Microbes and Human Functionality

The majority of our functionality comes from the microbes that reside in our system, right? So we have about 22,000 functional genes that code for all the things that we can do by ourselves.

22,000 functional genes. And that sounds like a lot, but an earthworm has 30,000 functional genes. A cockroach has 21,000 functional genes. So we're not that sophisticated.

So then the question is, well, how do we have all this functionality? We have almost two and a half to three million microbial genes in our system. And so the microbes that live in us afford us a whole new era of functionality that we wouldn't have without them.

Welcome to the TBD Fit podcast on Dr. Talks. I'm your host, Daniel Keeley, and I will be guiding you through this wellness journey in terms of optimizing health and longevity, where we unpack the science, the do's, the don'ts, and everything in between.

Come join us. Look forward to seeing you inside. Today, I'm joined by an incredible guest, Kiran Krishnan, who is a research microbiologist and health and wellness expert who's made it his mission to translate complex science into information that is accessible for all.

Podcast Introduction and Guest Background

He has co-founded and led several successful companies over the past two decades, including Microbiome Labs, who we use ubiquitously, which has become the go-to brand for microbiome therapeutics among healthcare professionals.

He's published peer-reviewed studies, contributed to scientific textbooks, holds global patents and is a highly sought after speaker worldwide. He's currently co-founder partner in three companies working to revolutionize wellness care.

In today's episode, we're going to dive deep into all things microbiome, which has obviously been my specialty and kind of area of research for almost the last decade now.

And so super excited to get him on the show and to highlight some of the products he's created in terms of enhancing patient outcomes. Welcome to the show.

Thank you so much for having me. We met not long back here connected at the microbiome labs conference, I believe, where you were showcasing, I believe, four of your companies at the event, all of which have validation, great science-backed production.

I appreciate kind of the level of detail and how myopic you are when you formulate certain things and we'll get into that later on. But tell me, how did you get started into this?

How did you start developing probiotics, if you will, once upon a time, if that's how you started? Yeah. So that was probably step two. Step one, when I got into the space, was really out of frustration that companies didn't have much research.

I was just a user of supplements. I was always a competitive guy. I cycled, I did triathlons, I did things like that. So I was always looking at supplements and taking protein shakes and all that.

But being a scientist, I also would call these companies and ask them about studies because there were always

claims on products with not a lot of studies that are referenced.

And the feedback I generally got was that they couldn't afford studies and that studies are, you know, the goal standard of studies are really designed around pharmaceutical products or randomized controlled trials with disease endpoints.

So I saw that as an opportunity to design more clever and affordable studies for dietary supplement brands or nutritional products. And so I opened a clinical research organization called Live Smart out of the South Side of Chicago.

And started doing clinical trials for companies. So I called companies and say, Hey, you know, it looks like you have some interesting products. I don't see any studies reference.

Are you interested in doing a trial on your product? And here's what we can do. So I designed and ran 50, 60 clinical trials through that. And that got me into the supplement space in terms of working with companies.

Then slowly companies started looking at me at, Hey, can you, can you consult with us on formulations? Can you work with us on ideation on new products?

And so that got me into the formulation world. And one of the other companies I started working with early on.

How Megaspore Was Developed

was Garden of Life. Garden of Life, this was back when it was actually still owned by Jordan Rubin, who was the original founder of it. And through our connections through a research group, we had the request from them to develop a new type of probiotic.

And this was back in 2010, some time ago, and they were looking at what would be kind of a new approach of probiotics. They were interested in soil-based organisms and so on.

And through the work that we did, we came to discover that floor-based probiotics were the most interesting to us. It met a lot of the criteria that we thought was important for probiotics.

And at the same time, we also came to find out, as we were doing testing, is a lot of stuff on the market really didn't do anything. And as a result, we said, okay, we can do something better.

It took us a couple of years to do all that work. We came back to them and he had sold the business to a much larger conglomerate and they weren't interested in any of this at all.

So then we decided, okay, this is too important. Let's take this to market ourselves. And hence Megaspore was born and Megaspore was the fruit. of that work, that investigation into probiotics and the realization that most probiotics out there were formulated without any real sensibility to it.

Most are dying in the stomach. They're not really doing anything, nor have they been demonstrated to do anything. So we developed Megaspore and we went to market to build our own company, which is Microbiome Labs, to make it available to people.

And we ended up doing like 18 studies on Megaspore. You know, I had this goal of making it one of the most well-researched probiotic formulas on the market.

Um, and I think we were, we were well on, on tasks to do that. So that's, that's how I got into that. Let's underscore Megaspore because I use that almost 100% with all patients, my patients with mold, mycotoxin exposure, certainly in testable permeability.

What goes into that formulation and speak to its efficacy or what you're trying to improve, target, et cetera. When

we were formulating it, so when I was thinking about what would be a perfect probiotic that would have kind of almost, I hate to use this word, but universal benefit, right?

Because we know that the gut impacts everything. And so you can impact the gut in a significant way. You should be able to impact everything. And that was a simple thinking.

Then I started exploring, well, what is the relationship that we have with microbes naturally, right? So we know when you're in utero, this introduction of microbes from mom's gut, dendritic cells from mom's gut actually bring bacteria from her gut to the amniotic fluid and to the cord blood.

So you're getting inoculations even in utero. Then when you're born, if you happen to be born C-section, like you're supposed to, you'll go through the vaginal canal, you get a massive inoculation there, you'll even come across I'm in contact with mom's fecal matter, inoculation there.

Then breast milk contains up to 600 different species of bacteria. So you get lots inoculation there and then close interaction with mom and dad, right?

So that's like where the microbiome starts. Now for the rest of your life, you're not being reborn in that way. You're not breastfeeding and so on. So then what is our natural interaction with microbes?

And it really turns out it's the environment. Right. And there's good data showing that people who live in more rural areas have healthier microbiomes and people who live in urban areas that being in more in contact with dirt, there's actual studies on this exposure to dirt improves your microbiome, your immune system and so on.

So then. There's something in the dirt. There's something with the microbes in the environment that play an important role in modulating your gut, your health, and so on.

So that's where we honed in on. Now, the vast majority of microbes in the soil, in the environment, aren't going to function like probiotics because they won't pass the first test.

The first test is that they have to be a live microorganism. Meaning they have to survive through the gastric system, our stomach acids and pancreatic enzymes and so on to get to the intestines alive.

The vast majority of bacteria in the outside environment are going to die through the stomach acid. So we ended up honing in on a set of microbes that can actually naturally survive the stomach acid, which is a fascinating feature of the microbe.

Then we said, okay, if they can naturally survive, maybe they're intended to survive from nature. What do they do? once they get into the gut. And then we started exploring and we found that what they actually do is they act like the police of the gut.

They can identify dysfunctional microbes and bring their numbers down. They can even identify beneficial microbes whose numbers are low and dramatically increase the growth of the beneficial microbes.

They also interact with the immune system and modulate unfavorable immune responses. They then seal up the lining of the gut. They upregulate the proteins that stitch up the lining of the gut.

They can improve mucus production, which is important for the lining of the gut. So they do all of these really important housekeeping things. that are the exact things that get dismantled in a dysfunctional gut microbiome that impacts mood that impacts metabolism that impacts hormones that impacts clearance right it impacts all of these things and we said okay this is the foundational probiotic right this is what we're supposed to be getting in nature by eating dirt and engaging with the natural environment, but we don't because we live in a sterile environment.

We live relatively sterile lives. And as a result of that, we just need to put it back in the system. And so our approach was really looking at nature for what it offered, understanding it, studying it, and then, you know, in a

somewhat clever way, putting it back.

In terms of the spore-based probiotics, the Megadis spore, which you formulated with a great degree of success. I mean, we, like I said, we use it very effectively with almost everyone.

Is there anyone that shouldn't use it? Is there a timing that you, when you should take it, whether without food, morning, day or night, it passes, obviously, as you said, the high acidity of the stomach acid.

So what are kind of the ramifications around it? Yeah, so we recommend you take it with food. To me, that's the more natural approach of it because you would normally be gaining exposure to these types of microbes when you're eating, you know, especially we're eating off the land, you're picking roots, you're digging up for roots and tubers and so on.

And it makes sense when you look at some of the things that they do, they do enhance digestion, they increase the production of stuff. digestive enzymes and so on.

And then of course they ferment some of the fibers.

What Spore-Based Probiotics Do

Once they get into the large bowel, they increase production of short chain fatty acids and then protect the liver in addition, because the liver goes through a lot of stress during the process of digestion.

So taking it with food makes sense. And we don't find that taking it any particular time of day matters. So any time of day with food is good. And in terms of contraindications for people who shouldn't be taking it, the only one we've ever spoken about is people who are on strong immunosuppressants.

Right. And this is because their doctor, whether it's a condition or maybe they just had a transplant recently. And so they're on strong immunosuppressant because their doctor doesn't want their immune system to accidentally reject tissue that's been grafted or things like that.

That's a rare thing for most people to where it doesn't really cover much of a population. And so outside of that, we haven't found any. How long can you take it for?

Is this for life or do you cycle on, cycle off? Yeah. Yeah, that's a great question. My position on it is that I think this is something that we need ongoing exposure to.

You know, I always go back to kind of evolutionary biology, like did this happen in nature in this way, right? If it didn't happen in nature in this way, then okay, we are circumventing a natural process or we are blowing up a natural process and often There's a consequence to doing that, right?

So when I look at it from a natural perspective, our ancestors got regular daily exposure to these endospores, which is part of the reason why I think they are transient.

Meaning when they get in the gut, they hang out in the gut for a period of a couple of weeks. And then they respore late and they leave, they leave through defecation.

So they're not designed to just stay in there and populate forever, which makes a lot of sense for a transient microbe that is quite ubiquitous in the very natural environments.

So I think take it all the time, take it every day, because the other thing is we know that these microbes protect the gut microbiome. They protect against pathogen overgrowth.

They protect against toxicity. They protect against inflammatory damage. They do so many things to protect the gut microbiome. And our gut microbiomes are constantly under assault.

And so unless there's a way of living a fairly pristine life in a pristine environment, where you may not need these spores, my recommendation is to take it every day.

I speak to my patients all the time in terms of we are no longer living in congruence with our biology or evolution. We're living in these temperature-controlled homes.

We go from one box to the next box in our cars to the office and back and forth, and rarely are we playing in soil anymore. We've sterilized our entire environments.

We pursue comfort at great length. It's just unfortunate to the detriment of our health go deeper in terms of probiotics. Now I know no better maybe person to speak to than you.

So the spore or soil-based probiotics, something that you suggest all the time, no issues. it will colonize certainly over time if you can consistently take it, correct?

And so you're now kind of revamping for the better in terms of immune benefits and hormonal benefits, mood, cognition, protection of the mucosal membrane.

What about other probiotics? Are all probiotics equal? Let's speak to maybe the differences in probiotics since that was a lot of your life's work here early on I see.

And then in terms of, again, spore probiotics, it sounds like that's not an issue to be on long-term. What about some of these others? And perhaps in the lens of evolution from populations that live.

All throughout the globe, right? When, when we look at some of the indigenous tribes and we have a lot of our microbes effectively are really unique personalization, right?

That's what kind of separates us from you and I, because I think we're what 99.9% genetically identical, but our microbes are really confer the autonomy.

And so if I look at patients from Asia or from South America. Yeah. Are we doing an injustice where we're trying to group everything into one and try to develop this kind of all in one signature, which is optimal versus maybe according to the evolution and where someone ancestrally came from, different microbes were protective there versus when they are here.

And maybe we shouldn't try to make everybody similar, if you will. Yeah. The same. Yeah. No, so that's a really important point. So there's an element of the microbiome called functional redundancy.

And the idea there is that you could have completely different microbes doing the same function in different people. Um, and functions tend to be preserved within the microbiome, but the players that conduct the functions can be vastly different.

Even within the same geography, even within the Western suburbs of Chicago say, you know, two people can have completely different microbes producing a lot of their short chain fatty acids or their.

urea and so on, right? But then certainly when you look across the globe, if you look at people in Southeast Asia or hunter gatherer tribes and all that, they can have vastly different microbiomes that are adapted to those environments.

One of the key things about all of this is this issue of your microbiome being properly adapted for your given environment. And so on a microbiome test, that is the beta diversity marker.

A beta diversity is how divergent is your set of species from the average individual in this geography. Now, that said, if you predominantly live in North America, Most people in North America will have a similar distribution of species.

They might have differences in some of the subtypes, but nonetheless, the functions are conserved, right? So there are still same goals across the board.

And the goals would be increasing diversity of the microbiome. So no matter who you are, what part of the US you live, or even what part of the world you live, increasing diversity becomes really important.

Number two is increasing keystone species. These are the really important microbes that hold up the rest of the microbiome. And number three is increasing the production of certain post-biotics.

And these are microbial byproducts. And this occurs from fermentation that they do in the large bowel, right? So short chain fatty acids is a great example of that.

Urolithins, lactic acid, these are foundational things that everyone's microbiome needs. They may be produced by different species and different people, but you want to conserve those functionalities.

Right? So you can feed and treat your microbiome in a way that supports those functionalities, even though the functionalities may be conducted by different species and different people.

Right? So as an example of that fiber, we know that fiber intake is generally good for most people and they feed diversity. They also increase the production of short-chain fatty acids.

They increase the production of natural GLP-1s, of serotonin, of dopamine, all of this good stuff. But each individual might have different set of microbes that metabolize the fiber and produce these byproducts.

But nonetheless, every one of those people could benefit from fiber. So when we look at the microbiome, it actually becomes less important to get so deep into an individual's microbiome where you're looking at individual species and what they're doing, where you really want to look at conserved functions and then support and feed those functions.

Choosing the Right Probiotic Type

Now, you asked an important question about other probiotics. So to me, the probiotic industry, if they were doing everything right, the way they should be doing, right?

With high integrity and only focusing on producing things that are going to be most beneficial and efficacious for people. You would have effectively maybe three categories of probiotics, certainly two.

Category number one would be foundational probiotics, right? So Megaspore would fit into that. These are probiotics that create global impact in the gut for foundational elements that are really important.

So for barrier function, for example, for immune response, for tight junction modification, for mucin production, for improving diversity. So these foundational elements that are really important to everyone and important for many conditions, right?

So you would have these foundational probiotics. Then the second category would be strain-specific probiotics that have narrow function. Right? So one that you're probably familiar with is the ZenBiome, which has the Bifidobacterium longum 1714. It's a psychobiotic, that strain, and it works most effectively by itself.

If, in fact, if you formulate it with other bifidobacterias and all that, it kind of knocks out its effect, but it's really specific for improving anxiety, mood disorders, depression, neurological inflammation, and generally things having to do with the central nervous system and the enteric nervous system.

So you would use that strain quite specifically for the patients who have anxiety or patients who have mood disorders or even sleep disorders because they have studies on sleep.

Then the cousin to that strain is Bifidobacterium longum 35624, which has a number of studies on it on IBS. So then that strain can be used in conjunction with Megaspore and all that, but specifically to dial in on effect on IBS.

So you'd have these singular strains that have known functionality. Some of those can function just as well when they're dead as when they're alive. And you would use those for specific outcomes.

And then on top of that, you would use a foundational probiotic like a Megaspore. or a Saccharomyces boulardii, or a combination of the two. So I think that's really the two categories.

The category that exists predominantly that doesn't make any sense to me, and there's been a couple studies that have come out that show that they could be potentially an issue, are what I call these kitchen sink probiotics.

So these are products with 15, 20, 25 strains and 30, 40, 50 billion CFUs without any rationale as to what strains are in there, why at what levels, why 50 billion, why 60 billion.

More often than not, those can cause more inflammation because the strains will be inflammatory in the gut. And they can also interfere with your endogenous species that are similar.

And that was two studies that were done out of research institute in Israel where they showed that these kind of kitchen sink type of formulas will actually slow down the recovery of your microbiome after antibiotics because this crazy jumbo mix of microbes are competing against your dangerous microbes for coming back and for binding sites and so on.

So that is the predominant category of probiotics and I think that category of probiotics doesn't really have much of a fit. You know, I think you'll go foundational probiotics that alter numerous important functions within the gut and then strain specific function, specific probiotics to really actually change in a specific condition.

When you said it's less critical to look species by species, um, there's a company that just sent me their, their test kit. I don't know if I should name the name or not, but it's looking at the entire kind of genome, uh, if you will, that we've now been able to establish, which you're probably familiar with.

And so, um, To me, that's interesting because you can evaluate where you have missing microbes, quote unquote, and you can begin to fill in the gaps. What I used to do early on is instead of the shotgun formulas, which I appreciate you speaking to that because I'm not a huge proponent, I would fill in the missing gaps with Rhamnosus or Gasserai or some of these other missing microbes.

Is that then would you deem more efficacious? Yeah, so, you know, looking at things at the species level can become problematic. I used to consult with and also made a small investment early on in a company that did that.

They looked at, they would take an individual's microbiome, they'd do full shotgun metagenomics, and they'd identify all the species that are present in the microbiome, and then would formulate a solution based on what species seemed to be missing.

The problem with that, though, is that at the species level, we can be very different, right? And a missing species, unless it's a keystone species, that's different because keystone species are present in most of us and are supposed to be present in most of us at a relatively high amount to the rest of the microbiome.

For example, Ficale Bacteria prosnitzae, in a healthy individual, It could be five to seven percent of the total microbiome, right, which is huge for one organism.

But most people are supposed to have E. calebacteria prosnitzi. So unless it's a keystone species, it becomes hard because you could be missing species, but not missing any functionality.

Right. And that's the part that becomes really important to dictate. And thereby the tests, I like the best, which is what we build with BiomeFX. And I think Tiny Help does this as well, where they look at the functionality that the

microbiome has, the capabilities.

Right. And the capabilities are made up of the microbes and their genetic elements and what they can do for you in your gut. And so I would say rather than trying to replace what would be perceived as missing species, it'd be important to focus on what are missing functions and or under.

rated functions, right? So a quick example of that is like if you look at your patient's microbiome, and they tend to lean towards proteolytic fermentation versus sacrolytic.

Proteolytic fermentation is the breakdown and fermenting of proteins. Sacrolytic fermentation is the breakdown and fermentation of starches and fiber.

Both are important, but when you have more proteolytic fermentation, the problem that arises is you start to produce a lot of inflammatory compounds. So pea Cressol is a good example of that.

Indole is another example of that where this individual starts increasing the production of pea Cressol and Indole because they're leaning towards proteolytic fermentation more.

That becomes a problem. You want to support the sacroiliac fermentation more. So you start shifting them towards more fiber, more fermented foods and so on, right?

Bringing that balance back. It doesn't really matter which organisms are doing the proteolytic fermentation and which are doing the sacrolytic, what you really want to do is shift the function.

So they do more sacrolytic and they're not producing those inflammatory compounds, right?

Microbiome Testing and Functional Diversity

So function is really the game when it comes to the microbiome because we don't know enough yet about each individual species and what they can do outside of the very well-researched strains.

And we also don't know exactly how the terrain affects what the species does. Right. So you could have, I could have a rhamnosus in my gut and you could have rhamnosus in your gut, but they may be doing different things based on what the rest of the context of my gut looks like versus yours.

So the context matters too. I'm a big believer that context matters and that's relevant in every single individual. But let me challenge that thought in terms of evolutionary biology again.

So just thinking, you got me thinking as you were sharing that. So what I'm trying to fill gaps in missing microbes, which I don't always do, but needless to say is.

My rationale is we are stronger as a community and what we don't understand sometimes is interplay with some of these microbes and how they feed off each other to then get stronger together.

So say if in our community, you know, you had a leader and you had like a queen bee and worker bees and say. One of those worker bees fell off. Well, you had another worker bee take its place, but is it like for like, is it a hundred percent?

So function is still accounted for, but is it optimal? And do we know the long-term consequence because function today is fine, but is it. sacrificed long term.

So that's my kind of challenge, I guess. Do we know when we are missing some of these microbes, function is still attained, but is it kind of at the cost of long term health sometimes?

I don't know. You tell me. Yeah. Yeah. I mean, And you can measure the propensity for certain functions based on

the number of genes that look at that, that conduct that function, right?

So an example of that would be sulfate reducing bacteria, right? So you've got a category of bacteria in your gut that are really good at reducing sulfur compounds or sulfates that come in from food.

And then they reduce sulfate into hydrogen sulfide. The problem with that is that hydrogen sulfide is very inflammatory. to the large bowel. And so it can create a lot of disturbance for people.

So if you have too much sulfate-reducing bacteria, then high sulfur foods like eggs and all that can be detrimental to that individual and cause more problem than benefit.

And the way you would know if you have too much sulfate-reducing bacteria is you get an actual genome count in a shotgun process. So it'll give you the relative abundance of that set of genes compared to the rest of the genome, right?

So it kind of gives you an idea of does this person do this sulfate reduction a lot compared to say, you know, another function that competes against the sulfate reduction.

And I think at the end of the day, one of the goals across the board is to increase diversity, right? And in part because we don't know all of the intricate interactions with the microbes, right?

So we don't know how they necessarily communicate with each other and function or feed off of each other in that much detail looking at the species level.

So it's always a benefit to drive diversity. And I think part of what you're doing when you're replacing missing microbes is you're bringing in more diversity, which is generally a good thing, right?

So I think that approach has a benefit and a merit to it from a diversity perspective because One thing we do know over the last 15 years or so of microbiome research is that higher diversity in the gut, the better.

There's been no contraindicating information that higher diversity is not good for you. You know, it's always higher diversity is better. So if there's a method of doing that, then absolutely.

Let's go back to what's passed from mother to kin. And so how we're setting up our children. for long-term health or unfortunate disease. How much of the microbes that we're passing on today is at a huge depletion compared to our ancestors, given our barrage of toxicity, whether it's from food, from soil, from air, from water.

I know you kind of spoke to that early on, but I want to then segue that into eczema, which again is one of your new formulations from what I understand that you shared with me.

with a high degree of efficacy, just incorporating again, probiotics or topical application to improve the dermis. So what have you seen in terms of missing microbes, if you will, again, from mother to child, which is unfortunately setting up issues later in life, but even earlier on.

So when you mentioned the bifidobacterium long and two specific strains, one we use very, very highly efficacious in terms of ADD, ADHD, a precursor of a kind of GABA production.

So anxiety, we think of that in terms of our aging population, but certainly with kids is becoming far more present, unfortunately. And I see when I'm looking at their microbial full-fire, whether it's from a, in the biome effects or other testing, we can see reduction in a lot of these healthy microbes and keystone species.

You mentioned one particular Ficalum prosinensis. Obviously, Acromansia is some of these other ones. How do you, also then to piggyback on that, how do you replete some of these keystone strains?

Because I know Acromansia now, one of the kind of darlings, if you will, a very hot, hot microbe. But some of these

other ones, Esterichia, you mentioned Ficalum, I don't know any probiotics that contain them.

Yeah. So you can't directly unless it's the fiber. Yeah. Yeah. How do you get them up? Right. So to go to the first part of the question, the passing down from generation to generation, in all of the topics around the microbiome, that's the kind of thing that keeps me up at night a little bit.

Because when you look at the data on it, it's scary. So just to put it in perspective for your listeners, the majority of our functionality comes from the microbes that reside in our system, right?

So we have about 22,000 functional genes that code for all the things that we can do by ourselves, 22,000 functional genes. And that sounds like a lot, but an earthworm has 30,000 functional genes, right?

A cockroach has 21,000 functional genes. So we're not that sophisticated. So then the question is, well, how do we have all this functionality? Well, we have almost two and a half to three million microbial genes in our system.

And so the microbes that live in us afford us a whole new era of functionality that we wouldn't have without them. And there's been lots of studies on something called nobiotic mice.

These are mice that are raised with no microbes at all. And when you look at the function of nobiotic mice, I mean, they have all the same physiology as any other mouse, but they die very quickly.

They can't mount simple immune responses.

Microbiome Inheritance and Modern Disease

They can't metabolize things. They can't produce things. So there's so many things that they cannot do that are basic to a normal mouse. And the reason they can't do them is because they don't have a microbiome.

Right. And so losing parts of our microbiome to me is like losing organ systems. So the analogy I give is like, what if we were told that our behaviors today mean that our next generation is born without a spleen?

And then ours and their behaviors means that the generation after that is born with no spleen and only one kidney. Right. We would be freaking out like, what the hell are we doing?

Right. We got to shake things up. We can't have our next generation of kids being born without a spleen. Well, that's, that's very similar to what's happening because we're not passing down an adequate ecosystem of microbes to conduct all of the important functions that our children need.

Right. And then thereby their children and all that. And in fact, I view it as a duty, as a, human, right? So we are the receivers and the benefactors of thousands of years of arduous process that our ancestors went through, hunting and gathering and foraging and pulling in all of these microbes into their system and then creating this kind of symbiotic organism, which is a human, and then passing those down to us It becomes our job to preserve that as much as we can to pass it on to future generations.

So we cannot squander our ecosystem or we'll run into trouble. And we're seeing that, right? I think to me, that is a big reason why we see certain, the prevalence of certain conditions increasing over time, autoimmune conditions.

We now have something like 130 defined autoimmune conditions. 40, 50 years ago, there was like 28. So we've created new diseases for us to deal with in that time period.

We see that with spectrum disorders. Spectrum disorders continue to increase in terms of prevalence, right? Going from something like one in 119 to one in 68 and one in 40 something now.

And yes, their diagnosis is improving and all that, but it doesn't account for the prevalence rate. Atopic dermatitis, allergies, asthma, all of these conditions just continue to skyrocket.

They're all directly tied to missing microbes and missing microbial functions. And so I think That we will get to a point if we don't shape it up and we don't pay particular attention to the importance of preserving our ecosystem to pass it down.

We will get to a point where we've lost so much functionality that the human is completely ill adapted to exist on earth. we have kind of screwed up our evolutionary advantage that we've gained.

So I think, yeah, I cannot say enough about the importance of preserving our microbiome and passing it down to the next generation. And then I think the second part of your question was around So it was a topic specifically given your formulation, but before we, before we go there, let me dissect something, which again underscores that we're no longer living in congruence with our biology in terms of evolution.

When you're suggesting the prevalence and rise of modern disease, we have made that as a norm. I think society has says cancer is inevitable, prostate cancer, one in two men after whatever the age of 60, something like that.

lung cancer which didn't exist before, smoking now it's quite common unfortunately. Many other cancers just in general and this is not a gene issue which we largely attributed to for so so long because we ask unfortunately the wrong questions.

This is a metabolic issue, this is a toxic exposure and this is a sterilization issue. Again going back to these missing microbes we now recognize the interplay of our microbiome on Uh, our gut bacteria, the whole ecosystem and its connection with every biological system in the body.

We are breeding weaker children. This is what I see as, as we are becoming more and more sick. I attend all these events. You asked me how, how I'm doing.

It's like everyone I see is sick. The question is just with what and to what degree you mentioned asthma allergies. That is so common, but yet people say, oh yeah, it's seasonal.

That is not normal. That is the sterilization of a microbiome. Same, if you're drinking alcohol in excess, you're killing off, you're, you're destroying your ability to fight against our modern invention of chemicals and so on and so forth.

Unfortunately, that has become so prevalent, but needless to say, it's, it's a sad reality. There's certainly, there is hope. The funny part is when we sit around and dinner, you know, we toast for, for good health, which is always very common in all cultures.

To me is I toast for healthier microbes. So I go to bed at night like praying that my microbes are healthy because there's whatever, a hundred plus trillion of them while there's only, you know, 30, 40 trillion human cells.

We're more bacterial DNA than we are human DNA. And to put it in perspective, again, you said a cockroach and who else did you mention? Well, a piece of corn has about 30,000 genes, interestingly, right?

Corn. Okay. So we, we neglect to realize that, um, what we really need to do is, is nurture, um, the environment that resides with us. So there is hope we can change the constitution.

Certainly you've demonstrated that with your formulations for some time now that we can shift things favorably. We just need to be mindful of this and we need to treat this, I think as priority number one, correct me if I'm wrong.

Furthermore, so highlighting a specific one, eczema, because what I wanted to address is I see this so common with kids, right? And the modern medicine to me is doing a disservice often enough.

And this can change relatively quickly under the right environment. The problem also is the external environment. Obviously, we have addressed that. Nutrition may be being order of operations number one.

I always suggest that nutrition is going to heal you or it's going to hurt you. There's nothing in between. Nutrition is

instruction. and it's instructing everything related to the topic of discussion today, our gut microbiome, both oral and GI.

The formulation that you were showcasing to me with a high degree of efficacy, I'd love to be able to highlight that. Yeah. Yeah. Um, and actually eczema is a great example of dysfunctional microbiome and, and the cascading effects of that throughout the body.

Right? So the formula that I'm talking about is this one is called sieve. It's a skin microbiome serum. Let's talk about where eczema comes from and, and.

affect why it's a bit of an epidemic with kids. And then it directly ties to allergies. It directly ties to food sensitivities and asthma as well, right?

There's something called the atopic march that occurs with eczema. So eczema is very clearly the presence of Staph aureus in arduous amounts. So Staph aureus is a type of pathogen that can exist on your skin.

It's ubiquitous, it's everywhere, but you're supposed to combat it with higher diversity of the skin microbiome and combat it with beneficial microbes like called Staph epidermidis, right?

So when we have a dysbiotic microbiome of the skin, we start to get an overgrowth of Staph aureus. Now what that Staph aureus does is it starts to break down the barrier of the skin similar to dysfunctional microbes breaking down the barrier in the gut.

The actual tight junctions, the fatty acids that protect the skin, they're called ceramides. So they break down that top layer, the stratum corneum of the skin, and they create a barrier issue of the skin.

Now, on top of that, what they do is they start making toxins that recruit the immune system to that area. On top of that, if you have a dysfunctional gut, then that dysfunctional gut skews your immune system towards a more inflammatory response to triggers, right?

So now you have a dysfunctional gut and you've got Staph aureus sitting on your skin. It's broken the barrier. It's producing toxins. Now your immune system shows up in that area very aggressively with a massive inflammatory response that's mediated by something called mast cells.

And that mast cell histamine response creates a massive amount of inflammation and further damage to the skin so when you actually can see the eczema lesion what you're actually seeing is the damage that the immune system has caused to that area and it's red and it's itchy because of the histamine and the leukotrienes that are released and then it gets dry because the ceramide which is the fatty acid layer that protects moisture on the skin that also has gotten damaged right so now you've got a dry, itchy, irritated patch where the skin barrier is no longer functioning like the barrier.

And it started with staph aureus overgrowing on that part of the skin.

Eczema, Skin Dysbiosis, and the Atopic March

And it was helped by dysfunction in the gut that's driving more of an inflammatory response to triggers. So it's a perfect combination of dysbiosis and a and a dysfunction of the immune system as it relates to that dysbiosis.

Now on top of that, it causes this problem of atopic march. Atopic march is this idea that You gain exposure to certain antigens like environmental particles, food particles, let's say a peanut protein, for example, through that eczema patch, right?

Rather than through the oral route. So what's supposed to happen is you introduce food and most things in the environment all end up going into the gut one way or the other.

And as they go into the gut, the lining of the gut has all of this immune sampling tissue where those antigens are sampled by the immune system in the context of a healthy microbiome.

And so that microbiome teaches the immune system not to attack that compound. It's something that you have to build tolerance against. So that is called oral tolerance.

It's mediated by a type of T cell called the Treg cell. Now, this is such an important topic that the 2025 Nobel Prize in Physiology or Medicine was given to three scientists that discovered this process of oral tolerance.

that discovered the T-reg cells that control unfavorable immune responses. And it becomes one of the key things that goes awry in most chronic conditions, especially chronic conditions that associate with inflammation, right, which is the vast majority of chronic conditions.

So this loss of tolerance, becomes an issue. Now, so what's happening is that since you're not sampling the antigens through the gut, where your microbiome can help your immune system build tolerance, you're sampling it through the skin.

Once an antigen penetrates through the barrier of the skin, it's going to elicit an inflammatory immune response. And that individual already has massive amounts of inflammation going on in that area.

And so the inflammatory portion of the immune system sees that antigen and decides that everywhere it sees it and it encounters this antigen, it's going to attack it with the same IgE histamine mass cell type of response.

And so penetration through the skin of food and environmental antigens causes hypersensitivity allergic reactions to those antigens in that individual.

So if you had a kid with eczema, That child has an eight-fold higher increased risk of developing allergies, food sensitivities, and asthma, right? Eight times.

So it's not 40, 50% increase. It's eight-fold increased risk because of this atopic march. And all of that starts with just a change in the ecosystem on the skin and a change in the ecosystem in the gut.

This child could be dealing with allergies, asthma, autoimmune diseases, and all that for the rest of their life. Right? So, and you're seeing, as you said in your practice, you're seeing more and more eczema, you know, and what does allopathic medicine have for it?

Steroid, steroid creams, right? That makes everything worse. It thins the skin further. It creates more dysbiosis. And I'm, you know, one of the reasons we developed this product is because I had more and more parents saying, is there another option?

Because they're getting in tune and they're starting to see like, okay, I don't want lifelong putting steroids on my kid. You know, there's got to be a better way.

And so, yeah, so we developed the spore-based serum. And when you apply it on the skin, what we tend to see is it competes against the staph aureus. So it brings down that problematic microbe.

Like in the gut, it also modulates the immune response on the skin and it increases the barrier protein production. So it seals, starts to seal up the barrier.

So a lot of what it's doing in the gut, it's doing right topically on the skin. It just requires the right type of formulation and delivery mechanism.

to make it do that, right? And that can alleviate a lot of issues. And this is what I asked you in person too, I recall is you're not even changing anything internally.

This is just explicitly internally, but then are you suggesting like the HE-58 or Megas 4 in conjunction? with what's going on? Yeah, exactly. In conjunction with it because we want to modulate what's happening in the gut, right?

Because a gut is dictating how the immune system responds to triggers throughout the body. We want to stop the negative trigger on the skin, which is the Staph aureus, which is what this does and facilitates a repair process.

But then we also want to make sure that the gut microbiome is modulating immune response so it doesn't do the five alarm fire for everything that you come in contact with.

So yeah, the combination is really effective. And they have an understanding of this kind of functional approach. When I had elucidated that we were using the spore probiotic very effectively here, he was suggesting not to do that because it will elicit a greater degree of immune response and it's thus more inflammation.

And I could see the rationale there because you're kind of pushing out the bad, there can be some sort of negative. a reaction, but if you're doing that properly, it should attenuate that response.

And so it was interesting to hear that another component that he suggested, which was novel for me, because he was presenting some research in terms of the benefit and efficacy of L-histidine, which in my mind would drive more histamine, but yet he was suggesting that kind of as an anecdote as well.

Any feedback? Yeah, so the first part about the spores, and we've actually tested this with spores, do they increase inflammatory response? Now keep in mind that you can increase immune response without the inflammatory component, right?

So the inflammatory component comes from dendritic cells or macrophages or innate immune cells expressing pro-inflammatory cytokines. But they can also express anti-inflammatory cytokines, like IL-10, for example.

And what we see with the spores is that they generally elicit an anti-inflammatory response. So that's the part he missed. He's probably not as familiar with the spores and the immunology related to it.

What they do is they upregulate something called tol-like receptor 4, which then increases the production of IL-10. and increases the expression of T-Rex, the regulatory T cells that the Nobel Prize is given for.

So they do an opposite thing. Now, the vast majority of probiotics do increase inflammatory responses, which is another reason why I caution against those kitchen sink probiotics.

that have 15, 20 strains because most of them will likely upregulate inflammation. On the second part with the histidine, yes. So what's interesting about that is what that would likely do is create a competitive, it's called an allosteric competition.

L-histidine could potentially compete for the same receptor sites as histamine does without triggering the inflammatory response that comes along with histamine, right?

Because it's an analog to histamine. So in the world of, you know, But biochemistry, we call them either allosteric or direct inhibitors of receptors.

So I think that may be what he's referring to that could kind of drown out the ability of histamine to create the response that it does. But to me, that's fine and that could help people for sure.

But ultimately what you want to do is get those mast cells to be less active. And the way you get mast cells to be less active is by increasing Tregs.

increasing secretory IgA and increasing tolerance, immune tolerance. Immune tolerance works against mass cell activation. And how are you best increasing Treg cells?

So the spores do that very well. Spores increase Treg expression. The bifidobacterium longum, 1714 that we talked about that you use for a number of indications, also increases Tregs and IL-10.

We also know that prebiotics will increase Treg expression. So oligosaccharides, even fiber, will increase Treg expression as well. Anything that up-regulates diversity in the gut microbiome will up-regulate Tregs because one of the ways in which Tregs increase is with interactions between dendritic cells and a diverse set of microbes that are non-pathogenic, right?

So non-pathobionts. that causes, that interaction causes the dendritic cell to actually convert a T helper cell into a T reg cell versus a T helper cell into a T 18 cell.

So the dendritic cell is sampling the microbiome and encounters a lot of pathogens. What it does is it activates in teen cells, which are going to be cytotoxic T cells and all that, that facilitated an inflammatory response.

If it encounters a lot of commensals, It up-regulates the T-Rex cells instead. Also, anything that supports the diversity of the microbiome is going to improve T-Rex.

Future of Microbiome Therapeutics

Yeah, the problem is most individuals who are sick with chronic conditions, autoimmune cancer, otherwise they're stuck in that TH2 dominance, which is incredibly inflammatory and unfortunately debilitating.

As a hyperbole, the reason why I asked that, I was hoping you might say carnivore as a joke. Cause obviously that they're, they're, it's devoid of fiber and capacity.

And so, um, I just wanted to hear our, our, for our community to hear that we're approaching time, which I have, I think like 22 more questions to ask you.

We'll definitely have to do a part two, which hopefully we can actually do in person because I would love to showcase some of the other formulations. Yeah.

That you made that I personally use that I can attest to that have tremendous benefits. So we only were able to showcase one briefly today and we can continue to expand upon that.

What is kind of on the forefront? I know you very briefly spoke about postbiotics. I know Thena is one in general. And so we're only kind of scratching the surface in terms of postbiotics, but what's kind of on the radar for the future for the microbiome?

Yeah, there's a couple of really, really interesting developments and I'm working with a couple of companies on this. One of them is getting much deeper and more detailed around what that mucin layer actually supposed to look like, right?

So the mucin layer, we just think of it as this glob of mucus, if you will. But in fact, especially in the small bowel, it's far more complex than that.

There are all of these structures in there like the glycocalyx, for example, the intestinal glycocalyx, which is a very important and very specific structural element that actually prevents the colonization of pathogens.

It increases the absorption of food by increasing the expression of brushwater enzymes. There's all of these components and there's ways of improving the growth of those structural components within the mucosa, within the layer of the intestinal barrier.

So that is becoming really, really interesting science. And there'll be a couple of products coming out. early next year or mid next year that will improve those structural elements.

That will make a big game changing difference. I think for people with like SIBO, IBS, it's going to be a game changer with that. The other part of it is actual postbiotics, which are microbial components.

especially polysaccharides or carbohydrates from certain types of bacteria, typically bifidobacteria. So bifidobacteria, there's a number of species of bifidobacteria that make something called exopolysaccharides.

These are basically long chains of polysaccharides that have a very specific function. Hey Chris! Good to see you, my friend. And what they do is they have very specific metabolic function, and you can dial them in with the specific bacteria and the specific structure of those functions to get the right metabolic effect.

So imagine an AI program. Let's say you have a patient that you dial in all the symptoms and output. You have an AI program that can pick out the right bifidos and how you cleave them to exercise the right polysaccharide to intervene in certain pathways within the gut.

That's actually coming in the next two, three years, right? So like true customized therapeutics for the microbiome is in the very near future. It's an exciting area.

To wrap this kind of up, going full circle, if there's one thing you would recommend for someone to start or to consider or to bust any sort of myths, obviously, but where does someone start?

Yeah, I think they start with looking at how they're feeding their microbiome. You know, what are they putting in and how that impacts the ecosystem? I think we get very focused on what we're feeding us for our needs.

Forgetting that the microbes that make up a bigger part of our digestive tract than our own cells, what do they need? Right? What do they need to flourish?

What do they need to function?

Feeding the Microbiome and Closing Thoughts

And it's going to be things like polyphenols and prebiotics and fibers and healthy fats are beneficial as well. So starting to get more perspective on feeding your true ecosystem.

And that will give you a better perspective on the choices that we make that can have a huge impact on our overall outcomes. This has been absolutely incredible.

Like I said, we're definitely doing a round two because only scratch the surface here. Last question that I end with all our guests is if you could have one superpower, what would it be?

Great question. I think I would love to be able to talk to microbes. I want to hear what they're saying, what they're doing, and then speak to them and be able to tell them to do things because they can do things that we can't do and they're doing stuff that we don't understand at all.

Holy cow, would we open up a whole amazing universe and we could just talk to microbes. I pray to mine every night. Religion aside, you know, the power of prayer, certainly that's not for today's discussion, but I also believe in science.

And certainly this has a lot of roots and it starts early on and this is passed down generationally. And when you mentioned, you know, Bifido, we see a huge reduction in Bifido strains and our kids who are expressing certain signatures of disease.

Again, that's the power of microbes and something that can be fixed. We'll do a round two and we'll look at some more anecdotes, if you will, the options, how we can fix different signatures, whether it's Alzheimer's or Parkinson's, metabolic issues like cancer, autoimmune, et cetera.

But this was awesome. We'll also highlight some of the other products that you created on the next part to call it. But until then, I genuinely appreciate your time today.

This was awesome. Yeah, I look forward to it. Thank you so much. We'll chat again. Thank you for tuning in to the TBD Fit podcast on Dr. Talks, where we unpack all things health and longevity.

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