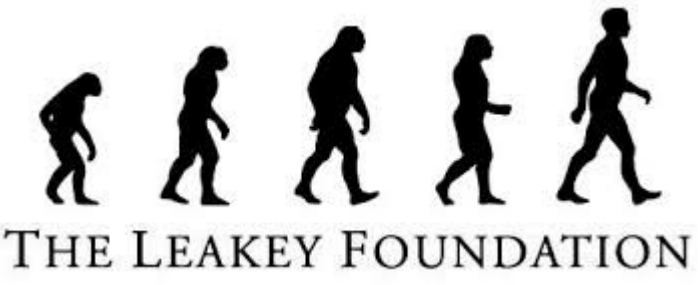

Origin Stories Episode 13: Evolutionary Arms Race

Meredith Johnson
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This is Origin Stories, the Leakey Foundation podcast. I'm Meredith Johnson.

On a previous episode for World Tuberculosis Day, we talked about new research on the origins of TB in the Americas and the terrible toll this disease has taken on humankind for thousands of years. In this episode, we'll take a deeper look at the evolutionary arms race between us and the microbes that make us sick. When Ebola started to spread across West Africa in 2014, it was terrifying. There is no cure for the disease and the only way to stop an outbreak from turning into a devastating pandemic is to isolate people who get sick and hope it doesn't spread. Pardis Sabeti is a Professor of Evolutionary Biology at Harvard University and the Broad Institute. She had been working in West Africa for many years in Sierra Leone at a place called Kenema. She was part of the team there focused on fighting a different disease called Lassa fever and when the first cases of Ebola started to arrive at Kenema, Sabeti, and her team jumped into action. Her lab sent advanced diagnostic equipment to Kenema so health workers there could quickly detect cases of Ebola. She knew that to stop this deadly disease from spreading they first had to understand how it was evolving and they had to do it fast. They needed some intelligence on the enemy. All the diagnostic tests, drugs, and treatments depended on understanding how the Ebola virus was evolving. To understand how she and her colleagues figured that out you have to understand a little more about this evolutionary arms race between humans and microbes.

Pardis Sabeti
Well, I think infectious diseases have always been really intriguing particularly from an evolutionary standpoint. Microbes are really fascinating. They're very powerful. They are one of the strongest forces shaping human evolution. They themselves evolve over time so they're always shifting and so I think it really is a true arms race because they are also in a struggle to survive.

Meredith Johnson
In the struggle between us and the microbes that cause disease Sabeti is deeply interested in both sides. She's a computational biologist who uses math and computers to study the genome and understand adaptation in humans and in the infectious microbes that have shaped our evolution. Basically for millions of years before we developed things like science, medicine, and hygiene the only thing we could do to fight microbes was evolve better defenses thanks to natural selection and evolutionary arms races are all about natural selection.

Pardis Sabeti
So when I try to explain natural selection it's this idea that if an individual, say a person, a ladybug, or a horse, any individual, if they have a mutation, a change in their genome in their genetic code that is somehow beneficial to their survival or to their reproductive success those individuals will then get to the age where they can reproduce and pass on that trait to their children and their children if they inherit that trait are more likely to survive, reproduce, and pass it on to their children.

Meredith Johnson
So for humans and ladybugs and horses, too important beneficial traits are ones that make you less likely to die from a disease that's going around or help you survive in the environment or make you more likely to have more babies over your lifetime. These traits are essentially mutations and if the mutation is a defense that helps you survive to reproduce.

Pardis Sabeti
And that mutation will spread very quickly in the population because each generation, more individuals are likely to get it.

Meredith Johnson
And those are the basics of the theory of evolution by natural selection described by Charles Darwin in 1858.

Pardis Sabeti
So this is an idea that has been percolating for a really long time and so it’s a really fundamental important point because rather than just sort of seeing this phenomenon happen they could actually explain why it was happening, but the interesting thing is it wasn't really until many decades later, not until the 1940s and 50s that we had an actual elucidated example of human evolution and that was when somebody named J.B.S. Haldane made a simple observation of the natural world.

Meredith Johnson
Haldane noticed that there were a lot of red blood cell disorders like sickle cell anemia in parts of the world where there was lots of malaria.

Pardis Sabeti
And malaria infects the red blood cells and they knew that and he began to wonder whether or not these disorders like sickle cell anemia or thalassemia, why would they become so prevalent and why in these tropical regions of the world and he began to think they might have done so because they somehow protect against malaria.

Meredith Johnson
And that hypothesis was shown to be true by another scientist named Anthony Allison just a few years later when he collected blood samples from lots of people in those regions; people who got malaria and people who didn't.

Pardis Sabeti
He took individuals who got malaria and those who were protected did not get malaria and he showed those individuals who were protected were more likely to have the sickle cell trait and that suggested that the sickle trait protected from getting malaria.

Meredith Johnson
And this first example of natural selection in humans was mind blowing.

Pardis Sabeti
What's interesting is infectious diseases, they are such powerful forces of human evolution and they themselves are evolving over time developing drug resistance and changing and so they're so interesting and it's really important that they were really the first elucidated example of human evolution. When Haldane and Allison were able to show that these red blood cell disorders were becoming very prevalent in parts of the world where malaria is endemic and individuals who carry those traits for these blood cell disorders were protected from malaria, we began to understand how humans were also evolving to their environment and the infectious microbes being that important part of the environment that was shaping us.

Meredith Johnson
Early in Pardis Sabeti's career, she decided she wanted to see that process happening. If these disease-resistant traits or other beneficial mutations were showing up and quickly becoming more common, she figured she should be able to see that in our genome.

Pardis Sabeti

So the genome is the blueprint, the book that reads out everything that makes up us. Everybody has their own genome and it's what we pass on to our children.

Meredith Johnson
And it's a really big book. The human genome has more than three billion letters. If you think of it as a book, the book would have a million pages and if I was going to read the human genome out loud to you on this podcast and I read for twenty-four hours a day it would take me a hundred years to get to the end of it.

Pardis Sabeti
In the late nineties and in the two thousands, we sort of transformed our technology, the ability to read out that book to see what all the letters were and is why we call it the genomic era.

Meredith Johnson
Sabeti was a Ph.D. candidate at the time.

Pardis Sabeti
And we were right at the cusp of the genomic era where the technology became so good that we could read out a lot of the human genome, the billions of letters that make up us very quickly and we were just trying to figure out how to deal with all this data. I started thinking about— the interesting thing is that a lot of what we do is we think about really simple principles; the principle of natural selection and then we try to figure out what would that mean? What would that look like in the genome and how you might develop it.

Meredith Johnson
So she wanted to see that natural selection in the genome. So she used her skills with math and computers to develop a way to comb through the genome and look for interesting patterns.

Pardis Sabeti
So knowing that natural selection is going to drive traits that are beneficial up in prevalence quickly in the population, then you just flip that on its head and say okay what I'm looking for is I'm looking for mutations that are prevalent and that have a young age. That's what I need to look for and what would— prevalent is easy to pick up. It's just you count how many copies are in the population and you say eighty percent of people have this mutation. Age is a little harder. How do you determine the age? I started to think okay what would that look like and it's this really fun process of saying okay what would the signal look like and what would you have to pick up?

Meredith Johnson

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And so for a long time she was just playing with the data.

Pardis Sabeti
You're just playing and you're trying to kind of look at it every which way and then finally thought of a way of calculating that change and tweaked away at it for a really long time.

Meredith Johnson
She developed an algorithm. A sort of code buster that could sort through the million page book of our genome and find the patterns that were hiding there and if it worked she should be able to see the regions of the genome where adaptations had happened.

Pardis Sabeti
So I actually applied it to genes that were known to be linked to resistance to malaria because that was the classic example that we knew about and so I applied it to genes that were linked to malaria and showed these like, very beautiful patterns. I often talk about that moment where like it was three in the morning and I had finished kind of this implementation of the test and I'd applied it to these genes that were important in resistance to malaria that I thought would have the signal if I was able to pick it up and the image appeared on my screen and I was just—, my mind was blown, like I could see exactly what you would expect to see if the trait was under evolutionary pressure and— but those are the moments. It's built on years of frustration and lots of notebooks, like page after page, but you have to love that kind of work and you have to love failing because most of research is just a lot of failures, but your career and your success and your fulfillment is based on the couple times it works.

Meredith Johnson
For the first time with this method, researchers could page through the book of our genome and highlight the sentences where recent human evolution with happening. They could see all this amazing stuff like evolving malaria resistance, like evolving the ability to drink milk into adulthood; other mammals only drink milk in infancy.

Pardis Sabeti
Though we see with the transition of the domestication of cattle this emergence of a lactase persistency; the ability to drink milk into adulthood and we can see those beautiful signals, very clear that this mutation emerged very recently in human populations within the last thousands of years and then and spread very quickly.

Meredith Johnson
And they found other things too.

Pardis Sabeti
We found a gene that's important in thermoregulation; the ability to sort of sweat and dissipate heat under strong evolutionary pressure in Asia and so we start to see these environmental pressures; the changing diets, the changing temperatures and climates, infectious diseases that are emerging, but over and over again infectious diseases emerged as a really strong factor.

Meredith Johnson
Using the genome like an archaeological record to look at human history and see what forces have shaped us. In the genomic era, the ability to read genomes on both sides is like a superspy power which brings us back to our arms race because their side is evolving too and much more quickly and more strangely.

Pardis Sabeti
We can only pass on those traits every twenty years to our children. They can pass on those traits to their communities. They can actually share their DNA between individuals in a population, which is very frightening because they can work so much faster or even if they're passing it on to their progeny, they're doing it over a short period of time.

Meredith Johnson
For most of our millions of years of human evolution we've relied on our naturally evolved defenses. Traits like sickle cell to protect against malaria and evolved responses like coughing to expel microbes, fevers to burn them up, but in the last century or so, really the blink of an eye when you think of our long history, we've started to understand how to be on the offensive. We've come up with amazing things like hygiene and vaccines and antibiotics and so for the first time we're able to act just as quickly as the microbes, but we can't get too comfortable. When antibiotics get over-prescribed or we don't take the complete course, it's like helping the other side get better at resisting our weapons.

Pardis Sabeti
A lot of people who don't understand evolution do understand drug resistance. They understand how a microbe at one point might be susceptible to a drug and then suddenly becomes resistant. That's actually evolution in action.

Meredith Johnson
And now some kinds of disease microbes are developing resistance sometimes even before the drugs get out of clinical trials.

Pardis Sabeti

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It actually has evolved to develop resistance faster and it's had to do that. It suddenly recognized in a way that these drugs were going to come at it and it's developed a way to quickly change its genome to work faster and so that is the frightening prospect for people working in the field of infectious diseases that these microbes, the more drugs we put at it, the more it's changing itself to be able to respond quickly to drugs.

Female Speaker 1
That's so scary.

Pardis Sabeti
It is. It is, but the thing about it is I have a lot of also faith in the ingenuity of human populations and so the fact of the matter is human innovation is also increasing at a scale we've never seen before, right? Year to year there's a quickening.

Meredith Johnson
While our bodies might adapt slowly, human culture and innovation is moving really fast. If human evolution can't keep up with disease evolution the hope is that our science can and this quickening has been critical in fighting outbreaks of emerging diseases like Ebola. Sabeti's lab is on the forefront of the battle against infectious diseases. They're sort of the intelligence division.

Pardis Sabeti
My lab is still really focused on understanding the genomes and developing tools to interrogate genomes and so we're one piece of the puzzle. We get the information, we understand what microbes are circulating and how much diversity exists in different microbial populations like the work we did in the Ebola outbreak to understand how quickly the virus is changing and what all diversity existed in the population.

Meredith Johnson
So back to Ebola. In June of 2014, health workers on the ground in Sierra Leone sent blood samples from infected patients to Sabeti's lab. Her team started sequencing the virus immediately and they released the results on a website in real time so scientists from anywhere in the world could see what they were up against. This was the first use of real-time DNA sequencing in the middle of such a deadly disease outbreak.

Pardis Sabeti
And that information becomes really important for individuals developing diagnostics and vaccines and therapies because fundamentally all of those things are based on the genome sequence of the microbe.

Meredith Johnson
From those sequences, Pardis Sabeti and her team were able to work out clearly that the virus was spreading human to human, not from mosquito bites or in the air or in the water. In fact, they were able to find that the virus had started in just one person and as the virus spread and multiplied they could see how it mutated. As it jumped from person to person it had a mutation about half the time and the picture that emerged was a virus that was more like a swarm of bees in a single organism. Because Sabeti and her team could look into the genome of the virus and watch how it was changing and evolving scientists could quickly update tests and diagnostics as Ebola shifted.

Pardis Sabeti
But one of the reasons why we want to keep doing it over time, we don't just get one genome sequence and leave it at that is because the microbe evolves over time, so we want to be tracking it in real time.

Meredith Johnson
And understanding our own adaptive responses is another big part of it.

Pardis Sabeti
You know, your human evolution is not happening fast enough that we need to be quickly responsive to it, but we do get clues from how we've evolved in the past so as we understand which mutations have allowed some people to survive the disease and others to succumb to it, we can begin to understand okay what would therapy look like? What might we target?

Meredith Johnson
Researchers can use the information about the responses that we've evolved and the ways the microbes are adapting to us and our medicines to develop completely new therapies that otherwise wouldn't be possible.

Pardis Sabeti
There's an importance in both things. There's an importance of quickly developing things that can translate into actionable diagnostics, vaccines, therapies, but there's also importance of really understanding the whole mechanism because that can get us to even something more powerful.

Meredith Johnson
In the evolutionary arms race between us and microbes in this high-stakes battle for survival, they might have numbers on their side, but we're the ones who have science and medicine and teamwork. Even though we haven't understood evolution for very long we're coming up with

exciting new ways to fight based on insights into genomes and how they evolve and I'm betting on team human.

Many thanks to Pardis Sabeti for sharing her work and her music. Besides being an amazing scientist who uses her understanding of evolution to help in the fight against infectious disease around the world, in her spare time, she is an indie rock band called Thousand Days. This is her music right here. We'll share a full song after the credits so look for links to find out more in our show notes.

Origin Stories is a project of the Leakey Foundation. The Leakey Foundation advances human origins research and offers educational opportunities to cultivate a deeper collective understanding of what it means to be human. We provide venture capital for scientists through research grants and share their discoveries through our podcast, website, and lecture programs. We also give scholarships to students from developing countries to attend field schools and earn advanced degrees. That's L-e-a-k-e-y foundation.Org. You can also find and follow the Leakey Foundation on Facebook and Twitter. For a limited time, all donations to the Leakey Foundation will be matched. So double your impact on science by going to the leakeyfoundation.org/donate and make a tax-deductible gift today.

This episode was produced by me, Meredith Johnson. Our editor is Audrey Quinn. Our theme song is by Henry Nagel.

Thanks for listening and here's "Turkana Boy" by Thousand Days.

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