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Scientists Cite Fastest Case of Human Evolution

By NICHOLAS WADE

Tibetans live at altitudes of 13,000 feet, breathing air that has 40 percent less oxygen than is available at sea level, yet suffer very little mountain sickness. The reason, according to a team of biologists in China, is human evolution, in what may be the most recent and fastest instance detected so far.

Comparing the genomes of Tibetans and Han Chinese, the majority ethnic group in China, the biologists found that at least 30 genes had undergone evolutionary change in the Tibetans as they adapted to life on the high plateau. Tibetans and Han Chinese split apart as recently as 3,000 years ago, say the biologists, a group at the Beijing Genomics Institute led by Xin Yi and Jian Wang. The report appears in Friday's issue of Science.

If confirmed, this would be the most recent known example of human evolutionary change. Until now, the most recent such change was the spread of lactose tolerance — the ability to digest milk in adulthood — among northern Europeans about 7,500 years ago. But archaeologists say that the Tibetan plateau was inhabited much earlier than 3,000 years ago and that the geneticists' date is incorrect.

When lowlanders try to live at high altitudes, their blood thickens as the body tries to counteract the low oxygen levels by churning out more red blood cells. This overproduction of red blood cells leads to chronic mountain sickness and to lesser fertility — Han Chinese living in Tibet have three times the infant mortality of Tibetans.

The Beijing team analyzed the 3 percent of the human genome in which known genes lie in 50 Tibetans from two villages at an altitude of 14,000 feet and in 40 Han Chinese from Beijing, which is 160 feet above sea level. Many genes exist in a population in alternative versions. The biologists found about 30 genes in which a version rare among the Han had become common among the Tibetans. The most striking instance was a version of a gene possessed by 9 percent of Han but 87 percent of Tibetans.

Such an enormous difference indicates that the version typical among Tibetans is being strongly favored by natural selection. In other words, its owners are evidently leaving more

children than those with different versions of the gene.

The gene in question is known as hypoxia-inducible factor 2-alpha, or HIF2a, and the Tibetans with the favored version have fewer red blood cells and hence less hemoglobin in their blood.

The finding explains why Tibetans do not get mountain sickness but raises the question of how they compensate for the lack of oxygen if not by making extra red blood cells.

Two other studies of Tibetans' adaptation to high altitude have also identified this gene as a target of selection. A team led by Tatum S. Simonson of the University of Utah and RiLi Ge of Qinghai University in China scanned the genomes of 31 Tibetans and reported in Science in May that HIF2a and other genes involved in red blood cell production bore the stamp of natural selection.

Independently, a group led by Cynthia M. Beall, an anthropologist at Case Western Reserve University, and Yong-Tang Zheng of the Kunming Institute of Zoology in China has detected a genetic change in the same gene in Tibetans and found that it correlated with having less hemoglobin in the blood. Their report was published in the June 22 issue of the Proceedings of the National Academy of Sciences.

Human adaptation to high altitude is a field of obvious interest, but another reason for the appearance of three studies on the same subject in matter of a few weeks may be that the technology to assess which parts of the genome are under selection has only recently become available.

The three new reports agree in finding the Tibetans' version of the gene has been favored by natural selection. But the Beijing Genome Institute's calculation that the Tibetan and Han populations split apart only 3,000 years ago is less likely to be accepted. Archaeologists say they believe that the Tibetan plateau has been inhabited for at least 7,000 years and maybe for as long as 21,000 years.

"The separation of Tibetans and Hans at 3,000 years ago is simply not tenable by anything we know from the historical, archaeological or linguistic record," said Mark Aldenderfer, a Tibetan expert at the University of California, Merced.

Dr. Aldenderfer said that there had probably been many migrations onto the Tibetan plateau, and that there was indirect evidence that pastoralists had entered the plateau from the north-northeast around 6,000 years ago. Earlier genetic studies have found that Tibetans are more similar to northern Han than to those from southern China, and have some admixture of genes from Central Asia, he said.

Geneticists have a more elastic view of dates than do archaeologists, and the estimate of a Han-Tibetan population split at 3,000 years ago could probably have been adjusted to 6,000 if the geneticists had taken any account of any other kind of evidence.

Rasmus Nielsen, a Danish researcher at the University of California, Berkeley, did the statistical calculations for the Beijing study. “We feel fairly confident that something on the order of 3,000 years is correct,” he said. But in a later e-mail message, Dr. Nielsen said, “I cannot with confidence rule out that the divergence time is 6,000 instead of 3,000.”

There is similar flexibility in the estimates of population sizes. The Beijing team calculates that at the time of divergence there were only 288 Han Chinese and 22,642 Tibetans. These estimates have bewildered archaeologists, given that rice cultivation in southern China started 10,000 years ago and that there was an extensive civilization by 3,000 years ago. Dr. Nielsen said that the figure of 288 people was meant simply to indicate a bottleneck in the Han population, meaning a time when it was very small, and that this bottleneck could just as easily have occurred 10,000 years ago.

Genetic differences between Tibetans and Chinese are a potentially delicate issue, given Tibetan aspirations for political autonomy. Dr. Nielsen said he hoped that the Beijing team’s results would carry no political implications, given that it is cultural history and language, not genetics, that constitute a people. There is not much genetic difference between Danes and Swedes, he added, but Denmark and Sweden are separate countries.