Humans Never Stopped Evolving

The emergence of blood abnormalities, an adult ability to digest milk, and changes in our physical appearance point to the continued evolution of the human race.

By John Hawks | August 1, 2016

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Natural selection is tricky to catch in action. As Darwin put it, "A grain in the balance will determine which individual shall live and which shall die." The grain in the balance—the slightly increased chance that organisms carrying one gene variant will fail in the struggle for existence—is the cost of selection. It is almost invisible, only becoming statistically evident when viewed across thousands of individuals, who may display only subtle differences in the affected character.

In the human population, the toll of natural selection is hidden within millions of deaths and births around the world every year. Everyone dies, many tragically young. And while obvious patterns sometimes emerge from early deaths—certain diseases, traffic accidents, drug overdoses—these are

often challenging to connect to the action of genes. Likewise, only by comparing the genes of parents with those of childless people, and the genes of large families with those of small families, can we begin to understand how natural selection is acting on births.

Six years ago, Yale University's Stephen Stearns and colleagues took advantage of a long-running study in Framingham, Massachusetts, to assess whether the effects of natural selection could be discerned among the people in the multigenerational study population. Over the last seven decades, public-health researchers have been monitoring the residents of Framingham, noting their vital statistics as well as blood sugar and cholesterol levels to understand the factors that lead to heart disease. As the initial group of research subjects got older, the study started to include their children, and then their grandchildren. The records provide a unique view of the health of a segment of the American population since 1948.

When Stearns and his coworkers analyzed the data, they found lots of evidence that selection was occurring, albeit with many curious patterns. Shorter women had more children than taller women, and heavier women had more children than lighter women. For men, height and weight weren't as correlated with fecundity. High or low blood-sugar readings in both men and women were associated with fewer offspring, and the age at which individuals had their first child also seemed to influence lifetime reproduction—people who had their first child younger ended up with larger families.[1]

The results left scientists frustrated. To what extent are these traits—stature and age at first birth, for example—heritable? What other factors are shaping the population? Age at first birth is surely influenced by cultural factors that can confound the attempt to tease out the contribution of genes.

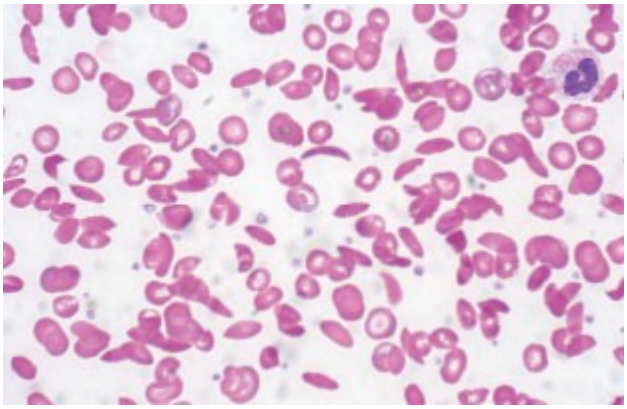
The advantage of lactase persistence was enormous, perhaps the strongest known for any RECENT human trait.

To get at those kinds of details, we need to combine records of traits with a look at the genes themselves. That kind of research is just now becoming possible.

Last month, for example, Harvard University's Jonathan Beauchamp published a study in which he compared known gene variants with relative lifetime reproductive success (rLRS)—a proxy for the number of biological offspring an individual has—in people of European descent living in the U.S. and enrolled in the Health and Retirement Study. In this cohort, Beauchamp found evidence that evolution may have selected against educational attainment, while favoring a higher age at menarche for women. Although he notes that cultural and environmental factors may have overridden the effects of natural selection, he makes the case that humans do continue to evolve.[2]

In the blood

The first solid evidence of natural selection in recent human populations was found in blood. Type B blood is common across central Asia, but much rarer in other places. Newly identified blood types outside the ABO system have also been found, and each has a distinctive geographical distribution. One of the most extreme is the Duffy blood type, which has three different versions, or alleles, just like the ABO system. One of these types, Duffy "null," occurs in up to 95 percent of people in sub-Saharan Africa, but is very rare among people whose ancestry comes from other parts of the world.



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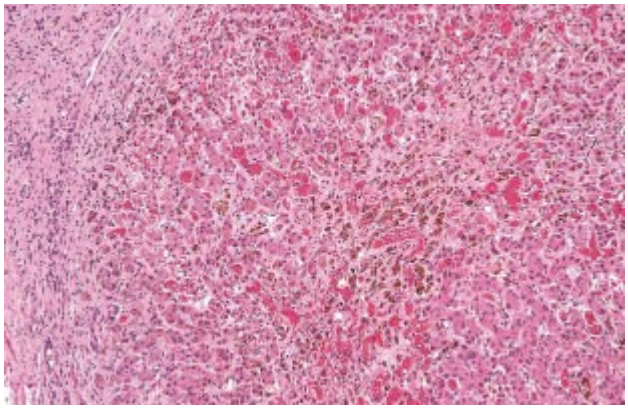
In addition to blood type, researchers have investigated the evolution of blood disorders and abnormalities. One of the most interesting is a deficiency of the enzyme glucose-6-phosphate dehydrogenase (G6PD), which helps maintain red blood cells. An insufficient level of this enzyme occasionally causes extreme, even lethal health problems, but is better known for causing a reaction to fava beans in people suffering from the deficiency. Other blood peculiarities include the sickle cell trait, reduced production of hemoglobin (alpha thalassemia), hemolytic

anemia (ovalocytosis), and abnormal hemoglobin types (hemo-globin C and hemoglobin E). By examining the frequencies of these conditions, researchers have found that these blood variations coincide with regions where malaria has been common throughout history. Further work revealed how small changes to hemoglobin can impede the malaria parasite's ability to break into red blood cells. The Duffy null allele, too, helped carriers to resist malaria.[3] The *FYA* and *FYB* versions of the gene both result in molecules on the surfaces of red blood cells that function in inflammatory reactions but also provide an avenue of attack for the malaria species *Plasmodium vivax*.[4] People who lack these molecules may avoid P. vivax infection.



RESISTANT TO MALARIA: Blood disorders and abnormalities such as the sickle cell trait (top) can impede the malaria parasite's ability to infect red blood cells and are more frequent in regions of the world where malaria was once common. But while these blood differences provided protection against the parasite, they are also associated with health risks, such as cirrhosis of the liver (bottom).
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These variations were not without consequences, however. While one sickle cell allele is protective against malaria, most people who carry two copies die young, usually without reproducing. It's no surprise, then, that malaria-free areas have extremely low rates of the sickle cell trait and other red blood cell variations.

Milk digestion

While the distribution of blood types and abnormalities was the first evolutionary pattern identified among recent human populations, perhaps the most famous is people's ability to digest milk beyond infancy. Around 30 percent of the calories in milk from humans and all other mammals come from a sugar called lactose, and to make use of the energy stored in lactose, the digestive system must be able to break it down into its two chemical subunits, galactose and glucose. This chemical reaction is catalyzed by the enzyme lactase, the gene for which is shared across all mammals. In most species, however, lactase is only expressed in young prior to weaning, leaving adults unable to digest lactose.

AGRICULTURAL ADAPTATIONS: As human populations began to domesticate animals and consume their milk, they evolved the persistent expression of the lactase gene, which breaks down lactose and is usually only expressed in young animals.
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Pre-agricultural humans followed, and many modern humans still follow, this same pattern of lactase expression in infancy only. Regular consumption of milk by an adult can sometimes spur a minimal amount of lactase production, but drinking a large amount of milk or other lactose-containing dairy products can cause severe digestive distress. People from China often have trouble digesting milk, as do many people from southern Europe. Yet in northern Europe and parts of sub-Saharan Africa, more than 95 percent of people produce the lactase enzyme throughout their lives and can thus digest milk as adults without difficulty. A smaller fraction of adults in other populations, such as those in the western half of Eurasia and other parts of sub-Saharan Africa, also have this persistence of lactase.

The persistence is not due to any change to the enzyme itself, but to the short patches of DNA outside the gene that regulate its activity. People from Ireland to India share one mutational change that prompts lactase persistence. In Arabia and sub-Saharan Africa there are four others. At least five times, ancient humans had a chance mutation that spurred lactase activity in adults and began to spread through the population. Not surprisingly, these populations live in precisely the areas where people domesticated cattle, sheep, goats, and camels for the purpose of consistent milk production. That domestication happened only within the last 10,000 years, and cattle became common in sub-Saharan Africa and northern Europe much later than this, placing an upper time limit on these genetic changes.

Lactase persistence is one of the most profound changes in recent human populations, and was one of the first to be investigated by scientists working with DNA directly from ancient skeletal remains, first by Joachim Burger of Johannes Gutenberg University in Germany and colleagues, and later by many others. Before 7,000 years ago, the ancient peoples of Europe lived only by hunting, fishing, and gathering; they did not farm or keep domesticated animals. Gene sequences from the remains of these people have never produced any evidence of lactase persistence. Only well after people began to keep cattle—as evidenced by milk residues found in pottery from early farming and herding contexts in Europe and west Asia—did mutations promoting lactase persistence arise. (See "What's Old Is New Again," *The Scientist*, June 2015.)

Once it appeared within these ancient populations, the numbers of people with lactase persistence grew by up to 10 percent per generation. Its advantage was enormous, perhaps the strongest known for any recent human trait. This kind of evolutionary advantage likely resulted from increases in fertility. Women on calorie-restricted diets have lower fertility, and they take longer after the birth of a child to conceive again. If lactase-persistent women could use the extra energy from milk to begin their reproductive lives a couple of years earlier, or could space their children a few months closer together, it would create a huge reproductive advantage.

Indeed, the frequency of lactase persistence has continued to climb substantially in some places even within the past 2,000 years. Just this spring, Stanford University's Yair Field and colleagues reported on a new study that sampled more than 3,000 human genomes from the United Kingdom to look at the effects of selection on genes. They found that lactase persistence is the largest single change within the British population since Roman times, increasing in frequency more than any other allele across the genome.[5]

Not so simple

The lactase example connects human populations and their cultural innovations. But in one important respect it is misleading: it is much too easy to understand. Unlike lactase persistence, most human traits are not the product of a single gene. Rather, they are influenced by many genes, and studying selection on such traits has proven very difficult.

Skin color is a classic example. One of the largest and most obvious physiological differences between populations, skin color is influenced by more than two dozen genes in a pathway that produces the pigment melanin and regulates the amount of this pigment in different tissues. Changes to these genes interrupt the generation of the dark pigment eumelanin, leaving skin with larger amounts of the reddish pigment pheomelanin, leading to various skin tones and patterns of coloration, such as freckles. Despite its complex genetics, skin color shows consistent patterns of evolution across the globe. People whose ancestors lived in the tropics tend to be dark-skinned, while those who lived further north and south tend to be lighter. One of the revelations of the last 15 years is just how recent this pattern really is. According to analyses of ancient DNA, people who lived in northern Europe only 10,000 years ago would not have had the extremely light skin of today's people in that region.

Other types of human coloration are also evolving. In their recent study, Field and colleagues found several genes related to hair and eye pigmentation that had markedly increased in the ancestors of modern Brits. These traits include one associated with blue eyes and two that are found in people with blond hair. Britain has experienced extensive immigration since Roman times, including the arrivals of Vikings, Anglo-Saxons, and Normans, but the genetic changes seen in this population are not due merely to migration; they mark the increase of particular genes above and beyond the contributions of immigrants. The British have become blonder over recent millennia.

Stature is another complex trait that has continued to evolve in recent years. Northern Europeans are a bit taller than southern Europeans, and looking at the genes that differ between them, Field and his colleagues found that the height differences were driven by natural selection for taller stature in the north over the last 2,000 years. This trend is not seen worldwide, however. The Framingham population and other studies in the U.S. have found that shorter women have had a reproductive advantage during the last few decades. On the other hand, a study from one sub-Saharan African nation, Gambia, showed a pattern more in line with the changes seen in Britain's population: taller women had more children.[6] For men the story is even more mixed. Dutch and Polish men have been under weak selection for taller height over the last several decades, but in other countries a man's stature seems to make no difference to his lifetime reproduction.[7]

The skeletons of ancient people likewise show physical changes over the past several thousand years.

Heads changed shape, becoming broader and a bit smaller over time in many parts of the world. We do not yet know which genes might be connected to such changes, just as we do not know many of the genes that might drive earlier reproduction. As we learn more about the genetics of human biology, studying the pattern of natural selection in genes may help us to uncover the biology of such traits.

Only a few of the recent evolutionary changes are obvious to us. Most are well-hidden, driven by genetic pathways we are still discovering. The record of ancient DNA from Europe is at the moment far more detailed than elsewhere in the world, but this is changing rapidly as ancient DNA samples from the Americas, Ethiopia, India, China, and other areas are coming online. We are already learning about the ancestry of these peoples from single genomes. Soon we will be able to look at past gene frequencies to map the history of adaptations that shaped their recent evolutionary history.

Humans across the globe have been living under very different selective pressures since our sub-Saharan roots, and the cultural differences that have emerged appear to have accelerated some kinds of evolutionary changes.

Evolving into the future

If there is one common theme in all this recent selection, it is that much of the human diversity we see around us today arose very recently. More than 90 percent of the heritage of every living human comes from sub-Saharan Africa sometime around 100,000 years ago. Fifteen years ago, many geneticists saw this recent common ancestry as evidence that human evolution had mostly drawn to a close. After diverging from our common chimpanzee and bonobo ancestors some 7 million years ago, hominins underwent massive changes in body size, diet, behavior, and brain size. Huge evolutionary innovations marked the beginning of upright walking, tool use, culture, and language. And those changes all happened before 100,000 years ago. (See “Uniquely Human” here.)

With such a dramatic picture from the fossil record, it is understandable that many scientists assumed that the final phases of human prehistory were fairly boring, at least from the Darwinian point of view. Across most of the genome, humans everywhere in the world are very similar to one another, much more so than to chimpanzees or most other kinds of primates. Modern humans vary profoundly in cultures and languages, but those differences are mostly learned, not coded in our genes.

Nevertheless, humans across the globe have been living under very different selective pressures since our sub-Saharan roots. And, in fact, the cultural differences that have emerged appear to have accelerated some kinds of evolutionary changes. The domestication of animals led to the invention of dairying, for example, a new dietary niche in which lactase persistence provided a huge advantage. Clearing tropical lands for planting domesticated crops and keeping water in pots changed human ecology in more-disturbing ways, making new habitats for mosquito species that afflict human populations with yellow fever and malaria and spurring protective changes in red blood cell morphology. Moving into new ecosystems also demanded new adaptations from the growing human population, from lighter pigmentation at high latitudes to maintain vitamin D production to improved oxygen metabolism in peoples living at high altitude.

Natural selection is fickle. Behavior that ensured survival in our ancestors’ environment may not be as advantageous under modern conditions. (See “Our Inner Caveman” here.) New evidence of how the human genome has changed over the last several thousand years points to a series of massive critical evolutionary changes, setting some aspects of our biology clearly apart from that of our forebears. And we are no doubt continuing to evolve today.

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natural selection, malaria, lactose intolerance, lactase persistence, human evolution, evolutionary genomics, evolutionary biology, evolution, disease/medicine and blood

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August 2, 2016

Anyone suggesting that natural selection is not continuing to effect humans or that humans are no longer evolving, should not call themself a biologist

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August 2, 2016

The only thing that surprises me in this article is the suggestion that many scientists thought that the human species had stopped evolving. But, I have seen a few papers in the past that did not recognize the pervasive and inescapable process of evolution in our species. Everything, including culture and social systems, affects evolution. Migration is very important. Birth control is very important. Government welfare is very important. Now we can observe new mutations between parents and children, and with very large populations a great deal of increasing genetic diversity can accumulate. Sexual selection, including segregation by intelligence, continues unabated.

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I'm surprised not to see any mention of the effect of modern medicine. In the limiting case where nobody dies, evolution is driven solely by fecundity.

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August 2, 2016

In 2008 The American Biology Teacher published an article entitled Evolution and the Cesarean Section Rate. In it, it is argued that the current lack of selection against a small maternal pelvis and a large fetus due to cesarean sections will lead to bigger babies, smaller maternal pelvises, and more cesarean sections. Evidence is presented that this has already occurred over the past 50 years in developed countries. Could this lead to larger newborn brains and greater intelligence in the future? A good argument is made for yes.

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August 3, 2016

There is a strong selection going on in developed countries in favor of RH+ people do to RhoGam. I'm not sure how available RhoGam is World wide but the majority of Rh- Moms will be given the RhoGam injection in the USA & I assume developed countries.
My Mom is Rh- my Dad Rh+. Before RhoGam was available my Mom was pregnant 10 times but carried only 5 pregnancies to term. All 5 of my siblings are Rh- but we should have a couple of Rh+ siblings...50/50 ratio. My theory is that all my Rh+ siblings didn't survive. I looked at my family and realized that there are many RH+ people alive today that wouldn't have been in the past. They will have children that will be RH+ if their partner is RH+(This is more likely do to RhoGam) & 50/50 chance of a Rh+ offspring if their spouse is Rh-(A small percentage of the overall available male selection do to RhoGam). It seems to me that the naturally occurring ratio of Rh- to Rh+ positive people could be changing very rapidly where RhoGam is being given. I've read about health differences dependent on Rh factor. I'm not sure it's been researched a lot....one thing I read was that O negative individuals are more susceptible to the Norovirus & have worse symptoms. I will not be going on a cruise ship. I'm interested in knowing how the ration of Rh- to Rh+ people have

changed since RhoGam became available.

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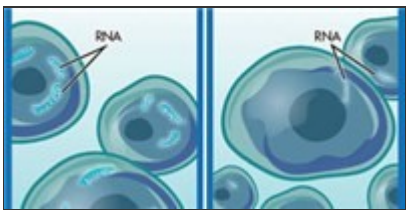

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