Michael Roesslein: Hello, everyone. I'm Michael. I'll be your host of this webinar today where we are going to talk about spore-based probiotics. And we are joined here with the person to talk about spore-based probiotics.

If there's anyone, this is Kiran Krishnan, the founder of Microbiome Labs, the formulator of Megasporebiotic, and probably the person who has educated more doctors and practitioners and experts on spore-based probiotics than any other living person, I would guess, at this point. So, Kiran, welcome.

Kiran Krishnan: Thank you. Thank you so much. And I would say we actually created the category of spore-based probiotics. It didn't exist until we launched it and created this language around this concept of spore-based probiotics. So when you look at, it's interesting, we see this addition in terms of market segmentation for probiotics. So if you buy one of those really elaborate and expensive economic reports on supplements and nutritional products, they always had probiotics as a category on its own.

And now, since 2016 or 2017, they create a sliver, a pie, in the probiotic space that's specific to spore-based probiotics. So it's a different category. And I'm proud to say that we played a role in creating that.

Michael Roesslein: Played a role. You guys are the only ones. So we're the only ones. Yes. I remember when we first, this is like a flashback, honestly, doing a webinar on spores, because we did a lot of these like almost 10 years ago now. And I remember, I watched, I watched your webinar called Forget Everything You Know About Probiotics or something like that. And I was like, what the hell are these guys talking about? What's a spore? I don't want to eat spores.

That sounds bad. That sounds like fungus. Like there was a whole level of like weirdness that you had to get around when you first started educating on them, because nobody knew what anybody was talking about. We had to start from like square one that like, no, these are not spores like killer fungus that are going to take over your body. Like the, because people equate spores with mushrooms, with fungus, you know, and so there was this whole level of questions that we don't get anymore. Because now people know about it quite a bit, especially anybody who's been around this industry. And that came from you guys.

And it's pretty incredible to see like how obscure of a concept it was the first time we did one of these. I don't know how many practitioners are using that product now, but it's got to be at least 30,000. Like the last number you gave me was around that, but I have no idea now.

Kiran Krishnan: And yeah, it's that or more. I mean, in fact, it's the so Megaspore is the number one selling practitioner probiotic. So it's surpassed all of the probiotics. And what's interesting about it, if you look at Fullscript as a marketplace, it's the biggest marketplace for practitioners, right? And they have something like 15, 20,000 SKUs. Megaspore is the number one selling product on all of it, even in, you know, including vitamins and enzymes and all of that stuff.

So and then of course, every other brand and competitors kind of come up with their own version of spore based probiotics, which I'm sure I'm sure will address. And keep in mind, this is the interesting part when Tom and I were first conceptualizing this. He had a relationship with Metagenics, I had a relationship with

a couple of other companies in our space. And the idea was really to take the concept to them and offer them the technology and all that so they can market it because we didn't have a company, we didn't have the ability to market something. And so we took it to all these companies and they all thought it was a dumbest idea ever. And so they all rejected it. And of course, over the last few years, every single one of the companies in that space all have their own version of a sport risk probiotic. But we were trying to get someone to pick up Megaspore as a product. And none of them, no one thought it made any sense. They couldn't get it.

Michael Roesslein: Good call, everyone else. Absolutely. On that one. So glad you guys did it though. And I mean, we saw so much immediate response and reaction because that's back when Facebook groups, when you were in a Facebook group, you would still see things that happened in that Facebook group.

Now, like, it doesn't work that way. But there are all these chronic illness Facebook groups of digestive problems and all kinds of wide ranging things and people who come on our webinars and they'd learn about Megaspore and they'd try it and it would work. And then they'd go back into the Facebook group and say, Hey, I just poop normal for the first time in six years.

And then we'd have like 50 new people on the next webinar from that group. And it blew up into this giant thing. And we couldn't, I mean, I remember sitting there waiting for the call from you guys that there was like more inventory in, because we would buy all your product and then it would be gone.

And then we'd buy all the rest of it and then we'd be waiting for more. And so it's been cool to see how far it's come. So let's get into talking about what we're talking about.

And it's just so fun to see like how what's changed in the last 10 years, I think it's been about 10 years. So yeah, I guess we'll start at the very basics. We say sport based probiotic. The word probiotic, you mentioned is its own category. We have a whole webinar on like what are probiotics, so we don't have to get into it super far. But just to start the conversation, when we're saying probiotic, what does that mean?

Kiran Krishnan: Yeah, so the scientifically accepted definition of a probiotic is a live microorganism. When administered in adequate amounts, confers a health benefit to the host. So when you look at that accepted scientific definition, there's really three parts that one has to meet criteria in order to be considered a probiotic. So number one is it has to be alive. So if it's not alive, if it's not a live strain, whether when you take it or even after you take it, if it's not functioning in a living manner, then automatically it doesn't qualify as a probiotic. Number two, it has to be administered in adequate amounts.

What does that mean? That means that there has to be some identification or definition of dose response, right? So which means you derive that from clinical work. So you have to have some sort of clinical trial to understand that there's a dose response to the microbe. And then the last part is it confers a health benefit to the host. You have to be able to show some sort of measurable health benefit to the host. There's lots of ways you can go in that direction, right?

Immune health, gut health, microbiome improvements, all kinds of things. But nonetheless, you have to show that. And those are the important components of the definition one has to meet. Okay.

Michael Roesslein: And there's a lot of probiotics on the market that don't meet all of those criteria. The vast majority, yeah. Yeah. And we've talked about that to an extent. But that just a little bit on, because when I found your guys webinar, I was pretty much going to stop trying probiotics because I had tried all of these fancy brands for professionals with my clients. I won't name drop, but there's like a handful of brands that at the time were like the leading brands. And I tried all of them. I tried some more obscure ones like, oh, you got to hear about this one, and you got to use that one. And it's got 80 bazillion CFUs in it and whatever.

And I got such mixed results that I was really considering just not using them with my clients anymore. Because it was so unpredictable what happened. And then I learned about you guys from Chris Kresser. And that's how I found your webinar. And so I watched it. And then it convinced me to give it a shot. And my first person I gave it to was my now mother-in-law and her allergies and asthma went away in like two weeks. And I was like, all right, what's going on?

And then we talked on the phone and you explained it to me. And why do most probiotics not meet the criteria of having research or provable results with the formula that they're like, what's going on in the probiotic markets where most of them give really mixed results or don't work very well? Yeah.

Kiran Krishnan: To really understand that, it's important to understand where this concept of probiotics came from. And there's a natural kind of evolution of that concept that has led to the vast majority of the way companies have decided to create probiotics.

And the other interesting thing, just like your experience, one of the reasons why we became so passionate about getting this out there to the market is when I met Tom, and I had met Tom just a few years before we started microbiome labs, we had met through a mutual connect. He's a, you know, he was a functional medicine holistic practitioner in the northern suburbs of Chicago. He had a practice that was very focused on gut health, like 90% of what he did was through the gut, right? It didn't matter whether he was treating, you know, immune conditions, skin issues, depression, anxiety, weight, he always focused on the gut, which resonated with me.

So already we had something in common. But the weird thing is that as a gut focused practitioner, he wasn't using a single probiotic in his practice. And that really resonated with me because I was like, what, you know, how is it that a gut focused practitioner that's seeing, you know, hundreds of patients all the time, he's working seven days a week, not using a single probiotic. And it was for the same reason that you had where he had tried many of them. And most of them were not consistent, they didn't really do anything.

So he kind of gave up on that concept, right? And so this was like, to me, like the reason to, to figure out what really functions as a probiotic and how you get it out there in the marketplace. So to give people a quick history lesson. So the first person that was really credited with this concept of a probiotic, although they didn't call it probiotic then, is a Russian scientist named Eli Metchnikov. He was using a fermented

milk product and he called the organism he was using, Bulgarian Bacillus. And he was treating, you know, severe gut conditions with it, right? So this was the first time there was this idea around a beneficial bacteria that can actually help you therapeutically, because prior to this, bacteria was really, really bad, right? We talked about the plague and other massive amounts of infections that people were getting. And then of course, antibiotics were a revolution in medicine because it saved a lot of lives. So then the mentality was bacteria is bad. We all, we have this awesome tool to kill it. If we encounter bacteria, that's going to save a lot of lives. He flipped the script a little bit and said, well, there's actually beneficial bacteria.

Here's one that I've isolated and created. And then he was using it with patients and actually won, he actually won the Nobel Prize for his work in medicine, right? So this was, it was such a novel concept. So from then, these fermented dairy-like products started becoming more and more popular and becoming clinically utilized. And then in the 1960s, there were two researchers named Lily and Stillwell that coined the term probiotic that, that encompasses many of these beneficial microbes, right? And the word probiotic, of course, means for life. So the idea is that certain bacteria are anti-life, they can kill you. And then these bacteria are beneficial for life. And so that's the word, that's where the probiotic came from.

Now, keep in mind up to that point. And then beyond that point for a couple of decades, probiotics were really thought of as fermented products, right? So fermented dairy, fermented vegetables, all things fermented. So they were starting to pull from traditional cultures and diets and identifying that, hey, this is made by a microbe in some cases fungus, in some cases pro-bacteria, but this has health benefits, has empirical data on it. They were starting to look at some clinical data on the health benefits of fermented foods. And so they were starting to isolate this idea of fermented foods, beneficial bacteria, delivery of probiotics, right? What they did not understand at that time, which is now very important to understand is that the bacteria itself that's creating the fermented food is not what is functioning in the individual, right? The benefit from the Bulgarian Bacillus milk that Elie Metchakos was doing and all the fermented foods that people would consume, the benefit comes from the ferment itself, right? So the ferment has all of these amazing components to it because when the bacteria breaks down the food substrates, like whether it's dairy or vegetables or whatever it may be, it's producing things like organic acids, it's producing peptides, it's producing all of these things that aren't normally found in that food.

And when you consume that food, you're getting all of those. This goes back to what the one thing that I saw Tom using all the time was this, there was this fermented product called Sagan. And it was in these little packets, it was super expensive, it cost something like four or $500 per month supply. And it was a ferment extract. So this doctor had figured out a long-term fermentation that he would do, a Japanese type of fermentation. And then he would pull out the extract and dry it and put it into these little packets.

That was the primary thing Tom was using. So he was using the ferment from fermentation that was far more beneficial than what he had available as probiotics. So that speaks to what Lily and Stillwell and Ily Meshnikov and all the initial pioneers of probiotics were doing, they were using fermentation. Now at some point in the late 70s, early 80s, companies started to, or marketeers really started to figure out, well, if this fermentation or this fermented food is beneficial, especially the dairy side of things, let's just take that bacteria that's doing the fermentation and deliver that instead, instead of the fermentation. So they started isolating fermentation bacteria, drying it, putting it in capsules and calling those probiotics.

Right. So this is why lactobacillus acidophilus became one of the more popular versions of it, because acidophilus is a very popular dairy fermenting bacteria, because it can ferment it at a lower pH. It's called acidophilus because it likes acid. The lower pH fermentation is beneficial because number one, it prevents the growth of mold, because once mold starts growing in that ferment, it changes the characteristics of the ferment. And number two, it creates less of a sour taste.

Right. So the initial capsule probiotics were grabbing fermentation strains and delivering them in very high amounts. That of course is not really going to do a whole lot because the benefit of those strains really comes from their fermentation.

Now there were a couple of researchers that found variations of those bacteria like acidophilus, you know, DDS1 was one of those that were discovered that actually does have a therapeutic effect on its own. But it would do that whether it was dead or alive. It didn't matter. Right.

It wasn't going in and colonizing. And so then this whole advent of just let's grab as many different bacteria as we can. The higher dose the better and the reason for the higher doses are trying to compete against their the competitive brand that they're going after and that brand has 30 billion CFUs. So they're going to go to 50 billion CFUs. They have 10 strains. So we're going to go to 15 strains. That became the whole market focus.

Right. And there were very, very few studies, if any, done on those kinds of products, the multi-strain high dose kind of products that they really did not build any scientific substantiation for having those as probiotics. Where we started to see the rubber hit the road on those products not really being effective is with practitioners like Michael, like Tom, who've been using those kind of products with a lot of promise and seeing that they're not really doing anything. Right. So supplement companies realize that overnight they could create some success because probiotics were really hot. And the two ways in which they wanted to compete with their competitors was number of cells and this and the concentration. That's all they thought about.

Right. They didn't care where they were getting the strains from. They weren't using any strains. Strain IDs, they would just call distributors out of China and Asia and other places and say, hey, give me acidophilus, give me gas or I give me this, they would get powders coming in. They weren't testing the powder to see if it's the actual microbe. They're just throwing it all together in capsules and calling those probiotics. Right. And then in 2015, a bunch of researchers from UC Davis took a whole bunch of probiotics from the shelf and did genetic analysis on them and found that 95% of them had the wrong strains in the capsule than what was claimed on the label.

Right. So all of that was a big mess because we just had marketers going after this crazy megalomaniacal idea and they nobody was investing in research around probiotics. And even up to recently, you have these brands that have a lot of Silicon Valley money and all that behind them doing so much marketing that still have 16, 18 strains in them, 50 billion, 60 billion CFUs. Those were probiotic ideas from the 70s and 80s before we even knew that the microbiome existed. Right. And so it's nice to see some companies

moving in the right direction, but that's why probiotics were the way they are. And still in many cases, that's the type of probiotic that most people have access to.

Michael Roesslein: Makes a ton of sense. And I was that person that was like, well, if this one has 200 billion, and that one has 400 billion, this one has 600 billion, that has to be the best one. Be better. Right. It has 16 strains instead of four strains. Why would I bother with the one that only has four strains? So I want the 16 strains and the 400 billion CFUs.

And then I wonder why I like crap my pants when I go to the, you know, and so it's, that makes a ton of sense though, how it would happen. And 95% of those companies were like, hey, people want this thing, let's make one of these. I know for a fact that one of the largest producers of supplements in the industry has said it doesn't matter what's in these pills, it's the name on the bottle. And I know from multiple people that heard this person say that thing.

And unfortunately, that's the case. So let's get into the star of the show, which took us a long time to get here. Apologize folks, but we're going to talk about the spores. And for the formulation with Megaspore Biotic, which is the product you guys formulated, that is the number one probiotics used by professionals today, there are five, right, five strains of bacillus species, spore forming organisms.

And I guess we'll start there. Why did you choose those five? And I know you could go for an hour on this, but like, why were those five strains chosen for the formulation?

Kiran Krishnan: Yeah, so we chose spores to begin with because of two main things. Number one is to meet that definition, the first part of the definition of what is a probiotic, right? So it has to be a live microorganism, which means that it has to be a microorganism that can survive through the gastric system.

So starting in the mouth, in the stomach, and then small bowel does lots of hurdles for bacteria. And it's there deliberate because these systems are called a gastric barrier in order to try to kill most microbes that are coming into the system, because we developed the ability to eat a huge variety of things. Many things may contain microbes on them that are not beneficial, they can make you sick. And so our gastric barrier, our pancreatic enzymes, our immune system, our IgA in our secretory fluids, all of those things are designed to neutralize and kill bacteria that may be coming in through food so that we can protect ourselves from infectious microbes.

And so, you know, it's a gauntlet for microbes to get through. And the vast majority of microbes that are isolated as probiotic bacteria are super sensitive. They live predominantly in the gut, right? They might adapt to some fermentation in big factories, but they're not designed to be robust because in nature, they don't exist outside of the body, right?

They've never existed in the environment. And so we wanted to find the natural microbe that has the robustness to exist outside in the environment where we would encounter them naturally and then can survive the gastric system. And that's where the bacillus came from.

So spore formers have that protective coating. Now, how do we pick the species that we pick? So two criteria there. Number one is it has to be a human derived bacillus, right? And a human derived bacillus is important because bacillus is a very ubiquitous genus. You've got lots of different species of bacillus, right?

Septillus, coagulans, clausae, all of these. And they're ubiquitous in that they exist all throughout the environment. They exist in every pole, the North Pole, South Pole, Tibetan plateaus. They exist everywhere in the environment. They're in the oceans.

They're in the desert. North Pole. North Pole, they're in the North Pole. Yeah, glacial ice cores.

They exist everywhere. They probably predate some of these tardigrades, right? And in fact, there's evidence that they are likely the seeds of cellular life on Earth because they can survive interstellar travel. So they're found on things like meteorites that come down to Earth from other planets, right? From the Kuiper Belt and all that stuff.

So the idea is that where did things like proteins and amino acids and cellular components come? Well, they're coming from outer space. So during early bombardment of the Earth when the Earth was developing, it was likely seeded with some of these spores. There's a study on bacillus subchilus surviving in the cold vacuum of space for seven years.

So it can certainly enjoy a journey from Mars to Earth on the back of a meteorite. So I mean, these are fascinating organisms that where they have been here way longer than we have. They're incredibly robust. They haven't changed much in the last few million years. When you look at the genetic homology of glacial ice core spores that are like three million years old who are still alive, they have 95 plus percent genetic homology to spores that exist in the environment now, right?

So they haven't changed much because they're so supremely adapted to this environment. And so you can find spores in all different corners of the Earth, but not all of them are adapted to living in the human gut, right? Some of them have developed the capability of binding to mucosal tissues. So they need the right receptors. They also need to be recognized by our immune system as friendly. So they don't cause an inflammatory response when you take them. And they also have to be able to map and control the microbiome.

This is the quorum sensing part of it, right? And I'll elaborate on that in a moment. So we wanted human isolates to begin with. So we went to Simon Cutting, who's probably the preeminent spore researcher in the world. He had over decades isolated lots of different spore strains from healthy human volunteers as he's building a catalog of the different spores that live in the human gut.

And so we went to him. We tried to find the best versions of the strains, meaning ones that we knew were very robust, that had strong competitive exclusion or quorum sensing, could form biofilms to protect the good microbiome, worked well with the immune system, all of that stuff. And we selected strains from there. Now, why did we select coagulants, clausiae, indicus, and so on is because they all have slightly different functions, right?

And they work best in a consortium. They support one and another in their endeavors within the gut to improve the host microbiome. So indicus, for example, produces high levels of carotenoids that brings down, dramatically brings down inflammation in the lining of the gut and allows the lining of the gut to repair. Clauseye modulates immune response so it can bring down inflammatory responses, not only in the gut mucosa, but in the lungs and other areas peripheral to that. We've got coagulants that produces a lot of L positive lactic acid, which is important not only to acidify the gut, which controls pathogen growth and fungal growth, but it also becomes a precursor to forming short chain fatty acids, which are really important.

We know, right, butyrate, propane, and acetate. Bacillus, subtilis, the subtilis version is really important because that's a very strong competitive exclusion bacteria. It's really good at identifying pathogens and bringing their levels down. It also produces high levels of short chain fatty acids. It also produces things like vitamins and other useful nutrients. And it forms biofilms. And it forms biofilms to protect the good native bacteria. It can also then degrade biofilms of pathogenic organisms. So they all work together slightly different roles. And that's how we went about formulating it.

Michael Roesslein: That's fascinating. That's the first time I've heard you talk about the theory of spores, you know, starting, you know, being involved in early life on earth. And it makes sense then that like life forms because they have beneficial functions inside the human gut, but also inside animal guts. And so it makes sense then that it's something we evolved with that there would be a synergistic relationship. Nature doesn't have accidents like that.

Kiran Krishnan: So totally, it's actually called symbiogenesis is the way you describe that, right? Where you take, you know, a couple of different species and you force them to exist in the same environment. Eventually they find a mutualistic relationship, a way of supporting one another. And what seems to be very clear from our relationship with the spores is that we consume them inevitably because they're in the environment. We consume them, they go in.

And then what we've the agreement we have with them essentially is that we'll give you a home, right? All our systems that normally impact other bacteria allow them to exist. So we're completely tolerant of them. Our immune system recognizes them as self, which is something to elaborate on with regards to other probiotics.

And at the same time, they clean up the system, right? They know better how to modulate the human microbiome in a favorable way than we do, right? So that's like millions of years of symbiogenesis, which is wonderful to be able to see. Now, I've mentioned a couple of times this idea of the relationship with the immune system, right? This is one of the things that made me nervous all the time before we launched Megaspore about the other probiotics.

This whole idea of just more is better, right? Knowing that these are biological entities, they have thousands of genes, even if they're dying, their systems, their cell walls, their cell membranes, the things within the cell themselves, whether it's mRNA or whatever it may be, or microRNA, those things are all immunogenic from many of these microbes. And so we started speaking about the risk of other

probiotics actually being inflammatory, more so than beneficial, because if you're getting microbes that you haven't specifically looked at the modulation of immune response, and you're just throwing it at hundreds of billions of CFUs, we thought that that could actually be detrimental to the microbiome and the immune system. As it turns out, two big studies were published showing that these multi-strain high dose probiotics actually slowed down the recovery of the microbiome after antibiotics, because these species, their components compete with our native bacteria for binding sites. So they're actually not good for the for your native microbiome.

And a lot of the work at the APC and University College Cork shows that most of these probiotic strains are actually inflammatory. They are not good for the immune system, because the body doesn't recognize them as self, right? The body sees them as incoming microbes at huge numbers. And so it activates all forms of inflammation and activates TH1, TH2, TH17. So when you put these microbes in, and you look at the the subject's blood markers, you get a huge array of inflammatory responses, versus with the spores, you actually get the opposite. Not only do you not get an inflammatory activation, you get an anti-inflammatory activation.

You get IL-10 going up, right, versus IL-6 or 12. So that's the beauty of nature, right? That's us being just smart enough to understand that nature has already given us these tools. We just have to figure it out, isolated, study it, and utilize it, versus this whole concept of trying to outsmart nature and do things that are quite un-net. I'm not sure.

Michael Roesslein: Outsmarting nature never goes well. I've seen enough movies to know that for sure. Yeah. But no, it all just makes a lot of sense. And there's so much more that's been learned since we first started having these conversations. So we were doing talks on sport-based probiotics and megaspore and seeing incredible results before you guys had even published a single study on this specific formula. I remember we were on a webinar and you were like, we have funding to do this study and we're going to do a study and it was really exciting and you were going to give it to college kids who were going to eat McDonald's and you were going to monitor their LPS. So LPS is determined, I'm probably going to use it in the emails when we talk about this. And then we have a whole webinar on LPS, which is lipopolysaccharide.

The first study that you guys published on this formula, and these are peer-reviewed published studies. And what you talked about at the beginning and I want to reiterate this is that what happens a lot is there might be one strain of organism that has demonstrated some sort of benefit to it. So then a company will produce a product that has some of that in it. And then it has like 12 other strains and they will list those benefits as the benefit of that product. When in fact, when you mix these organisms together, they tend to behave a little differently.

Or they can. They can behave differently and have different effects. So just because that one organism demonstrated a benefit on its own doesn't mean that if you mix it with 11 other things in a strange concoction and ratios and everything, that it's going to do the same thing.

So it was a big deal when you guys were doing the study on this formula, specifically. And the first one was on leaky gut. And the way that you measured the leaky gut was by measuring circulating levels of LPS

or lipopolysaccharide. So if you could just explain what LPS is briefly again, we have a whole webinar on LPS and what it is and what it does and why it's important to lower it.

But just in the shortest terms possible, what is LPS? Why did you choose to measure that? And why is it a big deal? Like what were the results of the study? And why is it a big deal that that's reduced?

Kiran Krishnan: So LPS is an endotoxin, right? So there's a key component to that word. Endo, meaning it's generated within. This is opposed to an exotoxin. An exotoxin is one that comes in from the outside. So like mole toxin in your house would be an exotoxin.

This is generated in your gut itself. And it is a toxin in that it has a toxigenic effect on the system. It's very pro-inflammatory.

It can damage tissues and so on. So you've got about, you know, half or more of the microbes in your microbiome that are classified as gram negative bacteria. What that actually means is that they don't have a cell wall structure. They only have a cell membrane. So those microbes have this LPS in their cell membrane. Now, the microbes use utilize it for lots of different things.

They use LPS for binding to things, to signaling to other microbes and so on. And it's not a problem necessarily when it's in the microbe living in the mucus part of your gut, where it becomes a problem is when that microbe dies and lices and opens up, the LPS gets released as an individual compound and it gets stuck in that mucus layer. Now, normally that's fine because then eventually it just goes out through defecation or if you have a really healthy microbiome, you've got other microbes that can metabolize that LPS or your secretory IgA will neutralize it and so on. But in people with leaky gut, what tends to happen is that LPS is released. It's sitting there in the mucosa and then given the right impetus, it leaks through the lining of the gut and ends up in circulation. So you can measure levels of it in circulation.

Now, why did we measure that? Well, that's because LPS has also been found to be the precursor to tons of chronic illnesses. In fact, the 2015 publication, and this is one of the one of the main publications I read on this, and which you got us super excited about just studying LPS impact itself. One of the main one of these publications, it's a meta-analysis paper, which means it's a study of lots of studies on the topic.

This is a 2015 publication in frontiers of immunology. And what they showed was leakiness in the gut that results in endotoxemia, that is the migrating of LPS from the lining of the gut into circulation was the number one cause of mortality and morbidity worldwide. It was a number one killer. Right?

It sounds crazy because you're like, what? That one thing is a number one killer. Well, it is because LPS is one of the biggest sources of chronic low grade inflammation in the body. And it's incredibly pervasive where it can get into almost any parts of the body. You find it at very high levels in the brain, in people with anxiety, depression, Alzheimer's, Parkinson's, and so on. It interferes with dopamine binding and serotonin binding.

It causes inflammatory damage to the brain. You find it in joints of people with RA. You find it in all over circulation of people with autoimmune conditions. You find it, you know, messing up the pain careers and interacting with visceral fat in people who are obese and have metabolic syndrome. So what it's been shown is that this migration of LPS into the body at high concentrations is the number one cause of chronic disease. So we said, OK, if we had a probiotic that can stop the migration of LPS by sealing up the lining of the gut and modulating the microbiome, then we have something here that would be quite profound.

So that's why we decided to study endotoxemia or LPS to see if the probiotic can actually stop LPS from migrating through. Now, the structure of the study was very simple. You take, you know, healthy young individuals and most supplement studies are supposed to be done in healthy individuals rather than a disease population, because if you do it in a disease population, according to the FDA, then you're treating the disease and then it becomes a drug, right? So then you're supposed to do it in a healthy population. Fortunately, and unfortunately for the population, but fortunately for us, a huge chunk of the quote unquote healthy population has massive amounts of leaky gut, right?

Again, it's a precursor to further problems, right? So a lot of people have leaky gut without knowing they have it and they may be fine for a while until the leaky gut becomes super profound. So how do you induce and test for this leaky gut when they have it, but they don't know it and they may seem totally fine. You do something called a food feeding study, a challenge study. So you sit them down, you give them a really high fat, high caloric meal.

The high fat, high caloric meal junkier, the better will induce amazing amounts of permeability in the lining of the gut if they don't have a healthy, robust microbiome. And then you can measure their pre meal LPS levels in circulation. And then we also look at all the inflammatory markers as it relates to that LPS. And then we do three and five hours after the meal. So post-prandial, we measure serum LPS levels again.

And we also measure all of the inflammatory markers that go along with it. What we found in the first hundred or so students that we screened about 55 percent of them had severe leaky gut, meaning every time they ate food, in this case, this was not a great meal, but it doesn't matter. It happens even when you eat healthy food. It's just a process of digestion and the volatility that's involved in that process makes it opens up the lining of the gut. They get a massive dose of endotoxins in their system. And then their inflammatory markers all go up. Now, some of them may feel this to a certain degree. They might feel a little flushing. They might feel a little loose, sorry, aches and pains and lethargy.

But many of them don't and they don't feel it until it becomes a severe problem. Right. So we took this. Then we took the group that had bad endotoxemia. We split them into two groups, gave one of them placebo for 30 days, give another one of them probiotics for 30 days or mega sports specifically. Had them come back 30 days later, do the same food challenge. They didn't change anything else about their behavior. They're still going out and partying, eating junk food, being stressed like college students. All they did was take the probiotic.

Right. When they came back, we saw over almost a 70 percent reduction in endotoxemia in these individuals. So we we were 100 percent of this of the students taking the probiotic responded, which was great, which means that 100 percent of them saw the effect. The average effect size was 70 percent, which is amazing, because many of them saw 100 percent alleviation of leaky gut and endotoxemia. Some of them saw 40, 50 percent. Right.

So you take the average is somewhere around 70 percent. Not only did we see a complete sealing up of the gut and even though we give them the same high junk food, high bad fat type of meal to challenge them, their gut is not becoming leaky now. Right.

Despite the fact that we're giving them the same bad food. Now, not only did we see the LPS endotoxins reduced dramatically. We also saw all of the inflammatory markers associated with LPS coming down dramatically.

Right. So these individuals went from being super inflammatory all the time, as we saw in the beginning, to being non inflammatory, anti-inflammatory. Actually, in that 30 day period, right? The placebo group, not only did they not see a reduction in LPS and endotoxemia. They actually saw a 30 percent increase in the overall rate of endotoxin and the severity of it. So they got worse in that 30 day period, and all of their inflammatory markers got worse concurrently as well. So we show this heat map picture when we do that, showing this one group went from inflammatory to non inflammatory, even under the conditions of eating a terrible, high fat, bad oxidized fat, high caloric meal. This other group started inflammatory and became more inflammatory in that 30 day period.

Right. And we saw lots of other things like triglycerides improving, gut brain function improving, all kinds of things. That was the foundational study for us.

And here's an interesting thing. We published it in the World Journal of Gastrointestinal Pathophysiology. It's a well known, decently impactful GI journal. Now, the reason we ended up publishing it in that journal was for two reasons. Number one was because it is a open source journal, which means you don't have to pay to get the copy. We wanted to be able to share this research with everyone, so we're going to be able to send them copies all over the place. Number two is the journal was so excited about the study that they actually forego all of their review fees about it. So normally when you submit a manuscript or journal to review, and you may submit it to three or four journals, so you hopefully one of them takes interest in it and it passes peer review.

So we submitted to a few. This journal saw the topic and said, barring that this passes review by our peer reviewer. So their peer reviewers are researchers in the field all over the world. They send the copies to and they come back with comments and all that. But the journal said, if it passes peer review, we would forego the cost of doing it, which is normally like four thousand bucks.

Right. And the reason is because they wanted to publish on a solution for endotoxemia, because as a GI journal, they had published the issues with endotoxemia before that. They had published how LPS endotoxemia causes disease pathology. This is the first time that they're publishing a solution for it. So

they were excited about it. And in fact, they called it a frontier paper. And it was in that, you know, edition of the journal, I believe it was there was a little blurb in the front page of the journal on this frontier paper.

So so that was really exciting. And then all our studies kind of stem from that. We started saying, OK, what else does LPS impact knowing that we could stop LPS? Oh, triglycerides. Let's start a study in people with elevated triglycerides. Rheumatoid arthritis. Let's study it in people with rheumatoid arthritis. You know, people with with IBD. So we started we did studies in IBD.

So we started doing numerous studies all from this idea that we are foundation only improving the microbiome, sealing up the leakiness in the gut and slowing down, if not stopping, one of the biggest drivers of chronic dysfunctions, which is endotoxemia.

Michael Roesslein: That is wild. I only knew about half of that. Every time I have you on to talk about spores, I learned more about LPS and the studies that you guys did. Nobody was giving me spores when I was in college.

I want like a redo just pizza and pizza and meat. I'm going to do better college with it. Yeah, I probably would have done better in college with that. And just in the chat real quick, Diana asked for posting citation. I just posted a link to a webinar that we've done with him in the past that goes over all 13 studies and has them all listed.

So you even found her paddle protection like liver protection is equal to milk thistle, which is the commonly used supplement for liver. I remember some of the studies I was like, how did you even think to study this? And so really wide ranging effects and benefits. I can't exaggerate if I tried how many people over the last 10 years have reached out to us and shared their story or shared their situations. It's been a staple in our family for the last nine years and you know, tens of thousands of practitioners. I can't believe it's the number one selling product on Fullscript. I didn't know that.

Kiran Krishnan: Yeah, and it has been for like four or five years. Yeah. And it has been for like four or five years. And keep in mind that, you know, we're not. I mean, we became better marketeers, but we didn't as a company, we didn't even have a marketing person or department until late 2018, early 2019. Right.

So for the first five years of the company, we didn't have marketing per se. And so because we just focus all our efforts on the science and talking about the science and presenting webinars with us.

Michael Roesslein: Yeah, exactly. Yeah, that was that was the extent of the marketing. Right. Now, so then how does it become the number one product? Well, we started surveying when we seeing this massive inflection of growth of practitioners 2017, 2018, 2019. We started surveying those practitioners and asking them why they can't why they opened up an account, right? Eighty seven, almost 90 percent of them said they did it because they heard about it from a friend or colleague, which to us then was like the biggest validation because you can get customers by fancy marketing, which is what a lot of supplement companies and probiotic companies do.

Michael Roesslein: They get the literally raise hundreds of millions of dollars for marketing and branding and all that. We didn't spend a dime on it and we were getting a massive amount of traction because it works so well and so many practitioners were so frustrated that they couldn't get any functionality to most probiotics that they had to call and tell their colleagues about it. And that that was to me the best validation. That's how it's scaled to becoming the number one product. It was not through any sort of fancy genius marketing efforts of us.

You know, we just were everywhere. I can vouch for that, that there was no marketing like the marketing was the practitioners using it at working. A lot of those practitioners probably started using it because their patients harassed them to try it. Because people were learning about it or hearing about it in groups and it kind of spread like organically on the internet, which was easier to do then. Now you'd have to have a bunch of money behind it for it to be able to do that because the internet doesn't let you just spread things for free anymore. No, the algorithms.

It's a lot more difficult. But I put links in the chat to Megaspore, Megaspore for Kids, and I included the Total Gut Restoration Trio, which has two other products in it that Microbiome formulated to be complimentary to Megaspore. We put them all on sale. There's a code there.

Save money on those products. It's in the chat. So check that out. We're also going to send out emails over the next few days with some more links, some more information to replay of this. I'll send out links to some of the other things that were cited. Actually, what we'll do is for the recording of this webinar, the page that it's on right below, we'll put some links to some of the other stuff that we cited here, the webinar on LPS, the webinar doing the research studies.

Like we've got you want to go down this rabbit hole. We have more videos and content on on Sport Probiotics than probably anywhere else on the internet, so we'll link a bunch of it on that page. And you guys can can check out those links, learn more about the products, grab them, try a sale. So here's the conundrum and I'm going to put you on the spot. So we have a whole bunch of questions. This webinar was an hour later than normal, so it's 9 p.m. here. I'm going to get in trouble if I stay on here much longer. So do you think it would be possible in not a super long amount of time, but not immediately right away to come back and do a quick sport probiotic Q &A and just all these questions at once instead of me staying here for another hour to answer the questions and then getting in big trouble when I walk out of this room, because for those who don't know, I have a baby who turned 10 months old yesterday and his bedtime is right around now and I'm normally helping and I'm not helping right now.

And if I continue to not help for the next hour, there could be problems. Yeah. Yeah. So would you be open to doing a Q &A just on sport probiotics and I'll pull all the questions from here and we can set that up for some time in the near future?

Kiran Krishnan: Yeah, we should do it very near future. Sometime in the next week or two. I'd be happy to because I know when people listen to things like this, they have burning questions and I don't want them to lose the interest in momentum and get their questions answered. I do want to make one of the comments that I mentioned earlier about other companies coming out with sport probiotics. Yeah. In

part, that was exciting to me because it was nice to see like, you know, sport probiotics now finally getting the recognition that they should.

Michael Roesslein: The problem with that. What's the?

Kiran Krishnan: Yeah, exactly. Imitation is the most. Imitation is the most. Imitation is the most. And the funny thing, of course, is many of these companies are ones that we took Megaspore to and said, hey, this is the next evolution of probiotics. And they said it's the dumbest thing they've ever heard.

So but then now, of course, once you create a market and you create, you create a need for it, then people come in. The problem I still see is they're taking the same approach as they do with any of the probiotic where they're just grabbing strains, they're throwing it together and they're not doing studies on them. Keep in mind that that spores, Bacillus subtilis, you know, H-U-58 versus another Bacillus subtilis can be very, very different in their functionality and that can be affected by just one or two genes.

Right. They can have five percent of their genes different and still both be Bacillus subtilis. And the five percent of the genes can completely change how that organism functions in the system. Our psychobiotic, you know, the Zen biome, the 1714 strain, which is a bifidobacterium longum, incredibly powerful strain in terms of anxiety, depression, all those issues, all of that is conveyed by one gene in that organism and you take that one gene out, it doesn't do any of those things.

Right. So so again, it's back to this idea that, OK, hey, here's these guys that brought spores to the market or have done all the studies are showing that spores are really effective. We're going to copy that and also do our own version of spores, ordering random strains, putting them together, saying, hey, this is now a new spore based probiotic, zero studies on the finished product. Right. That I think is where consumers really need to start demanding that supplement companies have studies on their finished product because you have no idea what the product does in your system if they don't have that study.

So be very careful and worry. I'm not aware of any of the other companies that have spore based probiotic formulations that have done any studies on the finished product. This they are using one or two strains that have studies on the strain itself. But again, they're combining it with other things and then assuming that the combination works well.

So for your money's sake, for your health and wellness sake, to protect your investment in your health, go with things that have studies on the finished formula. And that's such an important thing to do.

Michael Roesslein: I haven't seen any others, like you said, in the sport.

Kiran Krishnan: Nobody else is doing it. Category. It's very expensive. In one of our webinars, you talked about like what goes into running those studies. And so it's not just to throw everybody under the bus. A lot of supplement companies, especially if they're just starting out, like you guys couldn't have ran that study 10 years ago. The first time you like it had to grow first because it costs a ton of money to run these. I don't know how much that first study cost you guys to run. Like $400,000. $400,000.

Michael Roesslein: We didn't even have $400,000 in sales at the time. Yeah, just like scraping together money, hoping that it plus it's a huge gamble. Because if it was a small company scrapes together $400,000 and the study doesn't come out with favorable results, you're done then. That's it. Like you're over because you just spent more money than you actually have and that you're selling and you did it to prove that your product doesn't work.

Michael Roesslein: So bury that sucker right at the bottom of the pile. Nobody needs to see that. Let's not publish that one. But yeah, it's a huge gamble. It's a huge risk. It's tons of money.

It's really difficult to do. So it is. It's great. And you kept firing them out one after another after another.

So it just went from like five to seven to 11 to 13 before I was even able to keep up with what was going on. So I did post in the chat a bunch of comments ago, a link to our research summary webinar and then somebody asked for a SIBO. I posted a link to that one and then I posted again the products in the coupon. And that'll be going for a couple of days.

For anybody who wants to try out the spores, there is Megaspore for kids, which is a gummy and then there's Total Gut Restoration Trio, which we're not going to get into, but it involves Megaspore and has a couple of complimentary products. I'm going to stick around for a minute just to scan the the chat for a couple questions to see if there's anything I need to add. I've already copied the Q &A over. So I'll have that. I'll touch base with you. We'll make space in our calendar to do a Q &A follow up to this. And we'll get it done. We'll get it done soon.

I'm looking right now, but I'll have to move a couple of things around, but I'll make it a priority and we'll get it. We'll get it on the list or we'll get it. We could probably even do it next week.

So the thing I think we'll get next week, we could we could move. So that'll be fine. Let's just I'll communicate with you and we'll get it set up for for next week. OK, awesome. All right. Well, thank you. Thanks, everyone, for showing up.

Sorry for the issue with the Zoom link and the other link and everything else. The products used widely in the autism community should the person who asked that question in the Q &A. They are in the chat.

I mean, and. Yeah, thanks for showing up. Sorry about the link snafu. Thanks for everybody that got the email 20 minutes prior.

Mary Ann's the MVP. If she wouldn't have sent me a message and said, hey, Zoom didn't send the reminders. I wouldn't have known. Nobody would have got reminders.

And it would have been me and Kieran hanging out here talking about spores by ourselves, which we've done before. Done. Yeah. You guys be here. So thanks, everybody, for being here.

I will get the I got the questions copied. So there's one more that just got added. So I'll add that. All right, Kieran, you can jump. Thank you, everyone. I'm going to stick around for a minute, everyone, and I'll go through the chat and grab.

Yeah, anymore. We'll see you soon. Thank you. Yep. Thank you. Hey, everybody, thanks. Thanks for toughening it out with all my tech issues.

I'm scrolling through the chat to see if there's more questions that I can copy into this list. And I will get Kieran back next week to do a Q &A, which I didn't want to put out there, but he did. I don't usually expect him to do that fast of a turnaround. He's quite busy now, but that was nice of him to do that. All right, I'm copying any of the extra questions from the chat just so I get them all.

And is it right? Oh, OK. All right, I think I got them. No, you don't need to be monitored by a functional medicine doctor to take the product. We've had thousands and thousands of people over the last 10 years get it through us, and we help them if they have questions. As much as we can, we're pretty well trained on the products at this point. I could I could be a rep for microbiome labs at this point. I've interviewed Kieran like 60 times.

So I know the answers to most of the questions, but he speaks much more clearly and eloquently on them. Absolutely, it's fine with level thyroxine. I mean, talk to your doctor, but there's no interactions with with that medication. Thank you. Everyone's Mary Ann, so I don't know who I'm talking to.

You don't need to be monitored. Olivia, if your questions in the Q and A, I have it. I see it.

The Megaspore for Kids question. Enjoy the bedtime routine. Thank you for the congrats. Yesterday was 10 months. He's now starting to walk and he's eating food.

And he takes spores too in about three or four of his bottles a week that we give him. So the non-dairy prebiotic we can add we're actually having a whole new website built. That's not been announced yet, but there's a whole lot of things that are changing and coming. A new high production value podcast with this fancy camera that didn't work on Zoom today and a new website and some new branding.

It's rebranding the company a little bit and we're redoing the shop. We'll make sure to add that. We haven't added it because there was no demand for it really. And it costs a lot to do that kind of thing, but we're going to add it to the new site. And we can send you a link to get it if you want. Reach out to Mary Ann.

She can send you a link and we can figure out a way for you to get it, even if it's not in our shop. All right. I think that's all the questions.

Thank you, everybody. And it'll probably be next week, Tuesday or Wednesday. I'm not sure, but I'll hook up with Karan and we'll get it figured out and we'll get a Q &A set up. And I just realized there's some questions in my email too. So I missed those. So we'll we'll do all the questions.

Thank you. Oh, many days before you would feel a difference. Some people, it's quickly, we tell everybody, give it at least 90 days. But the studies were all done on 30 days worth of. I believe all the studies were 30 days. Like there's 13 studies that have been now done showing wide ranging benefits. And I believe the studies were done over 30 or 30 days, not 90 days.

I'm not entirely positive. But I think it's 30 days studies. So some people, it's quickly other people, I need to start really, really slow. And they still struggle if they take it too fast. So we didn't talk about dosing. We'll do that in the Q &A then also I'm going to make a note of that. So starting low and slow for people who are sensitive to things. This is on the website and it's with the product and everything. But we've had people start as low as like a quarter of a capsule every other day.

Who are really, really sensitive to stuff and then work their way up. Full doses, two caps a day with the largest meal. All right, I need to go do bedtime now. And for the question, can Kieran also discuss the physiology of the gut and how the bacteria interact with the immune system? We have a whole webinar on that. It's like 90 minutes.

It's probably the most comprehensive training on the subject anywhere. It's probably on the second or third page of videos on our website. But I'll try to include links on the recording for this.

And it's kind of top secret right now, but we're in the process of creating a microbiome optimization course with Kieran and it will feature all the content that we've ever produced kind of curated down and then an actual training course that he's working with us to put together and nothing like that exists. People have been asking for it for 10 years. We've talked him into it, but I'm going to do a lot of the heavy lifting of curating all the content, getting it all together, and then he's going to come in and fill the gaps and be the presenter and do all of that. And so that will be ready hopefully in August is what we're aiming for. But that'll be the first of its kind.

He's never done anything like that. And it'll be really, really cool. We've got some cool plans for it.

And it's a secret, so don't tell anybody. All right, just 81 of you. So all right, everybody, I got to run. Good night. And thank you, everybody. I got all the questions down and thanks, everyone. We'll see you soon next week.