glands, denser mammary glands, and smaller fat pads around those mammary glands. "This study was able to show there are other, more subtle effects" beyond hair thickness, says Joshua Akey, an evolutionary biologist at the University of Washington, Seattle, who was not involved with the work.

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To determine if these effects were also found in people, the team measured sweat gland density in Han Chinese in China carrying one or two copies of 370A. People with a double dose of 370A also had more sweat glands, the researchers report. They did not have an easy way to tell if mammary glands were different in this group, but they suspect, based on the results in mice, that these structures were also affected.

"It's one of the first papers that clearly shows that a change that was important in recent human evolution can be modeled in the mouse," says Wolfgang Enard, an evolutionary geneticist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, who was not involved with the work.

The group's analyses and computer simulations looking at how 370A arose and spread indicate that the mutation creating the variant gene happened more than 30,000 years ago in central China. China had been relatively warm and humid between 40,000 and 32,000 years ago and then got cooler and drier. But Kamberov thinks that summer and winter monsoons still created high enough humidity that those people who were able to cool their bodies with extra sweat glands would have done better. Alternatively, or in addition, the increased branching in the mammary glands could have provided an advantage for raising infants. "It's not clear which one of those [traits] resulted in differences" in survival and reproductive ability, Akey says.

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The work "pushes the field in novel ways, Akey adds, as very few studies have pinned down the functional consequences of genetic changes that have been selected for. Although "the mouse model brings you closer" to understanding how modern humans have changed through time, Enard says, "without a time machine we will never get all the relevant data."

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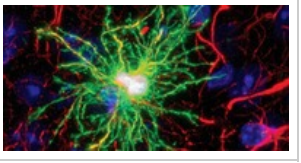

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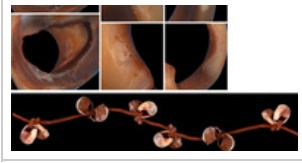

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