Michael Roesslein:

The webinar has started and the recording has started, Zoom likes to announce all of these things now.

Kiran Krishnan:

It does.

Michael Roesslein:

Let's see. People are trickling in, it is morning slash afternoon. Hello everybody, you are-

Kiran Krishnan:

[inaudible 00:00:16].

Michael Roesslein:

Is it 11:30 where you are?

Kiran Krishnan:

Me? Yes, 11:30. This is the earliest we've ever done one. It's amazing.

Michael Roesslein:

It is. Yeah. Everything changed when I moved over here because I'm not doing webinars at 2:00 in the morning, but it's, yeah, I think it's easier for some people to attend more in the evenings, but I can't do 3:00 AM for webinars. So-

Kiran Krishnan:

For sure.

Michael Roesslein:

All right. We'll let everybody trickle in. Let me know in the chat if you can see us and hear us okay and you might need to switch the... There's a little two above where you type in the chat and it can either say everyone or hosts or a panelist or whatever, make sure you switch it to everyone and then enter in if you can hear us and see us and where you are logging in from. And we will get started. I'm not seeing anything in the chat, so hopefully we can get some signal. Chat is disabled. Okay, great. I'm going to try to fix that real quick, attendees, there. I think I did it. Zoom always changes the default settings. So to keep us on our toes, things will change how their default settings are. And it looks like the default setting is now that the chat is disabled, but I fixed it. Good morning, Albuquerque, Vermont, working now, chat activated. Looks like people can see us and hear us.

So I'm Michael, I'll be your host. I think everyone here probably knows me at this point, Chicago, Utah, Southern Arizona, Mexico. And this is Kiran Krishnan, he is one of the co-founders of microbiome labs, formulator MegaSporeBiotic, now chief of North American operations for Novozyme, which is a Dutch... A Danish, Danish enzyme. Conglomerate giant that gives him access to a million new types of spores and probiotics and enzymes, which is fun and we have done about 1,000,007 webinars over the last eight years. And so since we're doing this series of webinars to launch a new site and announce a lot of really cool things here at Rebel Health Tribe, we figured bringing in Kiran for the first one would make a lot of sense. We're going to go over all the studies that have been published and are underway on MegaSporeBiotic, which is really cool. I remember when you were doing the first one, the first one was the one with the leaky gut study with the endotoxemia and the McDonald's and the college students, right?

Kiran Krishnan:

Yeah, that was.

Michael Roesslein:

Yeah. We'll talk about that one a little more, but it's crazy. There's so many now, and I know of about five or six of them, so I'm going to be learning along with everybody and I will be back on... Nika just popped in there. My dog is on the thing right here. These screen backgrounds are weird. I'll be back on, on Thursday to give a tour of a lot of the new stuff on the site. We've got new content, we've got a video library. We're adding 28 new products to the shop, expanding to have five new categories in the shop. A lot of new features and new things on the site. So I'm going to give a cool tour on Thursday at this same time and everybody gets to see some behind the scenes before it goes live next week.

And then we have webinars the following Monday, Wednesday, Friday, and Tuesday, after that with some new partners, we're bringing in some cool new products and companies, we're working with bio immersion, CellCore Biosciences, SymbioticA and ecoNugenics to have more products in different categories around brain and nervous system and mood and detoxification, and some general supports to go along with our robust catalog of gut and microbiome and digestion related products. So it's exciting time over here. And I will now stop rambling about all the things and what have you got to share with us today, Kiran? What studies are we going to learn about? I know about the leaky gut, I know about the liver, I know about the triglycerides and I know about one with Mega prebiotics showing diversity. So I'm sure we'll cover those.

Kiran Krishnan:

Yes. We'll definitely cover those. And then there's probably eight or nine more that we'll talk about. And I think before we start that, well, I want to talk about a couple of things. What you'll see today as I go through our studies is interesting because 99% of the probiotics manufacturers and suppliers we're talking about finished product companies, cannot sit up here and give you a list of their studies, right? Because they don't do any and that's a big, big issue in our industry. So when thinking about probiotics and you're looking at a probiotic to help with your health and wellness and your journeys that you're on, it becomes important to ask about studies on the finished product because a probiotic bacteria is not like a vitamin, right? It's not a mineral. If you took vitamin C ascorbic acid from this company and this company did a bunch of studies on their ascorbic acid and then this company can show that they have exactly the same molecular structure, ascorbic acid likely it'll perform the same as this company's.

And so they can utilize this company's studies to support what they're claiming, but it doesn't... That doesn't exist for probiotic bacteria because remember bacteria are living entities, they have millions of genes, they make hundreds of thousands of proteins. They have all kinds of metabolic functions. So most probiotic bacteria are different and they function different in different environments, right? So even when you have a probiotic, let's say it has seven strains in it and three of the seven strains have clinical studies on the strain themselves, right? And this is one of the things that companies do to claim that they have a scientifically validated product or research product is they have strains in their formula that may have studies on them but the strain studies are the strains by themselves at relatively low doses.

When you take those strains and you combine them with a bunch of other species and other active ingredients, you can't necessarily translate that those strains are going to behave the same as they did when they were by themselves, right? Again, these are biological entities that are very, very different from one another and are different in different environments. So it becomes really important in the probiotic space to know that the finished product you're using has studies on the final formulation as you're delivering the product itself. Now we also combine our product with other things. We combine our MegaSpore, as you know, with the MegaPre, we also combine our MegaSpore with the MegaMucosa and MegaPre. You have to do studies on those combinations as well, at least to some degree so you know that the benefits are additive. So what you'll see today are some of those as examples as well. So let's jump in

here and I'll talk to some of the scientific rationale around some of these studies. I think you could see this. So these are-

Michael Roesslein:

Before we jump in, hold on one second. I want to just ask you to speak real quick to why is it that so many supplement companies, probiotics and otherwise don't run the studies. I remember when you were doing the first one, you dropped some numbers and statistics and cost and time and really what's involved. I don't think a lot of people outside of the industry really know what it takes to run a controlled study involving X number of people over a certain amount of time. So could you just really quickly explain why that is that you don't see a lot of studies on products?

Kiran Krishnan:

Yeah, absolutely. So just to put it in perspective for people, it does sound easy, right? "Why don't you do some studies?" And in fact, prior to microbiome labs, I'd built a whole research company based on the idea that supplement companies did not have the wherewithal to do studies because there's a couple of complications for it. Number one is it's not easy to design a clinical trial. Most people can conceptualize a very high level way of testing things, right? You can go, "You just give this product to people with IBS and then you give a placebo to another group of IBS people and you see the difference." Well, at a high level, yes it can be that simplified but when you get down to it, if you're really trying to design a proper study, you have to make all kinds of considerations.

There's things called inclusion and exclusion criteria, right? You have to go through and go, who do we include in the study? Who do we exclude in the study? What are the things that they're taking? What are their histories, their medical backgrounds, all of that stuff, medical histories, whether or not they would skew the results in a positive way or negative way. How do you get the most balanced and appropriate data? Also how do you power the study appropriately? How do you get enough people? So you run relatively complex statistical analysis to try to figure out how to power the study properly. And then just the management of the study itself. How do you do the patient intakes and inform consents and all of the steps that go along with it, working through all the regulatory components of it. And then of course the cost of the study, right?

Because there's lots of liabilities, there's lots of costs, you have doctors involved, nurses involved, statisticians, researchers and all that. So to give you an idea, our number six study on here is actually our first study, that's the leaky gut study that we did. It was statistically significant, meaning the data reach significance, but it was a 50 patient or so study. That study costs probably about a half a million dollars, right? So to spend $500,000 on a study for a company we were in year like three and a half or four of our operations. We were probably doing no more than three to $4 million a year in revenue. So to think to spend more than 10% of any given year's revenue on a single study and not knowing if the study will work, that's the other risk, right? So you could spend half a million dollars on a study, take that big risk and the results are that your product didn't work. That's another massive risk.

So it's really hard for supplement companies that don't work off of 200% margins like pharmaceutical companies do to invest that kind of money in studies and take those risks. Very, very few supplement companies have the stomach to invest half a million, a million dollars into a study to find out that their product didn't work. We're doing studies right now that cost over a million and a half dollars, right? And that's for 100 patients, 120 patients. And the number of people involved, that million and a half doesn't count the number of your employees that have to help manage run all of the data and all of the nuts and bolts that come along with it.

Michael Roesslein:

It's a big undertaking, a big gamble, you better have a lot of confidence. And a lot of companies probably operate in that scope of finances that you're talking about, that you were in when you ran the first study. So it's like a huge, huge gamble to do that. I know that Dr. Kat Toups is a friend of mine and her and Dale Bredesen, Dr. Bredesen study

recently came out on reversing early stage dementia and they had, I think it was 25 or 40 patients or something over the course of a year and a half and it was two and a half million to run this study. So I just wanted to put it in context because to see that shows this list even more impressive because what goes into doing these studies is huge. So thank you for clarifying that.

Kiran Krishnan:

Yeah. Absolutely.

Michael Roesslein:

I'm excited to see what you've got cooking here. So I don't know if you want to go in order or if we want to-

Kiran Krishnan:

Yeah. And these are-

Michael Roesslein:

Want to run through it.

Kiran Krishnan:

Particular. I think these might be an order of, maybe publication. I didn't have time to put them in order of when we did the study, but I'll just go through each one on its own. So the way our philosophy worked, right? When it came to science and what we wanted to explore and validate really through clinical research and all that. And then here's the other thing, if you don't design the study well enough and there are gaps in your design and there are questions that arise, then you can't get it published, right? Because remember these are... All of these studies are published in peer reviewed index journals. So that means these journals are indexed on all of the literature databases like PubMed and then these are all peer review, which means that you have to submit your manuscript to a panel of research experts.

So these are published authors in the field and they will scrutinize your entire manuscript, your whole data set, all of that stuff to look for holes and gaps and they will have dozens upon dozens of questions that you then have to go back and answer. And if your answers don't meet their satisfaction, they will not flag it for publication. So you could spend a half a million dollars, 700,000, $800,000 on the study, the data could turn out okay and you're like, "Okay, we're excited about this, now we want to tell the world about it. So we want to publish it," because until you publish it, it doesn't have the validity that study normally would. But then you try to go through the publication process and nobody accepts it, right? Because there's two factors. One is how well your study was done. So it can easily get rejected and kicked out during the peer review process.

Number two, whether or not it's relevant for certain journals, because we've submitted studies to journals and they go, "This is really interesting, but it's not relevant to what we're focusing on," and they kick it back, right? So you have to also work through and try to find the right journal to get this reviewed to begin with, right? So all of the journals we've published in here like World Journal of Gastrointestinal Pathophysiology, Nutrients, the Integrative Medicine Journal, all of these journals are all peer reviewed index journals where you have to submit your study somewhere between four and six researchers in the field will review your information and scrutinize it for any holes, gaps, issues with the design and so on. So that's another very painstaking process that takes place. So the four or so studies I'll show you after this slide are ones that are going through that process right now and some of them have been going through it for like a year. So it's a lot of work. Now looking at-

Michael Roesslein:

I can imagine going through all of that, spending all of that money, having all of those people involved in the study, seeing the results and then having it be rejected by peer review. I don't think I'm cut out for that line of work. I think I would've a breakdown.

Kiran Krishnan:

It's the worst. It's the worst because you've just put... You've put at least a couple years of your time and of course you've put in a substantial amount of money and then it just gets kicked out over and over again. And fortunately that hasn't happened to us much. We had a couple of studies that did get lots and lots of questions and we've had to go back and forth with the researchers to really validate everything but... Which is a very painstaking process. It's not easy. But it's good though. It's a good process because you don't want bullshit signs out there, right? So you want to make sure that people are scrutinizing it to a certain degree before you're able to put it out there. So our philosophy and the research was relatively simple. We set off first just to solve big problems, right?

We set our eye on leaky gut as a first primary problem. We wanted to validate that we could resolve. We felt very confident in the product the way we designed it, the way we formulated it and based on existing studies on Bacillus endospores that we've... Including our own spores, these were studies that were done by Royal Holloway, which I'm not actually showing any of those studies here. So there are more studies than this on the strains themselves. These are just... This is just the work that we've done, but we felt pretty confident that it would help with leaky gut. The first study we did was a 30 day study on leaky gut. This is study number six that you see here on the list, you see here number six. That was the first study we did. As you could see, there's a... Did this zoom in weirdly?

Michael Roesslein:

Yeah, it zoomed in a little weird.

Kiran Krishnan:

Let me see. Let me stop sharing and reshare it again.

Michael Roesslein:

You could see them. I mean, I could see them, if anybody wants to comment on that, if you can see it okay without the zoom in, we can just leave it up, but I can... Close the thing on the left that has the... No, it still zooms in weird.

Kiran Krishnan:

Yeah.

Michael Roesslein:

So if you just close the section on the left, it'll make... That's showing the pages, it'll make the general one a little bit bigger.

Kiran Krishnan:

All I can... Yeah, all I can see is a weird zoom version. Let me just look at-

Michael Roesslein:

However it was when it was just up is fine. I think everybody can see that.

Kiran Krishnan:

Can see it? Okay.

Michael Roesslein:
I can see it fine. Yeah. They said they can see it in the chat. So-

Kiran Krishnan:
We just open up PowerPoint in general.

Michael Roesslein:
We can shoot out an image of that too with the recording of this that everybody can see.

Kiran Krishnan:
I see what's going on. Okay. Nevermind. Sorry. I got to zoom out a little bit.

Michael Roesslein:
No worries.

Kiran Krishnan:
Okay. Got it.

Michael Roesslein:
Yeah. Thanks for letting us know Sharon, Stephanie, that you can see it.

Kiran Krishnan:
Okay. Let me go back. Where's the sharing now?

Michael Roesslein:
I feel like we're in the old man generation now with tech things.

Kiran Krishnan:
Seriously.

Michael Roesslein:
All the restaurants over here, not all of them, but almost all of them have gone to the scan the QR code to see the menu thing and I feel like a grumpy old man. I'm always like, "Do you have a paper menu?" All right. Yeah, that looks-

Kiran Krishnan:
Okay.

Michael Roesslein:
That looks great.

Kiran Krishnan:

Okay.

Michael Roesslein:

Yes.

Kiran Krishnan:

So number six that you see down here was the first one. That was actually the first probiotic study that was done on leaky gut that showed any improvements at all on leaky gut, right? So we actually had the journal asking us to publish in their issue and they published it as what they call a frontier paper, which means that we got the cover, I believe of that... Or the cover of the very inside cover of that particular issue. And as you can see, that was published in 2017. That was our first study. And they actually waived the review fee, because that's another thing. Just to get a journal to review it, you have to pay them a fee for them to even consider reviewing the thing. But they were so excited about this. The reason they were so excited about it is because they a gastroenterology journal and they had published a number of studies on endotoxemia.

Endotoxemia is a scientific way of talking about leaky gut. It's basically when LPS, the endotoxin in the lumen leaks through and ends up in the blood. That's where the emia suffix comes from. So endotoxemia just means high levels of LPS endotoxin ending up in the blood and this is called metabolic or postprandial as you see here, postprandial dietary endotoxemia. That means the endotoxin levels rise very significantly after eating food. So when your gut is leaky, the most toxic time for your body is four to five hours after a meal. Your endotoxin levels rise very dramatically, six to seven times the normal basal level that's in the system and then all your inflammatory markers go up concurrently as well. So The Journal had published a couple of very big studies on endotoxemia showing that endotoxemia was in fact, a major driver of disease pathology so they'd shown the problem numerous times through different researchers who had looked at endotoxemia in different contexts, but they'd never published something that worked for endotoxemia.

So they were very excited to do that. That's the oral spore based probiotic supplementation, was associated with reduction of incidents in postprandial endotoxemia, a dietary endotoxin but we also saw changes in triglycerides and a number of disease markers because triglycerides came down when we resolved leaky gut, inflammation came down when we resolved leaky gut and the disease markers are things like interlukin-1, interlukin-6, TNF alpha, interferon-gamma. These are all very well known inflammatory cytokines that are associated with disease pathology and disease risk. So they were very excited to be able to publish this. And that was a landmark moment for us. So that was our first study. In our view, if we were able to help the system with leaky gut, then lots of other things were possible as well, right?

So we had to prove that out first. And just as a reference, we are currently going and doing a 90 day version of the study. This leaky gut study was a 30 day study and that was a risk, right? Because can you really resolve leaky gut or help it significantly in 30 day period, especially without doing anything else, right? Because leaky gut is multifactorial. It's driven by a number of things. And in this case we were not doing anything else. We weren't doing any dietary changes, lifestyle changes, they weren't taking any other supplements or support. These were college students. They weren't doing anything good for themselves in that period, in that 30 day period, all they were doing was taking the probiotics. So that was a big risk, but we calculated the risk because we said, "Okay, to really hedge our bets that the study works, we really should be doing other things.

We should be helping manage their diet to certain degree so they're not eating the worst things for themselves that month. We should maybe get them some things like glutamine and this and then colostrum and other things," but the problem with doing that is that you might hedge your bets that your data is good, but then you don't know what of those components are working the most, right? Or is it all of them? Do you need all of them at once or is it one of the components that's driving it, the other ones aren't really helping it, it causes too many questions and it doesn't really

prove the effect of the probiotic. So we took the risk and said, "You know what, screw it. Let's go for it. Let's just do the probiotic and then... And let's see what happens." Right?

Now here's another important thing to understand about studies. People say... I've heard people say, "Well, these don't count because you guys funded the studies." Well, it doesn't matter if you fund the studies, if you do it with academics or you do it with research institute or clinics, you don't get to be involved in running the study. So I'm involved with Dr. McFarland, for example, on this... On the leaky get study, I'm involved in the design of the study, right? I get to put my input on how the study's designed, what we want to study, what are the key outcomes and so on, once we decide on the parameters and the design of the study, then it's all him. We don't get to get involved in running the study, in looking at the data or any of that stuff and in fact, he's blinded because if this is a double blind study, which all of these were double blinded studies, then the researcher, the main principal investigator and their whole team cannot know which product is a placebo, which product is the treatment product, right?

We made the product. So we made the placebo, we made the treatment product, we code the product and then we send them coded product. They don't know which one is which, so they randomly assign people into different groups. And so we get no participation during running the study and then even collecting the data and analyzing the data. We don't get participation in analyzing the data at all. They get to analyze it and that's spelled out very clearly in the contracts and it doesn't matter if the data is good or bad, they get to decide whether or not they submit it for publication. So that's another risk when you work with academics and research institutes, because the decision to publish is theirs. So the data comes out unfavorable to your product and in fact, some people get hurt. Maybe there's a number of adverse events, lots of people had side effects. They will look to publish that because their goal is to publish stuff, right?

They don't care necessarily whether or not your product data was great or not, they want to publish something. So if your product sucks and the data turns out terrible and lots of people had adverse effects, they're going to publish it. So that's another risk you take as well. So it's important to know how that works, right? We sponsor the study by providing a grant. So we provide a grant to the university, but how they run the study, how everything turns out, you have zero involvement in that at all. And then in all of these studies in all these publications we disclose, and we have to disclose to the journal who funded the study and all that stuff too. So that's clearly disclosed.

Michael Roesslein:

If your product sucks, they'll publish that, is going to be the quote that we pull out of this webinar.

Kiran Krishnan:

Totally. It is a risk, right?

Michael Roesslein:

No, but that's... There's so many factors involved that people have no idea about. So I appreciate the behind the scenes about how these things actually work and that once the products are handed over, then there's no... It's out of your hands and it's like, fingers crossed, let's hope this works, let's hope it goes well, let's hope we see the results, let's hope all these things and it's just a big leap to take. So-

Kiran Krishnan:

Totally.

Michael Roesslein:

Sure, onto the next one, if you want to.

Kiran Krishnan:

Yeah. Yeah. And keep in mind the easiest thing in the world for supplement companies to formulate a product, use a bunch of borrowed signs to write your content, right? And make it seem as if the scientific validation on your product and then launch it, right? You're taking far less risk that way. If you are going to dedicate yourself to researching your products and really proving that it works in under the most stringent conditions. And then also lifting the science around this... Around the concepts that your product serves, you're taking a significant amount of risk and you're... But that shows the dedication to the science process, right? All right. The leaky gut was the first study, once we felt really confident that a product alleviates leaky gut, then we had a lot more confidence of studying a bunch of other things, right?

So I'll just start from the top here. The first one is looking at an ulcerative colitis, sorry, ulcerative colitis model. So this is an animal study and keep in mind that for having true consensus around scientific validation, it's actually not just human studies, because there are limitations on what you can discover in a human study. It becomes very hard to discover mechanism of action when you look only at human studies, right? So it becomes really important to do modeling systems, animal studies and human studies, all of them so that then you get proper consensus around the scientific effect because you can study things in animals that you cannot study in humans. You can do full pathology work after the end of the study to really dig into the organ systems and really look at how the product impacted each organ system. Clearly you can't do that on humans.

So being able to study mechanism of action becomes really important because ultimately the validity of your product is based on your ability to explain how it works, right? Showing that it does work is only one step, because if you can show it works, then it's black box technology or it's snake oil. You don't know how it's actually working. Once you can get in and elucidate the mechanism of action, that's when you really have strong, scientific backing to your product because you could talk about how it works. So in this case, ulcerative colitis, we wanted to study it on a very well validated rat model and the reason for that is we wanted to dig into, to figure out how it's actually helping under the... In a condition like ulcerative colitis. And this one is a study of our MegaSpore and MegaMucosa combined. That's why it says together with amino acids and immunoglobulin.

So the MegaMucosa of course has amino acids, immunoglobulins and polyphenols. So we used the actual commercial MegaMucosa and the commercial MegaSpore product on this model of ulcerative colitis and what we were looking at was a couple fold. Number one is can we improve all of the inflammatory markers associated with having ulcerative colitis? Number two, can we improve the microbiota in this case? And number three is the improvement of microbiota then also associated with an improvement in the pathology of the disease, the actual eating away at the lining of the gut, which is what occurs and also ulcerative colitis and the formation of these ulcerative lesions in the GI tract. And then finally, can we dig into the pathology and see tissue changes in these animals, in the region where they had all these ulcerative colitis type of lesions and sure enough, all of those were shown to be highly efficacious, where we were able to see a reversion in the pathology of the lining of the gut in these animals where they had these ulcerative colitis lesions.

And we were able to show that when you combine the amino acids, the immunoglobulins, polyphenols with the probiotics, it actually increased the impact because we did one of the arms with just the probiotic and we saw measured improvement but then when you combine it with the MegaMucosa we saw a significant improvement in the pathology of the condition itself, right? So this was part of how we showed that there's a synergistic effect between the MegaSpore and the MegaMucosa because lots and lots of practitioners use the MegaMucosa for these types of inflammatory conditions in the bowel. Going down, so we did this very... This study, next one was done with Cleveland Clinic. Cleveland Clinic has a couple of big microbiome labs, microbiome research labs, as you can imagine and Cleveland Clinic was one of the pioneers of integrative medicine. Of course, that was started by Dr. Mark Hyman, which most people know now it's a pretty big research and clinical Institute for integrative holistic medicine.

We were very excited to partner with them to study the impact of the spore-forming probiotic. In this case, again, the MegaSpore commercial formula on recurrent C. diff, right? And this was studied on mice as well, because of course it

becomes very hard to study C. diff in humans to really understand the pathways and the mechanism of action. We found some very, very interesting things in this study. Number one, this is a mouse model that Dr. Cressy had well established and had published a number of studies on where she's able to establish long term C. diff. So recurrent C. diff infection in these mice, right? So they can study all kinds of interventions to see how they function in these particular mice.

So they use this long term infected mouse model and what they were able to do is add the spore-forming bacteria against... Compared to other arms where they added just the carrier system and so on, but what they saw in the spore-forming group not only were we able to bring down the C. diff levels quite significantly, very similar to what they've shown with antibiotics being able to bring it down but more importantly, they showed a recovery of the lining of the gut, not only from the C. diff itself, but also from the antibiotic treatment because funny enough, one of the ways they get C. diff to actually colonize and stay long term in these mice is they first treat the mice with vancomycin. Vancomycin is the antibiotic that's used as a treatment for C. diff, right? So the treatment for C. diff will help establish C. diff as a long term infection in these animals, if you think about that.

So vancomycin damages the gut lining enough and the microbiome enough where it makes it easier for the C. diff to actually take hold and that's the way that they establish long-term infection in these animals, right? They use the prescription treatment for C. diff to establish long-term infection which-

Michael Roesslein:

I wish that surprised me, but nothing surprises me anymore.

Kiran Krishnan:

Right? It's absolutely crazy. When I first heard that I was just... I was basically laughing because it just... It's so crazy to think about that. And so what we got to study was twofold. Number one, can the spores, can the MegaSpore formula actually control C. diff and number two, what happens to the gut lining after you introduce MegaSpore after a course of antibiotics that clearly damaged lining of gut. So we actually got two really important pieces of data out of this study, which is published that showed that not only did the spores control the C. diff, but they also helped recover the gut lining and the damage that has occurred to it from the antibiotics they got to... They helped recover that and in the animals that were treated with the spores, they saw a significant improvement in the actual lining of the gut, the inflammatory and other damage that has occurred.

Now, here's the other really cool thing that we learned from it is we got to see how the spores go after C. diff, right? So in many cases, when the spores are going after opportunistic or pathogenic organisms, they'll actually sit next to them and produce antimicrobials. As it turns out, the C. diff is pretty hardy and perhaps some of the antimicrobials of the spores produce aren't effective against it. So they've come up with a new mechanism. The spores actually surround C. diff, right? And they chelate away iron and other minerals from C. diff. So they produce a chelating agent to starve out the Clostridium difficile because C. diff needs iron and other minerals, especially iron for its metabolic process.

That's part of why you bleed when you have C. diff infection, because C. diff is eating away at the lining of your gut to get to the blood flow. It needs the iron in the blood. And so what the spores have figured out to do is they surround the C. diff and they starve it by chelating away all the iron from it, right? That's a magical process in how it figures that out. We couldn't engineer a bacteria to know how to do that and yet nature has done this and we would've never known that unless we invested and ran this study in partnership with Cleveland Clinic. So that was so fascinating to find out. The next one is looking at... This is a human study, looking at patients with mild to moderate elevations of triglyceride. This is 12 week randomized double-blind placebo controlled trial that was run in a hospital.

Well, the reason we ran the studies in our original leaky gut study, we saw that a subset of patients had a significant reduction in triglycerides and these were on patients that did not have elevated triglycerides. The average triglyceride

in those patients were 150 and they still came down 28, 30%. So we wanted to see what happens if we take patients who actually have clinically elevated triglycerides over 200 and that's what this study was. And what we saw was a very significant reduction in triglycerides, which was very exciting because right now there isn't a good pharmaceutical that reduces triglycerides. Some doctors will use statin sort, but statins aren't really indicated to reduce triglycerides. And then the other option is prescription fish oils that have been shown to be able to reduce triglycerides. They bring it down somewhere around 25 to 28%. We were able to reduce it over 30%.

So we work just as well as a prescription fish oils to bring down triglycerides and triglycerides over cholesterol is a real measure of disease risk and health issues, right? So it was very exciting to see that we were able to do that. The next study is the idea of the gut liver access, right? So one of the things that we know very well when you study leaky gut is that the liver takes the brunt of the damage from leaky gut because all of those toxins flow past the gut and 85, 90% of those toxins will enter into the portal circulation, right? So meaning it's going to hit the liver first. So the liver is taking the massive hits from leaky gut all the time. And so we wanted to see, because we know the spores impact leaky gut in such a positive way. Do the spores also have the means of protecting the liver.

So this is the acetaminophen induce acute liver injury, where you basically take animals, you give them doses of acetaminophen over a couple week period, that acetaminophen over time, which is an well known NSET pain killer that acetaminophen over time is going to damage the liver. And then we-

Michael Roesslein:

Yeah, Aspirin, correct.

Kiran Krishnan:

Aspirin. Exactly. Yes. And that's... What we did is a three arm study where one was a control, so the animals didn't get anything. The second one was a prescription silymarin, which is a milk thistle out of... I think, Germany and Europe, this is a prescription grade product. And then number three was a spores. We wanted to see, can it protect liver as well as silymarin or at all? And sure enough, what we saw was that the spores absolutely protected the liver even under the condition of liver toxicity induced by overdosing of acetaminophen. And then when we did the actual liver biopsies and pathology, we found that the liver tissues actually was significantly improved and helped in the spore group.

So the probiotics spores have a way of protecting the liver through that portal circulation access. I think a lot of it is driven through short... The formation of short chain, fatty acids, like butyrate, acetate and propionate, acetate and propionate in particular make their way to the liver and are very anti-inflammatory and do support the liver a lot. I just did a whole Instagram live with Dr. Asia Muhammad, where we talked for about an hour on the unsung hero that is the liver, right? The liver takes the brunt of a lot of GI issues and most people don't look at liver as the liver, as a potential source of complications for their gut function because what's very clear is that basic liver function tests that AST, ALT they don't necessarily indicate fatty or dysfunctional liver.

You could have a fatty or dysfunctional liver and still have normal AST, ALT. So the encouragement has been, and that was what we concluded in our talk was that everybody, if you have a GI issue, you should go and get a liver scan. There's things called a fibro scan. You can just do a basic ultrasound at your doctor's office to look at fatty liver and fatty liver-

Michael Roesslein:

I was one of those people, by the way. I had extremely elevated AST and ALT numbers in my 20s-

Kiran Krishnan:

Yeah.

Michael Roesslein:

To the point where it was thought I might have hepatitis or I could have some... Something really bad going on with my liver. So I made it a concerted effort to deal with that and fix that. And about six years later, my AST and ALT numbers were down, which these are markers in the blood to the 20s or whatever, like is a normal number. And the doctor I was working with at the time, who I needed to write a script to do a phlebotomy for my high iron wouldn't do it unless I did an ultrasound on my liver. And I said, "No, no, no, my numbers are fine." And they're like, "You're not getting the script for the phlebotomy," which phlebotomy is a common way to treat hemochromatosis, which I have.

And I'm like, "Fine, I'll go do your ultrasound." And then they did the ultrasound and I still had what they considered mild to moderate fatty liver and that wasn't showing up with the blood tests and then more liver work, I did. Three years later, I went back, got another scan, liver looked fine, but my liver was considered fatty liver even though my blood markers were-

Kiran Krishnan:

Were normal.

Michael Roesslein:

Were [inaudible 00:43:05] kosher. So yeah, that's a thing.

Kiran Krishnan:

It's so important. And as the liver becomes fattier and more dysfunctional, it messes up the gut even more and of course it becomes toxic to the rest of the body as well. And there's a lot you can do to protect the liver. So this is one of the studies we want to do because we kept pushing with our clinicians that, "Hey, you need to look at the liver more often and it's not enough to do the biomarker or the liver enzymes, you have to do scans of the liver to really understand the role." And then if the liver is dysfunctional, we wanted to demonstrate that the probiotics can help. And that's sure enough what we did. The next study number five was a super interesting and exciting study. It's a study on irritable bowel syndrome as you could see. This was a patient study, a 90 day, 90 patient, double blind placebo controlled all of the bowels and whistles of the study.

Here's what was so interesting about it. So it's an IBS study. IBS studies, one of the things I don't like about them is they're mostly survey based, right? They're mostly symptoms scoring and symptoms scoring is fraught with error because it's really like people's perception and how accurately do they perceive their problem being there's a lot of placebo impact when you do a symptom score. So we did some of the symptom scoring, but we wanted a more quantifiable way to measure IBS response. And it surprises me that more researchers haven't used this. And I think I understand why, because it's not easy to use this, but there is a balloon mechanism to measuring IBS response, right? You might be thinking to yourself, "What the hell is you talking about?" So there's a well known procedure among gastroenterologists but it takes... But not all GIs do it, where you actually take a balloon, you insert it into the anus and you inflate the balloon incrementally at different levels.

And the person can only tolerate a certain level of inflammation and the studies are clear that when you have IBS, your tolerance of the level of inflammation becomes compromised, right? So if your tolerance can improve on the inflation of the balloon, you are actually showing that you're improving IBS symptom... The IBS condition, right? So we use this balloon measurement where you actually insert the balloon into anus and you slowly inflate it and you measure the mark in which they can't take it anymore. And it becomes very clear at what level the patients can't take it anymore. So we went to that extent to try to show that we can improve this crazy syndrome called irritable bowel syndrome, which again, I hate that diagnosis, but basically we had recruited people in that were diagnosed by gastroenterologists as having irritable bowel.

And what we compared it against was the standard treatment of Rifaximin and then a low FODMAP diet, right? So we did Rifaximin, low FODMAP diet and then MegaSpore, and what we found was that MegaSpore worked as well, if not better, than all of the other interventions in terms of improving IBS symptoms, right? So that was super interesting because... And this got published in Nutrients. If you guys aren't familiar, Nutrients is a pretty highly regarded journal in the holistic integrative medicine space. And they were excited to publish it because it was a pretty unique study on its own because nobody has really used that balloon because as you can imagine how invasive that is, and it's difficult to get patients to sign up for that, right? But we wanted to do that. Study number six is the leaky gut study we talked about. Study number seven is a super interesting one because we were really looking at the combination of the probiotic and then the MegaPre, right? And we were looking at the metabolic enhancement. This was, let's see, synbiotic concept containing [inaudible 00:47:09]

Yeah. So this was a study looking at metabolic improvements within the gut model. So this was a gut model study. We're looking at improving things like the production of short chain, fatty acids, other postbiotics, reduction of gas, improving of metabolic markers within the GI tract and so on, looking at the effect of the probiotic versus the probiotic with the prebiotic, right? So that's why the synbiotic concept idea came about because the idea here is that we're looking at the additive benefit of the prebiotic with the probiotic on all of these gut metabolic markers. The next one, number eight is treatment of spore-based probiotics in metabolic [inaudible 00:48:01] composition. This is a shine. This is also another gut model study, where we're looking at community composition of the microbiome. We were very focused on, can we improve alpha diversity within the microbiome? And then also, can we improve the growth of keystone species, right?

Akkermansia and [inaudible 00:48:23] bacteria pros, Nide, Bifido longum, Bifido animalis and adolescentis. So all of these different keystone species and then alpha diversity and then all the postbiotics that come out of those organisms. Because one of the things that we critically wanted to know was what does this probiotic and or probiotic plus prebiotic do to the gut community structure, right? And that's another very important thing that probiotic companies should be able to tell you about their product is what does it do to the rest of the microbiome? Because the probiotic itself and its functionality is one thing, well, its impact on the rest of the microbiome is where you're really going to see the changes, whether positive or negative. So this is one of the studies that we want to do. This is the use of MegaSpore in the shine model to study in depth the impact of community composition and sure enough, what we saw was a significant increase in alpha diversity when you use the MegaSpore in a gut microbiome.

We also saw a significant improvement in short chain, fatty acids in keystone species and so on. So that is the combination of studies here that we've done and published so far. We've done more than this, but not all of them have been published. Some of them we've done internally to verify certain things or work out or test mechanisms in our head so that we can design a proper clinical trial around that. And then this next slide, I didn't put the details in but these are five studies that have been completed that are going through the peer review process right now and they should be published soon. I'll tackle the first one at the bottom here, the MegaSpore and MegaPre weight management study.

This was a 90 day placebo, double blind placebo control study on overweight individuals, right? No change in diet, no exercise or anything, all they did was they took the probiotic and the prebiotic compared to a placebo in other half of the group. And we were doing full DXA analysis and we're also doing full metabolic panels to look at improvement in glucose control, in insulin response, in inflammatory markers and we were looking at visceral fat mass as well through the DXA analysis. And our idea here was that because we know from the previous studies, the ones that are published, that the probiotic and prebiotic increased butyrate production, increased Akkermansia, increased diversity, that we should be able to change the microbiome enough where people start to see metabolic improvements, even without dieting, even without exercising. And sure enough, that's what we saw. We see about a 38% reduction in visceral fat mass in that 90 day period.

That's a very significant reduction in visceral fat mass, because keep in mind, visceral fat is the most dangerous fat. It's that really inflammatory fat around the midsection and around the organs, harder to get rid of in many ways for a lot

of people and we saw such a significant reduction even without changing their diet or exercise. We also saw improvements in markers, indicator of insulin response and reduction in inflammation as well. So we're completely improving metabolic health just by adding in the probiotic and prebiotic and then if you add in lifestyle modification to that, the effects can be really, really quite phenomenal. The other two is MegaSpore SereneSkin. SereneSkin is an adaptation of the MegaSpore formula that we've increased the amount of the carotenoid producing strain and we've increased the dose of the subtilis a little bit as well. We've been working on acne for some time because acne is one of those big problems that need to be resolved because dermatologists are using lots and lots of long-term antibiotics for acne, which is just not a great approach, right? In our mind-

Michael Roesslein:

And some of the worst antibiotics too and-

Kiran Krishnan:

Yeah,

Michael Roesslein:

Like Accutane and all these other kinds of things that we have a lot of people in our audience that reach out to us and say, "Hey, I took this drug for seven years, what am I supposed to do now?" So-

Kiran Krishnan:

Totally. And the average time on the dosing is something like 130 days. That's the average time. So many of them go much longer than that, which to us, we're like no understanding the gut skin access and understanding that acne is an inflammatory and metabolic condition, we really need to be able to do better. So we've done two studies now showing very significant reduction in acne lesions. The first one is a 30 day study. We saw about a 35% reduction in acne lesions in 30 days, that's very impressive. So then the second study, it was the largest probiotic acne study ever done. And that study was done over a 90 day period because all the antibiotic studies on acne were over a 90 day period. And so we decided to do it so you can match... You can look at the data head to head.

And what we saw is a 65% reduction in all lesions, both in the face and on the trunk of lesion in acne subjects. And this is non cystic acne. So we can't study cystic acne because it's defined as a disease state and you can't technically study a disease state in the US using a supplement, right? So this is-

Michael Roesslein:

So what if it works? No, sorry. They said, "Because what if it works?"

Kiran Krishnan:

What if it works? That's not a good thing, right? For a number of industrial people.

Michael Roesslein:

I believe that [inaudible 00:54:12].

Kiran Krishnan:

Yeah, exactly. And so these are two pretty good size studies again, proving the same thing that through improved metabolic processes and reduction of this systemic inflammation, we can improve conditions. Of course we're helping the leaky gut already, but we can improve peripheral indications like acne. And so now SereneSkin, which is the

MegaSpore version for acne is really starting to scale among dermatologists and estheticians and nurse practitioners and all that. And then we did two studies on just the indica strain. The indica strain is the high carotenoid producing strain. This strain when it gets into your gut and this is a main strain and MegaSpore, gets into your gut produces high levels of carotenoids, 12 different carotenoids, alpha-carotene, beta-carotene, lutein, astaxanthin, zeaxanthin and RDA levels and it's producing it at the site of absorption. So the bio availability of these carotenoids through the probiotic is much higher.

So we did two studies looking at the ability to increase carotenoid levels in the skin with individuals by taking the probiotic because carotenoid levels in the skin are indicative of aging and protection of the skin because these carotenoid antioxidants are really important to prevent aging, fine lines, wrinkles, thinning of the skin and so on. Also prevent inflammatory conditions on the skin, but also UV damage, right? So one of the two studies we studied blue light damage to the skin from computers and cell phones and all that, which is a whole new risk now for the... For your skin on your face, beyond UV from the sun, blue light irradiation is a driver of aging and damage to the skin. And sure enough, we've been able to show with some of the initial indications that we can protect the skin from blue light irradiation.

So it's really quite exciting. And again, it adds to the war chest of clinical validation that these spores are highly effective, highly efficacious in the body and they work through very similar mechanisms in many of these conditions. So these are 13 of the studies and as I mentioned, we have others ongoing right now. Some bigger studies, we've got an antibiotic associated diarrhea study which is a pretty large, couple hundred patient study that's going on right now. We have a couple others in the works and we'll always continue to invest in research. And of course we have new species and all that, that we're discovering coming out as well. So that's a quick summary. Hopefully-

Michael Roesslein:

You guys have been busy, man.

Kiran Krishnan:

Yeah. We've been busy. We don't stop, right? And this is just this product, right? Not to mention, we've got the ZenBiome which has eight published studies. We've got the new PyloGuard, which is the H. pylori Product that has 10 published studies, two more ongoing right now. I mean, number of our products have so many studies already published and we're constantly working on the science bit of this. We're trying to set the bar high for companies in our space where we want to establish a level that says, "Hey, if you want to play in the supplement space and if you want to call yourself a science based company, here's what you need to do. Right? You need to take the risk and invest in the science because if not, you really just don't know what your products are doing." And so we hope to keep leading that charge.

Michael Roesslein:

You definitely are. Cheers to all of this and I can't wait to see these ones get published. I know this will make some noise, the metabolic improvement one, especially I know a lot of people are looking for that. And then I need to get on board with the SereneSkin. I don't know anything about that product. So you guys have been rapid fire releasing products so much that I've been busy, well moving to another continent and everything with the new site, everything else. So I've been out of the loop. So I'll have to look into that. We'll have you come back, talk about SereneSkin specifically and let's do... There's only a few... Is it possible to ask about any positive or negative effects with dosing MegaSpore or HU58 combined with berberine and quercetin. There wouldn't be any negative effect on your products from those two things would there?

Kiran Krishnan:

No, not at all. Not berberine or quercetin. We actually did a study with berberine. We did it with UCLA on prediabetes. It hasn't been listed here because we're still writing up the manuscript and all that. But we have looked at the data and berberine is effective for people with prediabetes because of its ability to improve insulin response and so on. It combines... It binds with the baroreceptors and the GI tract. So we did a study with it and I mean, there was no negative impact. And certainly of course, no negative impact at all. We in fact have used both together quite a bit. Of course, spores do go well, hand in hand for people with allergies and all that.

Michael Roesslein:

Great. Thank you. And Johnie wants to know how's Italy, Michael, is your wife doing better? Hi, Johnie. Yeah, it's hot, is how it is right now. Europe is being smothered by an insane, really dangerous months-long heat. I don't even want to call it a heat wave because it implies like... That, that's temporary or it's a standout thing, but it's getting very hot here. Things are good though, [inaudible 01:00:04] Mia'a doing great. We have not yet toured the enzyme company. We have not choreographed a dual visit to Denmark yet, but we will. And somebody asked about Crohn's disease. I saw one study you had on there that was colitis. Not exactly the same.

Kiran Krishnan:

No.

Michael Roesslein:

Mechanisms are probably similar. Do you have anything in the works, that's a disease you can't... Can you study a... Didn't you just say you can't do studies on specific diseases?

Kiran Krishnan:

No, we can't take Crohn's patients and study Crohn's itself, right? We have to take Crohn's patients and study auxiliary things like tolerance and safety and so on. And then if the Crohn's happen to improve, we might be able to report on that. But basically that's why we would do, that's why with the ulcerative colitis, we did the animal study because then you can do that. And we did that in Europe actually, but keep in mind that inflammatory bowel condition, Crohn's colitis, micro colitis, all those all have very similar pathologies, all are related to having low and bacteria [inaudible 01:01:13] having low diversity within the GI tract, having low production or short chain, fatty acids, being able to improve short chain, fatty acids, diversity, keystone species are all very supportive for those conditions. So you could certainly interpret that you can improve your health. You can improve your gut by improving those parameters, right? But yeah, we can't... I can't say that we did a Crohn's study and it reduced the disease state by X, Y, Z.

Michael Roesslein:

No worries.

Kiran Krishnan:

Yeah.

Michael Roesslein:

I wanted to drop in there. I totally forgot. We're celebrating Kiran studies and right now for, I think we're doing it 48 hours. MegaSporeBiotic only on our shop is going to be on sale. So I just put a code in there. MSB party is the code. I will link to the MegaSpore right now. And there was one more question about NAC in the Q&A and if NAC, if you guys dabbled with that at all or know anything about how that might relate to MegaMucosa, I don't know.

Kiran Krishnan:

I know lots of clinicians that have used NAC with MegaMucosa. We had actually NAC in our immune product. I think it, the MegaViron, but of course, NAC is coming under different regulatory scrutiny nowadays in the US. So the FDA is removing it as a supplement making it a drug, I think. So we're removing it unfortunately from the product, because we just have to be compliant with FDA. And so NAC, absolutely no issue at all. I mean, NAC can be really useful for the mucosal lining to induce some of the repair in the mucosal lining by mucolytic function. So I think NAC and MegaMucosa go hand in hand very well.

Michael Roesslein:

Perfect. Yeah, I've read that about NAC. I haven't seen it actually change, but I know if I was investing huge into supplement formulas right now, I probably wouldn't be including it because you can do that, produce 8 million bottles of something and then get a letter saying, "You can't sell this anymore."

Kiran Krishnan:

Yes. Exactly. [inaudible 01:03:25] Get it all.

Michael Roesslein:

So there's plenty of producers of NAC on the market that make fine products that you can use and make your own little mix there. But there we go. So MegaSpore two days, 15% off and I will let everybody know that for the party that starts next, the launch is Monday the 25th for the website, we're going to have a pretty cool sale that goes on for the end of July too on other stuff but for right now to celebrate these product, these studies and Kiran coming on here, we got a MegaSpore specific thing going on, it's right there in the chat. You'll get a recording of this. I can get that slide maybe from Kiran that has those studies on it.

Kiran Krishnan:

Sure.

Michael Roesslein:

And then we'll send that out with the recording and thanks for being here. Thanks for all the great feedback. Thanks for the questions and always appreciate your time, Kiran. Thanks for... I mean, I know what it goes into doing these studies that's why I wanted you to bring it up and talk about it and get to brag a little bit. I appreciate what you guys do and the high level of quality control and integrity. This is 10 times more than 95% of supplement companies out there are going to do for the cost and the time and the energy and the effort and the labs and the scientists and the... Everything that goes into it. So thank you so much. We're grateful to be able to bring this information out and we will do a enzyme lab tour at some point in Denmark and put that on the internet. So cool. Thank you so much. Thanks everybody.

Kiran Krishnan:

Thank you guys.

Michael Roesslein:

Have a great rest of your day.