The Pace of Evolution

A CLOSE LOOK AT THE HUMAN GENOME SHOWS THE SLOW AND STEADY BEAT OF ADAPTATION.

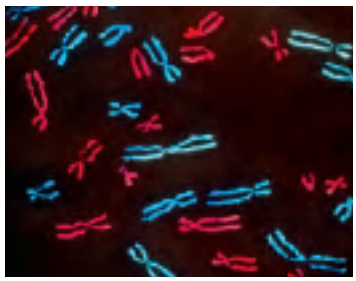
Here's how scientists have typically explained the emergence of a new genetic trait: A genetic mutation randomly occurs that gives its carrier an advantage in reproducing. Over a handful of generations, the mutation becomes more prevalent in the population, quickly becoming ubiquitous. It's called a "selective sweep" and has been the predominant explanation for how most new human genes have surfaced. Now here's Molly Przeworski's take: evolution is slow and complex and few human traits have ever emerged through such a speedy takeover.

Przeworski, an HHMI early career scientist at the University of Chicago, relied on the fact that if a gene mutation moved that quickly across the human population, most everyone would have inherited the identical genetic material bordering the mutation. If a mutation spread slowly, on the other hand, or arose more than once, it would gradually pick up other mutations in surrounding genes as it broadened throughout the population.

Using this reasoning, Przeworski and her team analyzed 179 human genomes collected through the 1000 Genomes Project. They looked at 40,000 genetic changes that set humans apart from their primate ancestors—some that might change a protein's function, others that are essentially silent. If the "selective sweep" model had dominated throughout human history, Przeworski's team would see more highly conserved regions around mutations that had functional effects. Yet they saw no differences between the variability surrounding functional mutations compared with the rest of the genome, they reported on February 18, 2011, in *Science*.

This finding must mean that "not many adaptations in our history have proceeded through sweeps," says Przeworski. "Selective sweeps must be really rare."

She suggests two alternatives that could explain how adaptations might spread more often. Preexisting mutations across the population can face a new selective pressure from a change in the environment—this process is called "selection on standing variation." Or, a trait can rely on many gene changes rather than one change with a large effect. "Height, for example, is controlled by thousands of loci," says Przeworki. "If the environment is selecting for height, that will happen through hundreds of gene locations." ■



Scientists looked at 40,000 genetic changes to determine the pace of human evolution.

–SARAH C.P. WILLIAMS

IN BRIEF

CELLULAR STRESS PATHWAY LINKED TO TRAUMATIC STRESS DISORDER

Researchers have discovered a genetic marker for post-traumatic stress disorder (PTSD) in women. They found that the gene's effect relies on the hormone estrogen and therefore is not linked to the disorder in men, who have very low levels of estrogen. Led by HHMI investigator Kerry Ressler at Emory University, the multi-institutional study could lead to the first blood test for PTSD susceptibility.

Ressler and his collaborators began with blood samples from 64 men and women in a highly traumatized population. Levels of a protein called pituitary adenylate cyclase activating polypeptide (PACAP) were higher in women who had been diagnosed with PTSD than in women without the diagnosis. A study in a larger group of women yielded the same results.

To understand PACAP's role in PTSD, the team looked for variations of the gene encoding the protein in more than 1,200 women at high risk for PTSD. They found that a mutation in the gene is associated with the presence of PTSD. The researchers then compared PACAP levels in female rats lacking ovaries, and thus estrogen, and in such mice receiving estrogen replacement. The mice with estrogen had higher levels of *PACAP* gene activity in regions of the brain associated with stress and fear, suggesting that estrogen controls this activity, the team reports in the February 24, 2011, issue of *Nature*.

This result provides the first evidence linking the PACAP pathway to PTSD. The pathway is normally linked to cellular response to stress.

MATING TRUMPS FIGHTING

In a tiny area deep in the mouse brain, a set of neurons ensures that mice don't mate and fight at the same time. Crude experiments from the 1920s had hinted that both behaviors were controlled by neurons in the brain's hypothalamus region. Now, HHMI investigator David Anderson has used modern techniques to resolve the details.

In his lab at the California Institute of Technology, Anderson and colleagues began by inserting electrodes into an area of the hypothalamus called VMHv1. Then they recorded the behavior—and firing patterns of 104 neurons in the region—of the male mice over the next several months.

When one male mouse encountered another male mouse and began to fight, a group of neurons in VMHv1 began firing. When a male mouse encountered a female mouse, however, a separate group of neurons switched on—and the aggression-linked neurons appeared to be actively suppressed.

Next the researchers engineered the male mice so that they could control the aggression neurons with bursts of light coming through an optic cable into the brain. When the light came on, the mice immediately fought—with a male, a female, or a nearby object. When researchers blocked the neurons from firing, the mice refused to fight, even around another male. Moreover, when researchers allowed a mouse to mount a female and then shined the light, the mouse did not engage in attacks. The results, published February 10, 2011, in *Nature*, suggest that the VMHv1 neurons activated during mating might inhibit fight behavior.

FLASH-FREEZING CELLS REVEALS BACKWARD TRANSCRIPTION

A new technique of freezing cells in liquid nitrogen allows scientists to view how a cell accesses information encoded in genes. The technique has allowed HHMI scientists to make fundamental discoveries about transcription—the process a cell uses to copy strands of DNA to single-stranded RNA.

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