“In some contexts, I’m a geneticist. In others I’m an anthropologist. And other times I’m an evolutionary biologist. I wear many hats.”

FAVORITE AFRICAN ANIMAL
Warthogs… or giraffes

INTERESTING FACT
Speaks Kiswahili

MUSICAL TALENT
Plays Beethoven on the piano

MISSES MOST WHILE IN AFRICA
A hot shower
Genetic Footprints

BY ERIN FULTS

Where did I come from?

What makes me unique?

What makes a human... a human?

These simple questions are not so easy to answer. We still do not know what makes you “you,” your mother “her” and your brother “him.” Nor do we know, precisely, why we do not look or act just like chimps.

Evolutionary geneticist Sarah Tishkoff doesn’t know the answers either. But these are the questions she asks every day as part of her job running a lab at the University of Pennsylvania in Philadelphia.

You might say Tishkoff has a long commute—traveling more than 8,000 miles to do her fieldwork in Africa. There, she collects data to help her understand evolution and its role in shaping human history and human health.

Working alongside African researchers, Tishkoff looks at DNA to trace the paths of human evolution. Her training in anthropology—the broad study of humanity itself—gives Tishkoff a unique perspective on genetic research, the study of heredity.

Tishkoff says that in many ways, genetics can begin to answer the questions of where we came from and what makes us unique—as individuals and as a species.

“What drove me to this work was being able to ask the questions philosophers ask,” says Tishkoff.

Every new answer brings with it a new question. And that means a lot of changing and adapting. With each project she meets new people and finds new diseases. The work is not always easy, Tishkoff says.

“Not easy” means setting up a lab in the middle of nowhere. It means using a car battery to power equipment, riding in a Land Rover® and colliding head-on with a bus, and sleeping in tents where zebras come to visit.

It also means: She’d hardly give it up.
What drove me to this work was being able to ask

Little Letters, Big Dig
A genome is all of the genetic information in an organism, stored in the form of DNA. This DNA is Tishkoff’s archaeological “dig site.”

Often called the code of life, DNA carries the genes you got from your parents.

To an extent, genes are what give you your mother’s eyes or your grandfather’s hair. Genes also affect your health—if heart disease runs in your family, you may be at risk for getting it yourself.

Of course, genes aren’t the whole story. Where and how you live, what you eat and whether you exercise, drink alcohol or smoke are all hugely important in your health and your appearance.

DNA has four different nucleotide “letters” that string together into gene “words.” Our bodies use genes as the templates to make RNA and proteins, which are the main workers in cells.

While the genome is mostly the same in all people, slight differences exist. This genetic variation makes up about one-tenth of a percent of each person’s DNA. These spelling differences, spread across many genes, are what make you unique.

This genetic variation is enough to distinguish you from your next-door neighbor, the president of the United States and millions of other people all over the world.

Genetic variation is inherited, so the more closely related two people are, the more similar their DNA is likely to be.

Individuals within a population have DNA that is more similar to each other’s than it is to that of people in other populations, because they share an ancestry that is at least partly captured in DNA variation. So people whose ancestors have lived for generations in Sweden will have DNA more similar to other Swedish people than to modern-day Koreans whose families settled long ago in Korea.

Medical researchers are interested in genetic variation because it helps them understand disease risk. For example, some people are naturally resistant to getting AIDS after becoming infected with HIV because they have a specific change, or variant, in their DNA. The variant is extremely rare, but examining the genetics of how it happens could lead to ways to prevent or treat this killer disease.

Scientists like Tishkoff who study genetic variation are actually studying evolution. Over time, changes occur in DNA, affecting the readout of the genetic message. If the changes are helpful to the organism, they have a greater chance of being passed on to future generations because they provide a survival advantage.

Of course, it takes many, many generations for these changes to catch on.

Into Africa
Tishkoff first got hooked on tracking evolution in the early 1990s while in graduate school at Yale University in New Haven, Conn. She had the chance to scan one of the largest collections of DNA samples from populations all over the globe.

One of Tishkoff’s first observations was that Africa was represented by genetic information from only two ethnic groups. That’s hardly enough to cover this vast continent, she thought.

At the time, Tishkoff explains, researchers hadn’t yet realized what

FIND MORE
Hear a native Xhosa click-speaker at http://www.youtube.com/watch?v=gytCi5a7AJg&feature=related
they were missing. “People had no idea how much genetic diversity there was in Africa. They thought, ‘well, any African population will do,’” she recalls.

Tishkoff made her first trip to South Africa in 1997. Working with a researcher in Johannesburg, she analyzed DNA samples and was amazed at what she saw. Tishkoff discovered that the hundreds of different African tribes who speak around 2,000 different languages also had a tremendous amount of genetic variation.

One thing Tishkoff didn’t fully appreciate until she arrived in South Africa was that she couldn’t take safety for granted. At the time, the University of the Witwatersrand in Johannesburg where she was working was in a dangerous part of town, and Tishkoff had to stay within the university’s walls. That meant a permanent curfew.

“I could work day and night,” says Tishkoff. “It kind of forced me to.”

Since she couldn’t experience the bustling city herself, Tishkoff learned about it from television. She watched interviews with people from different African tribes and started to pick up on cultural differences.

Tishkoff became interested in the phenomenon of click-speaking, tonal languages in which the same sequence of consonants and vowels can have different meanings depending how you say them. One of the most distinctive features of a tonal language is its many click consonants. For example, the !Xóõ language, with roughly 4,000 speakers in the South African nation of Botswana, has 83 click sounds—the largest number of consonants in any known language.

Because using clicks as a form of communication is very unusual, you might assume that click speakers are closely related. But they’re not as related as you might think.

Tishkoff looked for an explanation in their DNA and uncovered only a very distant relation between Tanzanian click-speaking tribes, but a common ancestry between some click speakers and a non-click tribe called the Pygmies.

Studying the click tribes and tracing tribal relationships is one example of a new science called molecular anthropology (see “The Big Family Tree,” page 6).

Molecular anthropology uses information from DNA and proteins to determine evolutionary links between populations. In this way, scientists like Tishkoff are molecular navigators who can investigate long-ago worlds.

Decoding Disease

Tishkoff, like other medical researchers, is very interested in how what happened long ago shapes genes that affect our health. This evolutionary information may translate into ways to understand, treat and prevent human diseases.

In Africa, Tishkoff lived in areas with high rates of malaria, an infectious disease that continues on page 6.
I want to know

This field of science uses a blend of methods to determine evolutionary links between ancient and modern people. It can also be used to reveal our connections to closely related species, like chimps and gorillas.

To connect the dots using molecular anthropology, scientists look at DNA. They look for differences and similarities in the sequences of nucleotides—the “letters” that make up the genetic material.

As different as people look, our DNA is actually amazingly alike. And, get ready for this: Your DNA is about 96 percent the same as a chimp and 85 percent the same as a mouse!

Molecular anthropology is important for understanding human origins and human evolution. Knowing our DNA roots can also help us learn more about diseases and genetic changes that our ancestors developed and passed on to us. This knowledge may be the key to finding new treatments and vaccines.

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disease spread by parasite-infested mosquitoes. Despite the fact that effective prevention methods exist—including bed nets and medicines like chloroquine—malaria is an enormous worldwide health menace. In Africa, where access to prevention and treatment is scarce in many regions, the disease kills a child every 30 seconds.

Yet some people inherit protection against malaria. Variations in a gene called G6PD are common in people who live in areas of Africa with widespread malaria. But although this variant of a particular gene guards against malaria, it also has a dark side, causing anemia and sometimes death.

Another example of a double-edged genetic variation is sickle cell disease, a lifelong problem in which the body makes misshapen red blood cells that don’t move easily through blood vessels. They’re stiff, gummy and tend to form clumps that get stuck, causing intense pain, serious infections and organ damage.

By any standard, sickle cell disease is not a good thing to have, except for the fact that people who have a sickle cell gene variant—along with one normal gene—have protection against malaria. As with the G6PD genetic variant, evolution tolerates the sickle cell gene variant and it gets passed on to future generations of people because it gives them a survival advantage.

But the story gets even more complicated. Just as the human genome adapts, so too does that of the parasite living inside the mosquito that transmits malaria. For this reason, Tishkoff laments, we will probably never be fully protected from the disease.

“We’re in an arms race with the parasite that causes malaria,” Tishkoff says.

The Big Family Tree

Where was your grandmother from? Your great-grandmother? Now how about your great-great-great-grandmother?

No doubt your family tree gets fuzzy the further back you go. But as humans, we can all trace our roots back to a common ancestor. Evolution and the migration of ancient peoples made humans a large and diverse population today.

But how do we find our ancestors? How do we learn where we came from and how we got here? The answer is molecular anthropology.

NOAH ROSENBERG, MARTIN SOAVE

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Molecular anthropology is important for understanding human origins and human evolution. Knowing our DNA roots can also help us learn more about diseases and genetic changes that our ancestors developed and passed on to us. This knowledge may be the key to finding new treatments and vaccines. —E.F.
what makes everybody unique.

However, all is not lost. Tishkoff thinks that by finding the genetic variants that contribute to parasites’ resistance to our drugs, scientists may be able to develop more durable malaria treatments and vaccines.

Got Milk?®
Tishkoff explains that the evolutionary race between the malaria parasite and human defense mechanisms is an example of co-evolution, where two species adapt and evolve in response to one another.

Other interactions occur, such as genetic adaptation to a cultural change. Take the case of humans who can drink milk and eat dairy products without getting sick.

Believe it or not, the inability to drink milk, called lactose intolerance, is very common in adults around the world. Most have a burned-out version of the enzyme lactase that digests milk and dairy products.

That’s in contrast to baby mammals, who need milk to survive and can easily digest it because their lactase enzyme is working fine.

Most adults who trace their ancestry to Asia or Africa cannot digest milk. However, some people from these African tribes are pastoralists, meaning that they keep domesticated cows. These people can drink milk long into adulthood.

Tishkoff wondered: Could there be a connection between raising cows and being able to drink milk as an adult?

She collected blood samples from different tribes in Africa and analyzed their DNA. Her hunch was correct: African populations with recent ancestors who were pastoralists had a genetic change in the gene that produces lactase, allowing them to digest milk.

Tishkoff also found a link between genetic and archaeological evidence. The genetic variant for lactose tolerance became common in East Africa between 3,000 and 7,000 years ago. Archaeological data suggest that cattle were domesticated in parts of Eastern Africa at the same time.

“To me, this was the ultimate find,” says Tishkoff. “It was everything I had been trying to do since college—tying together history, anthropology and genetics.”

So, a genetic change—the lactase gene variation—and a cultural change—the domestication of cattle—occurred at the same time and created a selective advantage. People with the genetic change could drink milk, become stronger and have more children, thus passing on the beneficial trait to more individuals and extending the benefit to future generations.

But which came first?
Did African farmers gradually gain the ability to digest milk after domesticating cattle, or did they seek cattle as a source of milk for protein?

Tishkoff is quick to point out that it’s not so clear. Right now, no one knows for sure.

Out of Africa
Tishkoff has recently turned her evolutionary focus toward height, weight, taste perception and metabolism. She has lots to do, since very basic traits like these are often the most complex at the genetic level. Height alone, she says, is thought to be controlled by around 100 genes.

FIND MORE
Every answer brings with it a new question.

Studying genetic variation and metabolism may have important health benefits. In modern humans, the ability to store fat and quickly increase blood sugar can lead to obesity and diabetes—widespread health conditions associated with many other diseases.

Tishkoff explains that in the not-too-distant past, these traits may have been adaptive. In times of food scarcity, the ability to store fat was an evolutionary plus. Now, with abundant food available in countries like the United States, obesity has become common.

Using molecular anthropology, Tishkoff will try to figure out how metabolism-related genetic variants evolved. In this way, she will effectively retrace the paths of many of today’s “civilization” diseases like obesity, high blood pressure and type 2 diabetes.

Aside from the obvious health implications, Tishkoff is also driven by the same curiosity we all have.

“I want to know what makes everybody unique,” she says.

Now 42, Tishkoff has visited more than 40 countries. She has made more than 10 trips to Africa, sometimes staying for months at a time. Her international travels have inspired a taste for exotic and ethnic foods and a rich appreciation for world culture.

It seems like forever since her first trips abroad, Tishkoff says, adding that she didn’t know what to expect that first time in Africa.

“I didn’t know where I was going to sleep. I didn’t know how I was going to do my labwork. I had no idea if anything was going to work at all,” she recalls.

“It was trial and error, and it was miraculous that everything worked so well.”

Now, with two young children, Tishkoff can’t just pack up and head to Africa as frequently as she used to.

“I miss it terribly,” she says. But it hasn’t stopped her research there, and Tishkoff still works with African researchers and looks forward to taking her children with her one day.

But for now, her graduate students are the ones peeking through the tent flaps, wondering just what that savanna sound was.

Mystery Malaria

Malaria, caused by infection with parasite-infected mosquitoes, is rampant in Africa.

The disease also devastates populations in Latin America and Asia, but the parasite culprit in these other regions, called *P. vivax*, differs from the African parasite in many ways.

Although *P. vivax* rarely kills, it does cause severe illness. And because it can lie dormant in the body for many years, those infected could get malaria again—months or years later.

Until now, researchers knew very little about *P. vivax* because they could not get it to grow in the lab. Now, parasitologist Jane Carlton of the New York University Langone Medical Center and an international research team have broken new ground by cracking the parasite’s genetic code.

Carlton and her team also compared the *P. vivax* genome with that of other malaria parasites and learned that *P. vivax* is unusual in many ways. She hopes that its evolutionary secrets will point to effective ways to control malaria or to eradicate the parasite in affected regions.—A.D.