

Still Evolving, Human Genes Tell New Story

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Providing the strongest evidence yet that humans are still evolving, researchers have detected some 700 regions of the human genome where genes appear to have been reshaped by natural selection, a principal force of evolution, within the last 5,000 to 15,000 years.

The genes that show this evolutionary change include some responsible for the senses of taste and smell, digestion, bone structure, skin color and brain function.

Many of these instances of selection may reflect the pressures that came to bear as people abandoned their hunting and gathering way of life for settlement and agriculture, a transition well under way in Europe and East Asia some 5,000 years ago.

Under natural selection, beneficial genes become more common in a population as their owners have more progeny.

Three populations were studied, Africans, East Asians and Europeans. In each, a mostly different set of genes had been favored by natural selection. The selected genes, which affect skin color, hair texture and bone structure, may underlie the present-day differences in racial appearance.

The study of selected genes may help reconstruct many crucial events in the human past. It may also help physical anthropologists explain why people over the world have such a variety of distinctive appearances, even though their genes are on the whole similar, said Dr. Spencer Wells, director of the Genographic Project of the National Geographic Society.

The finding adds substantially to the evidence that human evolution did not grind to a halt in the distant past, as is tacitly assumed by many social scientists. Even evolutionary psychologists, who interpret human behavior in terms of what the brain evolved to do, hold that the work of natural selection in shaping the human mind was completed in the pre-agricultural past, more than 10,000 years ago.

"There is ample evidence that selection has been a major driving point in our evolution during the last 10,000 years, and there is no reason to suppose that it has stopped," said Jonathan Pritchard, a population geneticist at the University of Chicago who headed the study.

Dr. Pritchard and his colleagues, Benjamin Voight, Sridhar Kudaravalli and Xiaoquan Wen, report their findings in today's issue of PLOS-Biology.

Their data is based on DNA changes in three populations gathered by the HapMap project, which built on the decoding of the human genome in 2003. The data, though collected to help identify variant genes that contribute to disease, also give evidence of evolutionary change.

The fingerprints of natural selection in DNA are hard to recognize. Just a handful of recently selected genes have previously been identified, like those that confer resistance to malaria or the ability to digest lactose in adulthood, an adaptation common in Northern Europeans whose ancestors thrived on cattle milk.

But the authors of the HapMap study released last October found many other regions where selection seemed to have occurred, as did an analysis published in December by Robert K. Moysis of the University of California, Irvine.

Dr. Pritchard's scan of the human genome differs from the previous two because he has developed a statistical test to identify just genes that have started to spread through populations in recent millennia and have not yet become universal, as many advantageous genes eventually do.

The selected genes he has detected fall into a handful of functional categories, as might be expected if people were adapting to specific changes in their environment. Some are genes involved in digesting particular foods like the lactose-digesting gene common in Europeans. Some are genes that mediate taste and smell as well as detoxify plant poisons, perhaps signaling a shift in diet from wild foods to domesticated plants and animals.

Dr. Pritchard estimates that the average point at which the selected genes started to become more common under the pressure of natural selection is 10,800 years ago in the African population and 6,600 years ago in the Asian and European populations.

Dr. Richard G. Klein, a paleoanthropologist at Stanford, said that it was hard to correlate the specific gene changes in the three populations with events in the archaeological record, but that the timing and nature of the changes in the East Asians and Europeans seemed compatible with the shift to agriculture. Rice farming became widespread in China 6,000 to 7,000 years ago, and agriculture reached Europe from the Near East around the same time.

Skeletons similar in form to modern Chinese are hard to find before that period, Dr. Klein said, and there are few European skeletons older than 10,000 years that look like modern Europeans.

That suggests that a change in bone structure occurred in the two populations, perhaps in connection with the shift to agriculture. Dr. Pritchard's team found that several genes associated with embryonic development of the bones had been under selection in East Asians and Europeans, and these could be another sign of the forager-to-farmer transition, Dr. Klein said.

Dr. Wells, of the National Geographic Society, said Dr. Pritchard's results were fascinating and would help anthropologists explain the immense diversity of human populations even though their genes are generally similar. The relative handful of selected genes that Dr. Pritchard's study has pinpointed may hold the answer, he said, adding, "Each gene has a story of some pressure we adapted to."

Dr. Wells is gathering DNA from across the globe to map in finer detail the genetic variation brought to light by the HapMap project.

Dr. Pritchard's list of selected genes also includes five that affect skin color. The selected versions of the genes occur solely in Europeans and are presumably responsible for pale skin. Anthropologists have generally assumed that the first modern humans to arrive in Europe some 45,000 years ago had the dark skin of their African origins, but soon acquired the paler skin needed to admit sunlight for vitamin D synthesis.

The finding of five skin genes selected 6,600 years ago could imply that Europeans acquired their pale skin much more recently. Or, the selected genes may have been a reinforcement of a process established earlier, Dr. Pritchard said.

The five genes show no sign of selective pressure in East Asians.

Because Chinese and Japanese are also pale, Dr. Pritchard said, evolution must have accomplished the same goal in those populations by working through different genes or by changing the same genes -- but many thousands of years before, so that the signal of selection is no longer visible to the new test.

Dr. Pritchard also detected selection at work in brain genes, including a group known as microcephaly genes because, when disrupted, they cause people to be born with unusually small brains.

Dr. Bruce Lahn, also of the University of Chicago, theorizes that successive changes in the microcephaly genes may have enabled the brain to enlarge in primate evolution, a process that may have continued in the recent human past.

Last September, Dr. Lahn reported that one microcephaly gene had recently changed in Europeans and another in Europeans and Asians. He predicted that other brain genes would be found to have changed in other populations.

Dr. Pritchard's test did not detect a signal of selection in Dr. Lahn's two genes, but that may just reflect limitations of the test, he and Dr. Lahn said. Dr. Pritchard found one microcephaly gene that had been selected for in Africans and another in Europeans and East Asians. Another brain gene, SNTG1, was under heavy selection in all three populations.

"It seems like a really interesting gene, given our results, but there doesn't seem to be that much known about exactly what it's doing to the brain," Dr. Pritchard said.

Dr. Wells said that it was not surprising the brain had continued to evolve along with other types of genes, but that nothing could be inferred about the nature of the selective pressure until the function of the selected genes was understood.

The four populations analyzed in the HapMap project are the Yoruba of Nigeria, Han Chinese from Beijing, Japanese from Tokyo and a French collection of Utah families of European descent. The populations are assumed to be typical of sub-Saharan Africa, East Asia and Europe, but the representation, though presumably good enough for medical studies, may not be exact.

Dr. Pritchard's test for selection rests on the fact that an advantageous mutation is inherited along with its gene and a large block of DNA in which the gene sits. If the improved gene spreads quickly, the DNA region that includes it will become less diverse across a population because so many people now carry the same sequence of DNA units at that location.

Dr. Pritchard's test measures the difference in DNA diversity between those who carry a new gene and those who do not, and a significantly lesser diversity is taken as a sign of selection. The difference disappears when the improved gene has swept through the entire population, as eventually happens, so the test picks up only new gene variants on their way to becoming universal.

The selected genes turned out to be quite different from one racial group to another. Dr. Pritchard's test identified 206 regions of the genome that are under selection in the Yorubans, 185 regions in East Asians and 188 in Europeans. The few overlaps between races concern genes that could have been spread by migration or else be instances of independent evolution, Dr. Pritchard said.

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