

Announcer:

Bulletproof Radio, a state of high performance.

Dave Asprey:

You're listening to Bulletproof Radio with Dave Asprey. Today's show is going to be really, really fun. It's Naveen Jain, who is the founder of Viome and has been on the show several times. This is the guy who cracked the code of what's actually going on inside your microbiome, inside your gut. My gut was wrecked for years when I weighed 300 pounds, 15 years of antibiotics every month because I had toxic mold in my home, which gave me problems with sinuses and all kinds of stuff, but eventually to actually see the data about phages and viruses and fungus and all those different bacteria. This is the guy whose groundbreaking company Viome, and by the way, full disclosure, I am an early investor, one of the first advisors. And I've just been the biggest cheerleader because this is the data that I quested for. And what I found out during Super Human was that I could quadruple the number of species of bacteria in my gut.

Dave:

How did I count them? I used Viome, of course, but today we're going to talk about some brand new stuff and I've got a new name and a new face for you. Who's a part of Viome. So Naveen Jain is a CEO and founders here, but also we have Ally Perlina the chief translational science officer at Viome. And Ally is here in order to really share the deep science as a systems biologist, a molecular biologist with knowledge about human genetics and the clinical side. This is the one who's actually looked at my poop, I'm embarrassed to tell you. And we're going to go deep on your mitochondria, your energy pathways, your cellular stress, your age, all these new tests. New data things that are available, that weren't available before. So both of you welcome to the show.

Naveen Jain:

Well, Dave first of all you know what an honor and a pleasure just to see your smiling face. And I got to admit that COVID here looks good. So if you want to keep that look I'm concerned. It's all good.

Dave:

I knew I should wash it. Now, when do I get to get like a hair microbiome test Naveen, tell me that's probably already coming out here your pathways.

Ally Perlina:

We'll sequence anything.

Dave:

You'll sequence anything. All right. I'll just take a tuft.

Ally:

[crosstalk 00:02:19].

Naveen:

So interestingly, if you look at this stuff and seeing our goal, our purpose in life really is to digitize the human body, to really understand at the molecule level what is going on. And you know what is really interesting, I think Dave, I think I remember four years ago when I was studying Viome, and we sat down

together on our first portable podcast and we talked about it. So, there are only three types of genes that are expressed in the human body, your mitochondrial genes that are inside the cell of human cell, that obviously all the human genes that are expressed and the microbial genes.

Naveen:

And what if you can look at all of them and start to see how this system approach to how each one of them impacts each of us? So how microbiome impacts what's happening in our human gene expression and how they impact what's happening in the mitochondrial gene expression or how my microbiome and mitochondria gene expressions are connected to together, how mitochondrial biogenesis changes the cellular response to things? So my point is, it is literally everything is connected. And for the first time in the human history, we have a chance to actually look at all of that and apply the AI and machine learning to not only just look at the wonderful steps, to actually figure out what to do about it. And I'm just so damn excited, that we're finally there, finally there.

Dave:

And a lot of listeners know about your background Naveen , but the idea that this is your seventh company, you're on the Forbes list and you're exceptionally successful. You don't have to do startups ever again. You just do these because you like changing things and disrupting and creating. So, that one of the things that attracted me to this, the other one though, is you went to Los Alamos national laboratories and you got \$2 billion worth of new weapons, grade, R and D on identifying things and said, "What if I took that and I turned it around from like a fear-based response." And said, now it's just data gathering at a high speed. And it's not about sequencing genes, which has been done before, but it's about looking at what behavior of things is doing with RNA analysis.

Dave:

So, that's kind of a quick introduction and you've been working for three years with Ally, and, oh, four years now. So it's one of those things where companies start out, you're small, you have this technology and you're doing this one thing is the gut, but I've been excited. I mean, you've said, "Dave, we have this new staff coming." And then, I'm going to be the first person to see it, right? At least one of the first, but all the same time, mitochondrial function, immune cell function, biological age and cellular stress. What do I have to send in besides my poop for you to know all this?

Naveen:

So basically the idea is, if you look at the things our human body is like a donut. There is a tube that goes through it, right? And our thought is, what if you can analyze at the top of the tube? And our thought is what if you can analyze at the top of the tube? So you look at your saliva, and what if you can start to analyze all the oral microbial activities. And I'm going to tell you some things here, and then you look at the bottom of the tube and you start to see what is the all the gut microbial activities that are going on? And then you look at the other side of the tube, which is the host, the humans. And you start to look at and say, what are the human gene expressions that are coming along? What is the mitochondrial gene expression that coming along?

Naveen:

So in this test, the health intelligence test that actually you can do today. So it's not some day in the future may come out. You can go to viome.com right now. And you can actually order this test. And when you order this test for the first time, you're going to start to see the schools and insights that are

all tied together. So it's not, this comes from your microbiome. This comes from your mitochondria. This comes from this. It is all tied together. So in a sense that when we look at your biological age, biological age is not somehow your microbiome are doing something or your cells are doing something or your mitochondria. It is all integrated approach to what makes you age. That means you may be chronologically, like me 61, but I am biologically maybe only 40. And if you ask my wife, she thinks I'm more like a 25 year old man, but that just depends on different things for different people, right?

Naveen:

But the point really is that we all age very differently. And our part was what if we can start to measure them at a molecular and cellular level, right? So we thought to look at immunity, the big thing now in this world of before it used to be all about flu, and now it's all about COVID. But the point is, why is it that some people catch exactly the same virus and they have almost no symptoms. And some people end up in the hospital. What is the difference between the two people? It's not their genes are somehow different. We all have 99.8% same genes. So it's not genetic. It is literally is how does the immune system response when they get infection, when they get this pathogen, how is the immune system primed for it, right? Is it too much inflammation in the body?

Naveen:

Because you're obese, you have diabetes, you have heart disease. That means you have inflammation going on in your body tremendously. And then your inflammation going on immune system is too busy trying to take it off what you already done. And now you hit the virus, and you think, all right, I'm done. And it just gives up. And suddenly you have all these issues. And that's the reason, what if you can build the immunity at a cellular level? And so we literally now give you your immune system health, right? We give you your mitochondrial health. We give you your cellular health, and we're going to describe you what all these different things are. What's included in them, including at the deepest level, every part that goes into your calculating, your cellular stress, that goes into calculating your mitochondria biogenesis.

Naveen:

And not just tell you what's going on, and then we say, here is what you can do now to go take care of it, rather than some generic advice, which I think where most people go wrong. They say, oh, I think I can just take glutathione because I think I got this, free radicals, I have a lot of ROS, I think I'm going to take glutathione. Without understanding that glutathione has very high amount of sulfide in them. So if you have very high sulfide production in your gut, dead probably the glutathione may not be the best one. Maybe you really need to be taking [inaudible 00:08:52], right? So point is, it is different reasons for different things. And then you have inflammation. It's not, oh, I'm going to just pick some anti-inflammatory drug, whether it's an anti-inflammatory supplement. So I'm going to pick curcumin. Well, the point is you need to understand what is the root cause of that inflammation?

Naveen:

Is it coming from cellular stress? Is it coming from pathogenic infection? Is it coming from some environmental stack, like tox, the mold toxicity, but if you don't know what the underlying cause of that is, you are going to just do things that may actually end up harming.

Dave:

As a systems biologist, as a systems thinker. And I'm a computer hacker, which means you're a systems thinker as well. Like from my background. How often is it one thing that's causing inflammation?

Naveen:

Very rarely. It's not just one thing. It's always the combination of many things that actually come together. It's literally, unless you have infection, suddenly you say, oh, that's the one major thing. But in general, there are a lot of things that have really come together. Environment, the food we eat, the lack of nutrition that we don't have. I mean, literally the inflammation in the body is, in fact without inflammation, we will die. So my point is not that people somehow think inflammation is bad. Inflammation happens because it saves us. Without inflammation, we won't be saved, right? So yeah.

Dave:

It's the wrong flavor at the wrong time, the wrongful inflammation.

Ally:

This is absolutely not wrong. I just wanted to add that when you have one thing, like a bad virus, it can cause inflammation. So, sometimes you can point it to one thing, but what pathways are going to be turned on as a cause of that, as a result of that causal, one thing of inflammation that is where it differs from person to person. So from some people you will have a great antiviral response, and then your system will know when to actually stop itself and be like, okay, wait, we got this taken care of. There's specific sort of breaks on the immune system that we know of. And some of these breaks like PDL and other things that are targeted by immunotherapy are the types of genes that we can see. And then for some people it will be uncontrollable inflammation.

Ally:

And once you have specific types of cytokine pathways turned on, if they're not controlled, well, then they keep recruiting and recruiting these immune cells, which can even lead to cytokine storm and things like that. So the different pathways that go in and trigger each other, that's thousands of things going on, but the cause, yes, sometimes it could be one or two really sort of culprit type of items. But as Naveen said, it also depends on your lifestyle. What you've been up to in your past, I don't know, 30 years, what you eat that will determine what are going to be those pathways once the virus, let's say comes in, what are going to be those pathways that will be turned? And based on that-

Dave:

Right.

Ally:

... you know whether you need to support some of these anti-microbial anti-viral type of responses, or you need to actually make sure that you tame your immune system at the right time and stage.

Dave:

For instance, let's say that you've been living off the standard American diet with tons of corn oil, soybean oil, all the inflammatory oils. So that actually the fat in your body is made out of those kinds of oils, which is what happens when you eat that way. And then you get, I don't have some kind of random virus that's going around that has a 1% death rate or something like that. But you're one of those people

gets really sick from that. I got to wonder, was it the fats and your diet and the fact that you primed yourself for massive inflammation, that was the cause? Whereas the guy standing next to you didn't eat that way. Didn't have any symptoms. So was it the virus or was it the lifestyle or was it the system? And I think we all kind of know where I'm going with that, but...

Naveen:

So it's [inaudible 00:12:52] morbidity. I mean, if you notice that, how many people have catch exactly the same flu, the same, this mysterious thing that somehow people think is going to kill the universe, right? That mysterious thing, there are a lot of young people, they don't even know they have infection, because they just literally, their body just deals with that, right? And other people who have a whole bunch of other comorbidities signals, right? So they have diabetes, they have heart disease, they have obesity, they got all types of things going on in their body. And suddenly they may catch flu or they may catch even the smallest of things. And the next thing they know, boom, they end up in the hospital, right? And that to me is really the key is that is your immune system, is your body actually ripe or essentially be into this situation? Are you honestly going to feel? Because they're literally at the cusp of feeling.

Dave:

When I weighed 300 pounds, I had that chronic inflammation. And if I got anything, I was like, oh geez, in three days, I'm going to have another sinus infection. And I would always go down the inflammation pathways. And I figured out how to turn that off. But part of that was lab tests, very expensive, weird lab testing, oh, you have too much [inaudible 00:14:11] or too much of this other inflammatory cytokine. And it's been very hard and expensive to quantify that.

Dave:

And it all does in my world, come down into the date, your mitochondria, but there's no solid mitochondrial test out there. I've tried every one of them. We've got one at upgrade labs. The only one that I trust until you guys just came out with this, where you ride a bike with a special algorithm, that's exclusive to us where you look at how well your body uses oxygen. That's the output of the system, right? You generate this much energy, because we can measure it from your legs and this much oxygen, and we'll tell you the percentage, but we can't tell you where's all that stuff that you're leaking. Where's it going? But you guys are looking at what specifically around mitochondria in your test?

Naveen:

So I think I'm going to have Ally describe, but there are two major parts to that. The mitochondrial health. One is the mitochondrial biogenesis. That means how well that your mitochondria itself is recreating reproducing, because, unlike the cell division, that only happens when you divide the cells. Remember the mitochondria is an organelle. It used to be an ancient bacteria. It is constantly dividing and it's constantly regenerating itself. So how do you measure the mitochondrial biogenesis? It has never been done. Because that is the one that constantly stuff does the cell repair, the DNA repair, the oxidative stress. And, but there's [inaudible 00:15:35], so [inaudible 00:15:35], all types of stresses dealing with that, right? So that's one thing.

Naveen:

The second part of [inaudible 00:15:40] that you talked about is most people think of mitochondria as energy production, right? And in the energy production, most people think of mitochondria as ATP cycle,

the Krebs cycle, right? They think that's what the mitochondria is about, but it is more than that, that more than that. And that's literally, we go through all of those pathways. So Ally, if you want to just geek out for a second here and just talk about all the things we look at, what causes the mitochondrial biogenesis, how do we look at the things? How do we recommend things? What are the things in the ATP production? So just geek out for a second here, so that Dave knows that you actually know your stuff, your molecules.

Ally:

Time my second. So, let me try to just kind of recap. So, some of the things that you said, mitochondria is an energy, a furnace, is the energy generator for the cell, and it needs to rise up and actually deliver that energy at any occasion, when we need more of it. When there's some kind of demands, stress, maybe you're fighting something, maybe you have, not enough of the types of nutrients. So a mitochondria actually can sense when you don't have enough energy from something let's say called AMPK, that senses the ratio of AMP to ATP. ATP is that energy molecule. And we get ATP from mitochondria. So mitochondria has a way to know about this, but to know about this, the signaling pathways need to actually tell mitochondria, Hey, we don't have enough energy, so can you make some more please?

Ally:

And for that, you need to have, first of all, enough mitochondria and all of the compartments and components of it and all the proteins, they need to be functional. So when mitochondria knows that it needs to produce more energy or metabolize certain things for you, for the cells, there is a master regulator of mitochondrial biogenesis called PGC-1 alpha. And this gene is what signals to mitochondria to be able to function optimally, and to actually deliver what the cells need. So that's one of the things that we measure, and that can be in response to different stressors, or just the ratio of AMP to ATP the energy molecule.

Dave:

For people listening going hold, I just got lost there. So ATP is adenosine tri phosphate. So this is the energy molecule, and it goes down to ADP when you use it. And if everything's working right, it goes back to ATP. So it goes from three down to two, down to three. And AMP is what happens when something got screwed up. And now you're a busy three part engine. You just lost the first part. Now you lost the second part and you've got AMP. And AMP, you either pee it out, which a biological expensive valuable molecule just got wasted in your urine. Or if you can get enough energy, you could rebuild that and reuse it again. And if you're good at doing that, you'll probably live longer. Did I get it right?

Ally:

Absolutely. Perfect.

Dave:

Alright, just checking.

Ally:

That's excellent.

Dave:

Now everyone learns, AMP, ADP, ATP in that order, like one, two, three. Keep going.

Ally:

[inaudible 00:18:42] try. Exactly. Exactly. So, in response to AMPK activation, PGC-1 alpha activation, mitochondria is news to crank up its functionality basically. And in order to give you the energy you need, first of all, you need to get the fuel, which can come in either a carb or fat sources. So if it comes from, let's say, long chain fatty acids, different types of fats, they need to be transported into the mitochondria before they can even be processed, metabolized, oxidized. And for that you need, that's why some people need some help with that. They need L-carnitine, that's one of the reasons they might take that. Other sources, glucose and glycolysis. There's a very well-known pathway where you break down different sugars.

Ally:

It's more than just glucose that can come into the pathway. You can get that pathway activated with fructose and with breaking down of more complex carbohydrates. But the point is, then you get to the Krebs cycle. And after the Krebs cycle also known as the TCA cycle or citric acid cycle, you are able to generate some of the molecules that then also contribute to electron transport chain. When as a series of different transformations, you finally get the most of that ATP pumped out through the pump. And you need all of these different components. Now, all of these components, then there's a cytochrome C. There is ubiquinone ubiquinol shuttle. You need to know what are the personal gene expression and pathway profiles that you need most. Because if you just, if you take everything, some of the things may not be very beneficial for you. For some people, you may not need L-carnitine, you do not need any more of the protein. And then, I mean, no ammonia sources in your body. Whereas other people, you need more of the CoQ10.

Dave:

It is so important. My statement, look, I take 150 [inaudible 00:20:41] a day, and I've just, people say, well, you might be wasting money. I'm like, great. I'm happy to have the world's most expensive pee, I've no issues with that. What I don't want to do is I don't want to be in a situation where I'm taking something that doesn't actually benefit me. And I finally figured out after a while, if I take too much acetol L-carnitine, which is in a lot of cognitive enhancement formulas, but not everyone needs it. And not even everyone with optimized metabolism like me even needs it. When I take it, I actually get a little bit of a headache and I get jaw tension, which is a side effect. Because I have enough acetyl L carnitine in my system and it actually doesn't work. It raises my acetylcholine levels more than I need.

Dave:

So how would I know that? Because I'm a biohacker, how would someone who's taking that going, I have headaches all the time and I'm grinding my teeth. Well, you just wouldn't know it. And so some supplements in excess are not going to help you. And people say, Dave, tell me what you take. I'm like, I'm not telling you what I take. Are you a former 300 pound guy who had autoimmune issues? Who is my age?

Dave:

Oh, might you be 150 pound woman? Who's a different age? Just don't do what I do, optimize. And for me it's been an evolutionary process with a million dollars. And what you guys did is said, why don't we

spend \$2 billion of basically military spending plus all of the AI research you've put in over the last four or five, however old we are now. But all of that and saying, okay, maybe there's a way someone can get the test and then say, oh, these are the things that the gut bacteria, plus the combination of my body's actually doing, that's going to tell you the supplements with the highest ROI, and all I care about is ROI, the show is based on ROI, right? Go listen to the show. Was it worth more than an hour of your time? If so, give us a four star, or five star review or whatever. If not, don't.

Naveen:

Every time I listen to your show, it is one of the best Ottawa I get. I mean, I think there are very, very few people. I honestly believe the level value every time with every guest. I mean bar none, I mean, there's literally what I find is you talk about actually learning and learning the valuable life lessons, something you can take home and apply. I would give that a five star every day.

Dave:

Thanks Naveen , that means a lot coming from you. And Ally, I know that you can pretend like you listen, you don't have to listen.

Ally:

I actually read on your website of that, I'm a fan.

Dave:

Cool. Thanks.

Naveen:

By the way, I feel like I didn't tell you that, some of our best people that we have hired have come from people who listen to our podcasts together.

Dave:

Oh cool, that's fantastic. But walk us through that mitochondrial thing?

Naveen:

I was going to just take you one step further and I'm going to announce something that I didn't want to announce, but now that you brought it up, I'm going to tell you that. So we just launched this health intelligence service now that actually looks at your mitochondrial gene expression, human gene expression, and the microbial gene expression that got all together. And now we're going to be actually launching the preseason supplement, designed and made to order for each individual after doing the tests. When they do the tests, we say, you need 22 milligram of [inaudible 00:23:50], you need 11 milligram of buprenorphine, you need seven milligram of [inaudible 00:23:54]. And we literally made those capsules, it capsules, whether you need 35 ingredients, whether you need 16 ingredients, we make them for you on demand for each individual completely made to order. And that will be launching on August 1st.

Ally:

That's right. That's right.

Dave:

I'm pretty stoked to see what you guys think I need to take. Because, is it going to be accurate? I think it will be based on the science, but will it have that weird Japanese ingredient that Elkaime five, five, six or five eight, whatever that, so it was probably not, I think there's room for tweaking on top of it, but you're going to get everyone's major categories. And if you're a weird biohacker like me and you're like, okay, I'm going to take this cognitive enhancer. I'm going to do this. You can still play, but get your basis covered. How much magnesium do I need? I don't know. You guys should tell me, right?

Ally:

Exactly.

Dave:

And that's what I want.

Naveen:

Our job is to look at 90% of everything that you, give you everything you need and nothing that you don't need. And then you go in there on your own and actually do the biohacking. You literally personalize even top of that personalization, because it doesn't matter how much we learn. There is so much in the human body we're still going to learn. So as we get millions and millions of people doing it, it is going to get better and better and better, and just have someone else be able to improve that goes down in docs. But we are not there today. So I would be absolutely telling you that today you can do that. Maybe 40 years from now is going to get more and more difficult because we will know everything by then. So I think, yes.

Ally:

Can I just say why we call it precision, precision supplements? Why you refer it that way? precision nutrition? Can I just say why we call it precision, precision supplements? Why you refer it that way? Precision nutrition. Because nowadays, if you look at what people mean, when they say personalized nutrition or personalized supplements, it's more categorized than it is personalized. It's like there is the nootropic category, there's a weight loss category. There's an insulin category, there's a performance endurance, whatnot category, the cardiovascular health category.

Ally:

And then if you actually think, well, I need that support too, I need this to be, just prophylactic. I need improvement in my disease. Then you cover all the categories. You're going to end up actually with 500 supplements for all, and that can be harmful because it can overload, even your liver and kidneys can be overloaded with this. Plus all of the things that go into supplements that sometimes contain heavy metals. And when you add up too much of that, and then all of the fillers and things like that.

Ally:

So, how do you then narrow it down to what you need? And this is when, it's a way of personalization that is based on molecular level precision, and you can only get molecular level precision if you can understand, system wide, what is actually happening down on the molecular level to meet your molecular needs. So if somebody needs more NAD plus precursors in order to fuel your electron transport chain or your crab cycle, then that is what you need. And you can take nicotinamide riboside

or other ones, or if you need more of the ubiquinone in order to fuel the ubiquinol ubiquinone shuttle inside also the mitochondrial, or you need more of the L-carnitine, some people do. And so with this molecular level of precision, and also looking at what is going on in your microbiome, what else is happening in terms of your stress response, your inflammation, only then you can make these molecularly precise supplement recommendations and or food recommendations.

Ally:

And so for recommending any one thing, so like a cookie 10, or there's a berberine, for instance, if you recommend this one thing, our philosophy is that you look at what a person has gone on and all of these different functional levels, integratively and functions are painted by all of the different activities of the pathways and microbial contribution as well. You look at what is going on integratively and the ingredient that serves most purposes for you to kind of readjust and fine tune those knobs. For the fewest number of ingredients, that is what's going to give you that personal level of precision. So that's why we kind of take the systems approach to give you this functional integrative precision supplement, precision nutrition offering.

Dave:

It makes so much sense to be able to do that. I'm excited, but I have a question here. I feel great when I take my stack of supplements.

Ally:

All right.

Dave:

And I tune it on a daily basis, like you know what? I didn't sleep that well last night, my aura ring tells me as much. And I feel like, ugh, or like you see a little bit of puffiness around your face. Whatever I had for dinner last night didn't always work. So, alright, I'm going to take extra of this and less of that. And there's a daily tuning, but if I was to say, run the health intelligence test tomorrow, and I've been taking this stuff, what was evolving stack of stuff for 20 plus years, aren't the results going to be based on my supplement stuff? And then if I quit taking those supplements and I started taking something new, wouldn't I have to get a new test?

Naveen:

But so remember Dave, this is all about snapshot of what's happening in your body, right? So we look at, for example, your histamine signaling, in terms of what is your histamine signaling telling you right now? So even though you're taking supplement to actually maybe take care of it, but the signaling is still happening. So we look at histamine signaling, we may be looking at your prostate glenndon biosynthesis. We are looking all the stuff like tissue remodeling and repair. So wound healing is very interesting is that, some, obviously the body is designed that in case you get wounded, it releases things like combo sites and platelets to take care of it.

Naveen:

But what happens is sometimes the people have this mechanism turned on, even though there is no wound and the body's constantly producing it, then it starts to get really, really harmful. So we look at the cytokine signaling, we're looking at antiviral and antibacterial response, right? So we're looking at all of those signaling to figure out how your immune system is being activated. And even though you're

taking supplements to deal with them, but the fact is the activation is still happening, right? And that's how we know what you actually need.

Dave:

So then the idea would be that someone comes in, they do the health intelligence test. Then they save so much on the supplements they're taking. Because now they're taking the ones that they need on subscription and all of that, that they can actually get another test in six months or a year and sort of see how is it working and then tweak.

Naveen:

And actually, honestly we do that. It's included. So when we launch our supplement the test-

Dave:

So its included, okay.

Naveen:

... we include it, so that means we actually do the test. Look at every insight, give you all the insights in the body, then give you the procedure and supplement and then send you to another test four months or six months later, and then reformulate and redo the things again. So in a sense that you're constantly seeing what is going on. We give you what you need to do, and then prove it to you that it's working and tune it again. And then we keep doing it. Another test of [inaudible 00:31:16] testing [inaudible 00:31:17]. And the idea is keeping your body in that optimal phase, keep retuning your body just like you tune your car every year you retune body every four or five months.

Dave:

This has been sort of every bio-hackers dream and frankly, most people who are aware, wow, I didn't have enough magnesium or zinc or something last year. And this year I probably do. So what needs work now? It's been a real pain for me. I have a directory on Dropbox or something full of all of my different lab tests going, oh, what's my level of red blood cell, this and plasma that. And it becomes a little bit overwhelming, especially for, I'm just going to say, mere mortals, who aren't professional bio-hackers.

Dave:

So the idea that it's kind of an automated system, or you send a sample in every now and then, and it's built in, and it looks at the system of your guts and your oral microbiome and your cells. That to me is one of the most attractive things is, I mean, I've spent countless tens of thousands of dollars on that's getting disrupted and replaced. So that's go Viome.

Naveen:

Thanks a lot, Dave, one other thing I was going to tell you was that, most of us will look at the symptom. We wait until we start to see some symptoms, whether it's a puffy face or something that symptom, but we don't know pre symptom, the things that are going on inside at the cellular level, right? So for example, and we all know there's a cellular stress always going on, but is that cellular stress coming from oxidative stress? Is it coming from genotoxic stress? Is it hypoxia inducing stress? Is it antioxidant expressed that? So my point is we know exactly what is causing the cellular stress, that sooner or later is

going to end up showing you the symptom. So if you can prevent it by actually taking the action earlier, you don't even notice it.

Dave:

That is the dream. So you don't know the bullet that you dodged. And one of the things that's fascinating to me is you're talking about all these different pathways and Ally, I had a specific PGC, one alpha question for you to go back a little bit in the interview. So I'm perhaps the world's biggest and only PGC-1 alpha fanboy. Tell me a little bit more about what PGC-1 alpha does in the body for us?

Ally:

So it sends the signal to support and build up more of the mitochondria. So mitochondria, it's not enough to just produce energy and to crank out this electron transport chain, you actually have to produce more of the building blocks of the organelle, and you also need to know how to be ready to make more mitochondria. So when cells need to divide, when you need to actually have more mitochondria within the cell. So all of the different pathways, they kind of converge and then diverged through PGC-1 alpha because it's a master, a mitochondrial regulator. And yes, of course it does stimulate the metabolic reactions themselves, even the glycolysis and TCA cycle enzymes, they get induced in one way or another through PGC-1 alpha and paper gamma and other type of transcription factor signaling.

Dave:

So it's miracle grow for mitochondria. So you have more of them, so you can make more power onto math.

Naveen:

That's great. [crosstalk 00:34:37].

Dave:

I translated that. Now, how do you raise it?

Ally:

So there is a whole number of supplements that actually raise the expression and activity of PGC-1 alpha. The point I think is how do you pick the one that's right for you? So actually some people say, it almost makes it sound like PGC-1 alpha is great. Therefore everybody should have more of it. But the thing is, if you have too much of this mitochondrial activity, the byproduct of that is reactive oxygen species. So if somebody has enough of the metabolic activity and they have oxidative stress, then you don't need to stimulate PGC-1 alpha.

Ally:

So the point is, it depends how you ask the question. Is it like a miracle for everybody? And we should then have more of it or not? So of course there are a lot of supplements and herbs that have specific ingredients that will boost your PGC-1 alpha, but you may want to actually concentrate more on the redox and antioxidant and detox type of pathways because your mitochondria is already performing, performing so well. That is a byproduct. It's making these reactive oxygen species that can then damage membranes of mitochondria itself and of your other cellular organelles.

Dave:

So that's beautiful. So your environment is polluted or isn't fertile enough and you pour miracle grow on your mitochondria. You're not going to get what you want. But the things that I was hoping you would say is that exercise is one of the easiest ways to raise.

Naveen:

Absolutely, absolutely true. It is true. Exercise is one of the best way to increase the PGC-1 alpha. In fact, it goes to, I think, induction of AMP activator, AMPK activity, right?

Dave:

It does. Now, what is another thing that's not coffee that raises PGC-1 alpha as much as exercise?

Ally:

Well, there are some polyphenols, okay, not coffee, but some herbs and polyphenols have specific ingredients that raise PGC-1 alpha. I mean, it depends which one is best for you. So it could be like fisetin that you can get from strawberries, or it could be

Dave:

And I love that stuff.

Ally:

... something that has more of a neotropic effect, depends on what you need.

Dave:

It's in the nightshade family. It's a hint.

Ally:

You honestly want to say, want to share with us, because baby, I want to...

Naveen:

[crosstalk 00:36:57]. It's nicotine.

Dave:

Nicotine. It's nicotine, the nicotine is one of the most potent ways-

Ally:

[crosstalk 00:37:02].

Dave:

... to raise PGC-1 alpha. So here's my question. Are you guys going to tell me to start using nicotine? Not smoking, smoking's bad, but nicotine raises PGC-1 alpha. That's why everyone gets thin and looks rift when they smoke and eat a bunch of crap. Even though I don't recommend you do that, but is nicotine going to be on the list of things to pay attention to?

Naveen:

Well, [crosstalk 00:37:20].

Ally:

You should always [inaudible 00:37:21] to nicotine, but [crosstalk 00:37:23].

Dave:

I know you guys are going to tell people to start using it. I do that.

Naveen:

So Dave, we do look at things like [inaudible 00:37:28]. [inaudible 00:37:28] also-

Dave:

That's good.

Naveen:

... goes to PGC-1 to [inaudible 00:37:31] gamma. Ursolic acid, so [inaudible 00:37:35].

Dave:

Big one.

Naveen:

So a lot of different ones that can actually support other PGC-1 alpha through different mechanisms. So I would say, yeah, the exercise is really good for you. There's no doubt about it. It goes through the induction or [inaudible 00:37:49]. It induces the AMP activator, AMPK activator site. You can look at the things around other things, other supplements, including nicotine, if that is something you are willing to do. So answer is yes, the nicotine is one of the things that actually does, and there's no two ways about, it does increase the PGC-1 alpha activation.

Dave:

If someone smokes, what are we going to see in their biome, their microbiome, their oral biome, or in their mitochondria, just the counterpoint.

Naveen:

So actually we see, so smoking and by the way, vaping and lots of other things that are clearly shown to impact significantly, they're all microbial activities. In fact, we have filed with FDA and in fact, we should be expecting next week, the breakthrough devices, that is where we are able to show that auto microbial activities determine the stage zero and stage one oral cancer. And we actually show-

Dave:

Wow.

Naveen:

... that how so we... so we literally can look at pre-malignant and the stage one oral cancer, just by looking at the order of microbial activity, then we showed the people who actually smoke or people who chew tobacco or the people who are in fact doing Listerine or whole bunch of things, how especially vaping, vaping causes a massive, massive amount of change in the auto microbiome. And you start this mysterious disease that people are talking about, people who were vaping in their lungs, that will be coming from auto microbial activities being completely changed other than some mysteriously that disease was coming along.

Dave:

Wow.

Ally:

I just wanted to say that it depends what your metabolic reactions are going to lead your nicotine to do, so you can have more of a, like a niacin input or you can have the nicotine in my right beside precursor, which then goes to NAD plus, which fuels your energy. And we can see the enzymes, the genes that code for these enzymes, that convert NADH to NAD plus and NADP NIDPH all of these different redox reactions. We can see if those are active. And we can also see in the microbiome, if nicotinate, and nicotinamide pathways are activated by your microbes. And so microbes can actually give you some energy. They can even do some detox for you. They have their own glutathione and sod and catalyts and all of these things.

Ally:

And they can also give you some B6 or B12. So maybe you're getting already a lot of B12. You don't need any more, but maybe your microbiome can help you with a little bit extra B6, which you need to actually make use and produce more serotonin. So you need to take all of these things integratively into account. So, and nice in for instance, it's not actually, it doesn't work out great for everybody. For some people, it can contribute to this positive, [inaudible 00:40:50] nicotinamide energy type of pathways. And for other people, it just causes a lot of flushing. It does not naturally convert to NAD. It's not a short path. So, for some people that conversion actually depends on enzymes, that expression of which we can also see and it declines with age. So that's another thing that could play into your overall biological age score.

Dave:

I'm just so blown away at all the different little questions, niacin, before you go into sauna, who the heck knows, the first time I took niacin, I was probably maybe 28 and I'm turned bright red and you get hot and feel all weird and it's not pleasant at all. And other times it doesn't do that much, but it's dose dependent and I've done tons of NAD. And so like, okay, make sure that you have sufficient levels, but being able to be precision about it. I think this is going to really change a lot of people's lives time. I'm pretty darn excited about it. And the mitochondrial picture is, oh my goodness. I mean, I've spent a thousand dollars on a test last year where they took my live blood. I think it was live, it must've been, and then they expose it to hydrogen peroxide.

Dave:

Like, look, you can make good antioxidants, your mitochondria good for you. I'm like, what do I do with this? It doesn't do anything, right? But good for me. They weren't bad at that. Maybe I should take some more vitamin C, but I couldn't do anything with it. I'm like, great. I lost a thousand bucks and I didn't

learn anything that was useful. And so the idea of, okay, what changes would you make? Not just for the history of Viome is. Change this that you put in your mouth and you get this different in the activity of what's in your gut. That was step one, step two, all these other cellular things going in the body. I'm pretty excited. And I can't wait to get my results in on this.

Naveen:

You'll be getting them soon Dave. I think I'm going to send you the kit and you're going to analyze it by the way I have one at home right now. So I'm going to be doing that tomorrow.

Dave:

Good deal. So this is brand new stuff. I know that, I know I've learned a lot just my historical ones. And Ally, one thing that you did say earlier about fillers and binders. So I take, I've taken make super clean supplements and I'll blend it myself in a blender and hold my nose and drink it if I have to. But, when you guys got my results, we had a phone call, and I said, well, okay, where can I be getting this PEG polyethylene glycol? And so it turns out I was taking SARMS and I did a whole blog post on firearms. I put on 29 pounds of muscle in six weeks. I raised my PGC-1 alpha beyond normal levels and did all sorts of crazy stuff. But, they my PGC-1 alpha beyond normal levels and did all sorts of crazy stuff. But, they were available in that solvent.

Dave:

And you said, well, you're getting a lot of this stuff and it's messing up your gut. I'm like, what's going on? So I looked and now if I'm going to do SARMS, I will put them in vodka and use a magnetic stirrer. So I'm getting ethanol based, but that was directly from my biome things. And when you say you can tell, you guys could tell, because I didn't tell you any of that. And you looked at my poop and said, "You've got this going on and it changed your bacteria." And so if you're listening to the show going, what else am I doing that changes my bacteria? You have no clue and none whatsoever. And there's no way you would, because I eat a really clean diet. I raise my own animals. I raise my own vegetables. I know everything going into the soil that went into the animals that went into the kitchen and what kind of cook, where I use, and where the oils came from.

Dave:

I do everything and still, I don't know all that. And maybe I should be using 20% more olive oil. Hell I don't know. I think what I'm doing works, but if I can get the data, it's going to be another level for me. And if you're probably not where I am, because it hasn't been your life's passion, it's a few hundred dollars and then you're good to go. Because you got more data than I ever had. And I'm kind of jealous. I wish I was just starting to be a buyback right now, because it would be way easier than it has been. What about-

Naveen:

It can't be that much fund Dave.

Dave:

That's true the fund wouldn't be there. What about age? You're talking about biological aging. I've seen all sorts of DNA powered things. I was saying we're going to look at [inaudible 00:44:53]. How are you determining biological age? Because I think you're different.

Naveen:

So I think, I want Ally to talk about cellular stress. And when you talk about a little bit about all the other things we're looking in terms of aging, because I really think that is so unique that anybody has ever done.

Ally:

So many of the things that we just talked about play into cellular aging. And cellular aging, well, how do we know that it's aging? It's not by looking at the actual calendar or the clock. We look at more of the cellular markers of that aging clock. So, the decline in essential functions of the cell, they have specific pathways that signify that, okay, these cells are not coping well with all of the proteins that need to be transported somewhere, with all the post translational modifications in order to know where to traffic, the deliveries of certain proteins, for instance, and then when to take the extra protein or misfolded protein and then degrade it. So processes of ubiquitination when you target something for degradation processes, for correct export, even processes that make cells specific immune cells pick something up and display it on the outside of the membrane to say that this is like a foreign type of a particle or substance so that your immune system can target it.

Ally:

All of these functions, they actually can decline with age. And one of the reasons is the reactive oxygen species and oxidative stress. So oxidative stress happens when you have those reactive oxygen species and your ability to mitigate them is actually not keeping up with the rate at which they are produced or introduced into the cell. So all of the things we talked about so far, actually, if these functions in one way or another, are declining with all the wear and tear that cells go through, then that contributes to cellular aging, and telomerase is also included. And so this functional, progressive decline of the cell is senescence and cellular aging. And all of these things go into that. Mitochondrial health obviously very much plays into that.

Naveen:

So I mean, looking at all that, I mean, all this stuff from the cellular center sense, you're looking at this function of how make protein, degrade protein. You're looking at the damages to the DNA that's happening, how we are repairing it, the regulation of telomeres and oxidative stress or even apoptosis, right? To see really are we killing these cells or they're just essentially going out of control.

Ally:

Right. So some pathways will signify that the cells are undergoing programmed cell death or apoptosis. But if you just have this low enough level of damage or stress that it doesn't send cells to apoptosis, it actually just makes them less and less efficient at many different processes and pathways. Then you have this progressive dysfunction happening, the loss of really essential function. So you don't get enough stuff where you need it and when you need it. And signs of that, the aging cells is what we can pick up with the gene expression that lights up all of these different pathways.

Dave:

That is a very different picture than sort of this one thing just determines how old you are. So I'm pretty excited about that. The one thing that you're not including that I really, really like is one of these, it's called a dynamometer and measures your grip strength. And it turns out this is one of the cheapest measures of how old you are, is how hard can you squeeze and this digitally measures that. But I don't

think that's necessary because I'm pretty sure that the Viome age is going to be a little bit more accurate than how hard can you squeeze.

Naveen:

I mean, literally you can measure your biological age by measuring your inflammation in the body because systemic chronic inflammation also causes you to age because all of that causes your cellular stress, right? So my point is by looking at all the cytokine marker, looking at all of the systemic chronic inflammation, that is another great sign of aging. So some people think, oh, I'll just look at the methylation. I would just look at the telomere. Well, guess what? That's just one of the many, many things that go into the systems of aging, right? So I think as you said, mitochondria is one of the big thing, but DELMIA, doesn't tell you that how bad your mitochondria is doing, or how badly it is doing. And if your mitochondria is not going to produce energy, you're going to age, that's how you get wrinkles.

Ally:

And constant metabolic stresses as well can induce oxidative stress and inflammatory response and different aging processes. So it's all actually truly interconnected. That's the system's view, and you have to figure out that which place in the system you need to act. So I was just remembering that there's a set of pathways that people, for some reason find very amusing from the microbiome that are part of protein fermentation that lead to production of spermidine and spermine, and those are byproducts of microbial protein fermentation that actually anti-aging.

Naveen:

You know why that's funny.

Ally:

[crosstalk 00:50:04].

Dave:

By the way I take spermidine orally, you can get a [inaudible 00:50:11] out of spermidine. I've been looking for a long time. I wrote about it in Super Human and yeah, it kind of smells like you'd expect it to smell. And, yes, it was discovered there first. And if you guys don't know what I'm talking about, that's okay. Because you're young and innocent, you can stay that way for a while longer.

Ally:

You know how you see the product quality check. Yes.

Dave:

But it is necessary. In fact, I take a specific strain of probiotics that are shown to increase spermidine production in the gut and are correlated with increasing your lifespan.

Ally:

Right.

Dave:

That's a good thing to do. And I think that in fact, when I send them my next sample, you'll probably see them go wait, oh, this guy has the best spermidine I've ever seen. And that's how I roll.

Ally:

Well, we'll tell you that. So all of these things, it depends what your microbes are doing and what the host response is like, if you need more of the amino acids and protein substrates that will make your microbes give you even more natural spermidine, or you actually don't have the kind of microbial functions active that give you spermidine. And they're more likely to take it and make more ammonia and putrescine which can be toxic and harmful, not even just for the gut environment, but it can also leak through the intestinal barrier into the bloodstream. So those different pathway factors can help us be more precise and personalize different recommendations for you.

Dave:

I think it's one of the problems that have been out there for a while on the paleo diet, the old Atkins diet, and even some of the things like you're getting into a Whole 30 and another diet, it's like that all of which are infinitely better than the standard American kind of random food diet, but it's this excess protein, and the ammonia problem and the [inaudible 00:52:01] problem. They are things I've written about in the Bulletproof Diet. That's now, the book came out six years ago. So I was doing the research about eight, nine years ago because when I was on a high protein diet, you do that. And people have been to a gym where people on high protein diets, there's a reason that it doesn't smell very good in there. That's putrescine, but putrescine was named for what cadavers smell like.

Ally:

And cadaver is another one we see microbes spread [inaudible 00:52:23].

Dave:

Oh, sorry, cadaverine was, not putrescine, they smell putrid, but cadaverine is there yet. Thank you.

Ally:

So a cadaverine is more from a lysine, and putrescine is [inaudible 00:52:34] or anything pathway. So we could see if there's too much a sulfide as well, which can come from sulfate or sulfite, or it can also come from the sulfur amino acids. And sulfur amino acids, people sometimes overdo on the whole cystine and different forms of cystine, which are good for multiple things. But if you have too much of that sulfur profile going on with some of the more toxic or pro-inflammatory sulfites happening, you don't need that. You actually can do better if you substitute for a different type of amino acid or for more bioavailable amino acid sources, like in specific types of sprouts and you may even need digestive enzyme to help your protein digestion so that you don't have, your microbes digesting the protein, making these harmful byproducts, which will then cause inflammation and oxidative stress and yourself that we can measure from the host side.

Dave:

One of the big things that's been in Super Human, just all along it's guys the type of amino acids matters more than how much protein or how much meat or whether it's plant based or animal based. It's really about these building blocks and then the peptides, how they're glued together. And one of the things that popped out is like the amount of glycine, the amino acid that you eat in proportion to cystine or the other amino acids that are inflammatory is really important. Most of us are low in glycine. So you eat

some collagen, get your levels up. Do you guys provide specific information in the test about your ratio or the amount of glycine versus these other amino acids that are essential, but inflammatory?

Ally:

Well, we don't actually measure the amino acids themselves. We measure the activity of all of the pathways that are needed to let's say convert one amino acid into another, like the Sistine homocysteine methionine, all of these pathways. And we see genes for that and differential expression between people within the microbiome and in your human blood transcriptome. So that gives you a unique perspective into more than just that one final readout of the amino acid. You see exactly which routes along your biochemical pathways, you're more or less likely to activate. And based on that we want to actually be proactive to help you rebalance. I'll tell you just one example where something called trimethylglycine I'm sure you know, but a TMG betaine, it's given in different forms, there's the betaine HCL, which can help your digestive issues and including protein fermentation and digestion on the GI track of things.

Ally:

And then there's [inaudible 00:55:06] and hinderers that you can take for like the methyl donor and all of the cardiovascular benefits that it gives. But some microbes will take that trimethyl glycine and they will take that into the methanol genesis or methane production pathway. And you will end up making more methane than you know. And methane gas, if it's not really overly produced is not an issue and you may not have that microbial profile, but we can measure in your pathway analysis, in your results. If you have the kind of microbial profile Arcadia basically are the ones that are methanogens. If you have them actively making methane, then you may not want to look at TMG, you may want to take something else for your digestive issues. And if the digestive issues are of one kind, you may benefit from bromelain and bromelain will also hit some of your inflammatory and some of even fluid retention type of issues.

Ally:

But if your digestive issues are because of, let's say opportunistic microbes, then back to berberine, berberine has antimicrobial properties, and it can also help back to your AMPK and all of these different metabolic pathways. It can help with that. It can help reduce your fat and sugar levels. And so looking at multiple things you need to hit personally and things that you do not want to introduce into your system because you have enough, or it can actually be harmful. That is what drives our nutrient prioritization for you.

Dave:

That is exactly why we go to multiple functional medicine appointments. And then someone who is well-trained that is going to ask, okay, what kind of inflammation, what did you do beforehand? What do you think caused it? And then, okay, let's maybe quantify some of your cytokines and all. And they'll help you to dial in on it. And I think we're still going to need that for a very long time, but I think you guys are going to get at least half of that, just because it's the easy stuff out there, and then we'll get the weird stuff, right? And the more of the tests you have, the more the weird stuff becomes less weird because the data sample goes up. So this is big. It's really big in the world of living a lot longer and performing a lot better. And just knowing, man, I don't know, should I spend 25 bucks on this supplement or this supplement or neither one, and be able to just to make an optimal decision.

Dave:

And so I just, my thanks. I mean worked at it for a long time, but just thanks for continuing to push it. And Naveen particularly, you're not doing this for money, man. I know you very well. You're already very comfortable. You're doing this because it's cool. And because you think it matters and I'm truly grateful there. And for bringing in people like Ally. Ally being a systems biologist and having that knowledge and that way of thinking is very unusual. It's missing from Western medicine entirely where there's one drug will save everything and you're like, yeah, what about your PGC-1 alpha?

Dave:

Thank you for doing that and thinking that way, we need more humans who are systems thinkers. And I think you're doing fantastic work with Viome. So thank you both for being on the show.

Naveen:

Thanks a lot Dave, really appreciate it.

Ally:

Thank you [crosstalk 00:58:12].

Dave:

For people who are listening, viome.com, V-I-O-M-E, Naveen , and I've teased him about this. He still says yome, but it's actually Viome. So there you go.

Naveen:

Exactly what Dave said.

Dave:

And I just, I've got to say yes, I have a small financial interest because I'm an advisor, but seriously, this is so cool. Have you been listening? It matters. It's awesome. So please, if it's within your means and you're interested, you should sign up for the tests because you'll learn something, on that note, have a wonderful day.