I study the population history and genetic diversity of Africa, human evolution, and the evolutionary dynamics of complex disease risk. I'm Sarah Tishkoff, a professor of genetics and biology at the UPenn School of Medicine, AMA!

SarahTishkoff [1] and r/Science AMAs[1]

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Abstract

Hi Reddit! I'm Sarah Tishkoff, a professor of genetics and biology at the University of Pennsylvania's Perelman School of Medicine and School of Arts and Sciences. My lab studies human evolution, ancestry, genetic variation, and disease risk in populations around the world. We aim to answer fundamental questions about human origins, focusing on Africa's role as the place where modern humans originated and thus the region with the most genetic diversity. We also look at complex diseases with a genetic influence, like heart disease and diabetes, and how historical evolutionary pressures may have kept these relatively common in modern populations. Next year, I'll be joining the Board of Directors of the American Society of Human Genetics, which meets next week in Baltimore. If you're interested in human genetics issues, check out the [meeting's agenda](: http://www.ashg.org/2015meeting/asp/soe/webroot/soe.shtml) and keep an eye out for the many interesting findings that will be announced. I will start answering questions at 1 pm Eastern (10 am Pacific, 6 pm UTC). Thanks Reddit, I'm wrapping up now because my kids are asking where mommy is! But I've really enjoyed the opportunity to share my research interests with you and if I have a chance, I'll check back later to answer more questions. Have a great weekend The views expressed in this AMA are my own and do not necessarily reflect the views of the University of Pennsylvania or ASHG.

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Science AMA Series: I study the population history and genetic diversity of Africa, human evolution, and the evolutionary dynamics of complex disease risk. I'm Sarah Tishkoff, a professor of genetics a

SARAHTISHKOFF R/SCIENCE

ABSTRACT

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I often read about how Africans, and especially Khoi-San peoples, have much greater genetic diversity than non-Africans. Are there any tangible examples of this, e.g. traits where Africans have several different phenotypes while Europeans or Asians would only have one or two? Or is the diversity all at the sequence level.

iorgfeflkd
First of all, I'm glad to have this opportunity to participate in AMA! I see a lot of great questions including this one. You are correct that Africans have the greatest levels of genetic variation compared to non-Africans. This is true if one were to pool populations by continent and is also true for nearly all African populations if studied individually. There are also high levels of genetic differentiation among African populations. This is a result of their demographic history. Modern humans originated in Africa around 200 thousand years ago and a small subset of people left Africa in the last 50,000 – 100,000 years, resulting in what we call a population "bottleneck". A lot of genetic diversity was lost during this event. Africans have also maintained a larger long term population size compared to non-Africans. They are also sub-structured—populations have been separating and diverging for long periods of time. Then in some cases people migrate, admix, and diverge again. There is also a lot of variation in

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climate, infectious disease exposure, and diet in Africa, resulting in adaptation to local environments. It is for this reason that you see a lot of phenotypic variation in Africa. In regards to whether or not Africans have more phenotypic variation amongst populations compared to, say, Europeans or Asians, this is still an outstanding question that would need to be quantified. It also will depend on how you define a "phenotype". But a couple of examples that come to mind are height and skin color. Africans have some of the largest variation in height ranging from short statured central African hunter-gatherers (often referred to as "Pygmies") who are typically under five feet tall to the tall and thin East African and Central African pastoralists who are tall and thin (typically over 6 feet tall in some groups). There is also a lot of variation in skin color just within the continent which many people aren't aware of. For example, the Khoisan, who have the oldest genetic lineages are the lightest skinned people in Africa and the pastoralists who originate in southern Sudan are the darkest skinned people in Africa. So, there is a very large range compared to indigenous populations from Europe, for example. But note that due to adaptation, there are also very dark skinned people in India, Papua New Guinea, Australia and elsewhere and there are populations with very short people among certain groups in the Philippines, New Guinea, and South America, possibly due to adaptation to a tropical environment.

You said that heart disease and diabetes had evolutionary pressures keeping them common? What do you mean? How did they help?

Are there any others like that that we normally would think are just horrible diseases, but they serve a purpose?

nnutcase

What I mean by that is that until 10,000 years ago, ALL human populations practiced hunting and gathering. As a species, we've also been adapting to very different climates. According to James Neel, an influential human geneticist and anthropologist who was a professor for many years at the University of Michigan, he thought that diabetes might be prevalent due to the "thrifty gene hypothesis". The argument was that "thrifty genes" which contribute to risk of diabetes in modern environments may have been adaptive in past environments when we were hunters and gatherers. For example, high blood sugar levels and increased fat storage could have been adaptive during times of famine but when people started eating McDonalds, these same genes could contribute to predisposition to obesity and diabetes. This would imply that common diseases like diabetes could be due to ancient genetic variation, not new genetic variation, and some studies have supported that hypothesis. But note that the thrifty gene hypothesis is contentious and some argue that they don't see evidence for this. However, because traits like diabetes and obesity are caused by many genes and environment, it's tricky to find the genes that play a role in these diseases. And finding signatures of natural selection at these genes could be even trickier. So, this is still an interesting outstanding question.

Regarding other horrible diseases that are common because they may also be adaptive in certain environments, the first example that comes to mind is sickle cell anemia in which people who have one copy of the sickle cell mutation and one normal copy have increased protection from malarial infection. Another recent example was the identification of genetic variants at a gene called APOL1 which are strongly associated with risk for kidney disease in people of recent African origin. However those same variants are also protective against certain parasites that cause sleeping sickness which can be a lethal disease. Some have hypothesized that the protections against sleeping sickness caused these mutations to reach high frequency. However, note that these genetic variants may have multiple effects, including protection against other infectious diseases and we're still trying to figure out why they're so common.

My question is about race. I am almost a complete layman on this subject so I am interested in your expert opinion. Having studied sociology I have been taught that race is largely a social construction. I had a professor who essentially claimed four things:

1: there are no definitive categories for race nor has there ever been. A lack of scientific consensus points to a fundamental problem in the concept of race.

2: the genetic differences in humans in terms of race is not significant. There is more genetic diversity amongst members of one race than between races and there are very few universal rules we can say are true for all people of a certain race.

3: a lot of what we know in terms of disease, intelligence, and predisposition to certain activities and race is actually more likely to be based on culture and economics than genetics. For example a poor person is going to be more likely to have diabetes than a rich one, and someone who lives in a poor African country is more likely to be interested in running than skiing.

4: most human populations have not lived in isolation from each other and for hundreds of thousands of years have been intermingling, wandering and breeding with one another. Additionally many racial categories we imagine today are defined by man made borders that have only existed for 50 years or so. So human populations have not existed in isolation from each other long enough to evolve into entirely separate races.

It's been a while since I studied this and as I say I am a total layman here but is there any truth to any or all of these claims? What is your opinion on the matter?

scruntly

Well, this is definitely a challenging question to answer! Overall, I agree with most of what your professor says. I've participated in many discussions involving geneticists, historians, sociologists, and clinicians about whether or not race is a useful term for studies of human diversity and for biomedical research, diagnosis and/or treatment. Inevitably, we always get stuck at the level of trying to define race. This is because race, as we use it today, is often defined based on a combination of biological, cultural and sociological characteristics which are nearly impossible to separate. Furthermore, race has historically been used (or perhaps I should say misused) to classify populations in a hierarchical manner and to justify abuses including the killing of millions of peoples based on their "racial" classification. However, in my opinion, there is no "objective" way to define race. If we base it on morphological features like skin color, this doesn't work since skin color is thought to be an adaptation to UV exposure and we see people with dark skin, for example, in many indigenous populations of the world. Another example would be the use of "Hispanic" as a racial classification. Based on genetic studies, people who self- identify as Hispanic may have varying amounts of Native American, European, and African ancestry (and other ancestry as well). If we base definitions of race on patterns of clustering as inferred from genetic data (someone asked about Edwards paper described below), the problem is that the clustering patterns observed very much depends on the algorithm used and the populations included in the analysis. For examples, there is a commonly used program called STRUCTURE which uses probabilistic methods to simultaneously infer the number of "ancestral population clusters" (labeled as K) as well as individual ancestry from those clusters. But it's up to the user to define a priori the number of "ancestral populations". People have debated what sort of threshold to use but there is not a consistent way to do this. Furthermore, this analysis is very much influenced by which samples are included. For example, in a paper by Noah Rosenberg and colleagues published in Science in 2002 at K = 5, they observe that individuals cluster into five major geographic regions that some people would argue correspond with common notions of "race". But note that at K = 6, the Kalash population from Pakistan become distinct on a global level! And in our Science 2009 paper, in which we included a large number of diverse African populations, we found that K = 14 best fit with the data on a global level and we observed more genetic substructure among Africans than amongst all other populations on the globe! When we breakdown the analysis by geographic region, you can see even more fine scale subdivisions. In fact, there is a new method called fastSTRUCTURE which looks at even more fine-scale substructure present in small geographic regions, like Europe, for example. I disagree a bit with your professor about people intermingling for

hundreds of thousands of years. It's absolutely true that modern humans, as a species, like to migrate and admix with many different people. In fact, when our species migrated out of Africa, it appears that we even admixed to a low level with archaic populations like Neanderthals! But there certainly were some geographic boundaries for long time periods between some regions (for example people became more isolated in the Americas after the Bering land bridge which connected the Americas to Siberia became covered with water). But it is also true that there are typically no hard and fast "boundaries" and that people who live in geographically intermediate locations often have mixed ancestry. In fact, within the African continent, I have found that admixture between populations tends to be the rule rather than the exception! So, I think that we should be thinking in terms of ancestry rather than race. Could ancestry impact risk of disease? I believe it can (for example we know that there are certain genetically influenced diseases like Tay Sachs that are very common in people of Ashkenazi Jewish ancestry). However, environment and culture is also having a big impact and we must consider both jointly.

Africa is quite diverse in terms of human culture and environment, in addition to human genetics. In what ways does your research take the interaction between genetics and environment (cultural and otherwise) into account?

Thank you for taking the time to do this AMA!

neurobeegirl
We are very interested in co-evolution of culture and genetics. For example, we have studied correlations between linguistic, geographic, and genetic variation. Generally, there are strong correlations but with some exceptions. This is because some populations have migrated over long distances and some languages have been replaced. Another classic example that my lab has studied is the genetic basis of lactose tolerance. We identified several novel genetic variants that are associated with lactose tolerance in East African pastoralists which arose independently from each other and from the mutation associated with lactose tolerance in Europeans. These mutations occur in populations that have domesticated cattle and drink milk. We showed that it is under very strong selection in Africa (and also in non-Africans) and has rapidly risen to high frequency in populations that practice dairying. What is particularly cool is that the age of the mutations correlates really well with the origins of the practice of cattle domestication as indicated by the archeological record. For example, the earliest evidence for cattle domestication based on archeology is in north Africa and the Middle East around 8,000 – 9,000 years ago. We estimate the age of the European mutation to be around 9,000 years. But cattle weren't introduced south of the Saharan desert until around 5,500 years ago which correlates really well with the inferred age of the east Africa variants to be between 3,000 – 7,000 years old. I love it when we can integrate genetics with cultural, linguistic, and archeological records!

Hi Professor Tishkoff,

Thanks for doing this AMA. I hail from Rwanda but appear more North Eastern African. Could you tell us why people in the Rift Valley of the horn of Africa appear different, from say, the central or western and southern parts of Africa? Were there mass migrations fro-and-to middle east and back to Africa that may have led to people from HoA having caucasoid features? Do you know of any studies on this?

Thanks

teknikalglitch
Thanks for asking this question. My research career started when I was studying populations from Tanzania and I have continued to focus on studying the population history of people from the Rift Valley and their relatedness to other populations. There are some populations thought to be

indigenous to that region for tens of thousands of years. These include the Hadza and the Sandawe, traditionally hunter-gatherers who speak with clicks, a language classified as "Khoisan". In fact, there has been a lot of interest and debate about whether or not this language is related to the click languages spoken by the San in southern Africa. Many linguists would say that the Sandawe language is related but the Hadza language is very divergent. In anycase, one hypothesis is that the original inhabitants of that region were click speaking hunter-gatherers who separated from each other tens of thousands of years ago (and some would argue that the San in southern Africa originated in East Africa). Today, the rift valley has populations that originate from many regions. The pastoralist populations that speak languages classified as Nilo-Saharan (like the Maasai) originated from southern Sudana and then migrated first into Kenya (and other surrounding countries) and then into Tanzania within the past few thousand years. People who speak Cushitic languages and are agro-pastoralists (and who have some of the Eurasian features that you mention) migrated into the region from Ethiopia within the past 5,000 years. The populations in Ethiopia are themselves admixed with non-Africans. Then there are people who who are agriculturalists and speak Bantu languages. Their ancestors originated from Central/Western Africa and came into the Rift valley within the past few thousand years as part of the "Bantu migration" originating from Nigeria/Cameroon. There have also been more recent migrations of people from the Arabian peninsula along the coast of Kenya and Tanzania (i.e the Swahili people), and of course even more recent admixture with people from many regions of the world, particularly in populations living on the coastal regions and/or in urban regions.

Do you consider mental "disorders" like OCD, ADD, and psychopathy diseases or evolutionary traits? Also, can genetics explain the liberal/conservative difference in people, or is that purely environmental? Thank you!

curtify
Regarding psychiatric conditions like OCD, ADD, etc that's an interesting outstanding question. We know that there are some genetic factors contributing to these traits (but also very strong environmental factors) and as I mention in one of my answers above, because genes can have multiple effects, they can be associated with risk to these disorders but at the same time could be associated with things like creativity. So, I think it's "possible" that these conditions could result from variants at genes that were adaptive but we have a long ways to go to answer this question definitively (finding the genes associated with these conditions is extremely challenging since they're due to many genes of small effect together with environment). Regarding genetics of liberal/conservative difference in people, I'm skeptical that we will ever find such a gene(s)! Keep in mind that behavior is very complex and is certainly due to complex interactions of hundreds of genes and environment (and frankly, I'm pretty certain that environment is having the biggest impact on whether someone identifies as liberal or conservative!).

Are there are regions of Africa that distinguish themselves as less diverse, genetically speaking? How about regions of increased diversity? Can you say something about sickle cell anemia and if certain peoples aren't affected by it? Also, does darkness of skin have any effect on ability to survive sicknesses/diseases? (I'm thinking elementary things like water retention and fighting high temperature fevers)

Thanks!

drewblair36
In a paper we published in the journal Science in 2009, we look at over 2,500 people from more than 120 populations in Africa and compared to 1500 people from across the globe. We didn't observe any African population with less diversity than non-Africans except the Dogon from Mali. However, we did not have high quality DNA from that population and there could have been some artifacts because of that. I think that analysis should be repeated using better samples and my prediction is that they will be as diverse as other Africans.

Among the African populations, the populations with lowest diversity are groups like the Beja pastoralists from northern Sudan and some East African pastoralist groups like the Dinka and Pokot. This could be due to smaller population sizes and/or higher levels of inbreeding (for example, it is tradition amongst the Beja to marry first cousins). But, interestingly, some groups that are very small today such as the Hadza hunter-gatherers who have a census size of only 1000 maintain high levels of genetic variation, though they also have amongst the highest levels of identity by descent (regions of the genome shared amongst individuals) compared to any population in the world.

Regarding sickle cell anemia, the answer is yes, there are many populations not affected by this. This is because sickle cell anemia is thought to be at high frequency because people who have one normal copy and one copy of the sickle cell mutation are protected from malaria, a disease which causes very high mortality in Africa, particularly amongst children. So, we see the highest prevalence of sickle cell anemia in West Africa where malaria is most endemic and where this mutation may have arisen. However, because of a large migration of people who speak the Bantu languages who originated from Nigeria/Cameroon and spread across sub-Saharan Africa within the past few thousand years, this mutation has been introduced to other regions of Africa. There is a nice map of the distribution of the sickle cell mutation in this paper http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3708126/.

Regarding whether dark skin could be protective against infection, that's a great question! To my knowledge, we don't currently have an answer to that. But please note my answer above in which I discuss the huge amount of variation in skin color in Africa. My lab is currently studying the genetic basis of skin pigmentation in Africa and we hope to be able to say more about this soon.

Are we getting more genetically "unhealthy" than previous generations due to modern medicine weakening natural selection? If so, could this be a problem in a few generations if we do not implement some sort of genetic "screening" to remove the bad genes?

Talciuma
Wow, that's an interesting but tough question! The short answer is that it would take a very, very long time to change the gene pool of "bad" genetic variation. Also, importantly, most genes have what we call pleiotropic effects—that is they influence multiple traits. So, a gene could have both a "good" and "bad" effect and it would be a bad idea to get rid of it. Some people would argue that this may be the case with genes that influence ADHD or bi-polar disorder. Many very creative people who have made important contributions to our society have been diagnosed with these disorders. Also, as time goes by, medical treatments will improve so I don't think society is going to suffer.

Where do you see human evolution going? Doing a historical analysis on where we came from, do you have any hypotheses on what we might look like in a few thousand years?

hs7296
Wow, this is an interesting question to ponder! I don't think we're going to "look" very different as a species other than that we will continue to be more admixed (and this can only be a good thing from a genetic perspective since it introduces more genetic diversity!). However, one thing to remember is that infectious disease is one of the major continuing sources of selection which could potentially wipe out huge numbers of individuals unless they have innate resistance. We've recently seen this happen with the Ebola outbreak. For reasons we don't entirely understand, as many as half the people infected in Africa did not die from the disease but others did. Also, it's taking a long time to come up with a vaccine. So, I definitely think we will see ongoing evolution in regard to immune related genes.

Malaria was an incredibly important driver in human evolution.

What other diseases known or not widely known may have had such an impact on our species?

MorsOmniaAequat

As I mentioned in my answer above, infectious disease is likely to have had (and continue to have) the largest selective pressure. Undoubtedly other infectious diseases have had a major impact including bacterial infections (think about the black plague!). TB is also a major killer today but both TB and malaria have been overshadowed by HIV as the biggest cause of mortality in regions such as sub-Saharan Africa. I also mentioned the ebola example above. This is an area that I'm very interested in studying--how do populations differ in their response to infection and what is the genetic basis of this? There is still a lot to be learned! (also, see my response above about sickle cell and malaria and variation at the APOL1 gene and kidney disease).

Hi Professor,

I'm having a robust discussion with a friend about how many generations it takes to change human traits.

For example, apparently about a third of people have the enzyme to digest milk. I was thinking that if the seven woman who generated most of Europe (is that even still in vogue that idea) survived when others didn't maybe it was because they had lived with cows for long enough that they had evolved to get nourishment from milk as well as meat.

My friend says I'm just wrong because evolving the enzyme would take longer than the time since domestication of cattle. He's probably right but I'm interested to hear how long you think that kind of thing would take.

Thanks for your time if you have it :-)

kookaburralaughs

OK, I should clarify a few things. As someone commented below, all of us have the gene that codes for the enzyme lactase which is expressed in the small intestine and breaks down the complex sugar lactose, present in milk, into glucose and galactose which are readily taken up into the blood stream. However, most mammals and most humans, for that matter, shut down expression of this gene shortly after weaning (by around age 6). But in populations that have domesticated cattle and practice dairying, the have a genetic adaptation which results in this enzyme being kept on into adulthood. I discuss this question in more detail in one of my responses above. The answer to your friend's question is that this trait has evolved very rapidly over the past 3,000 - 9,000 years in populations that traditionall drink milk. Also, I am not aware of any evidence that seven women were the ancestors of most of Europe!

I heard that the oldest known Y chromosome goes back over 300,000 years. It was discovered in the Cameroon area.

It this verified? Is this a Y chromosome of the Homo Sapiens lineage (this was before our species actually became distinct) or does it represent interbreeding with another Archaic lineage?

Your thoughts are appreciated.

Albacorewing

This is a super interesting outstanding question! It was a big surprise to many of us in the field when a Y chromosome lineage was identified in Africa which diverged from other lineages more than 300,000 years ago (other studies of the Y chromosome had observed divergence around 150,000 years ago). We still don't know the reason for this and I think it will be informative to look at Y chromosome variation in more Africans. But I think you're absolutely correct that this could represent inbreeding between anatomically modern humans in Africa with archaic populations, just as has been observed for

non-Africans with archaic populations such as Neanderthals and Denisovans. In fact, we demonstrated evidence for archaic introgresion in Africa in a paper published in Cell in 2012 http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3426505/. Several other groups (such as Mike Hammer and Jeff Wall) have shown this as well. The problem is that we don't have any good genetic material from African fossils since they don't preserve well in the wet climate of Africa. But I do believe that some day we will be able to obtain ancient DNA from Africa and when we do, we'll have a much idea of how much introgression there was with archaic population in that region.

Ooh your topic of study sounds so interesting! What got you into that area?

ALittleOpus
I started out with an interest in Anthropology. When I was in high school I read a book by Margaret Meade on cultural diversity of Samoans and I decided that I was going to be an Anthropologist and that I wanted to do field studies. So, I declared Anthropology as my major at UC Berkeley. But at that time, there was a professor named Allan Wilson who had founded the field of molecular anthropology. I became increasingly interested in how we could use genetic data to answer questions about human evolutionary history. So, I switched to a double major in genetics and anthropology. Then for grad school, I decided to get a PhD in human genetics and went to Kenneth Kidd's lab at Yale. He and Luca Cavali-Sforza at Stanford had one of the largest collections of DNA samples from populations around the world. But at that time, the populations they were using as "representative" Africans were central African Pygmies! Because there were so few samples from Africa, I started writing to the few people who had samples from that region like Trevor Jenkins from University of Witwatersrand in South Africa and asked if we could collaborate. I then discovered that there was much more variation among African populations that among populations from other regions of the world. But at that time, I was tied to the lab bench! After I got my PhD, and before joining Andy Clark as a postdoc studying population genetics, I did a short postdoc with Dr. Jenkins at WITS. While there, I attended a meeting in Cape Town on the cultural and genetic history of the Khoisan people. It was a great meeting with geneticists, anthropologists, linguists, and historians coming together with representatives from the different Khoisan tribes. I asked people what they thought the most interesting outstanding question was and they said that I should study how the Hadza and Sandawe hunter-gatherers from Tanzania, who also speak with click consonents, were related to the Khoisan from Southern Africa. So, when I got back to Andy Clark's lab, I joined forces with Joanna Mountain who was also interested in that question and we wrote a joint NSF grant which was funded. That enabled me to do field work starting in 2001 when I was a new faculty member at the University of Maryland. I went off by myself for 3 months (well, actually my husband came with me for the first month) and without knowing at all how it would work, together with my African collaborators, I started collecting DNA from blood. That set off a life long passion to study African genetic diversity in order to learn more about human evolutionary history, African population history, and the genetic basis of disease risk. After I had kids, I had to pass the "fun work" of doing most of the field collections to students and postdocs (actually, it's incredibly hard work but for those of us with a passion for this sort of thing, we keep wanting to do it!). Just recently my kids got old enough to be able to join me in Africa so I'm hoping that soon they will be my research assistants!

Hi Sarah! How have geographical or cultural isolates and/or small populations that may exhibit increased genetic drift informed your research? Populations like these might represent outliers on the spectrum of evolutionary effects- can you share with us some things we have learned from them?

p1percub
Hi! I recently published a perspective about this in Science https://www.sciencemag.org/content/349/6254/1282. Many studies today of complex traits like height and weight have focused on studies of hundreds of thousands of individuals. This is often necessary

because these are very complex traits that may be due to hundreds of genetic variants, together with environment, and each genetic variants is having a small effect. Scientists often refer to this as the "genetic architecture" of a trait. But this genetic architecture may differ among ethnic groups, particularly if a trait is under selection. For example, a recent study in Science of Inuit populations from Greenland identified genes that are associated with height and weight which are adaptive to a very cold climate and a diet high in fat from fish. This study relied on relatively small sample sizes--an initial size of just a couple of hundred individuals to find targets of natural selection in the genome and then a genotype/phenotype association study in several thousand individuals. Interestingly, at least one of these variants also impacts height in Europeans but was missed in prior studies because it's not common in that population but is common in the Inuit population, possibly due to adaptation. We have also been studying the extreme short stature trait in central African hunter-gatherers (commonly referred to as "Pygmies"). This is clearly a complex trait and we still have lots to learn about the genetic basis of this trait. However, using a relatively small sample size we have already identified a pathway associated with this trait (the GH/IGF1 pathway) based on genetic data and also several candidate genes. I think that there's lots to learn by studying a broad array of ethnically diverse populations. Also, it's important that these populations will benefit from genetic studies and the development of better therapeutics.

Just how unique are the Khoisan people of southern Africa?

dghughes

Well, that depends on how you define "unique". First I want to make it clear that ALL modern humans are genetically very similar at the genome level. What is unique about the Khoisan people of southern Africa is that they have the oldest genetic lineages in the world when you look at mtDNA, Y chromosome DNA or autosomal DNA. This does not mean that they are an ancient population!!! Remember that all populations in the world have been evolving. However, they descend from a population that was ancestral to all others. So, they're an interesting group to study if we want to learn more about modern human origins. They're also interesting because they have some interesting morphological characteristics, including fair skin color and it will be interesting to determine if this was an adaptive trait and what the genetic basis is of this trait. Also, from a cultural perspective they are very interesting. They speak a language which contains click consonents. The only other languages that also contain clicks are the Hadza and Sandawe populations from Tanzania, as I mentioned in another post. Until recently, they practiced a traditional hunting and gathering life style and have adapted to living in very dry climates such as the Kalahari desert. I think they will continue to be an interesting population to study from both a genetic and anthropological perspective.

Assuming that my family and I are of Mexican descent (from the area if Durango, Mexico and the northern part of the state of Zacatecas) and have very limited indigenous features. But, some of my family has very dark features. I'm curious just as a starting point, what could my DNA look like given the existing knowledge about the bearing migration, the Spanish conquistadors, the Moores in Spain, slave migration, and other factors that could influence DNA?

lowmigx3

My answer relates to one of my prior comments about "hispanics" and the fact that people who self identify as hispanic may have native American, European, and African ancestry (and other ancestry) to varying degrees. Many genetic studies of the Americas have shown evidence for high levels of admixture between indigenous populations and people of European and African descent.

Hey Sarah! I used your paper, "Distribution and frequency of a polymorphic *Alu* insertion at the plasminogen activator locus in humans" from 1996 recently to solve the conundrum of a double banding pattern I was seeing with tPA primers and human genomic DNA template for an assay I

was developing at work. Thanks for your work and those insertion site-flanking primer sequences!

AbbaZaba16
Wow, that's great! That was one of my earliest studies. Glad to hear it was helpful!

Which people from "Africa" do you study? Does it include Arab Africa? And white people of southern Africa?

Michaelpr
Mainly sub-Saharan Africans from all major regions.

Hi Sarah, fascinating topic! Thanks for doing this AMA.

We're constantly hearing about the effects that the human race is having on ecosystems and other biological organisms and how often they go extinct and/or become endangered because the environment changed too fast for them to adapt. I wanted to know if you could speak to whether you've looked at whether these changes have affected the human genome at all, e.g. if a native African vs a 2nd/3rd generation person from the same community living a western lifestyle will have any differences in gene expression, and whether that might affect some of the more "modern" diseases that we have now.

puffz0r
Good question! Believe it or not, there are some human populations that may go extinct as well. For example, there are some small Amazonian tribes that have been living in isolation and if exposed to infectious diseases for which they have no immunity, may all die. I also study a hunting and gathering population called the Hadza who live in Tanzania. There are only 1000 of them. Sadly, partly due to the influx of other populations to the region, and the rise of "ecotoursism" which has resulted in a high incidence of alcoholism and a concomitant shift in behavior, HIV has been introduced into this population. They are resistant to taking western medicines and already HIV has spread to at least 15% of the population. I worry what will happen to them in 50 years.

But you raise another interesting point which is the effect of the environment on gene expression. Scientists refer to this as epigenetic effects. We know that environment and epigenetic changes are definitely influencing gene expression in populations. I think it would be a really interesting question to study epigenetic differences in populations practicing indigenous lifestyles vs those that have recently moved to urban areas and are living a western lifestyle. Epigenetic factors certainly could be contributing to disease risk.

I've read that the genetic form of diabetes isn't present in African lineages. It was hypothesized that interbreeding with Neanderthals could explain its deep roots. Has there been any movement on this theory?

Thank you

wearemostlywater
No, this isn't true! In fact, many studies have shown a higher prevalence of diabetes in people of recent African origin who are living a "western" lifestyle. Indeed, I have rarely seen diabetes in Africans practicing an indigenous lifestyle but it's very common in urban areas and some think that it may be due genes that increase risk for disease in a western environment (and see the discussion above about the thrifty gene hypothesis). I think what you're referring to is an interesting study published in Nature http://www.nature.com/nature/journal/v507/n7492/full/nature12961.html. In that study they looked for regions of the genome in non-Africans which may be derived from admixture with archaic

populations like Neanderthals. They found one such region which is common and has been associated with risk of diabetes. But this is probably an exception rather than the rule.

How has the 1000 genomes project helped your research?

What other resources like this do you value for your research and how could they be improved?

merwinn
The 1000 genome project has been a very important resource to myself and other scientists. It's important to me personally because I'm able to compare the populations I study in Africa to the globally diverse populations included in the 1000 genomes project. It's also been of help for many biomedical studies because they've identified a lot of novel genetic variants, some of which may be functional. I think that resources in the future that would be particularly useful would be those that include a broader array of ethnically and geographically diverse populations, that have high coverage sequence data so that we can have more certainty about calling variants, and that have phenotype data which can be linked to the genetic data so that we can better understand the genetic basis of phenotypic variation, including disease risk.

How significant is the Homo naledi finding and what are you hoping to learn from it?

Veagles89
This is a really exciting finding because it represent a new species which has a mixture of archaic features similar to the genus australopithicus but also some features similar to the genus Homo. But what I'm waiting for is for them to be able to place a date on the age of the specimens. That will help us to interpret their place in the history of our species.

I am interested in understanding the evolution of language. Do we know when this ocurred in human evolution and which of our ancestor species also likely had language?

quality_is_god
We still don't know the answer to this question. Some people think that language is what is unique to our species Homo sapiens sapiens. It's difficult to study because we don't yet know the genetic factors influencing language and it's hard to infer from fossils. But some day we may be able to find these genes and also to use the study of ancient DNA to address this question.

Some diseases are even harder to eradicate because they have genes that can be beneficial in other environments. (For example, one mutated gene for cystic fibrosis can help prevent against typhoid.)

Are more prevalent diseases more likely to have beneficial side effects? Does the environment dictate the rates of disease or is it all pretty uniform throughout populations? (So like in the example I provided above, would areas more at risk for typhoid have a higher rate of people born with CF?)

Lastly, do you think diabetes or heart disease could have some positive side effects? If not, is there a way to manipulate the disease so that it can? Seeing as they're both so rampant, it'd be amazing to reap some sort of benefit out of them.

Thanks for your time!

Girthanthaclops
I've already addressed some of your questions in my other replies. But I'll just quickly state that one

general characteristic of diseases that have a genetic basis is that they tend to vary in frequency amongst ethnic groups. This could be due to adaptation to diverse environments but it could also simply be due to their demographic history and to random genetic drift (i.e. random changes in the frequency of variants which tends to have a bigger effect in small populations). It's an interesting outstanding question right now to determine why some disease are so common and how much is due to selection vs drift.

Hi Dr. Tishkoff, I do a bit of work in a lab for evolutionary medicine and I am very curious about complex disease evolution. Has your lab come to any conclusions about where/when complex disease arose in the human genome and how certain diseases (such as diabetes) are currently evolving in the global population?

aheshke_jada
Please see responses above.

Without getting into controversy as these topics often can be, at what point does genetic diversity result in a new species? I have always wondered with so many different ethnicities represented in Africa alone, surely enough one of these must be varied enough to be considered a separate species, or given enough time may be very close to speciating. This does not only apply to Africans of course, I have also wondered this about the uncontacted tribes around the world, or communities such as the Amish, which allow very little genetic diversity to enter their communities, in theory is it not possible that these groups could become a new species of hominid given enough time, and at what varying degree of genetic diversity would they have to have to be considered a different species. I know classifying species can be difficult however. Thanks so very much for this AMA.

qna1
Well, I'm sure this comment will generate controversy! There are many definitions of species. One commonly used definition is the inability to produce produce viable offspring when individuals from two species mate. Species can also be distinguished based on extremely divergent morphological or behavioral differences. But I can tell you with 100% certainty that ALL human populations are from the same species and that the difference in any particular group are not sufficient to reach the level of species. Keep in mind that we all have a relatively recent African origin (non-Africans arose from Africans in the past 50,000- 100,000 years which isn't very long from an evolutionary perspective). Also, small founder groups like the Amish may differ in terms of frequencies of certain variants but overall, every genetic study has shown that there is more variation within populations relative to between populations.

People tend to believe race is an innate biological feature, as if there were a "race gene". This is wrong, but it is hard to convince people of this because though race is a socially constructed category, it is a category (often) based on physical traits, and traits are in a broad sense part of a person's "biology". What is a good way of explaining this?

I saw a talk once given by a statistician at CMU that showed plots (it was a while back but I think they were colored PCA plots) that showed populations in Africa that had closer genetic ancestry with populations in Europe than other populations in Africa. It occurs to me that this is a good way to demonstrate the dissonance between conceptions of race and actual genetics. Can you point to such a graphic? Is there anything better than PCA at this point?

Edit: Found it, a clustering method based on Spectral Graph Theory

osazuwa

Please see my response above. Also, note that many of the physical traits that people associate with race may be due to adaptation to particular environments and in some cases they may result from random genetic drift (ie. random changes in allele frequencies over time). So yes, there are morphological differences among people (in fact all of are unique in that way) and yes they have a strong genetic basis, but typically morphological features can't be used to define race for the reasons that I describe above.