Michael Roesslein:

And we are recording. The product spotlight for MegaMucosa, that's going to be the topic today. The last one we did, the MegaSpore one, was a ton of fun.

Kiran Krishnan:

Yeah.

Michael Roesslein:

We don't have to talk about you blowing all your initial funding money for the company and going to work seminars that maybe or maybe wasn't going to work and all that fun stuff about throwing all the money on the table hoping this is going to work. So, if you didn't hear that, he gave the whole breakdown of pretty much how Microbiome Labs got started in the MegaSpore one of these product spotlights and the background on how they got into probiotics and MegaSpore. But, most [inaudible] a lot of history there behind the company that was really fun and interesting to hear. And it must seem like forever ago that you guys were at a conference and nobody knew who you were and you weren't one of the speakers, and you're trying to hustle at lunches to get people to listen to you.

Kiran Krishnan:

Oh my God, yeah. And then getting one or two people at the lecture. Crazy. Speaking to a crowd of two.

Michael Roesslein:

I've had a couple of things go sideways like that. And when I used to teach in-person classes when I was living in Chicago, I had two or three people show up one time. And you have to still be on your A game.

Kiran Krishnan:

Totally. Yeah.

Michael Roesslein:

You're giving the same speech feel as if you were giving it to 200 people to those two people. So it's-

Kiran Krishnan:

Yeah, you can't do a disservice to them. They spending their time with you. I can tell you, it feels much better to talk to crowds of two to 300 than two, but absolutely grateful for those two.

Michael Roesslein:

Yeah. For sure. It's got to start somewhere, right?

Kiran Krishnan:

Mm-hmm (affirmative).

Michael Roesslein:

Yeah. Our first webinar that we did probably had no more than 50 people on it, and then we've done some for hundreds as well. Let's just get rolling. Like I said, we covered the MegaSpore in the first product spotlights. Now we're back to do MegaMucosa, which is actually Microbiome Lab's second most popular product. So we're

probably just going to go down that. That'll be how we cover them is, that's the determining factor. But this is ... It wasn't the second product you created, that was the K2, was it?

Kiran Krishnan:

Right. Yeah. And the K2 straddles a little bit in gut health, a little bit in [crosstalk] overall health. So, it didn't necessarily fit into the system of rebuilding the gut. But I think there was another product before MegaMucosa, but we were conceptualizing the idea of MegaMucosa for some time because we knew that we were missing a couple of critical pieces in the idea of completely repairing the gut, right, so we can go into the why story for MegaMucosa.

Michael Roesslein:

So spores can't do it all?

Kiran Krishnan:

Yeah. And the spores are like, if you have a broken car, the spores are like the mechanics. And they have all the intelligence, they have lots of capabilities to fix it, but there are some components of it where they're going to need special tools, right, and the Mega Mucosa provides certain key tools. So, a couple of the things that we noticed going through the research and of course we're always looking for more and more these, the opportunities to create more profound effect for people. In going through the research, we realized that a big part of repairing the gut is based on what is going on in that mucosal tissue, right, and the fact that you have leaky gut means that the mucosal tissues is damaged in a certain way. Because your gut doesn't necessarily become leaky until the mucosa gets damaged because the mucosa's sitting on top of that intestinal epithelium.

So when the mucosa starts getting damaged, that's when there's access of all the toxigenic things to the intestinal epithelium, which will eventually make that leaky. So we knew that with the spores, we were starting to fix the dysbiosis. We were starting to the leakiness in the intestinal epithelium itself, but then we weren't necessarily addressing everything that's going on in the mucosa part of it. And that's really important. So, the rationale behind how we thought about it was, "Okay, number one, what are the components of the mucosa like, what is it made out of that we need to add into the system to make sure that we had adequate building blocks to rebuild the mucosa?" So once you have the components, then number two is what are the stimuli that are required to create that rebuilding response, right, and then number three, what would prevent the rebuilding from occurring should you have the components and the stimuli? So that's just a simple way that we thought about it.

And, A, the components are four key amino acids, right, those four key amino acids in L-form, are the amino acids that get glycated or they stick a sugar component on it. So then you end up with this glycoprotein matrix, which is essentially a gel. And that is done by goblet cells, right, so goblet cells in your intestinal epithelium do that all day long, but they need those four amino acids in order to build that mucosal structure. And when we were looking at the research, it was clear that when you have a damaged mucosa, if you've got a regular diet of amino acids coming in, you'll get some rebuilding going on because you'll get some of those amino acids. But then when you supplement specifically with those four, it increases that rebuild by like 95%, right, So to us, I was like, "Oh my God. Okay. That's an important piece we've got to stick in there." So then we dealt with the issue of the building block.

Then the second part of it is, what's the stimulus to get them to rebuild. Well, the stimulus was already being addressed by MegaSpore to a certain degree, because the stimulus comes from a short-chain fatty acid production, which MegaSpore on its own increased the short-chain fatty acid production a significant amount. And then number two, the growth of Akkermansia. Akkermansia is a really important microbe for sending

triggers to rebuild a mucosa. MegaSpore on its own increases Akkermansia to a certain degree. However, another really potent way of increasing Akkermansia is through the use of polyphenols. Akkermansia loves polyphenols. And so polyphenols have been shown to increase the growth of Akkermansia.

So we said, "Okay, we've got short-chain fatty acids pretty much covered. We need a boost to give Akkermansia some growth potential." So that's when we added in the polyphenols. So now we've got the building blocks, the four amino acids, and we've got the stimulus to rebuild taken care of. The polyphenols played two roles because it also helps with the components that may prevent the rebuilding of the mucosa, right, so what are those components that may prevent the rebuilding of the mucosa?

Well, the big one is inflammation in the mucosa. So a chronic inflammatory response in the mucosa, because of how the immune system is now recruited into the mucosa, because it was leaky and damaged for some time and then the tendency of the immune system to shift towards this pro-inflammatory response to everything that's coming in there, that creates a net inflammatory blanket, if you will, in the mucosa and inflammation negates repair, right, we know that from even basic from your skin, right, that's no different than if you cut your hand, if you continue to inflame it each day by rubbing it, the cut will never heal properly. So the cut needs to be left alone in order for it to actually heal. So the mucosa is in a similar manner, that if the inflammatory response to the mucosa was continuous, then it would really slow down the rebuilding process.

So then we said, "Okay, the polyphenol actually does help with that because the studies that we have, the clinical trials on that polyphenols show a measurable reduction in the inflammatory markers associated with mucosal damage, so it's doing that already." And then that's where we went to the IgG because we said, "Okay, we also want something in there that can neutralize toxins, neutralize things that create this toxic load in the mucosa, neutralize bacterial toxins that may be being produced by a dysbiotic gut that drives inflammation in the mucosa. We also need something that has been shown in conditions that are associated with a damaged mucosa to be able to repair that mucosa." And fortunately the IgG has those kinds of studies. So they've got a published study on pediatric ulcerative colitis showing a reversal of the index within ulcerative colitis, which means that the pathology of the condition is improving, which is in large part, the mucosa. And then even in HIV enteropathy, they have published studies in that, showing that they were able to modulate the immune response in the mucosa in HIV enteropathy, which is a severely inflammatory condition in the mucosa itself.

So those kinds of studies told us that, "Hey, this is one of the really important components we need in repairing the mucosa." So, that's how we built the product out with that kind of thinking. And of course, I'm simplifying the thinking for you here, but this takes a lot of research into the pathophysiology of gut dysfunctions and immune dysfunctions. They really identify where the big issues are, where the pain points are in the recovery process and how we can reverse that and go backwards so that we can make the improvements.

Now, the product was a hypothesis, right, based on really good signs, the hypothesis was, when you add this to what the spores already do, then the benefit should be measurably better. And sure enough, we launched the product. It's a difficult conversation, even with practitioners, to talk through and explain all of this, but people started trying it and they started to understand the importance of the mucosa component of it. And very quickly, within, I would say the first eight months of launch, it very quickly became the number two selling product within our whole line. It still remains there today because of the impact that it has once you're already taking the spores. So the additive benefit on top of the spores is really quite profound.

And then we started getting people telling us about all kinds of effects that we didn't even really anticipate, effects on their lipidome or their lipid levels in their blood, effects on anxiety and mood disorders. And all of those things, when you go back to it, are tied to the presence of dysfunctional mucosal, immune response, pathogens in the mucosa that are producing toxins, all of those things that get addressed with this particular product. So, it became very exciting to us.

We actually just completed a study on ulcerative colitis. This was in an animal model because you can't do these kinds of studies in humans, but we were comparing the effect of a well known treatment for UC flares, which is prednisone. We're comparing the response of just doing MegaSpore or MegaSpore with MegaMucosa against the standard of care, which is prednisone. And what we found, and hopefully this paper will be published sometime in the next four or five months, it's hard to predict, but what we found was that the combination of MegaSpore and MegaMucosa was more powerful than the MegaSpore alone. And the MegaSpore alone was actually similar to the prednisone. So the combination seems to be clearly additive. It's one of our favorite products, it's one of the ones I take all the time and we get just amazing responses from it.

Michael Roesslein:

Cool. There's been a lot of research that's happened since I think this first came out, which is when I first got briefed on it. So, I know you have some joint studies going and I've heard from others that are in the research world that peer reviewing and publishing and things right now are tricky with everything's backlogged and sideways, the rest of everything.

Kiran Krishnan:

Yeah. [crosstalk] aren't even reviewing papers right now. They're so backlogged that you'll send them and they'll just send a reply back and say, "Thanks for sending it. We can't look at anything for a year." But we're very confident it'll get published because it's a pretty well done study and it's very relevant, because it speaks to the current state of how you treat flare-ups in the gut.

Michael Roesslein:

Yeah, which almost all involve damaged mucosal layer. But while we're talking, we're assuming that everyone knows mucosa mucosal layer to an extent. Could you just give super short what are we talking about regarding mucosa and mucosal layer? I don't remember the exact subject line, but one of the subject lines for the emails for this, I said something about mucus is awesome or let's have more mucus or something. Because mucus gets a bad rep. Everyone thinks, they think, "Oh, it's like when you have a cold, blow your nose, whatever." But actually when you're sick, it's helping you out by being there.

Kiran Krishnan:

Absolutely.

Michael Roesslein:

So, is that the same, like the mucus in the nose and the head that everyone thinks of and then the mucosal layer and the gut it's one system?

Kiran Krishnan:

One system, yeah. And what's happening in your sinuses or in your head, in your nose is constantly being translated to the gut microbiome. And the gut microbiome is creating effects in those localized areas as well through the mucosa, which is a really important component of your entire immune system. But let me show you this diagram just to help explain it a little bit. So, when you look here under the, this way, under the healthy mucosa, you've got your intestinal epithelium. These are the cells that line the intestinal epithelium.

Above it, you've got this mucosal layer. Now, in your gut, you've got a dual layer to it. You've got this mucin-2 layer, which is an inner part. This is the closest area to the intestinal cells. And then you've got this mucin-1 layer, which is where all the microbes and all live, right, and then up here is the tube, the tube where food goes

through. So the hollow part of the tube, called the lumen. And then down here is where your circulation is. So, if something gets all the way through both layers of the mucosa and then passing intestinal epithelium, now it's entering into the bloodstream, right, so this whole thing is the really important barrier that separates the outside world, which is up here, the tube, from the inside world, which is down here in the circulation.

So this is what your mucosa looks like. It has two distinct structures. When the mucosa starts getting damaged, it starts to look like this, where the inner structure gets eaten away and gets damaged, which means all the bugs in the outer structure end up flowing in. And when all those bugs flow in and end up close to the intestinal lining like this, then you start getting a panicked immune system that starts recruiting immune cells to this region because the immune system is anticipating basically an invasion of microbes into the system, right-

Michael Roesslein:

Pulling the fire alarm.

Kiran Krishnan:

Exactly. Yeah. If all these microbes are allowed to move in, it's basically bacteremia or sepsis. So this is your body's protection against sepsis, and that occurs chronically. So when your mucosa is damaged, you chronically have a translocation, is the official word, of microbes into that inner part. That chronically triggers immune responses. And you've got chronic inflammatory response going in the mucosa.

Why that is so impactful in the rest of your body is because the gut mucosa is a central command center for the rest of the immune system. What's happening in the gut mucosa gets translated to the rest of the body. If you've got this massive inflammatory response going on in the gut, then it's sending that signal to all the other mucosal tissues going, "We need more inflammatory responses in all the mucosal tissue," because it's trying to protect the entire system, right, so all of it is a singular mucosal system and it all gets translated. And so if you have chronic sinus infections, if you've got a chronic UTIs, you've got chronic BV, you've got infections in other parts of the body chronically, oftentimes because the mucosa in the gut some sort of dysfunction going on with it.

Michael Roesslein:

So what's going on up here would mirror what's going down there and vice versa. So if you eat certain stuff and you get all head coldy and flammy and snotty and whatever, that's probably happening there too then.

Kiran Krishnan:

Totally. Yeah. And in fact, it starts there, right?

Michael Roesslein:

It's starts there in the [inaudible].

Kiran Krishnan:

Yeah. Because the food goes in and goes into the gut mucosa first, and then you feel it right here in your sinuses and all that. I have the Asian glow problem, so when I have a glass of wine, the alcohol and the phenols and all the stuff, the sulfites in the wine are going in my gut. But as soon as my gut mucosa starts reacting to it, I feel it here and I get red in the face and all that from that, right, it translates to almost immediately.

Simon [Cutting], where we isolated our stranger originally, he did a study where he took a tetanus antigen. Everyone knows about tetanus, the pathogen. You take the antigen and you stick it on the spore and then you

swallow it. And then once you swallow it, within two hours he was able to show anti-tetanus antibodies being produced in the vaginal mucosa in women. So that's how quickly the message got translated, right, so the women got exposed to the tetanus antigen in the gut mucosa. And in this case, it's along with the spores. So the spores actually really interact with the immune tissue really well in the gut. And that created this systemic response against tetanus that you could measure even in the vaginal mucosa within a couple of hours.

Michael Roesslein:

That's crazy.

Kiran Krishnan:

We had talked about, I think a while ago when I did the microbiome control of the immune system, I mentioned how the mucosa on the inside is actually the largest surface area in your body, right, it's a little over 4,000 square feet in surface area comparing that to 40 square feet of skin that we have-

Michael Roesslein:

I'm proud of myself. I looked that up and found that number, and put it in an email for this webinar and I was almost accurate. And we didn't talk to each other. I knew that I remembered something from your last, the other presentation about the surface area. I was trying to get across to the readers how vital the health of the mucosa really is. That it's not even just in the gut, that it's every hole that we have where the outside can go on the inside has mucus.

Kiran Krishnan:

Yeah. It enters through a mucosa. Yep. Everything. And most of the entrances end up in the gut actually, because if things go in your eye or your nose or your ear, all of these things drain into the throat, right, so the ear has eustachian tube that drains into it. The nose of course automatically drains into your throat. Your eyes, through the tear ducts and other glands, it'll end up in your throat.

So, everything is filtered into the gut. And even if it goes through your skin, below the epidermal layer is the mucosal layer, so it's going to enter a mucosa there. If it goes through your urogenital track if you're a woman, it goes through the vaginal canal, or even for men, if it goes through the urethra, it's going to end up in a mucosal tissue. That's the largest sampling site in the body. And that's where all of the decisions are being made by your immune system as to how to react to the thing that's entering in. Whether it's a environmental particle, it's a food component, it's a virus, it's a bacteria, it's making those decisions. And then with immune dysfunctions and gut issues, those decisions often the wrong decisions. It's attacking everything, right, in the case of food intolerances, allergies, and so on.

Michael Roesslein:

That's when that dam is broken, it's just-

Kiran Krishnan:

Exactly. When that dam is broken-

Michael Roesslein:

... chaos [crosstalk] everything.

Kiran Krishnan:

... things are infiltrating through. And then as a consequence of attacking everything in that region, it ends up attacking your own tissue. And that's the onset of auto immune conditions and other similar conditions that start damaging your own tissue over time, like inflammatory bowel conditions.

Michael Roesslein:

Okay. So with the ingredients in this, specifically the goal, is to increase and build and rebuild the blue on your chart, right, on that chart. It'd be the blue, the mucin-2 layer, right?

Kiran Krishnan:

Yeah-

Michael Roesslein:

But a little bit in the mucin-1 as well because the bugs and everything likes the polyphenols.

Kiran Krishnan:

They do. And here's the key to it. The mucin layers are built from the bottom up, right, so when the goblet cells here, I think the green in this diagram, are making mucin, they're making it down here and eventually moves up and then sloughs off. So you lose the very top part of the mucin layers through defecation. If you have really bad diarrhea, you're going to see a larger amount of this mucin coming out. You might even see slimy looking poop, right, that's actually the top part of the mucin layer. But the mucin-2 layer over time becomes mucin-1 and then sloughs off.

Michael Roesslein:

Oh, okay. So it's just giving it what it needs to do that process of coming from the ground up.

Kiran Krishnan:

Exactly. It's no different than how your skin rebuilds. Your skin of course comes in, is built from the inside out. So what used to be a subcutaneous layer or a dermal layer now becomes an epidermal layer when it moves all the way to the top and then-

Michael Roesslein:

Becomes dust.

Kiran Krishnan:

Yeah. Then becomes all the dust in our room, right?

Michael Roesslein:

Yeah. What do you think it is when you dust the shelves, that you're dusting is your arm. So, I heard a statistic one time, I don't remember what it was, but it put the amount of weight that a human being dusts off in skin cells in one year. And it was something in ounces and it was just, if you could see-

Kiran Krishnan:

It a lot. 90% of the solid matter in dust is human skin cells, right, and then 30 times that is bacteria because for every one skin cell, you've got 30 microbes sitting on that one skin cell.

Michael Roesslein:

Crazy. Alright. So we covered the importance of mucus is not your enemy and that it's essential there. And you mentioned polyphenols are in there. That's like colorful fruits and vegetable stuff, right?

Kiran Krishnan:

Yeah, exactly. A lot of it comes from colorful fruits and vegetables. In this case, we focus on citrus polyphenols. So they come from citrus type fruits, and they have some specificity for Akkermansia.

Michael Roesslein:

Okay.

Kiran Krishnan:

Oh, and then of course, polyphenols, just another mention about this, these particular polyphenols as well have been shown to increase diversity in the microbiome. Because polyphenols are really important, what we call, cross feeder in the microbiome, right, so the microbiome has this layering system of feeding. You've got primary fermenters that break down the big macromolecules, the proteins, the carbohydrates, the less complex ones. And then they will create secondary metabolites that'll feed the next layer of bacteria. They will then metabolize that and create a tertiary metabolize that'll feed the next layer.

Polyphenols are really interesting because in the middle layer there, there are a number of bacteria that do a really good job of converting polyphenols to other usable compounds that the body needs, including things that protect us from metabolic processes, things that protect us from reactive oxygen species, oxidants and so on. And then also really important compounds like urolithins that are created in the gut from digesting polyphenols that are really important for our own mitochondrial function. So those become really important for the intestinal epithelium that has to keep turning over and producing new cells to keep the gut integrity really solid. That's a whole other line of why the polyphenols are so important in the barrier system of the gut.

Michael Roesslein:

Polyphenols also, I get brought up a lot when Mira had her first flare and was in a lot of inflammation, a lot of people recommended get more polyphenols because they can quell inflammation as well. And so I think they feed bugs that produce things that quell inflammation or something direct. Alright, well, let's just jump into some questions. I have, what are, you might've answered this when I was writing down the questions from the email and they might've asked it before you answered it, but the four amino acids specifically.

Kiran Krishnan:

Yeah. Off the top of my head, I think we've got cysteine, valine maybe, isoleucine and ... Let's see. We can pull it up. Oh, I have a product label right here somewhere. I'll tell you in a second. Okay.

Michael Roesslein:

Threonine.

Kiran Krishnan:

Threonine, yeah. That's it. [crosstalk] proline, serine, threonine and cysteine.

Michael Roesslein:

It's on our site. Product label's on the MegaMucosa listing on our website. But, someone asked why not glutamine. And glutamine, I've had a lot of people in our group over the years have really negative reactions to glutamine, who can't convert it to GABA and so it becomes excitotoxic and causes anxiety symptoms and a bunch of other things. Did that play in your decision?

Kiran Krishnan:

Yeah. And glutamine's effect on the lining of the gut is a very indirect effect, right, what it's supposed to do is provide energetics required for your own system to repair the lining. We did a whole metaanalysis on glutamine. That was one of the projects that I had a couple of our research team people do. I said, "Put together all the research for me on glutamine. I want to understand exactly what it's doing," because that was like the staple in our industry for gut barrier issues. And the research is very unclear. Number one, you need really high doses for it to do anything. You need five to 10 grams a day. And then there were a good number of people, again, that had that cytotoxic response. So then you had to worry about people that had snips on whether or not they could metabolize glutamine appropriately.

And then ultimately, glutamine is really supposed to be providing the energy for the intestinal epithelium to repair itself. But that doesn't resolve the issue of the mucus and all the other things I talked about, right, the building blocks, the short-chain fatty acids to provide the energy to the goblet cells or preventing all of the things that prevent the rebuilding. We just didn't find it to be necessary. And we felt very strong and confident that with this formula, we could probably do way more than glutamine would. And adding glutamine to something like this, in the doses, we would need to add-

Michael Roesslein:

You'd have to take like six scoops of it.

Kiran Krishnan:

Totally. It'd be a crazy dose each day. And then there'd be too many people that would have a negative effect from it.

Michael Roesslein:

Okay. Let's see. Lisa, just wanted to say that the combination of MegaSpore and MegaPreBiotic and MegaMucosa helped me resolve my histamine intolerance. That's awesome.

Kiran Krishnan:

That's great. And then that's exactly the kind of thing that we work towards by creating that total gut restoration, because we would see in really complex conditions like histamine intolerance, although the name is simple, the actual pathophysiology of what in the world is going on with histamine intolerance is really complex [inaudible]. And we saw a product like MegaSpore can get you there a little bit. You really need a much more comprehensive system to repair those kind of problems. So, that's a perfect example. So thanks for bringing that up.

Michael Roesslein:

Yeah. Positive effects from MegaSpore in the histamine circles on Facebook were one of the things that blew up our webinars in the first place. Because a bunch of people got relief there, which is that's a rough condition. Then the whole group flooded into our webinars and then a whole bunch of people tried it and liked it.

Kiran Krishnan:

And histamine intolerant people classically just had a really bad go with probiotics in general, right, because many other probiotics actually made them worse.

Michael Roesslein:

What are the other components or factors besides inflammation that can prevent rebuilding of the mucosal lining?

Kiran Krishnan:

Yeah. So, inflammation being one of the biggest ones. Number two is the inadequate supply of the building blocks. And then lack of Akkermansia and then finally lack of short-chain fatty acids. So you need butyrate. Butyrate is the main fuel for the goblet cells that reproduce the mucin. And then you need Akkermansia to turn on the genes that are required in order to rebuild a mucin.

Michael Roesslein:

Okay. Regarding the leaky gut diagram, is that the small intestine or the large intestine? That'd be both, right, more in the large because there's more bugs in the large, but-

Kiran Krishnan:

Exactly. Yeah. That is a generic representation of in between the two. The biggest difference between the two is the thickness of the mucosal structure. So, in the large intestine, the volume of the mucosa is bigger. In part because, in the small intestine, you do want some transit opportunity here, right, because you're expecting small molecules like food components and all that to make its way through here. So you don't want the barrier to be too big. But in the case of the large intestine, this barrier actually becomes much thicker because there's no real absorption happening in the large intestine unless it's being carried and it's a specific compound. And then of course the volume of bacteria is much bigger. So then that mucosal layer [crosstalk] deeper.

Michael Roesslein:

So that's an in-betweener.

Kiran Krishnan:

That's an in-betweener, yeah. It's to illustrate what the structure looks like. The big difference between small and large is the depth of the mucosa.

Michael Roesslein:

Okay. I personally just drink a thing about this size and I put some prebiotic, so mucosa, and I have a little bit of magnesium I take and a couple of other things that I put in there. And then I just drink this over the course of a few hours. Does it matter? Because there's a few questions in email and a couple of questions here regarding dosing with food, away from food. I mean, because it's a powder in liquid, I probably wouldn't recommend drinking the whole thing with a meal just because that dilutes everything. So, is that a good approach to just sip it through a morning or something?

Kiran Krishnan:

That's exactly what I do. I actually start the sipping, because I don't want to take in any calories, I start the sipping with my first meal. But then I'll be drinking the drink for a few hours after that meal is done. That's the drink I make with my first meal of the day, which will be usually in the afternoon, a lunch meal. And then I'll likely be drinking that same drink through my afternoon work and then all the way up to dinner time. That's a great way to do it. And then that's the same because if I combine the prebiotic in the mucosa as well, and so I'm getting both of them at once. Sometimes I'll put in maybe a little vitamin C powder in there depending on the time of year and what's going on. Sometimes I'll put a little magnesium in there like you do. But that's my afternoon sipping drink.

Michael Roesslein:

Okay. The dosages, like you mentioned, studies with some of the ingredients and you're doing some joint studies with this, was the one scoop the standard dose, is that what's used in the studies, is that what you would recommend? Is this a more as better thing or if you guys dosed it to where it's pretty enough to just do the one?

Kiran Krishnan:

Yeah. One scoop will give you full clinical effect of the product. I'd probably do a little bit more. I probably do maybe one and a quarter scoops, only because I do a very generous scoop of my own. So I would say a heaping scoop, which is probably more than the five gram volume that we did all the calculations based on. But, you don't need to and there's no issue if you do more.

Michael Roesslein:

Okay. Any concerns, I'm 99.9% this is no, but this woman that, I believable, I don't remember the name, so I don't want to use Tinder, it was when an email has seen TSH go down and T4 and T3 go up by taking the spores. So very excited about this. Those are thyroid markers. They take thyroid medication, I believe thyroid hormone. There's no concern with this interacting with that in any way, is there? Because thyroid meds are taken in the morning and they're not supposed to be certain stuff around them, but I don't think this matters.

Kiran Krishnan:

No, not at all. You can of course deliberately space it out but it doesn't matter. It won't create any sort of metabolic change in how you break down your medication.

Michael Roesslein:

I figured as much. Is there a better time of day? I do from after my first meal, before the late morning, early afternoon. This stuff doesn't really matter when it gets in. I wouldn't chug a giant thing right before bed, just for obvious reasons. But other than that, it doesn't really matter, right?

Kiran Krishnan:

It doesn't. No. As long as you're getting it into your system, you're good. It works throughout the whole day. It's slowly providing the building blocks, the energetics, all of that stuff, throughout the day. So it doesn't really matter. Whatever's convenient for you really.

Michael Roesslein:

Is there any weight dependent dose for kids?

Kiran Krishnan:

Mm-mm (negative). My kids do take some of the mucosa, I give them about a half a scoop just because they won't drink that volume. It's so hard to get them to drink any liquid throughout the day to begin with. So if I have to mix a whole thing this big for them, it'd be impossible to get them to drink this whole thing throughout the day. So I do about a half a scoop of the prebiotic, half a scoop of the mucosa, and then every few hours I've got to go remind them to take a drink out of their cup. So, whatever you can get into them is going to be beneficial. That's the thing with kids. If you can do half a scoop of each, you're going to do a lot of good for their gut.

Michael Roesslein:

Okay. I had two people ask, and it is related to the mucosa so I'm trying to stay really on point with the only asking the MegaMucosa questions, but how do you feel about Zonulin as a marker for leaky gut? I guess Chris Kresser recently sent out something that said he doesn't feel it's a very effective marker to use for assessing leaky gut. A couple other people emailed me and said the Zonulin is over 2000, so I obviously have leaky gut. It's not really something I've ever personally used to assess that, but I know that it is in some circles. Do you have an opinion on that?

Kiran Krishnan:

Yeah. We've looked at Zonulin a lot because every time we do our studies, we're looking for the best end points to study. But in my research, I find that Zonulin is very inconsistent with its ability to predict leaky gut. And in people who clearly have leaky gut that's measured through other methodologies, Zonulin could be completely normal. There's the lactulose mannitol test. There's of course, LPS endotoxemia. And there are studies on there that show contradicting information on the level of Zonulin. So it's not a great predictor, no. It doesn't mean if you have elevated Zonulin, doesn't mean for sure you have leaky gut. And it certainly doesn't mean if your levels of Zonulin are quote unquote normal that you don't have leaky gut. So we don't use it in clinical research because it doesn't afford that stability in prediction of results.

Michael Roesslein:

Okay. Where does this fit in the total gut restoration sequencing? I have several questions about that like, I take the spores, when would I add this or when would I add something else? It's under my impression that it goes spores, then prebiotic then mucosa about two weeks apart. But, is there an official story right now?

Kiran Krishnan:

That's it. Yeah. That's the general story, right, so if people can remember this circle. So it's the recondition all the way up here. That's the spore state, that's the first thing. And then reinforces the prebiotic component of it. And then rebuild is the mucosal component of it. So this is essentially stage one, two, and then at the bottom is three. That's the general thing. In some cases, if it's a really sensitive individual, maybe they have lots of sensitivities in how they respond to things, we'll actually start them with the spores and the mucosa at the same time. That's totally fine too, because there's a lot that's in the mucosal product that actually will help negate some of the detox effects that can happen with the spores.

So you can start with step one and three together if you need to. If you're a highly sensitive person, you tend to react to things. There's no issue with that. It's just that then you'd want to, when you get to the second phase where you're adding in the prebiotic, you want to stay on the mucosa and you're effectively combining step one and three. And then when you add in the prebiotic, you're basically in the last phase where you're doing all three at once, right, so those are the adjustments you have to make. There's nothing wrong with starting with

the mucosa and all that. We started making those adjustments in the clinic here in Chicago based on the patients that were coming in. Not everybody fit well in the going one, two, three, right?

Michael Roesslein:

Okay. All right. I'm through all the email ones, I guess. We got some here, phlegm and chronic clearing of the throat, is that too much mucus? Would MegaMucosa have anything to do with that or is it primarily only function on the gut?

Kiran Krishnan:

Yeah, MegaMucosa is only functional in the gut. So the overproduction of mucus is a completely different immunological artifact, right, and that can be effected by certain dietary components. There's this idea that increased dairy intake increases mucus production. It makes sense scientifically. There are a couple studies that disprove that, that were done by the American Pediatric Society and a couple of big research groups. But, I still see it anecdotally. Like with my son, for example, from time to time, he can get stuffy depending on what's happening in the season. And if he's taking a lot of dairy, he gets a little bit stuffier. And the moment I reduce it, it's less stuffy. And so, to me, there's some tie there. How it's connected is still a little bit unknown. But, when it comes to the mucosa, it's not about producing that phlegm like mucus, it's about reinforcing the gut component of the mucous. So it wouldn't trigger any of that increase in mucus production.

Michael Roesslein:

Okay. Allergies and chemical sensitivities, can MegaMucosa help with that? My understanding is the more that that barrier is damaged, the more likelihood of things like allergies and chemical sensitivity. So I would say not directly, but indirectly.

Kiran Krishnan:

Yeah. It's addressing one of the potential root problems of people that have sensitivities to compounds, right, because a big driver of why your body starts reacting adversely to things that you should be tolerant of is because of this damaged mucosal lining, is because those kind of compounds are now entering the body but getting too close to the intestinal epithelium and getting caught up in a immune battle that's already going on. So then next time your body sees that compound, it's going to react to it in that same way. So now you've got a sensitivity. So even though it's not going to specifically target that compound or those compounds, what it's doing is it's supporting that basic normal tolerant immune function, which is going to be critical to trying to make progress on your sensitivities.

Michael Roesslein:

That makes sense. I love and understand the science behind MegaMucosa, but when I take it, I get rashes and histamine reactions. I suspect it's from the sweet stuff in there, or maybe the citric acid. It is in a fermented form. I do fine with MegaIgG2000 in this regard. So wondering if maybe it's something just to revisit later. PS, I take MegaSpore without an issue.

Kiran Krishnan:

What I think it is, it's actually probably the amino acids. We found some people respond really strangely to amino acids. And there's a number of pathologies and snips in particular, it may not have to do with your gut necessarily, it may have more to do with your own DNA in the metabolic processes of amino acids. And so it's rare, it's not something we see very often, but we have seen it. And typically, those people like yourself are

perfectly fine on MegaSpore, perfectly fine on IgG. It'd be worth you trying to take a polyphenol product on its own, see how you respond to that. And then it would narrow it down to the amino acids really being the issue. There's very little reason for response to things like monk fruit that's in there that's providing the sweetness. It's much more likely that's the amino acid.

Michael Roesslein:

Okay.

Kiran Krishnan:

The aminos-

Michael Roesslein:

Yeah. And the immunoglobulins help in their own kind of way, just not necessarily as well rounded of approach. Does the prep phase for a colonoscopy impact the mucosa?

Kiran Krishnan:

It does. Yeah. In fact, there's a couple of studies on how the prep phase can create longterm dysbiosis in people, especially people who've had multiple colonoscopies in a year, right, because you've got a certain progressive level of inflammatory bowel conditions. So it can. And I think if you've had to undergo colonoscopy or you're going to undergo one, you have to treat the recovery from that no different than you would treat anything else that may damage your gut like antibiotics or something, right, so, it's not innocuous. It does have an impact. And it has impact on your mucosa and the microbiome as a result because of the changing of the ecosystem that's sitting there in the top of the mucosa.

Michael Roesslein:

Have you considered making any of these powder formulas without any of the sweeteners in them? I'm guessing with the ingredients that are in them, it would taste terrible. So they have patients that don't like the taste or react badly to [inaudible] thus are not compliant.

Kiran Krishnan:

Yeah. So we were able to do that with the prebiotic. What we were able to do is just encapsulate it.

Michael Roesslein:

Encapsulate it, yeah.

Kiran Krishnan:

Yeah. In the prebiotic, the dose overall is lower. So we're able to do it and keep it I think it's like six capsules is a full dose, which is not bad. But this product, if we had to do that at the MegaMucosa, it would be something like 12 or 13 capsules a day, which would be a crazy dose and compliance would be really bad. And there's no way anyone would consume this without flavoring sweetness. In part, because, or in large part, because the amino acids are extremely astringent, right, when you take singular amino acids, it's like licking a battery.

Michael Roesslein:

I used to take leucine when I was in grad school in exercise physiology because that was the hot amino acid supplement to get buff. And it tasted like just total garbage.

Kiran Krishnan:

Totally. It's terrible. And cysteine is really bad too. Cysteine is very bitter. And the polyphenols themselves don't taste that good. So it's a difficult product to flavor and we understand people who are either sensitive for whatever reason, would prefer not to get monk fruit or the steviol or the rebaudioside A in them. But in general, the benefit completely outweighs any sort of minuscule risk that there may be. And there's no way you would take an unflavored version. I don't care how dedicated they are. There's no way, I would never take it. The experience has got to be manageable as well.

And then let me speak to the capsule thing, because not only is it a lot of capsules that you have to take per day, but the cost to take this powder that's in here and encapsulate it increases the cost of production of the product by a significant amount, right, this is, from a cost standpoint, a very expensive product based on the ingredients that are in there and the doses that the ingredients are in. This would end up being a retail $85 product if we had to encapsulate it. So we said between the idea that people would have to take 13, 14 capsules a day-

Michael Roesslein:

I don't want to do that.

Kiran Krishnan:

Yeah. [crosstalk]

Michael Roesslein:

I take plenty of capsules already.

Kiran Krishnan:

Totally.

Michael Roesslein:

I actually like the powders because of that.

Kiran Krishnan:

Same here.

Michael Roesslein:

Yeah. I get it. It's pretty like some people are averse to the sweet, but I have taken straight amino acids several of them, and it is not something I would wish on somebody. It's explanation makes sense. That's why we ask, so that patients stop complaining. Just cut this video and show it to your patients.

Kiran Krishnan:

Yeah. And believe me, we thought about all this stuff. We go through everything when it comes to the production and the design of the products. And yeah, we have the patient's compliance and experience in mind as well.

Michael Roesslein:

I don't know how this [inaudible] but do your products, again, help with reactive oxygen species?

Kiran Krishnan:

Yeah. So polyphenols play a big role in reducing the oxidative effects of ROS. ROS is a natural thing that's going to be generated in the gut because of metabolic processes. All of the metabolic processes that the microbes are doing in the digestive system are going to generate ROS as well to a certain degree. Of course, your own cells generated a lot of reactive oxygen species. One of the key things is polyphenols, and then the secondary metabolites of polyphenol digestion by the microbiome actually produces compounds that really quench reactive oxygen species. So yeah, absolutely. That's a big driver of intestinal damage and inflammation and so on. It's part of the reducing the measures that prevent the rebuilding of the mucosa.

Michael Roesslein:

There are some sequencing questions. We did just cover that, regarding sequencing, probiotic, prebiotic mucosa. It's already been addressed in the video. So, I'm going to just ask that you watch the recording that you get because we already went through that. Can this, the mucosa or the prebiotics or MegaSpore cause heart palpitations? I don't know how that would be possible.

Kiran Krishnan:

I don't know. Unless you've got a interesting response to the amino acids, maybe. But not something that we've seen before. In some cases, the herxheimer reactions can cause people to feel like they're palpitating. And it's got this excitatory effect because of the release of certain toxins within the gut. That could happen. I wouldn't say that it's completely out of the realm of possibility, but it's not something we see very often at all.

Michael Roesslein:

Yeah. That's not one that I've heard. I've met a couple people who have that kind of reaction to anything that they take and it wasn't specific to that. It ended up being like a [inaudible] situation or some other highly sensitive, highly toxic type of situation. Alright. I think we're good. Look at that, 54 minutes. That has to be-

Kiran Krishnan:

Wow.

Michael Roesslein:

I don't know if we've ever had one under an hour. Somebody ask a six minute question. That was really thorough, really great. These do wonders for helping people educate themselves as far as what might be right to try, when and how to use it and how to combine things and how to know when is the right time and the rationale. The practitioners learn a lot here because they learned the rationale behind the ingredients and how to explain it to patients and how to explain why it's sweet and doesn't taste like battery acid. And ask their patients if they want to take 14 capsules but-

Kiran Krishnan:

But 20 bucks more or [crosstalk]

Michael Roesslein:

Yeah. Pay 20 bucks more to take 40 capsules. So it's really helpful. These are a great service and a great value. She's laughing. It does taste not good. She was laughing at my battery as a comment, but the leucine ... I wrote a paper in my grad school and they had to choose the supplement and I wrote it on leucine. Because I was reading the muscle and fitness magazines. And at the time, that was the hot porn. I don't know if it still is. I don't read that anymore. So I wrote it on there and the pros were all this stuff. And I listed all these studies and I couldn't find any contraindications or any negatives really That's harmless to take leucine. And then the only con I could come up with, I put tastes like battery acid. And the professor thought that was great to do.

Cool. Well, yeah, this is great. Thanks everyone. Thanks for bringing awesome questions. Thanks for emailing all your questions and bringing them here. And it's always fun. We will send this out. I don't know what day is this, Wednesday? Probably Friday. Oh, by the way, I have a discount for you. That's important.

Kiran Krishnan:

For me?

Michael Roesslein:

No. Well, you don't need a discount.

Kiran Krishnan:

They do send it to me for free.

Michael Roesslein:

Yeah. It just comes in the mail. Let me see.

Kiran Krishnan:

Goes up in the mail.

Michael Roesslein:

Oh man, I'm pretty sure I had a coupon made. I guess you're going to have to wait because I don't see it right now. That is my fault. But we have coupon that we're going to get you 10% percent off of this. Oh, it's M-M 10 off. That's what it is. I'm going to put that here. That is M-M 10 off. And then I'm going to link right now. Sorry. I'm usually way more on the ball than this. I'm off my game. I can't manage the chat box and the Q&A box and the emails and talk to you and get this queued up. I'm slacking in my ... I crossed 40 and everything goes to hell.

I'm going to put the link here, even though we're leaving and there's a code, M-M 10 off, which we'll do 10% off MegaMucosa. One time use. There's no limit to that. If you want to get three of them, get three of them. It's always free shipping on our site over 75 bucks. So there's the link. We will email out the recording on Friday. So anyone who's registered for this will definitely get that. And it'll just go out to the general email list. I'll post it in the Facebook group and you can watch it there. And there's your code M-M 10 off off. And there is the link.

So thank you everyone. We're still three minutes under an hour. It's not even barely dark outside there in Illinois, which is another record. So, thanks a lot, man. Are you going to get back out of the road yet, is it happening, are things-

Kiran Krishnan:

Zero. Zero opportunities to be traveling, so nowhere.

Michael Roesslein:

Wow.

Kiran Krishnan:

Yeah. Last year I flew 390,000 miles. This year I've only found 80,000 so far. It's a huge difference. I'm about 300,000 miles behind. So, it's just crazy. But I'm also trying to maximize my time at home. I do have these little children at home that seem to be enjoying my presence. That's been a good thing.

Michael Roesslein:

That's good. It's a silver lining.

Kiran Krishnan:

Exactly. Yeah.

Michael Roesslein:

Let's do that. I'm sure that's nice. And you'll look back at the quarantine time as fondly.

Kiran Krishnan:

Exactly.

Michael Roesslein:

Alright. Thanks everyone. Thank you. See you guys later.

Kiran Krishnan:

Bye.