

The goal of much of modern medicine and culture is effectively to stop evolution. Is that happening?

## Are Humans Still Evolving?

The news made headlines around the world: Blonds were going extinct. According to CNN and other media, a World Health Organization (WHO) study concluded that the gene for blond hair, which was described as recessive to dominant genes for dark hair, would disappear in 200 years. The BBC announced that the last natural blond would be born in Finland and suggested that those who dyed their hair might be to blame, because “bottle blonds” were apparently more attractive to the opposite sex than natural blonds were and thus had more children.

Fortunately for blonds, the whole story turned out to be a hoax—“a pigment of the imagination,” as the *Times of India* later put it. WHO announced that it had never conducted such a study, and hair color is probably determined by several genes that do not act in a simple dominant-recessive relationship. The story, which may have originally sprung from a German women’s magazine, apparently simply leaped from one media outlet to another.

Although the story was untrue, the ease with which it spread reflects popular fascination with the evolutionary future of our species, as well as the media’s appetite for evolutionary pop science. Today, Oxford University geneticist Bryan Sykes is receiving voluminous coverage for his book, *Adam’s Curse*, which predicts that continuing degeneration of genes on the Y chromosome will leave men sterile or even extinct in 125,000 years. Many biologists say that the question they most often receive from students and the public is “Are humans still evolving?”

To many researchers, the answer is obvious: Human biology, like that of all other living organisms on Earth, is the result of natu-

ral selection and other evolutionary mechanisms. Some say the question itself betrays a misunderstanding of how evolution works. “The very notion that ... we might not be evolving derives from a belief that all other life forms were merely stages on the way to



**Modern mismatch.** Overbite is widespread among modern humans, but evolution may not be to blame.

the appearance of humans as the intended end point,” says primatologist Mary Pavelka of the University of Calgary in Canada.

But other scientists point out that in developed countries, culture, technology, and especially medical advances have changed the evolutionary rules, from survival of the fittest to the survival of nearly everyone. The result, they say, is a “relaxation” of the selective pressures that might have operated 50 or 100 years ago. “Biologically, human beings are going nowhere,” says anthropologist Ian Tattersall of the American Museum of Natural History in New York City. University College London geneticist Steven Jones agrees. “The central issue is what one means by ‘evolving,’” Jones says. “Most people when they think of evolution mean natural selection, a change to a different or better adapted state.

In that sense, in the developed world, human evolution has stopped.”

Yet millions of people in developing countries continue to live under the combined stresses of poverty and disease. Under these conditions, even skeptics of ongoing human evolution agree that natural selection may be favoring genes that confer resistance to disease or enhance reproductive fitness in other ways. Indeed, researchers are now tracking how deadly maladies such as AIDS and malaria exert selective pressure on people today. “As long as some people die before reproducing or reaching reproductive age, selection is likely to be acting,” says geneticist Chris Tyler-Smith of the Sanger Institute near Cambridge, United Kingdom.

Even in developed countries, where survival tends to be prolonged for almost all, recent studies suggest that there are still genetic differences among people in fertility and reproductive fitness, an indication that natural selection is operating. “The question ‘Are humans still evolving?’ should be rephrased as ‘Do all people have the same number of children?’” says Pavelka. “The answer is that we do not make equal contributions to the next generation, and thus we are still evolving.”

Over the past few years, a wealth of new data has begun to illuminate how natural selection has shaped—and may still be shaping—humanity. The human genome project and genetic data from people around the world have powered an explosion of research seeking signs of natural selection in human DNA. “A lot of the tools we are now using to search for selection were developed by people working on flies and other organisms,” says evolutionary geneticist Bruce Lahn of the University of Chicago. “But once researchers began to discover examples of ongoing selection in humans, it opened the door and gave them confidence that they could find even more.”

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So far, the number of confirmed cases of genes under recent selective pressure is only “a handful,” says Tyler-Smith. But that is likely to change once the results of the International HapMap Project, a multinational effort to determine worldwide variation in the human genome, are released later this year. Because genetic variation is the raw material on which natural selection works, favoring certain alleles over others, Tyler-Smith says the HapMap should “give us an overall view of the regions of the genome that have been under selection.”

### Drifting toward modernity?

To science-fiction fans, the future of human evolution conjures up visions of dramatic changes in our bodies, such as huge brains and skulls. “Many people see us continuing on the righteous path of increasing intelligence,” says Pavelka. “But we will not head in the direction of larger brains and crania as long as infants are required to pass through a woman’s pelvis to get into the world.”

Whatever lies in our evolutionary future, scientists agree that the modern human body form is largely the result of evolutionary changes that can be traced back millions of years. The uniquely human lineage dates from about 6 million years ago, and many studies have demonstrated that our divergence from chimpanzees was accompanied by strong selective pressure, for example on the human brain. Yet researchers caution that not all morphological changes—the ones we can see in body shape and size—are the result of natural selection; some may not be due to genetic evolution at all. For example, the increase in average height seen in many developed nations over the past 150 years or so is probably due mostly to better diets rather than natural selection.

Even very early evolutionary changes in the hominid line were not necessarily due to natural selection. Take the hominid face, which has changed dramatically in the past 3 million years from the heavy-jawed mugs of the australopithecines to the relatively small and gracile skulls of modern humans. Anthropologist Rebecca Ackermann of the University of Cape Town in South Africa and anatomist James Cheverud of the Washington University School of Medicine in St. Louis, Missouri, analyzed hominid faces over time, using formulas that model natural selection as well as random genetic drift, in which some traits or alleles become more common simply through chance. They



**Cold adapted.** Natural selection may have favored the Buriats’ broad skulls.

concluded last December in the *Proceedings of the National Academy of Sciences (PNAS)* that natural selection probably drove the evolution of facial form up to the birth of early *Homo*. But they also found that genetic drift could explain most of the changes in the human face after the birth of *Homo* about 2.5 million years ago. “Selective pressures on the face may have been released” when humans began using tools and so did less biting and chewing, says Ackermann.

The take-home lesson, she says, is that “genetic drift has played an important role in shaping human diversity. This is evolution, too.” Drift has continued to shape modern human faces and skulls in the more recent past, according to other studies. For example, researchers have examined

regional differences in head shape—parameters such as width of the skull, height of the nose, and length of the jaw—to see whether certain traits were favored by natural selection in response to differences in climate or environment. In most cases, the differences among populations turned out to be no more than expected due to random drift. But there are a few exceptions: Anthropologist Charles Roseman of Stanford University in California last year reported in *PNAS* that the skulls of the Buriat people of Siberia are broader than predicted by random drift. Broad skulls have smaller surface areas and so may be an adaptation to cold climates. That fits with previous work by anthropologist John Relethford of the State University of New York College at Oneonta. Relethford concludes that random drift and migration can explain cranial differences in “most cases,” with the exception of people like the Buriat and Greenland Eskimos, who live in very cold environments.

Although the evolution of measurable traits such as modern human skull shape may be due to random drift, some changes in human body form may have more to do with cultural and environmental factors such as diet. “Over the past 10,000 years, there has been a significant trend toward rounder skulls and smaller, more gracile faces and jaws,” notes anthropologist Clark Larsen of Ohio State University in Columbus. Most of the change, says Larsen, is probably due to how we use our jaws rather than genetic evolution. With the rise of farming, humans began to eat much softer food that was easier to chew. The resulting relaxation of stress on the face and jaw triggered changes in skull shape, Larsen says. He adds that the dramatic and worldwide increase in tooth malocclusion, tooth crowding, and impacted molars are also signs of these changes: Our teeth are too big for our smaller jaws. Numerous studies show that non-Western people who eat harder textured foods have very low rates of malocclusion, he notes. Similar changes are found in monkeys fed hard and soft diets. “With the reduction in masticatory stress, the chewing muscles grow smaller, and thus the bone grows smaller,” Larsen says. “It is not genetic but rather reflects the great plasticity of bone. It is a biological change but heavily influenced by culture.”

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### Signs of selection

Even if random drift and other nongenetic forces have helped shape modern humans, there is

## Candidates for Recent Selection in Humans

GENE OR GENETIC LOCUS	HYPOTHESIZED SELECTIVE PRESSURE
Lactase	Improved nutrition from milk
G6PD	Protection against malaria
Duffy blood group	Protection against malaria
Hemoglobin C	Protection against malaria
TNFSF5	Protection against malaria
CCR5	Protection against smallpox and AIDS
H2 haplotype	Unknown but only in Europe
DRD4	Cognition and behavior
MAOA	Cognition and behavior
AGT	Protection against hypertension
CYP3A	Protection against hypertension
TAS2R38	Bitter taste perception





**Battle for survival.** AIDS and other deadly diseases may spur a rise in resistant gene alleles.

growing evidence that natural selection has also played an important role, even if its effects have been more subtle. Human evolution researchers are now mining the riches of genomic data to spot genes subject to recent selective pressures (*Science*, 15 November 2002, p. 1324). Geneticists have a large arsenal of “tests of selection” at their disposal, all of which exploit the genetic diversity of human populations to determine whether individual alleles or larger blocks of the genome—called haplotypes—are behaving as would be expected if they were only subject to random drift and were not under selection.

Some tests look for evidence that mutations in an allele that alter the protein it codes for have been favored over those that cause no change; others examine whether certain alleles are more common than expected. A fairly new and powerful approach compares the frequency of an allele in a population with the genetic diversity within a haplotype to which it belongs. If the allele is common due to random drift over a long time, the adjacent region of the genome should show considerable variation due to genetic recombination, the exchange of DNA between chromosomes during meiotic cell divisions. But if the variation is less than expected, the allele may have risen to high frequency in a much shorter period of time—a telltale sign of selection. “These tools are powerful,” says Lahn. “Where we are lagging behind is in good data.”

By deploying such methods, geneticists have identified more than two dozen genes that appear to have come under selective pressures since the rise of *Homo*, and several of them may still be subject to such pressures

today. Some of these favored alleles apparently arose at highly critical periods in human evolution. Such is the case of *FOXP2*, the so-called speech gene, which is implicated in the ability to talk, shows signs of strong selection, and arose no more than 200,000 years ago, coinciding closely with the first appearance of *Homo sapiens* (*Science*, 16 August 2002, p. 1105). Other genes under selection are linked to cognition and behavior, and still others are involved in defense against diseases such as hypertension, malaria, and AIDS (see table, p. 235).

In some cases, the new tests for selection have helped nail down long-suspected cases of evolutionary adaptation. One classic example is lactase persistence, the inverse condition of so-called lactose intolerance. Most adults cannot drink milk because they produce little lactase, the enzyme that breaks down lactose, which is the major sugar in milk. But a sizable number of people can, and their geographical distribution correlates closely with the spread of domesticated cattle out of the Near East. Thus, more than 70% of Europeans, who have a long history of drinking milk, have lactase persistence, as do some African pastoralists. In contrast, the percentage is very low in most of sub-Saharan Africa and Southeast Asia.

Last year, researchers clinched the case for selection at the lactase gene. A team led by genome researcher Joel Hirschhorn of Harvard Medical School in Boston identified a haplotype more than 1 million nucleotide base pairs long that includes the lactase gene and confers lactase persistence on people who carry it. This form of the haplotype is found in nearly 80% of Europeans and Americans of European ancestry

but is absent in the Bantu of South Africa and most Chinese populations. Hirschhorn and colleagues concluded from the unusual length of the DNA block that it is young, because it has not yet been broken up by genetic recombination. They calculate in the June 2004 issue of the *American Journal of Human Genetics* that this haplotype came under very strong selective pressure beginning between 5000 and 10,000 years ago, corresponding to the rise of dairy farming. Thus a cultural and technological change apparently fostered a genetic one. “This is one of the best examples of recent selection in humans,” says Tyler-Smith.

Although being able to drink milk as an adult has its pleasant side, as any chocolate-shake lover can testify, most people in the world get along fine without the beverage. Yet in some cases, having a certain allele can be a matter of life or death. Thus, the genes most likely to be under strong selective pressure today are probably those involved in providing resistance to infectious disease, says Sarah Tishkoff, a geneticist at the University of Maryland, College Park. “In Africa, people are dying daily [of infectious disease], and those who have genotypes that confer some resistance are going to have more offspring. That is natural selection in action.”

AIDS and malaria are arguably the worst scourges of humankind today, and they may both be exerting selective pressure on African genomes. Several genes have alleles that provide resistance to malaria, including those that code for hemoglobin C and an allele of the so-called Duffy blood group found only in sub-Saharan Africa; accumulating evidence suggests that they have both been under recent selective pressure. Four years ago, Tishkoff and colleagues showed that two different alleles of a gene called *glucose-6-phosphate dehydrogenase (G6PD)* have also been favored by strong selective pressure. The mutant alleles, A<sup>-</sup> and Med, are found only where malaria is or recently was a problem and offer resistance against malaria, although they can cause blood diseases.

Tishkoff and her co-workers used the known geographical variations in the *G6PD* gene to estimate that the A<sup>-</sup> allele probably arose in Africa about 6300 years ago and then spread rapidly across the continent; the Med allele, found in southern Europe, the Middle East, and India, is estimated to be only about 3300 years old (*Science*, 20 July 2001, pp. 442 and 455). These estimates are consistent with archaeological evidence that malaria only became a major health problem after the invention of farming, when the clearing of forests left standing pools of water in which the vector for the disease, the *Anopheles* mosquito, could breed. Thus a cultural change again led to a genetic one.

The case of AIDS, and the virus that causes it, HIV, suggests that the selective advantage of a gene can shift over time. As HIV infects T cells in the blood, it docks onto a cell surface receptor called CCR5. In the mid-1990s researchers discovered that a mutation in the *CCR5* gene provides strong protection against AIDS in homozygotes, people who have two copies of the protective allele. The mutation, called delta 32, is found in up to 13% of European populations but is extremely rare in other groups, including Africans. Researchers dated the origins of the delta 32 mutation in humans to about 700 years ago and concluded that a strong selective event resulted in its spread; this finding was confirmed in 2001 using sophisticated selection tests.

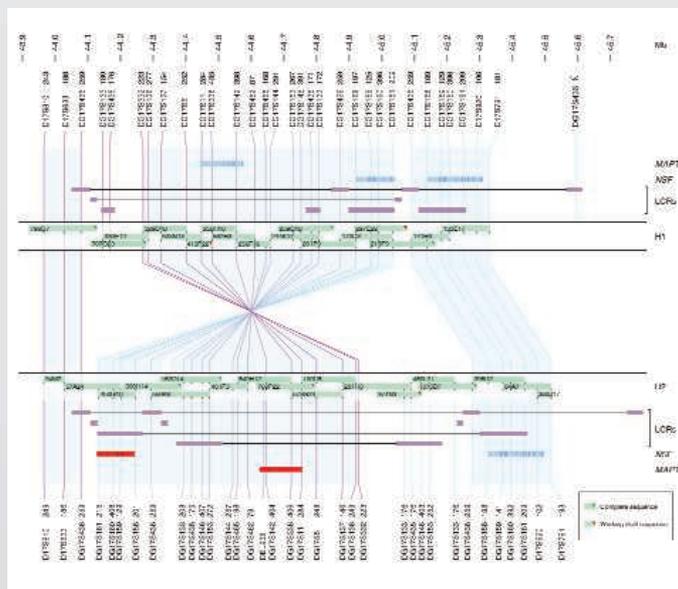
Yet because the AIDS epidemic dates only from the late 1970s at the earliest, researchers believe that the selective pressure on the delta 32 mutation must have been from some other factor. Researchers have debated whether the plague or smallpox, both of which ravaged European populations in the past, is more likely, although some recent studies have leaned toward smallpox.

### Icelanders evolving?

Although researchers scouring the human genome for signs of natural selection have uncovered a few examples, direct evidence that a particular allele actually boosts reproduction—the sine qua non of natural selection—is hard to come by in humans. But that's just what researchers were able to do in one dramatic study in Iceland. For the past several years, scientists at deCODE Genetics, a biotechnology company based in Reykjavik, Iceland, have been gathering genetic information on the nation's 270,000 citizens, in a government-approved effort to isolate disease genes (*Science*, 24 October 1997, p. 566). In the course of this research, deCODE researchers discovered a variant of human chromosome 17 in which a 900,000-nucleotide-base-pair stretch of DNA was inverted; this inversion was associated with a previously identified haplotype called H2, which they estimate arose 3 million years ago. H2 carriers make up about 17.5% of Icelanders and 21% of Europeans, but only about 6% of Africans and 1% of Asians.

To see whether the relatively high frequencies in Europeans represented natural selection, the team genotyped 29,137 Icelanders born between 1925 and 1965. When these data were correlated with the island's extensive genealogical database, the evi-

dence for positive selection was stunning: As the team reported in the February 2005 issue of *Nature Genetics*, female H2 carriers had about 3.5% more children than H1 carriers. "This study has large implications," says anthropologist Osbjorn Pearson of the University of New Mexico, Albuquerque. "The European version of the H2 haplotype could sweep the entire human population if it conveyed the same reproductive advantage in other people and environments." But deCODE CEO and research team co-leader Kári Stefánsson says the low frequencies of



**Baby boost.** Women with an inversion in this region of chromosome 17 have more children.

H2 outside Europe suggest that for some reason, its advantages are limited to that continent. "Why, I can't tell you," he says.

There are several genes in the H2 region, but it is not at all clear which ones cause H2 carriers to have more children; one nearby gene is implicated in pregnancy complications. The deCODE team is looking at the genes to see whether differences in expression might create the selective advantage. One lead, Stefánsson says, is that H2 carriers also show a higher rate of recombination during meiosis. In an earlier study, his team found that mothers with high oocyte recombination rates also tend to have more children, possibly because this genetic shuffling helps protect against errors in meiosis, which are a major cause of miscarriage in older mothers. H2 carriers also appear to live longer on average. "It is fascinating to think that there might be an advantage associated with a DNA variant at both ends of life," Stefánsson says.

### Our evolutionary future

To many researchers, the limited but growing evidence that natural selection is cur-

rently acting on the human genome means that humans are still evolving, even if in subtle ways. But can we actually predict the course of future evolution, à la Sykes's disappearing males or the vanishing blonds? Most researchers' predictions are considerably more narrow and cautious and are tied to known selective pressures.

For example, researchers predict that delta 32 and other protective *CCR5* mutations may become more common in populations widely infected with HIV, especially in Africa. "If there are no more advances in the treatment of AIDS and people continue to die, we would expect selection pressure to increase [the mutations'] frequency over time," says Tyler-Smith, who adds that he sees "no reason why they should not go to fixation"—that is, replace all other alleles of the gene.

Whether or not these patterns will make a significant difference in the way humans look or live is another question. "There will be minor fluctuations over time and space in the makeup of local human gene pools as humans respond to local conditions," predicts Tattersall, "but they won't be directional. I find it hard to foresee that under current conditions a qualitatively new kind of human is ever likely to emerge. But if conditions change, all bets are off."

Evolutionary predictions are tied to speculation about just what kind of environment we may face. Some researchers suggest that changing climate conditions may diminish the benefits of culture and medicine, creating a new era of natural selection. "There has been a relaxation in selective pressures in industrialized societies," says evolutionary geneticist Peter Keightley of the University of Edinburgh, U.K. "But our ability to sustain that relaxation is probably temporary. We are using up our energy resources, our population is growing, and the climate is changing. All this is bound to lead to greater difficulties and renewed selective pressures."

Despite such concerns, however, most scientists remain leery of long-term forecasts, in part because of the way evolution works. "Evolution is not directed towards a goal," says Tyler-Smith. "It always takes the short-term view, operating just on what allows us to survive and reproduce better in this generation." For now, predicting humanity's evolutionary future may be little more than crystal ball gazing—better suited to science fiction than scientific research.

—MICHAEL BALTER