Episode 39 – Ali Torkamani: Preventing heart disease with personalized genetic testing

Drew (00:03):

Good day to you listeners, and welcome back to Science Changing Life with your host Drew Duglan. Today we look at the power of our genetic code to predict our health and future risk of disease. I'm joined by genomics expert Ali Torkamani, who is at the forefront of using digital apps as a way of helping people cut their heart disease risk. So let's join Ali as he explains his early interest in evolution, which then primed him for his eventual academic path in genetics and data science.

Ali (00:30):

Born and raised in Los Angeles, California. My mother is a math professor and father, a computer scientists, both of Iranian background and I guess a a lot of Western Asian or Asian countries. I guess in general, academic performance and achievements is, is pretty important. You know, it's like number one, <laugh> on the list practically, you know, they really pushed academic performance, kind of the importance of science and obviously mathematics as well. So I would say my mother really like exposed me to just various topics, uh, pretty early on, scientific topics. And one of them was evolution, essentially. And I thought it was fascinating and sort of wondered, you know, about it, why are we here? You know, why are, why are we there way we are? And all that Darwinian evolution really just relates, uh, relates to genetics, evolution of genomes. So really kind of like comes from like an existential place almost.

(01:39):

It's like, well, why are we here? What's our purpose? Why are we the way we are and why do we make the decisions that we do and all that? And I think a lot, a lot of that relates to genetics. Of course, genetics is unlike the only driver of, of these things, but I sort of feel like basically if you had enough information about someone, then you could predict what they would like, what they're gonna do next, uh, that sort of thing. Yeah. And genetics is a, is a big player that, so yeah, that, that's pretty much like how I first got interested in genetics and it kind of grew from there into the, the more computational sciences and that sort of thing.

Drew (02:18):

And when you were talking about your path there, you sort of used genetics and almost genomics interchangeably, and you are the Director of Genomics at Scripps Research. So can you sort of break down what that difference is there? Because I think people will have heard of genetics, but can you just remind people of what genomics is and the differences?

Ali (02:36):

When you think of genetics, you think more specifically of like inheritance, genetic inheritance, how do particular genes influence downstream traits or diseases or whatever? Versus in genomics you might be thinking more about the overall function of genes, how they relate to one another. Uh, and but that ultimately trickles down into how they're inner relations with, uh, one another lead to genetic phenomenon like inheritance of traits and, and diseases. So for me, they're very much tied together.

Drew (03:13):

Got it. But I guess it's more the full sets of genes with genomics and sort of the broader relationships then.

Ali (03:19):

Yeah, that's right.

Drew (03:21):

Cool. So within your sort of genomics team then at the Translational Institute here at Scripps Research, what is it that your team does broadly then, and what kind of problems are you trying to solve?

Ali (03:30):

So my research itself, I would say is broadly focused on genome interpretation. Is, is sort of how, how I would summarize it more or less if you have someone's genome data, their genetic data, uh, whole genome sequence data, for example, with or without, but usually with other types of data, health data, essentially, what can you tell them about themselves? So it could be a rare disease, for example, someone with a rare disease where you're using their genome to kinda identify the cause of, of the rare disease and, and hopefully a strategy to ameliorate the rare disease. Or it could be something somewhat more complex in thinking about like common diseases like heart attacks, strokes, diabetes. Then, uh, you know, you can also use genetic risk factors plus non-genetic risk factors, combining 'em together, make predictions about risk, and then hopefully again, come up with strategies to offset that risk.

Drew (04:36):

I know there are so many different technologies around now that have just really advanced the field of genome sequencing, as it were, including some of these consumer products like the 23andMe. So I mean, has that just been a massive revolution in the field and just allowed you guys to study so much more?

Ali (04:54):

Yeah, de definitely. So if we start from, let's say, when I started my PhD, basically the human genome had pretty much just been sequenced a couple of years beforehand, cost billions if not millions of dollars. And nowadays whole genome sequence you could get done for less than a thousand dollars. So yeah, I've seen it go from like one genome being this huge task that required like an international consortium of investigators to now, you know, pretty much anyone can go, you know, drop off a blood sample or whatever and get their genome sequence back in a matter of two weeks or, or even less, less than that really. And genetics is all about populations, basically. And the influence of each genetic variant on especially common traits is pretty small. So you need, you know, these thousands, hundreds of thousands or even millions of people with genetic data to kind of start relating genetic variation to outcomes.

VOICEOVER: Drew (06:09):

To try to get access to this population level genetic data Ali's team has developed a free downloadable app called MyGeneRank. This app looks at hundreds of different individual variations in regions of DNA and integrates the information to produce what's known as a polygenic risk score. This is the influence of multiple genes and how they might contribute to your risk of certain conditions. And Ali has been using these tools in a research capacity to try and understand the risks of cardiovascular disease as well as potential interventions.

Ali (06:40):

The purpose of of that app is really to collect genetic data and help data from people calculate their genetic risk score, return that back to them, and see what they do with that information. So in the, in the case of coronary artery disease, not only does, you know, having a high genetic risk or increase your risk for disease, but that's not really the most important practical use of that information. What I think is more important is not only do you have higher risk, but the benefit that you get from common preventative medications, statin therapy, which reduces your cholesterol levels, the benefit, uh, of those medications is enhanced in these people with high risk scores. And there's essentially a problem with adherence. People don't really like to deal with their health risks or reduce their health risks until something is actually going wrong, more or less. So we think genetic information, this genetic risk information could be one way to, to bridge that gap by identifying the people that are both at increased risk that isn't measured by the common ways of measuring risk, like your cholesterol levels, your blood pressure levels, uh, et cetera. And also knowing that you get more benefit from going on these preventative therapies. So yeah, encouraging, you know, the highest risk people and those people that would get the most benefit from taking these preventive actions.

Drew (08:13):

Right. And you've mentioned the risk of coronary artery disease, and I take it that's sort of one of the main, like the big main risk factor for having a heart attack, right. And heart, heart disease.

Ali (08:25):

Yeah. They're almost interchangeable. They are slightly different, but yeah, we use them kinda interchangeably, coronary artery disease, heart attack. Yeah. You know, number one or number two, depending upon when it's measured cause of death in, in the United States and, and developed, uh, world. So something you definitely wanna try to reduce.

Drew (08:46):

Got it. What is your opinion on the degree to which heart disease heart attacks heavily genetic versus all the environmental triggers that we are exposed to?

Ali (09:00):

So it varies from condition to condition, but for heart attack and coronary artery disease, the estimate is that it's about 50/50, it's about, uh, half genetics and half environmental factors. Actually, that's the case for many common complex conditions. What you can do is estimate how much genetics explains the variability of these traits in the population overall. For many of them you find that close to 50% or even more than 50% of variation in these traits is explainable by, uh, genetic factors. So that doesn't, that doesn't mean that for each individual it is 50/50. It does just means on average in the population overall what it amounts to. But for any individual, your genetics might be the primary driver or your lifestyle might be the primary driver. So there's gonna be a lot of variability from individual to individual. But overall, it's about, uh, 50/50.

Drew (10:03):

Have you used the app to look at your own genetic risk score? And if so, has it prompted any changes to your lifestyle?

Ali (10:13):

Yes I have. I am borderline high genetic risk. So we consider people in the top 20%, 80th percentile or higher to be in the high genetic risk group. And I think I was like 82 or something, uh, like that 82nd percentile. I didn't start a statin yet, although it started my gene rank. I was under 40, but now I'm over 40, so maybe I might have to start thinking about that. I would say I leaned more heavily into dietary behavior change and checked my cholesterol, made sure it was low. I did end up lowering my cholesterol pretty substantially through just lifestyle changes. Although maybe there's some, I've reversed some of that now, so who knows, I might, I might have to go <laugh>, go back and uh, and adjust that. But my father takes statins, he has high cholesterol levels. So to some degree, my family history sort of inspired putting this together and making the information available. To some degree I am a little bit worried about it for, for myself cause of, uh, my family history.

Drew (11:21):

Now, in terms of the big population level data that you were discussing with the, uh, genetic risk scores for heart disease, have you seen major differences between, say, men versus women, different racial or ethnic groups? What does that demographic difference look like? Do you know?

Ali (11:41):

Yeah, so, you know, men versus women, in terms of the risk for coronary artery disease, there's no real differences as far as I've seen, but in terms of like ethnicity or genetic ancestry, there, there are at least differences in how well we can measure genetic risks. So most of these large studies have been done in populations, mostly European origin. So the genetic risk scores are most effective for identifying or predicting risk within that population. The other interesting part of it is that different genetic risk factors have different frequencies in different populations. So if you look at just like the raw distribution of genetic risk scores in different populations of different ancestry, you get different averages essentially, where some populations have a higher average than others. Now whether or not that means that they have a higher genetic risk or not is, I would say not a hundred percent clear or maybe not even correct.

(12:47):

Cause many of these genetic markers are not directly causal, they're just sort of correlated to risk. So we return genetic risk information on this zero to a hundred scale relative to people that are similar to you in terms of genetic ancestry. What we're doing is essentially comparing you to people who have similar genetic ancestry and sort of normalizing you to that scale. So you're on a zero to 100 scale relative to people with that have similar genetic ancestry as you do. So that's still sort of a, a big unresolved problem in the use of these genetic risk scores is making them equitable, making it so that, you know, e every while everyone does get information out of these scores, but making it sort of equally useful, uh, across all genetic a and that's kinda, you know, it's just a question of data essentially.

Drew (13:44):

And in trying to build this bigger data pool, do people worry about privacy? What has kind of the response been with some of these tools?

Ali (13:51):

Yeah, absolutely when I go say talk about the app to a non-scientific audience, just to sort of inform them about it, uh, you know, maybe encourage them to sign up, that sort of thing. Pretty much the most common question I would get would be something like, are you related to or work with any pharmaceutical companies or insurance companies? They're like, no, you know, it's just, just for

research. Uh, we won't share your data with anyone. Keep it private. Uh, but yeah, it's, it's certainly on people's minds privacy, especially as, as it relates to genetics and I think rightfully so. So I, I think overall we need laws better protections in terms of like non-discrimination as it relates to genetics to encourage people to use, you know, generate that information, use it and, and share it. Uh, really.

Drew (14:49):

Well. Broadening this up to other diseases, I did have something that I wanted to get your take on. So it seems like some people with certain blood lipid profiles that put them at risk for cardiovascular disease may also have increased risk for neurodegenerative disease. I've heard like Alzheimer's. So could your app potentially predict that kind of risk as well and other areas of study like that which are, uh, currently of interest?

Ali (15:13):

Yeah, absolutely. So we probably wouldn't say, you know, get your coronary artery disease genetic risk score. And that might relate to your say, Alzheimer's disease risk. But for any common condition you can think of like, you know, Alzheimer's disease or other neurodegenerative diseases, there is another genetic risk score, another polygenic risk score that would relate to that, that would be predictive. Our ability to predict them varies from condition to condition. But yeah, absolutely. I think any condition that you can, that there's like a common screening approach for is a good candidate for the use of genetic risk information. So like breast cancer, prostate cancer, colorectal cancer, those are the ones that really come to mind, uh, for me as where you can use genetic risk information to either encourage people to go get screened or accelerate their screenings. So the screening for these cancers tends to be age-based essentially.

(16:14):

It's just like a blanket, but again, that's like just a population average. But if you know your individual genetic risk, then let's say, you know, you're supposed to start screening at age 40, let's say if you have higher risk at the age of 35, maybe you have the risk of an average 40 year old individual. So you might start screening at the age of 35. And then, you know, getting back to the topic of neurodegeneration that you brought up, depends on who you ask, but there's experts of the opinion that basically even lifestyle change, that sort of thing doesn't change your risk for Alzheimer's disease. So there's not really much you can do about it. Now, not until there's therapies out there, but genetic risk can inform you in other ways, like life planning. You know, maybe if I have an ultra-high risk of Alzheimer's disease, I might wanna plan for long-term disability insurance or, and make sure I can get a caretaker, you know, so I don't burden my children when I'm older, that sort of thing. Anyway, point is that if it applies across a large set of conditions and there's a lot of different decisions that you can make using genetic risk information.

Drew (17:20):

Definitely. Yeah. And it's good that you brought that up, not just possible health changes, but also just thinking further ahead with all the other logistics in life. And you know, as we think further ahead, how do you think these apps, like MyGeneRank and other genomic data is gonna be integrated with other tools we have in the future?

Ali (17:40):

Yeah, so absolutely it can and should be integrated using all of these various ways of collecting help information about yourself from biosensors to other digital devices, to other genomic approaches like

the microbiome. The way I think about it is that your genetics, your polygenic risk score, or genetics in general sort of defines your potential at birth to experience, let's say these different health outcomes. And then as you age and interact with the environment, then your genetics or your risk gets expressed in various different ways, like your cholesterol levels or like the composition of your microbiome or your heart rhythm, you know, that could be measured by a biosensor, for example. So then when you start incorporating these other tools like biosensors, continuous glucose monitors, et cetera, now you're getting more detailed information about your current health status.

Drew (18:44):

Well, when you're not consuming genomic data, Ali, how else do you like to spend your time outside of the, uh, institute?

Ali (18:52):

Yeah, you know, when you sent this to me, I was like, this is gonna be the hardest question <laugh> that you asked me. Cause I don't have a good answer, really. No, I, um, you know, I like working out, I like going to the gym. That's like my hobby probably.

Drew (19:04):

See that's for getting your risk lower, surely <laugh>.

Ali (19:07):

Exactly, exactly. Yeah. You know, multiple benefits, you get the, you get the stress release. Yeah, you get the, uh, you know, being strong is nice, the being able to move really and uh, and all that. And uh, yeah, I think, I mean, I think working out is, is fun actually. You know, and then besides that, kids, my kids occupy a lot of my time these days. They're six and eight years old, so Oh

Drew (19:33):

Wow. Busy.

Ali (19:34):

They always want my attention. And then yeah, if I get the chance to play some video games, uh, also, but that happens a little bit less these days.

Drew (19:43):

<laugh>, <laugh>, Hey, are your kids interested in evolution and <laugh> Darwin?

Ali (19:50):

You know, I haven't pushed anything on them. I've taken the opposite, uh, strategy I guess as my mother. I just, uh, I just sort of let them be on their own. Sure. You know, we take the, take the, MyGeneRank empowerment approach, I guess, you know, show 'em how to use a computer, show them how to access and retrieve information and you know, let them go discover whatever they want to discover <laugh>. I see. So, no, they, they haven't gotten into, into the genetics yet. They're, you know, they're more on the video game, uh, side of things.

Drew (20:23):

Cool. Well maybe they'll be data scientists then?

Ali (20:25):

<laugh>. I hope so. That, that's what I sort of subtly encouraging my, uh, my son, especially the old older one to, you know, get him to do some Minecraft, uh, programming. Uh, for now there's some like block programming you can do in there. Yeah. His first kind of step towards becoming data

Drew (20:43):

Scientists. I'm sure plenty of software engineers got their start playing video games.

Ali (20:48):

So Oh, I'm sure. Yes.

Drew (20:49):

Cool. Well, hey, with my final roundup question I wanted to ask you, you know, if you could give one piece of advice or your wisdom to anyone in the realm of work or career progression or life health, whatever it is, what would it be and why?

Ali (21:04):

Good question. Pursue your passions and play to your strengths. Uh, I think, so for me, you know, being a professor at Scripps studying genetics, uh, et cetera, it's a job, obviously, but at other time when you're just doing the research, it doesn't, you know, it doesn't feel like a job. It's like a feel feels like a, a, a hobby or a passion. And I think that's a, that's a big part of why I've been able to kind of get where I am in, in the field. I think it's that combination of something I'm passionate about from the computational side, it matches the strengths that I have. You know, it just makes work and life more enjoyable, I think. So, yeah, I think don't follow a path just because you feel like that's the path that you've been told you need to go down or it's the, you know, the right path or whatever. I think it's really important to, you know, follow your passions and, and, and play to your strengths.

Drew (22:04):

Solid advice there from Ali. And that is certainly a winning combination of passion and strengths. Many thanks to him for joining us today and showing us the ever-evolving nature of precision medicine. In the show notes, we'll have more information on Ali and these digital tools, as well as links to the latest features, profiles, and videos from the Scripts Research Magazine. If you enjoy what we're doing here, please subscribe and leave us a review as it will really help with those podcast algorithms. We'll have more fascinating discussions coming your way soon. So until then, stay curious and be well.