Whats the difference between genetics and actiionable genomics? It's all in the reporting.

Dr. Joseph M. Raffaele, M.D.
Kashif Khan

Dr. Joseph M. Raffaele, M.D.
Hello, welcome to another episode of the "Telomere Summit". I'm your host, Dr. Joseph Raphael. Today, I am very pleased to have on the show, Kashif Khan, the founder of The DNA Company. He is the chief executive officer and founder of The DNA Company where personalized medicine is being pioneered through unique insights into the human genome. With the largest study of its kind globally, The DNA Company has developed a functional approach to genomic interpretation, overlaying environment, nutrition, and lifestyle on the genetic blueprint to create personalized and deterministic health outcomes. Welcome Kashif to the "Telomere Summit", I'm really looking forward to having you. I looked at your bio and you have a lot of interesting details in there, but why don't you tell me a little bit about your story and how you came from not being in healthcare as an entrepreneur and then to creating The DNA Company.

Kashif Khan
For sure, yeah, it was for me a need, I was sick. As many people you find that sort of get into this journey of healing themselves really. It gets driven by that a lot. And so, I come from a completely different industry, I was a PR and marketing guy, so I used to help startup to midsize companies grow. The advisory they needed from the PR marketing to everything else that they didn't even know they needed. And in that journey, I got pretty sick. I'm 42, I was 35 at around the peak of it and I had eczema, psoriasis, constant migraines, debilitating migraines. My business partner used to have to drive me home because I just couldn't function. Acid reflux, I had depression issues, anxiety issues. There's just a whole bunch of stuff that made be almost dysfunctional. So, in that, I was going to various clinicians that were solving all these things as a multitude of different problems. A pill for this, a cream for that, to scan for this. And that's what I believed was the correct path, because you grow up with your doctor, which I did, and you kind

of feel like they know me in years. I do need to mask each one of these things and get rid of them, that's the check mark for success. The eczema's gone. You don't even ask why I got the eczema, but let's just get rid of it. And it was in that the things weren't gone, it kept manifesting in different ways where there was multiple things. So, I took charge as many people do. I started speaking to friends that I knew that were into functional medicine that understood sort of root cause. And I started to slowly heal things and there was still this threshold I couldn't cross of being healthy. The problems were gone, but I didn't feel great. I was still not in good shape, et cetera. That's when I landed on genomics, because the true deep dive of why was I getting stuck? Well, I need to understand how different choices are different for me versus another person and another person and another person. And your genetic blueprint, that code, that is not just about ancestry and what color your eyes are. There's so much more to it if you understood it. That's what made me cross that line from masking symptoms to truly being healthy. I'm not sick anymore. I'm probably in the best health of my life. I'm 42 years old and I haven't had a cold or flu in four years, I don't have allergies anymore. So, by digging deeper and deeper and deeper and peeling back those layers, I got healthy to the point where I took my marketing company, gave the keys to the staff and literally walked away and said, "Thank you for your work, you keep it." I found what I got to work on and I personally poured my own money into it and we built it and here we are today.

Dr. Joseph M. Raffaele, M.D.
Wow. That's a fascinating story. I mean, when we do hear it, at times, people have a challenge that they have to confront. "Lorenzo's Oil" for instance, that movie, where they have to find the cure for their kid's illness and you had to find, really the basis of why you were suffering from these things that were being treated in sort of a whack-a-mole kind of fashion with allopathic medicine, the way it goes at it. So, you started The DNA Company at that time, or you were in a different business, a supplement business--

Kashif Khan
Yeah, it's funny, I actually met you around the time, right around this time. We were at A4M, you were there and of all the people there, I really sort of appreciated what you were working on 'cause you were going beyond how do I mask the system and you were trying to determine people's biological age. And things like you kind of inspired me also. And I saw that there's so much more to how our body is wired than just the symptoms we're trying to suppress. And we can learn so much more. And so yes, we started off developing solutions from the genome, which is how I carried myself. I learned, and we can get into these things--

Dr. Joseph M. Raffaele, M.D.
Yeah, tell me a little about that, we have time.

Kashif Khan
So, one example, I talked about depression, I have family that as I grew up, I saw addiction everywhere. My uncles, my cousins, all alcoholics, all successful also, but all alcoholics. And when I get to the genomics of that, it will make sense. There was also a lot of illness, a lot of asthma, eczema, all these types of things and there was depression. So, now what I understand about myself, I'm also entrepreneurial like my family and when I look back now that I've learned, ancestrally, my grandfather, great-grandfather, they were all entrepreneurs. I have what's called warrior genetics up here. There's warrior or worrier, those are kind of the extremes and then most people are in the middle.

Dr. Joseph M. Raffaele, M.D.
Warrior or worrier, like worrying about things.

Kashif Khan
Exactly, yeah. With the same context, two different results.

Dr. Joseph M. Raffaele, M.D.
So, fight or flight, warrior or worrier kind of thing. Very interesting.

Kashif Khan
Why is that happening and what does this have to do with depression and addiction and all these things? And entrepreneurial-ism why is it all the same bucket? So, when it comes to pleasure and reward, those two things that you feel. You require dopamine for those. So, dopamine is deployed, you then bind it and you experience that pleasure reward. Well, there's one gene called DRD2, which determines how dense your dopamine binders are. And I have the least sparse, slim to none density. So, I feel things way down here. Then there's a gene called MAO, which is breaking down the dopamine in an attempt to bring you back to your normal state. There's an enzyme produced by COMT, another gene which is well-known, which then clears, it's a clearance enzyme. So, I have the least density of dopamine, I have the fastest MAO that as I'm experience this thing, it's already being broken down and I have the fastest COMT that's sweeping everything away. So, I hardly feel, and when I do, it lasts this long and it's gone.

Dr. Joseph M. Raffaele, M.D.
So, you need a dopamine drip, basically.

Kashif Khan
I just don't get it. And so there's really three potential outcomes and I've experienced all three. Depression, 'cause you're not getting that hit, Addiction, because you go down the pleasure route and you feel that with pleasure and you need more and more and more and more or achievement because you go down the reward route. And you're fueling it with, "Whatever I did yesterday isn't good enough." And why does a marketing guy walk away from his company and go invest into biotechnology when he has no business doing so? Because that reward and that opportunity is too much for me, I need it. So, this is why me, I have been through depression, I have been through addiction and why was my family, they were all successful business people, all addicts at the same time? Because they would reach that plateau in their business and they wouldn't push for more and then they would go down the pleasure route and go into addiction. So, that one simple profile, there's so much more to "genetics". From this gene means this, this gene means that, to the functional, "How does the body actually work? And how do we reverse engineer what genes are instructing each step in that process?" And now the condition, depression, addiction, achievement, being a condition like you're striving for it, can be unpacked into why is it happening? Flip opposite.

Now imagine I had the maximum dopamine receptors and I had the slowest clearance enzymes, I would then appear as opposed to being reward-seeking and constantly saying, "Yes, yes, yes, more, more, more". I would be more flaky and not interested. And by the way, my business partner is that, he's the exact opposite of me. And for the first two years of working together, we had a lot of issues, there was constant friction 'cause we'd be in a meeting and we'd leave with our 10 action items. I could not rest until I worked on them. He would not even touch them and think that he already did them because his sense of reward was so easy to get that he wasn't really pushed by these things, but give him that thing that truly gave him that sense of reward and he would binge and get lost on it. That's the difference between addiction, which is constant elevation in seeking reward to binging where you don't need to do it every day, but when you do it, you're lost for eight hours. So, he would come back, the two things that he actually enjoyed working on, this stack of paper like this, like, "How did you do that?" For me, it's all calls, notes and summaries, but I get everything done.

Dr. Joseph M. Raffaele, M.D.
Right.

Kashif Khan
Right. So, that one simple thing can completely change the way you think about yourself. And that's just one of the things I heal and it goes on and on and on from there.

Dr. Joseph M. Raffaele, M.D.
So, initially you recognizing those things as helpful, but there were supplements that you took and you had a company that .

Kashif Khan
So, what is it about genomics that has not been actionable? There's been these hardcore diagnostic, "You got a rare genetic cancer", or, "You have sickle cell syndrome". That's a genetic condition. It's maybe 2-3% of healthcare. We know that of our $4 trillion healthcare budget, 90% is chronic disease, which you're not born with, these are not genetic conditions. These are environment, nutrition and lifestyle conditions.

Dr. Joseph M. Raffaele, M.D.
Or polygenic, many, many genes involved.

Kashif Khan
Yeah, all these systems that interplay with each other and all of a sudden that profile is at a high-risk. Versus, "Hey, this gene means you got an 80% chance of Alzheimer's."

Dr. Joseph M. Raffaele, M.D.
Right. Exactly.

Kashif Khan
What does that do for me? Other than, okay, now I have anxiety for the next 30 years, or to ask the question, "Well, doesn't that mean that 20% didn't get Alzheimer's with the exact same genetics?"

Dr. Joseph M. Raffaele, M.D.
Yeah well, I think with the Alzheimer's, or the Apolipoprotein E gene, that is one of the most highly characterized ones for Alzheimer's disease risk. And we know what it is, we know what the variations are, two, three, and four. But what's interesting to see is many people, and we know people that inherit two fours and have tenfold increased risk of Alzheimer's disease, what are the genes around it that enabled some people to not express the Alzheimer's and that's sort of the genomics that sits around it. Yeah, you know you have this really bad thing, but it's not like Huntington's, or at least maybe there's something about Huntings that we don't know about that could fix that. But is there something to look at as Dale Bredesen does in his protocol, a multimodal approach. And that's, I think what you're talking about, is functional

genomics versus genetics and genotyping, which maybe you can talk about how your... Because there's a lot of DNA companies out there that do DNA sequences. I'd be interested to know how your approach, what you do, is different in your company. Well, just sort of talk about generally what gets done.

Kashif Khan
Sure, so that what you just described is the key element. It's the interpretation. Anybody can go run a DNA test, in fact, anybody listening here can go buy a sequencing machine, put it in their basement and start running their own DNA.

Dr. Joseph M. Raffaele, M.D.
At this point, it's getting to that, yeah, exactly.

Kashif Khan
What does it mean? What do you gleam from that information, the interpretation? That's the difference between a great clinician or somebody that's more like an order taker or prescription writer, it's the interpretation. Same thing genetically. I can tell you about your APOE gene and what does it mean, but then how am I interpreting, again, that multifaceted insulin resistance. It's another co-factor.

Dr. Joseph M. Raffaele, M.D.
Sure, absolutely.

Kashif Khan
Your reward seeking behavior, how do you actually deal with food? Are you an addict or a binger? Do you lean on food as a coping mechanism because your serotonin levels are screwed up? Those types of things. So, when you start to package and create these profiles that are functional in nature, meaning don't tell me my risk without telling me what to do about it. And they typically can't tell you what to do about it because they haven't understood why they get to the risk. Let me give you an example. I'll give you a great example that really paints a picture. So, and I'll pick cardiovascular disease because that's what touches the number one group of people. It's the biggest killer in the United States, 18 million people globally last year. 50% of people, unfortunately, in the US are expected to have some sort of cardiovascular issue. And then you wonder why. And if you go to most genetic testing websites, they will tell you, "We deal with this condition, this condition, but cardiovascular is a lifestyle disease." Meaning that you have to make wrong choices to get it.

Dr. Joseph M. Raffaele, M.D.
That's not true

Kashif Khan
Yeah, so those those wrong choices are the load on the suboptimal genetics that just makes it express faster. It's like I have a Ferrari. Great, beautiful. But what if I take the Ferrari off-roading? That's the difference between that answer of you're not born with it, you're gonna get it. What did you do with what you were given? Those cards you were dealt. And that's environment, nutrition, lifestyle, which leads to what we call epigenetics. So, that load that we create. So, cardiovascular, let's use that as an example, really paint the picture for everybody. My good friend who was actually our first investor in the company, he's a pharmacist. And he came to us because for an entirely different reason, he had been on Lipitor at the age of 38 and his cholesterol numbers just wouldn't stop rising, kept going up. He said, "I'm a pharmacist, I can't figure this out. Do you guys have a Pharmaco genetics test?" Which is very common nowadays, where you can figure out what type of drug you need to what dose, what gene metabolizes the drug. I said, "Before we get into that, what if you don't need the drug? What if we can get you off of it?" He said, "No, that's not how this works." He's a pharmacist, right? He said, "I just need to know what dose I need." I said, "No, just let me work on this for a bit.

And if we don't get it, then I'll help you with your thing." So, we ran his genetics and what do we find? That 9p21, which determines what quality of endothelial, that inner lining of the blood vessel, what quality you have, stainless steel or paper thin. He had paper thin. Worst quality hardware. And we know that cardiovascular disease typically isn't in the heart, it's usually in the arteries around the heart, calcification, plaque buildup, all those things. So, he had really bad quality hardware, which means more prone to inflammation. Again, take that profile, put it on a beach in Aruba with nice fish out of the sea and good sleep and everything, he's not getting sick. You have to have the load. Then we looked at his glutathionization pathway, your detox pathway. And this is where we look at something unique, called a copy number of variation. So, anyone here that's done a genetic test has probably received a list of what are called snips. It's like a spelling mistake in the gene and if that spelling mistake is there, one letter as a T instead of a C, the gene is functioning different. What if you don't even have the gene? Literally you didn't get it.

Dr. Joseph M. Raffaele, M.D.
Deletions, or copy number variation.

Kashif Khan
Or there's an extra copy. You could have an extra copy of the gene. So, now imagine if this snip or spelling mistake is so impactful, what does it mean when you don't even have the gene? You don't have the instruction for that function. So, in glutathionization, we look at three things. We look at first line of defense here. How do I filter things that I breathe in? 'Cause that's where things enter my body.

Dr. Joseph M. Raffaele, M.D.
Can I just interrupt you for a second? You're saying glutathionization, I'm not familiar with that. Sorry, do you mean glucoronidation or is?

Kashif Khan
No, glutathion, the actual use of glutathione to bind on the toxins to send them to the liver to metabolize and then clear.

Dr. Joseph M. Raffaele, M.D.
So, that's based on levels of glutathione or what is it?

Kashif Khan
It's based on the instruction to glutathione and that's literally what I was just about to tell you, that what are your genes telling whether it's... And this is why precursors work so well, because they don't need the instruction, they just get the work. Like NAC's , alpha lipoic acid. So, if you, in your blood, you're supposed to have these soldiers going around collecting and binding onto toxins to instruct to clear. The GSTT gene, it's possible to have a copy number variation. Meaning you didn't even get it from mom or dad. And we have many clients who have zero copies like this friend of mine. So, anything that enters the bloodstream is not being cleared. That core process of clearance, he just wasn't doing it. There's also at the gut, that's another place where things enter your body, you're meant to clear. There's a gene called GSTM1, he didn't have it. Forget about what version, what quality, he didn't have the gene. So, this instruction, and then you wonder why are some people so much more prone to colitis, Crohn's, leaky gut, et cetera? Well, if I don't have the instruction to clear toxicity of the gut, imagine the inflammatory load that's being caused. Then there's GSTP1, which is kind of first-line defense of the lungs. And this one, you can't have a copy number variation, it's about the snip, but he was also suboptimal there. So, now we know that he was probably suffering from a toxic load. Then we look at methylation, which is the anti-inflammatory response, because if he has this toxic load, he's gonna be inflamed. These free radicals are free flowing, causing damage to the vasculature.

and we already know he has a bad quality endothelial. So, it's more easily damaged with abrasions, inflammation, et cetera. The body is supposed to methylate. There's a methylation cycle, it's not just the MTHFR gene that everybody hears about. There's a whole upstream and downstream that support it. And now you can look at that whole system to understand how well somebody's doing that. If you're sub-optimal in that whole system, I have the toxins free flowing. I have a bad quality hardware, it's now getting inflammation and I don't deal with the inflammation well. Now we've understood the profile. Full of toxins, bad quality hardware, can't deal with the inflammation. Even then this person may never get sick because something has to cause the inflammation. Then we ask him, "What do you do?" What was he doing? He was golfing four days a week. When you're golfing, you're in a golf course for four hours at a time breathing in all those toxic pesticides that he did not have the genetic ability to clear. And in Canada where we are, it's even worse because there's no regulation because we have a heavy winter and we need to sort of keep up. And so, there's a heavy toxic load in that greenery that makes it so nice that he was breathing in for four hours at a time, four days a week that he could not clear, now wreaking havoc through his system. That's coming in from the outside. There's also mitochondrial clearance, which is in your cells in the process of using oxygen and nutrition to create energy. They also create oxidants the by-product. There's different genetic levels of being able to clear that oxidant or by-product. He was way down here. So again, the load on the cells was very heavy.

So, now we know that he has inflammation here because of all this toxicity, he's not dealing with inflammation well. What is the body's response to inflammation in the endothelial? It will actually deploy cholesterol as a hormone to reduce the inflammation. What happens when cholesterol meets toxicity, it hardens and gets deposited and you get the beginning of that cholesterolemia for which he was taking a pill to treat that very last layer of the onion. There's so many more things that are happening for 5, 6, 7, 10 years prior to, which is why chronic conditions are the way they are. You're not born with them. You're not born with type two diabetes. You have to do something wrong for a number of years to get to it and then when you're in it, you have to solve the wrong problem to stay in it. And that's what was happening to him. He was masking the symptom as opposed to understanding he just doesn't detox well, or at all we should say. And now he doesn't deal with the inflammation from that well and he is weak in his hardware here, so he's gonna get inflamed here and the body's gonna try and help him by sending cholesterol, which then creates that buildup. So, he no longer is on a pill, by the way, he's off Lipitor, he's healthy.

Dr. Joseph M. Raffaele, M.D.
So, his cholesterol actually came down. Cholesterol being deposited in the walls is different from creating circulating cholesterol. It's kind of interesting that his cholesterol, did you have a

coronary calcium score or anything prior to that to see how much damage he had? He had probably had a CIMT, he did for the thickness of his intima, which is the measure of the endothelium basically. But in any case, I mean, I guess there wasn't a lot of longevity in his family either, probably.

Kashif Khan
Well, this is why him being Pakistani background, why are all Pakistanis and Indians told that cardiovascular disease is in your genetics? The heart is fine, it's all of this around it. And the thing you just said, it would have been even more exaggerated if his lipid transport was so optimal also, which it wasn't. That would have been another layer. And here's another layer, brown people, sub-continent people, Indian, Bangladeshi, Pakistani, have the same insulin response from saturated fats as everybody else does from starches and sugars.

Dr. Joseph M. Raffaele, M.D.
Now that's fascinating, that's not something I knew. I had a couple Pakistani patients who have had pretty bad cholesterol at younger ages and evidence of heart disease in their late thirties. I had a guy that used to swim at my club, a really fit guy, is there every day doing laps. Probably because he had a family history of heart disease. And then one day I didn't notice him and then for another week I didn't notice him. Somebody told me he had died of a heart attack at age 30-something. Crazy stuff. Now, also incidentally, some of those have had very short telomeres as well. The patients that have had early cardiovascular disease. So, we can talk about that in a little bit more. So, there are some pretty big differences then in genetics between certain populations and risk for cardiovascular disease. And that's something that people need to... And also you don't know necessarily. People don't always look like they necessarily are from Pakistan or have those genes in them. We're all finding out from these services that we have. Other ethnicities in us that we may not even know. So, it'll be good to open that door. Sorry, I interrupted your story.

Kashif Khan
No, no, that's fine. And that's the challenge, cardiovascular disease is one of those things where it's completely silent until it hits you. And 64% of women die on their first cardiovascular event.

Dr. Joseph M. Raffaele, M.D.
'Cause it's underdiagnosed for sure.

Kashif Khan
Undiagnosed, completely silent, no previous warning sign. And then that takes us down another path. Well, why has it hit women so hard versus men? Well, there's other layers of

inflammatory in cell that compound like estrogen toxicity which men don't suffer so much from.

Dr. Joseph M. Raffaele, M.D.
Or a loss of estrogen in menopause, which is the opposite side of it. Right, exactly.

Kashif Khan
All back to what you said, you have to interplay the systems and take it from this probability based, "You got 80% chance of something" to a certainty. Here's you, here's who you are, here's what your risks are.

Dr. Joseph M. Raffaele, M.D.
So, when somebody orders a test from your company, you obviously highly annotate it and do you do some... And I also read that you have the largest DNA database in the world, is that correct?

Kashif Khan
Yeah, for clinical reviews, meaning that this is the other guy. So, me coming from the outside, it was very easy to see what wasn't working. And what wasn't working when I came into the industry was that geneticists study genes, they don't study people. And then all of a sudden they're supposed to provide solutions to chronic conditions. This is why if you ask genetic companies, "Well, no, they aren't related to chronic diseases". No, you just haven't met any patients. You don't understand how things connect. So, what we set out to do, we said, "We need to meet every single one of our patients, at least during our research phase." So, we sat in front of 7,000 people, one by one by one by one by one, to understand. "Give us your healthcare history. Tell us about your family." Let's look at the phenotypes. How did things manifest?

Dr. Joseph M. Raffaele, M.D.
Oh, so that's very interesting. So, for your first 7,000 subjects or I guess, patients that you did extensive phenotyping on them from family history. What other kind of markers did you do? Out of curiosity.

Kashif Khan
Even physical traits. We've gotten to the point now where we can ask you questions that assume your genetics with a very high level of accuracy, because we've seen over and over and over again, when somebody's balding by a certain age, it equals a certain hormonal pathway, which also leads to prostate enlargement. When a woman is having certain physical traits, it is a very glaring red sign for fibromyalgia coming, or a rocky menopause coming, and we now

know what to do about it. So, those types of things work 'cause the same physical traits that equal this aren't limited to that they also equal other things.

Dr. Joseph M. Raffaele, M.D.
Yeah, sure. So, with that, so you then did some deep data analysis on your first 7,000 to make correlations between various changes in genetics, copy number variations, snips, et cetera, deletions. So, a lot of companies will specialize in what you were talking about earlier, the genetics of the mind, dopamine receptors, et cetera. Some companies will focus on 9P21, like Boston Heart you can get that for heart conditions. Some will do it for pharmacode genomics. You're, I take it a broader approach because I remember when I got my whole genome sequenced by Illumina, when they were doing it back in maybe a dozen years ago. The "Know Your Genome" thing, I got access to my genome, but it really is kind of useless to me because they told me, whether I had a risk for atrial fibrillation, whether I had a balding gene, whether I had a few traits that basically 23andMe gives you now. Aspirin sensitivity, that kind of business. But I could browse through it and look up RS numbers and snips but it was kind of useless. What's really important is having the phenotype that goes with the genotype and then analyzing it and telling a person exactly what does it mean. How is it actionable? What are your risks? So, maybe you could tell our listeners about what a typical report will cover from your company and how you go about doing that, that's different from what they've done with 23andMe, or people upload to Promethease or whatever to analyze their genome.

Kashif Khan
So, and what you explained is exactly what I experienced was broken. I knew that my genome was my blueprint. It's literally your human instruction manual, but the level of insight that I was being provided by genetic purveyors was not personalized enough. It was all general information and it wasn't pointing to the big problems. So, that's really what we did. We said in those 7,000 reviews, let's keep banking the insights, what are we learning? And take it away from genetics to profiles. Meaning, again, you can't be certain or actionable, clinically actionable unless you understand how things intersect, and that means building profiles or multiple things combined to one person. So, in doing that, we then said, "Well, how do we make this available to everybody? Because our clinicians know this, we know this, but we can't teach it and train it and expect doctors to use it when they're already so busy, that's difficult." So, we built an artificial intelligence platform that, it blew my mind when I saw this number, but it covers 200 trillion data points in order to populate the reports. And I had no idea that that's the level of computation that was going on in our heads when we were sitting with patients and working with them, but that's what it took. So, starting with people don't care about their genetics. If I give you a DNA report, what I want to know is what's wrong with me and how do I fix it? In plain English, tell me. And great, if you give me all the supporting stuff for me to spend

my time on in the evenings at some point, but right now, tell me what's wrong with me and how do I fix it? So, what we said is, well, that's where genetics is broken. I don't need to give you a list of genes, a gene report. I need to give you a list of conditions and how you rank in them.

Dr. Joseph M. Raffaele, M.D.
Conditions, your risk for conditions that you may even currently have that you don't know about and things that you may be doing, or that could cause you to have more risk or things that you should be doing to have less risk? That kind of stuff. Let's get into a little detail about that. Choose a particular one.

Kashif Khan
We broke it up into six main areas where after going through these 7,000 people, this is what everybody kind of needs to kind of optimize themselves and be a better version of themselves. And it's not clinical yet where we need an MD in between to diagnose.

Dr. Joseph M. Raffaele, M.D.
Okay, great.

Kashif Khan
So, what are those areas? Sleep, which we all know now is so important. But when you look at our sleep report, we could not make it without first understanding the brain, without first understanding diet, nutrition. 'Cause they all inter sync, like you said. So, sleep is a big one, mood and behaviors is the biggest report of the six that we provide. If I have your DNA, I don't ever need to speak to you to know how your personality works, how you deal with fear, anxiety, trauma, are you prone to PTSD, are you a procrastinator? Should you have been an accountant instead of a doctor? We know this about you.

Dr. Joseph M. Raffaele, M.D.
That's a big statement to make. I mean I'm not saying that you can't support it, but that's a big statement.

Kashif Khan
We literally work with executive teams to help them build their team at a consultative level 'cause we understand what people are actually... It sounds crazy but if you understand the dynamics of just understanding what neurochemicals drive what behavior, and then knowing the blueprint for how much you deal with these, how much do I create, how much do I bind, and how much do I clear? It's very simple in the end of the day. And we already know, it's already studied what these chemicals do. We've just never, other than measured in real time,

we've never understood the foundation, the blueprint, how is this person wired? And we're literally saying, here's your wiring, here's how your brain is wired, so that's the other one. Cardiovascular is a big one for us. So, diabetes, hypertension, stroke, cholesterol, anemia, all that stuff. Then we get into diet nutrition. So, it's not just your typical genetic diet report of eat more greens, eat less of that, we start with the brain. Are you a binger, an addict? Are you more emotionally driven towards food? The time of day when you should eat? Then there's carb metabolization, fat metabolization, insulin response, micronutrients like vitamin D, A, B, C, et cetera. Then we get into hormones and fitness. So, how is your hormonal cascade determining what your body looks like? Everyone gets stuck at these plateaus often because they're chasing goals that aren't relevant to them. I'm not designed to be a linebacker. I can't deadlift 400 pounds, but if I do work out the right way, I can look like captain America, perfectly fit. I'm not gonna be huge, so you have to understand who are you even designed for. And I give this example, it's funny, but Kim Kardashian and Kendall Jenner, they're sisters, but look at them. They have a different father, so the hormonal cascade is--

Dr. Joseph M. Raffaele, M.D.
One's an olympian, the other is not. So yeah, you definitely got different genetics. But you're absolutely right about that. I'm curious, so there's other companies that give athletic-type genetics and it's particular genotypes and I forget which snips it is, you either have propensity for fast-twitch muscles or are more slow-twitch, your mitochondria... How about, I just read something about elite endurance athletes having the most amazing mitochondria and do you look at mitochondrial genetics at all?

Kashif Khan
Yeah, we do, and that was the last of the six that I didn't mention was the immunity, inflammation and detox. It's your immune response, which is where we look at the mitochondria. So, the SOD2 gene determines how well you deal with oxidative stress.

Dr. Joseph M. Raffaele, M.D.
SOD2, Superoxide Dismutase 2?

Kashif Khan
Yes, exactly, yes. And that's where if you're not doing well there, you look at these marathon runners that are in their sixties. They're kind of retired and there's some that look great and some are all haggardly with their skin is all wrinkled. And why did they age so fast? Because of the amount of oxygen stress they put their system through that they weren't able to cope with because genetically they weren't wired for it. So, that whole ability to deal with mitochondrial, which supports so many other things. Disease is rooted in inflammation, we know that.

Inflammation is rooted in cellular health. If you don't understand how your cell is ticking, like what's going on there and what is it actually capable of, versus the load you're putting on it? Well, you're probably gonna get a disease of some sort, some chronic condition.

Dr. Joseph M. Raffaele, M.D.
Yeah, so that sounds like that's very actionable for people early in life to know about whether or not they should be one of those people who thinks it's a good idea or likes to, for some reason, do 10 marathons in a year. Maybe some people just aren't set up for that. Or if your company has some research in the report that shows what you can do to mitigate that, less, not healthy, but less capable genetic inheritance for a lot of endurance training. I mean, I have some patients that are ultra marathoners, they go run 100 miles in 24 hours, kind of stuff. You think that that would cause a lot of oxidative stress, but I guess the ones that are successful, it doesn't so much, or they just have great willpower, who knows what, but are there then in your report, things that you can, that you suggest based on the literature that can mitigate a lower functioning or a lower express level of SOD2?

Kashif Khan
Yeah, exactly that. So, now that we've identified what's going on, where do we need to focus, now what do I do about it? And in the reports themselves, we create some generalized recommendations that kind of cover how do you deal with these various conditions. When we get more prescriptive about something, we need a health coach or somebody in between. And so, we do offer programs where people can get coached by somebody or even at the clinician level, even working with clinicians like yourself to say, "You deal with the patient, we just provide the information and help you guide them through it." That also happens quite a bit. With us, we work with a lot of functional medicine doctors, et cetera. But yeah, the action items are built right in. They're in the reports because ultimately, okay, going back to that 80% chance of Alzheimer's, what did that really change in my life? I need to know why, and I need you to know what to do about it. That's really what the patient needs and that's what we brought things to.

Dr. Joseph M. Raffaele, M.D.
And so, your sort of patient will then get the tests, I take it's a buccal swab or something like that?

Kashif Khan
It's a saliva, yeah--

Dr. Joseph M. Raffaele, M.D.
And then how much of their genome do you run? Is it you have specific genes that you're looking at? It's not a whole genome sequencing?

Kashif Khan
No, and here's the other thing, just like yourself, how many people out there have had their whole genome sequenced to be completely underwhelmed?

Dr. Joseph M. Raffaele, M.D.
Yes, completely underwhelmed.

Kashif Khan
You've given me my encyclopedia, but I don't know how to read this thing. It's in a different language. And other than pointing out a few genetic conditions, which I don't have, I would already know that I had them. It didn't really do much for me. In the future, maybe, yeah. Something might come out of that. So, what we say is data's dumb unless you know what question to ask it. Data's just a pile of information. And this is another gap and it's kind of like a dirty secret, I would say, in the genetic industry where you wonder why is there so many concerns about data privacy and data being sold, et cetera. 'Cause to be straightforward, the DNA testing business is not a good business because I only need to test you once, your DNA doesn't change. It's not like bloodwork we're gonna come back to me every six months or year.

So, the model, it started off great and then the 23andMe of the world, those types of people that you mentioned, their investors started to say, "Well, what else are you gonna do? You sold this guy a test, this guy, then what?" They said, "Okay, well, what we can do that's reoccurring is we can sell data." But in order to sell data, that means your product is not designed for the person that's buying it as a, "How do I get my reports", it's designed for the buyer of the data. You have to collect what they need. 'Cause they're paying you a lot more money than what the test buyers are paying you. So, that's what ended up happening, we have these... Let's gather as much information as possible and then the AI and analysts and geneticists will comb through to find that needle in the haystack that may lead to some kind of therapeutic. And this is why, I think it was 2018 or '19, 23andMe raised $300 million from Glaxo, GSK. Well, you wonder why they're the ones that gave them $300 million, right? Because there's an endless pool of data to come out of it. So, what we said is that we know of the 22,000 genes in your body. Most of them, we're not gonna take action on. In fact, we only cover about 100 of the 22,000. And we test for about 600 'cause we believe there's others that are going to eventually be actionable. But

today-today, the report you get back gives you information on about 100 of them. And those 100 are in these systems. Hormones, which is so impactful, detox, methylation, mood and behavior, and some other various snips for diet nutrition, cardiovascular, some here and there things that we think are important. So, there's about 100 genes we look at. From there, I would literally, as a cliche would say money back guarantee. If we didn't give you more information than you got from a whole genome sequence. Because we interpreted it better by focusing on what actually matters and drawing more insights out of the important stuff. We give you hundreds of pages of information that's actionable, that's insightful. As opposed to here's your encyclopedia that you need to now go hire scientists to comb through that maybe to might tell you something.

Dr. Joseph M. Raffaele, M.D.
So, of the 100 genes you're looking at, are they in genes where there's a high percentage of variation in a population like the MTHFR gene where 30% has this and 2% has that? I mean, you're not really looking for rare genetic mutations. You're looking for ones that are more common, but when in combination with other ones. And so, you'll put them together, you'll say, "All right, you have X, Y, and Z. And this combination means this." That's different from something that says that you just have this snip, "Here are the papers that show what it's associated with, go read them and have a good time." You're giving a more... 'Cause I mean, the hundreds of pages and stuff to read about is great, but frankly, nobody's gonna read those. It's really, they're gonna want to read what is telling them what I need to do, how strong the evidence is behind it. Clinicians are gonna want that as well. I'm sitting here thinking, I want to order this test now and I'm really curious to see what it says about me. And these six areas that you mentioned. Is there interaction between the genes in area two versus area six that you also look at? Because there's probably companies out there that measure the snips in each one of these areas, right? You'd have to put them together perhaps to do it. Just how's it? Is there a single dashboard page as well where it's sort of like, this is you.

Kashif Khan
Yeah, so your first question about rare conditions, we don't do that. We believe that that's what the genetic industry is doing well, they're focused on it. They don't believe that genes mean anything more than that. Let them do that. We also believe that 90% of healthcare isn't that, it's chronic disease. So, the outcome of what we provide is three things. Prevent chronic disease or if you already have it, reverse it. Slow down aging, 'cause we understand why it happens and optimize performance. If you're healthy and you just want to know how to get the best version of yourself out there, we can do that for you. So, how has that reported back in terms of, yeah, everything intersects. If anyone tells you that this gene means this, without it correlating to other systems, they're only giving you 60-70% of the information because everything is affected

by everything else. And that's why our AI triggers 200 trillion data points. It's not just what does this snip mean? What does this snip mean if you have this and if you have this and if you have this and then if you don't have this and if you don't have that, 'cause it changes. So, in those reports, it's designed where you can look up anxiety and you can understand what is your risk and we'll tell you why, why do we say that you're more prone to anxiety because it's different for different people. And now you know exactly what to do about it. As opposed to saying, I have anxiety, I have to take a pill. Let me give you an example. My niece, she's now 14, just turned 14. Last year at this exact same time, November of last year, she had an anxiety attack. First time in her life, 13 years old. My mother, my sister and my niece lived together. So, my mother called me saying, "Get over here, your niece has an issue." So, she couldn't breathe, I called my pediatrician friend. He said, "Sounds like classic anxiety issues. Call me if anything happens again." Sometime later my mother called me. I was unfortunately on a call like this, so I didn't answer. And she was texting me, texting me, texting me.

She said, "Come over now, come over now." My niece had another anxiety attack and she fell over and hurt herself this time. She couldn't get up, she hurt her leg pretty bad. So, I called my pediatrician friend again, I said, "I don't know if she has a fracture or something. Can you help me?" He said, "I'll get you into this clinic." In Canada, it's all public healthcare, so there's long wait times. So, I went to this urgent care walk-in type hospital and we spent eight hours there. And the net result, there were scans, there was questions. The net result was if it happens again, let us know. The same question and answer I got the first time. And by that time I knew what it meant. It meant that if it happens again, we have to give her a prescription for an anxiety pill. That's what that meant. So, it happened again. But what happened this time is my mom called me crying that, "Your niece has left." I said, "What do you mean left?" She said, "I see a note here and she's gone." I said, "That makes no sense." The sweetest, most innocent girl, you would never even guess, there's no problems.

So, my mom's in an apartment building. So, I get over there and my niece is outside the front door. 'Cause that's how innocent she is, for her running away is like, "I went outside by myself." So, I went and picked her up, got her in the car. I said, "Let's go for a drive. What's going on? Are you being bullied? Tell me, I don't care, there's no judgment here." So, she actually didn't know. She said, "I just feel horrible, I just need to get out of there." She was actually just running away from herself, from being in that space. And then I just kind of slapped myself and said, "I have the girls genetics and I did what any concerned parent would do, call the doctor, "How do I fix this?" I said, "I have her genetics, let me figure out what's going on" and I didn't do that. Then I realized, wait a second, my mom's been calling me like monthly. So, I looked at the text message, and it was on the last one, and it was like clockwork a month prior. So, I asked my mom, "Is this timed with her menstrual cycle?" She said, "You know what, now that you

mention it, yeah." She said it's right before the cycle, like a couple days before. I said, "Okay, that's interesting." So, I look up her hormones, slim to none. She's highly androgen dominant, very low hormone levels. And we know at the beginning of the menstrual cycle, is when you're already very low and she's even ultra compounding that. So, even then it happened in November 2020. Why then? Because that was when for the first time in her life, she didn't go outdoors for months. Because she was being homeschooled because of COVID. No vitamin D, so this thing was happening before, this low hormone level. But because that key other hormone that we call a vitamin, vitamin D was also extremely low because she wasn't getting any, was triggering an exaggerated response. And just like me, she has hardly any dopamine receptors. So, she was experiencing it in her mood and behavior.

So, I looked at this, I said, "In three minutes, we just figured this out." And it's been three months of her having this issue. So, I called my pediatrician friend and I said, "What do you think about this?" He literally was speechless. He said, "If you speak in terms of biochemistry, what you just explained to me is 100% on." I said, "Why are you framing it as, if I speak in terms of biochemistry, is it right or wrong?" He said, "My problem is we don't have this in our toolkit." He said, "What you're saying to me, theoretically, 100% sounds accurate, I just don't know what to do about it." So, what did I do about it? I gave her a whack load of vitamin D. I gave her L-theanine to boost her dopamine levels. And I said to my mom, if it gets worse, we should probably put her on birth control pill as an emergency just to get the hormone level balanced. The first month we didn't do that and she had no problems. Since then, it's been a year, literally almost exactly a year, has not had the problem once since then.

Dr. Joseph M. Raffaele, M.D.
Yeah, otherwise she might've been consigned to Xanax.

Kashif Khan
For God knows how long. And how many young girls complaining about mood issues, anxiety issues, that get treated as the symptom they're complaining about. The pain point that people, and this is true of most conditions. The pain isn't the problem, the pain is your body's screaming to you that there's something wrong, we need to dig into it. And hers was a hormone problem and a vitamin D problem and a dopamine problem. That combination led to this expression of collapse, "I'm beyond my threshold, can't take it anymore, I have anxiety."

Dr. Joseph M. Raffaele, M.D.
That's a very interesting sort of case history. I know it's your niece, but... So, you also mentioned that one of the areas is longevity, and this is a telomere summit. I'm kind of curious about, I guess some of the things we're looking for longevity are the detoxification enzymes and

glutathione levels, et cetera. Have you considered, or do you look at any of the telomere mutations that can take place? There's something called a telomere biology disorder, which is extreme 50% loss of telomerase activity. And that's a little less than 1% of the population, maybe less than a 10th of a percent, depending on how you define it. And those people have the classic cases, dyskeratosis congenita where you have three things, the tongue and hairy leukoplakia, et cetera. Then they go on to have bone marrow failure and pulmonary fibrosis if it's the first-generation. But just as in most things in genetics, there's other mutations within the telomerase enzyme that causes a lesser level of telomerase activity. There's genes like the TERT gene, T-E-R-T. So, have you considered, or do you test for any of those multiple mutations? I know last time I looked, there's dozens of them.

Kashif Khan
Yes, so that's literally the next thing we're building is our longevity report. So, the thing that I just said, where we don't do what the genetic industry does, which is this gene means this, this gene means that. The one area, literally the one area where we think that's important is longevity. Otherwise it's all about genetic conditions. So, we have literally right now... So, first of all, the way our platform works, you asked about dashboard, it keeps getting updated. So, people log into it six months later, there's more information. And the report gets better and better and better. And it lives with you forever. So, we're now doing that next stage of what do we do better? And there's two things we're working on, female hormone health 'cause we just find that there's so many women that are underserved and second is longevity. So, we launched the longevity report, it's live now. The telomere science is now being added to it. What now exists in it, the first snip that we added was around a gene called FOX03. And what that is, your longevity, literally your longevity gene. How well do you deal with getting rid of mutated proteins and stem cell production and all these types of things. So, literally your ability to have a long, healthy life. So, in that journey, we started working on the telomere stuff. So, I would say to anyone listening that that report you get today, as it keeps getting updated, that you'll be one of the first people to see that new round. So, the longevity report is live today with the FOX03 and we've reinterpreted the brain in terms of how to optimize for longevity. We reinterpreted diet nutrition, things like insulin response, et cetera. Bone health, skin health, hair health, all these things and what drives them. And the next thing we're adding is the telomere stuff to that.

Dr. Joseph M. Raffaele, M.D.
And the telomere stuff would be... So, the difference between, that's why I brought up the telomere biology disorders, that is what geneticists do well, they test for that. That mutation that causes a high penetrance and significant disease and is usually relatively rare. However, there are specific single mutations that take place within telomerase or within the sheltering

complex which binds the whole telomere complex together. But there's a large variation inheritance in telomere length, it's sort of the most important part, 70% heritable. And that's outside of telomere biology disorders. So, it's probably, not probably, it's almost assuredly poly genomic. And so, looking at, this is perfect for a company like you, looking at a sort of a telomere mutation score or short telomere risk score, or even a long telomere risk score. Some people say that super long telomeres can be associated with increased risk of certain cancers. I think that's debatable, but that's for another time. But I would love to see a company like you take 10 of the most highly published mutations and see if then we'd have to do telomere testing as well to see is it associate with cardiovascular disease? We know that short telomere length is highly associated with cardiovascular disease. More of a risk factor than cholesterol and hypertension, or at least on par with them. Because that way we will be able to predict who probably should get a telomere length test to see whether they actually have short telomeres, and if they do, there's a lot things you want to do differently if you have really short telomeres. You definitely don't want to smoke. You don't want to do that anyway but you really don't want to smoke. So, that would be in addition to FOX03, which I think is a great one. Klotho would be an interesting one. That whole area would be great for a company like yours and be interested to see what you do with that. The longevity is available. So, you're gonna look at the 7,000 that you previously had and all the phenotypes that they have, and then kind of put together a longevity report based on that.

Kashif Khan
Yeah, the same sort of way we operate in terms of what we've done today, we're now applying to longevity and why? Because of the demand, that's what people are asking for. "How do I slow down aging?"

Dr. Joseph M. Raffaele, M.D.
That's what people are asking for.

Kashif Khan
Yeah, so we've done that and now it's... Yeah, so we're gonna take our same functional approach and basically what you just described and apply it to this area where it hasn't been applied to yet. So, the net result, it's gonna be a lot more actionable.

Dr. Joseph M. Raffaele, M.D.
Well, that's great. Well, I mean, it sounds like you've been doing amazing work in the last five years since we, or so, spoke for the first time, and is there any parting thoughts you'd like to leave for the listeners about... You told what your next steps are, maybe you can just tell them what your website is, et cetera.

Kashif Khan
Firstly, anyone that's here today are already taking that first great step because how many people actually even think that they can manage their own health. We've taken for granted that 50% of Americans have a chronic condition by the age of 50, by the age of 60 you have two. That's just like the American dream, it's supposed to happen. But it doesn't have to happen, specifically for chronic conditions. You can manage, mitigate, reverse, prevent, do all of those things if you understood why they happen and listening in on something like this today, first of all, is a real big step, making it a priority. But use all the tools available to you. Do not take for granted that somebody is gonna take care of you. The technology, first of all, is so accessible now, not only what we do, but what you do with all the testing. There's so much you can be doing, there's no real excuse other than I didn't do it. So, it's just about what choices do I need to make? How do I personalize them? Yes, DNA can guide you, there's other things that will also guide you. In terms of product, I know our team put together something so that people can dive a little deeper.

I know that there are some questions in terms of, "Hey, I want to buy the DNA test, but actually want to know a lot more than just the DNA test." On our website, thednacompany.com, that's our website, thednacompany.com. I think right there, you can go register that if you were part of the "Telomere Summit", that there's an event you can attend, so they can learn a lot more and just go register there. You can learn, or you can just go straight to the website and buy a test and learn for yourself. The nature of who's listing here today, we're gonna have our coaches ready if you want to get into coaching. To learn more and dive deeper. 'Cause I understand, again, the nature of who's here. Really want to sort of take charge of their health, so we've made that available to our coaches that have been trained in longevity so they can help with that. But really, that's it in a nutshell, you can go to the website, grab a test and learn. Sign up, set yourselves up for the webinar and learn more or just contact us if there's any questions you have, we're here.

Dr. Joseph M. Raffaele, M.D.
Well, that's great. It's been really wonderful talking to you. Fascinating discussion. I look forward to checking your test out myself in the very near future. And I hope we get to speak again at another conference or what city are you in?

Kashif Khan
We're in Toronto.

Dr. Joseph M. Raffaele, M.D.
You're in Toronto. Yeah, I used to go up to Toronto a fair amount when I had, I still have a licensee up there and I used to know some hockey players up there too, actually. So, I'll wait till the spring though, how's that? You be well, Kashif. Thank you again.

Kashif Khan
All right, good talking to you.