Relationship Goals: Your Gut Microbiome and Immune Function – Kiran Krishnan, Ph.D., with Dave Asprey – #864

Announcer:

Bulletproof Radio, a state of high performance.

Dave Asprey:

Today has a live audience from the Upgrade Collective. No, that's not poop. I'm sorry guys, I was just calling you names. The Upgrade Collective is my membership and mentorship group who I tease mercilessly as we go through the year, learning all of my books. If you're interested in being a live studio audience, Ourupgradecollective.com, it's super fun. And there's, oh, dozens of people dialed in right now, watching this episode, hearing all the weird stuff that I'm saying to today's guest before anyone else.

Today's guest, speaking of such things like poop is a research microbiologist and he studies the human microbiome and how it affects your gut, your immune system, and things like that. This is someone named Kiran Krishnan, and he's been on the show before. He's with Just Thrive, a probiotic and other gut health kind of company. But there is so much going on around immune systems, and around what we're learning very recently about your gut. So Kiran, it is so good to have you back. I love just geeking out with you.

Kiran Krishnan, Ph.D.:

Thank you, sir. Thank you, Dave, for having me. It's awesome to be on-

Dave:

Not all microbiologists have a sense of humor and if they do, it's super nerdy. So you have a pretty good one, I'm going to give you a pass on that.

Kiran:

Thank you, Dave. No, they don't let most of them out of the lab. I somehow broke out and I was like, "Listen, let me among the people so I can translate all the things you guys are doing for the people." So, that's become a big part of my role is just translating the world of the unseen microbes to meaningful information for people to be able to utilize [inaudible 00:01:48] change their lives.

Dave:

That's the problem, and I've been struggling with this for years. Okay, you fast forward or fast forward reverse, whatever that is called. Fast backward to 20 years ago, okay, I was the room clearing guy anytime I ate. And people would ask at the beginning of the Bulletproof Diet, "Hey, what's your advice if I have really bad gas?" And my advice was always, "Get a dog, so you can blame the dog." And, because this was one of my mini strategies to deal with the problem before I got to it and then I said, "Oh, I think it's a fungal microbiome thing. I think it's a bacterial."

And then you find out there's tens of thousands, if not a hundred thousand bacteria that could be there. And, then there's the ratios and balances, and turning into actual information has been a very long journey for me. But, what I do see is the ratios of bacteria, dere, acuities. They shift when people go Bulletproof, but how the heck do you know now what to do in the gut when you're looking at this incredible complexity versus what you knew 10 years ago? What's different?

Kiran:

Yeah, so the biggest difference that we now have at our fingertips is the use of meta-genomics which is a sequencing technology, right. So, that gives us an opportunity to not only figure out exactly who's there because the crazy thing about it is the vast majority of microbes that live in your gut can't survive outside the human body. Many of them are even seconds. So they're mostly anaerobic, right. So, the moment we bring them out in stool and then we start trying to plate them from stool, meaning grow them in Petri dishes, most of them end up dying. And so you can't study them when they're alive, so the only way to really understand who's there and in what quantities to study the DNA that's present.

So, you have to become a sequencing detective and you need massive amounts of computing capability to look through all of that DNA, right? So just to give an example, our human DNA, we have somewhere around 22,000 functional genes when we sequence a whole human genome front to back. In our gut microbiome, we have over two and a half million functional genes when we sequence all of the bacterial DNA in there. So it's a massive data stack, and then making sense of that data is really the hardest part about it, right. So you can sequence it, you get millions of pages of data and then you have to run all that data through software that assembles all of the bacterial cultures, and ecosystems and all of that. So, that advancement's really given us the insight into understanding this ecosystem.

Dave:

So, there are variety of ways of looking at what's going on with your gut bacteria, right. And, I feel like I've interviewed many experts in the field and this is your third time coming in here. It seems like every two years I'm seeing, oh, there's a whole bunch of new species. Oh, we didn't know this or this species is associated with Parkinson's or not having Parkinson's, and all this sort of stuff. And I'm sitting here going, "All right, I'm going to say I like to think I'm smarter than the average bear. Or, at least I'm more informed than the average bear." And I'm having a hard time knowing, all right, what's actionable when I see a study that says, "This species is really good for you." Because either you take its food, which is usually polyphenols or fiber, or you take the probiotic version if you can buy it. Are those the only two tools we have?

Kiran:

Then the other tool is our microbes that have a way of affecting the ecosystem.

Dave:

Oh great, so they all fight each other? So, you might take the enemy of the good one or something.

Kiran:

Yes, there are ways of doing that and here's what's interesting about it, right. So, we as a species ourselves have not developed any capability of kind of going in and modulating our own microbiome, right. All of these organisms, trillions of cells, thousands of different species live in our GI tract and live in our body, on our body and everywhere else. We don't have the capability of going in and manipulating that ecosystem in order to affect change in a positive way. Right, so we count on other microbes to be able to do that for us, and the assumption in nature is that there are certain microbes that we were always going to be within close proximity of or work within a symbiotic manner. And, those microbes are the ones that we've outsourced this job to and that's a really interesting concept.

When you think about we have such limited amount of genetic capability as a species, right. We barely have enough genetic material as an earthworm does, and so we're not that cool or sophisticated. What makes us that sophisticated as we are, is the two and a half million or so microbial genes in our

system. And, so being able to outsource functionality to microbes is a big part of being human. So there are sets of organisms that we have outsourced through the course of evolution, the ability to modulate and monitor the rest of the microbiome. And so we're finding that when you start putting in these microbes back into your system, you really start getting the positive changes. They start refereeing the ecosystem, and making things more balance and improved.

Dave:

I think I get it. Or basically, you have a herd of cats or you have an ecosystem. I also am not sure, and I want you to stress test this for me. You say the human genome is limited, but what percentage of our genome is from viruses?

Kiran:

That's within our system itself, right. So, viruses probably make up somewhere around eight to 10% of the total genetic material in our system. The virome is pretty large and the virome is pretty diverse, but it's not anywhere as close as the microbes, the bacteria at least. But they're there, they're present and they do make up a measurable amount of the genetic material that's within us.

Dave:

And the genetic material, I don't mean viruses floating around in your gut or in your tissues. I mean, that are incorporated into human DNA, right. That's the 90%?

Kiran:

Oh, sure. Yeah, and it's hard to say where our genes came from, right. We know that each one of our cells have ancient pleiotropic bacteria in there are mitochondria, essentially ancient bacteria. So, we've got a lot of DNA that we've collected from many different organisms, including-

Dave:

From bacteria and from viruses.

Kiran:

And viruses as well, yeah. Mm-hmm (affirmative)?

Dave:

So, there are a group of people and I think they're right, who believe that some part of evolution is driven by picking up viruses from the ocean. Which is as a lot of people don't know, incredibly full of viruses. In fact, you want to get a cold with a 30% greater chance of getting a cold, go swimming in the ocean.

Kiran:

Mm-hmm (affirmative), yep. For sure.

Dave:

Because you pick up viruses and it's not a bad cold, it's an immune modulating cold. So, that means that the human genome is extended into our environment because we pick up new genes when necessary, or maybe when we don't want them from viruses that are floating around and it's kind of a normal part

of what humans do. So you can either say, "I am an island." Or, "I am part of this ecosystem that includes all these viruses that are part of my genome." And, I'm starting to think that they're part of our genome or we part of the earth genome. Do you ascribe to that or am I a little bit too hippy for you?

Kiran:

No, I think you're right on the money. I mean, I've always referred to the human system as a walking, talking rainforest, right. We are a holo biome which is a super organism. We are an organism made up of a collective of organisms that together in a certain balance will function and work. But we are also in constant osmosis with the ecosystem, and we're designed to be that way. I think that the success of the homo sapien, sapien comes from our ability to adapt to our environments by picking up features and all that from the environment.

A great example of this, and this is not virus specific, but it's ocean related. If you look at Japanese people, right, when you look at their microbiomes of the Japanese people, they have these unique genes that code for an enzyme called beta [inaudible 00:10:30] that helps them break down seaweed. That's not a normal gene to have, and their microbes seem to have it. And it's not normal for those versions of the microbes to have it, but as it turns out, their microbes picked up that gene from microbes in fish as they keep eating fish, right. Because, now that's a sustainable important feature for them because they eat a lot of seaweed.

So, yeah we absolutely are in constant osmosis with the environment. We're picking up DNA, RNA from viruses, bacteria, amoebas, protozoas, virtually everything. And, there is also lots of what we call inter kingdom communication. Meaning, from completely different kingdoms on the phylogenetic tree, we can pick up DNA from things like plants, from leaves, right. This micro RNA which are these tiny little things of RNA that can swim from a plant cell that we're eating, and then get into our genes and change gene expression within our system. And, that may be some of the ways that these nutrients benefit us actually by changing those gene expressions.

Dave:

And, that's the so same micro RNA that's in the most controversial new medical drug that's out there. Well, not exactly the... It's the same type of thing, but different mRNAs can do many different things. And this is why guys, you're listening to the show, I am extremely interested in mRNA technology. Okay, I believe that about 40% of aging is caused by inflammation and inappropriate immune system activation. And by the way, 30 years from now, when I'm still looking and feeling exactly like I do now if not better, I'll be saying, "I told you so, I told you so, I told you so." Mark my words, episode whatever this is. And maybe it's 39%, but I'm within a standard deviation of 40%.

So if that's the case, we need mRNA and we need it from our food, and we probably need to take control of that so we can use mRNA to turn off diabetes, and heart disease and all that. So, do be an anti-vaxxer because you might want a vaccine for something that is a clear and present danger to you as you age, where you look at the risk and the benefits and you go, "Oh my God, that's totally worth it." Oh, and I got clean data. The other little problem we have right now.

Okay, so don't say drugs are bad, don't say any technology is bad. Okay. You can use lasers to shoot you down bad people or to heal a wound faster. So lasers aren't good or bad, neither are shovels. You can hit people with them when you dig holes. So, don't be a zealot for or against anything except for butter and kale. Be against kale before butter, as long as you have those right, everything else is optional. All right, so sorry, I'll get off my high there but mRNAs are not inherently bad. Nature uses them. Is that what I just heard?

Kiran:

Oh my God, we have thousands of mRNA fragments in our system every single minute of every single day. That's how things go from DNA to protein, right, mRNA's the messenger in the middle. And, we just did a metabolic health study looking at changes to the microbiome and improving metabolic health. One of the ways that we study changes in our own metabolic health is by doing an mRNA blast which is a huge sequence check on all the mRNA in our system. It's massive, massive amounts of data. Every single second of every single day we're generating mRNAs. That's one of the things that puzzled me about this whole crisis that's going on. I'm like, "All of a sudden mRNA is some sort of weird vicious, toxic thing when we have millions and millions of strands of mRNA in our system every single day." So, yeah I think you're not off on that at all. It's-

Dave:

Okay, it's nice to be able to have the freedom to select which mRNAs are floating out. There's that whole biological autonomy thing which I am absolutely supporting here. So, this is not say that you should allow others to inject you with any bodily fluid without your permission or anything else without your permission. It's your body, you get to say.

So one of the things I about your work Kiran, is that you're not just kind of in the lab looking at stuff. You're doing human clinical trials. And you've done dozens of them, but you've done some really cool stuff around leaky gut. And I take that personally, because leaky gut was a major part of unwrapping what was going on with me and I have a lot less and usually none. But I mean, none is a very fine thing to say. And, all of us have some degree of stuff that passes through or we probably wouldn't have very functioning guts. So, what have you learned about leaky gut in the trials you've done now that's very different than what we would've known 10 or 20 years ago?

Kiran:

Yeah, so a couple of really interesting things. One of the interesting things is that you cannot tell who has leaky gut, right. So you would think that people are somewhat symptomatic of it, you would think that you could look at somebody and predict how healthy their gut is and how healthy their intestinal lining is. But, it's impossible to tell. I mean, one of the studies we did and we published, we use young, healthy, normal individuals, right.

Now of course, healthy, normal is a very gray definition but the way the FDA defines it is really people without any diagnosed chronic illness, not being managed for anything, not on any medications, no reported symptoms or issues at all. The average age is about 22 and they were all of normal body weight. So within the spectrum of just having normal composition, and 55% of them had very severe leaky gut to a point where it was very dramatic on the inflammatory response of the leaky gut created.

So the way we understand it as we've progressed through the different research that we've done, is that you likely have some degree of leaky gut all the time, right. We have, of course, 20 feet of intestines, so any portion of your intestines can be leaky at any given time. The moment you start exceeding a certain limitation on the amount of your intestines that are leaky, that's when it starts becoming really clinically relevant, right.

So as your intestine becomes leaky for what reason, a bad meal, a toxin you got exposed to, whatever it may be, your system is designed to fix that. And, then some other part gets a little bit leaky and then it fixes it. Another part gets leaky and it fixes it. But as the repair slows down with dysbiosis, and more and more of the intestinal lining comes leaky, over time that becomes clinically relevant. And, so it's not a people think of leaky gut as a static state like, "My gut is leaky." Or, "My gut is not leaky." It's

a dynamic state. It's constantly somewhat leaky, but if the net result is a significant leakiness in the gut, then it's going to become clinic relevant.

Dave:

How quickly does the lining of the intestine turn over?

Kiran:

Oh, so you can completely turn over full lining of your intestine within about two or three days.

Dave:

So, two to three days?

Kiran:

Mm-hmm (affirmative), so we've got a really great opportunity to constantly be healing it, repairing it, keeping it fresh. And, so there's a few parts of the body that turn over that quickly, right. So, the insides of your mouth often turn over and heal pretty quickly. So, certain other soft areas with a lot of abrasion and damage because of eating and things like that are designed to turn over and repair pretty quickly, and your gut is one of those areas.

Dave:

So, it's easiest to think of it almost like a treadmill. A treadmill takes three days to go around all the way and that's your gut. And so if you did something bad one or two, or three days ago, you could still be feeling inflammatory effects, well, possibly even up to 10 days later. But, most of the research that I've seen says usually within four days most of it hits you.

Kiran:

Yep, absolutely.

Dave:

Right, and that's because the three day turnover, right?

Kiran:

That's right. Yep, but here's the most important aspect of that turnover and that repair is that much of the repair and the turnover is dictated by the microbes that live there, right. So again, we've outsourced these things to the microbes because we have limited capacity to do these things for ourselves. And, so we're counting on certain types of bacteria in order to be able to do that.

So I'll give you an example of that, one of the keystone species that's really well known for repairing the gut lining, maintaining low inflammation in the gut lining is a bacteria called faecalibacterium prausnitzii. And those that have low levels of faecalibacterium prausnitzii tend to have much higher increased rates of inflammatory bowel disease. So Crohn's and colitis, and so on. The reason for that is faecalibacterium is a very important member of the repairing committee of your large bowels lining.

And, so we all have all kinds of damage occurring in our large bowel all the time. But if you have faecalibacterium, it's constantly repairing it. If you don't have faecalibacterium, at some point, the

damage overcomes the repair and you start getting significant inflammation in lining which then puts you at risk for things like inflammatory bowel disease. Right, so we're constantly battling this state of damage, oxidative stress, inflammation, and all that, and then repair recovery and so on. And then as it turns out, microbes are so important for that repair and recovery phase.

Dave:

What was the name of that bacteria again?

Kiran:

It's called faecalibacterium prausnitzii.

Dave:

F-A-E-C-L-U-M, what?

Kiran:

Yep, F-A-E-C-L-E-A, faecali. Bacterium, B-A-C-T-E-R-I-U-M.

Dave:

Bacterium, just an [crosstalk 00:20:31].

Kiran:

Yep, and then prausnitzii is P-R-A-U-Z-N-I... I think it's N-I-T-Z-I-I.

Dave:

All right guys, I'll put those links in the show notes. You go to Daveasprey.com/podcasts. You always find transcripts and all that, so those are interesting things to pay attention to. When you're looking at this sort of three day, okay, you're going to injure your gut when you eat almost anything. And more likely a seed or a grain is going to cause more damage, or many vegetables are going to cause damage. But that's not say it's harmful damage, but they're going to go through there and then you're going to have to regrow stuff, right.

And I don't know, I'm assuming that meat and fat probably because it's less abrasive, has less damage, right. It's designed to heal quickly, so I'm not saying damage like oh, into the world. Although frankly, some of those grains might not be good for you. But, is it a safe assessment then that less abrasion is going to be good for leaky gut?

Kiran:

So, abrasion is one aspect of it. The other aspect is what is the immunological response to the food? Right, so certain things like dairy proteins, for example. And a lot of people will elicit an immunological response, whether immunological response itself creates a damage. So, it kind of depends on the individual to certain degree, and it depends on their lineage, and then it depends on what they normally eat. So, if you take somebody who's normally meat and potatoes, Midwestern, US person, and then you all of a sudden send them over to Sweden and they're eating all kinds of fermented stuff and all that, even though those that food is perfectly normal-

Dave:

Sweets are weird, man.

Kiran:

They eat a lot of interesting things, right. So, a lot of fermented fishes and things like that. They will create inflammatory responses in their bowel, because their immune system and their microbiomes aren't used to seeing those food, and so that will create damage temporarily. But again, damage is one thing. Repair is the key, right. So at the end of the day, that's the same thing like working out, right. The whole purpose of working out is to create damage, whether it's oxidative damage to your cardiovascular system and all that. And then of course, to your muscle and all that, you create tears and damage, but that adaptive repair is what kind of gives you that next level of fitness and so on. So-

Dave:

So, then what we want to do is we want to create less damage, right. And, I'm assuming the first one of them would be abrasion. The second one would be you eat something you're allergic to, it triggers toll like receptors that trigger mass cells to de granulate, they release heparin, they release histamine and basically set off little nuclear bombs inside the gut. Because, see why I think aging might be related to immune inflammation? I don't know, is that an accurate picture of the other major cause?

Kiran:

That's right. Yeah, so the inflammatory response, I would say is the biggest driver of gut related damage that occurs. Now you can also, of course, in the modern day eat foods that are absolutely toxigenic to your microbiome, right. So, foods that are [crosstalk 00:23:46]-

Dave:

What's the worst? Tell me it's kale. Come on, tell me it's kale.

Kiran:

I would say the inflammatory one would be first, because the damage is pretty immediate and quite profound, right. And that profound immediate inflammatory damage has a cascading effect not only in your gut, but then for the rest of your system, right.

Kiran:

[inaudible 00:24:00] effect not only in your gut, but then for the rest of your system. You can measure that kind of inflammation in your brain a few hours after eating. You can measure it in your periphery and so on. And then the toxogenic effects, like if you are eating food that has high levels of Roundup in it or other preservatives and antimicrobials and so on, that's going to cause dysbiosis and then drive more inflammation over time and then you abrasiveness and foods like seeds and tough things that get stuck in the little out pocketing of your intestines and all that. That can drive inflammation over time as well. But that inflammatory response to food can be quite damaging to the system.

Dave:

Okay. So we have abrasion, inflammatory response to food.

Kiran:

Mm-hm (affirmative).

Dave:

And then the other thing, and I'm leading you down a path here is you can probably tell, but this is so people have a framework for understanding, "Okay, there's all these insults I'm throwing on my little treadmill." And then we're going to go into, what do we do to make it heal faster because it's going to take hits. It just is. That's what it's there for. That's why it heals so fast, right?

Kiran:

That's exactly right. Yeah. And that's why it has so many repair mechanisms in place. And the gut lining has all of these layers to it that are designed to provide a little bit of fallback as damage occurs. Lot of feedback loops to tell the system that it's damaged and then lots of microbes in that area. That's where 70, sorry, lots of immune cells in that area. That's where 70, 80% of your immune system lies, is in your digestive tract. So your immune system is there, ready and waiting to help with the situation. That's also the largest site of exposure that you get to the outside world. So that's another reason why for the proximity of the immune system, to the gut, almost everything that you get exposed to in large quantities goes through your digestive tract in one way or the other. So everything's sitting there waiting and ready to repair if your system is in the right position.

Dave:

One of the compounds that has profoundly affected how I think about guts and brains and just the whole anti-aging and biohacking world is good old lipopolysaccharide. Can you talk about what that is, where it comes from and what it does to your gut?

Kiran:

Oh my God. So lipopolysaccharide is... It is the unknown villain of virtually everything. Before this, I actually just gave a couple of lectures on it. One of the lectures are gut brain lectures. So I went through all the research on how damaging lipopolysaccharide or LPS is to your brain. And then the one before that was a lecture on lipolysaccharides and metabolic disease. And so-

Dave:

There you go.

Kiran:

You know how damaging it is, how it's the number one driver of diabetes. For example, there's a study called the cordial prep study. This is a 60 month study... Sorry. Yeah. 60 month study, 490 individuals. They took individuals that were pre-diabetic and they were following them over 60 months with all kinds of biomarkers that they were measuring to see which biomarker was the best predictor of going from pre-diabetes to diabetes.

And there was only one that they found was the level of LPS lipopolysaccharide in serum. That was the only biomarker that was predictive of going from prediabetes to diabetes. It's mind boggling how disruptive it is. And so when you have this lipopolysaccharide, which we all do, because it's made by something called gram negative bacteria in the gut microbiome. So every bacteria in your microbiome can be distinguished as gram positive or gram negative and that's just a matter of staining them with a particular stain under the microscope called gram stain. And if they have a cell wall structure, they pick up the stain. So you can look at them and go, "Ah, they're stained so they're gram

positive." If they have no cell wall and just a cell membrane, they don't pick up the stain, so they're gram negative.

So those gram negative bacteria that don't have a cell wall, they have this LPS lipopolysaccharide all throughout their cell membrane. Now the bacteria use it for lots of things. The bacteria use it for communication and for adhesion to the lining of the gut, for receptor binding to other bacteria, nutrients and so on. So when it's in the bacteria, it's not really an issue, but what's happening in the gut is your bacteria's constantly dying and regenerating and so on mm-hmm and every time the bacteria dies, it releases this LPS so the lipopolysaccharide, now this thing is free floating around in your lumen, in the mucosa and if it's in the lumen, it's okay. It's not really causing you a whole lot of issue, but if that's allowed to leak through the lining of your gut and enter circulation. It's going to cause little mini nuclear bombs all throughout your body and that a big driver of aging.

Dave:

There you go. And it's a tiny molecule. Lipo is fat and fat is something that can penetrate your gut lining. It's meant to do that. So small droplets of fat, we use that like liposomal glutathione, small droplets of fat, the drug companies use liposomal delivery system to bypass all the protections. But the polysaccharide that's a complex sugar configuration that can stick onto molecular locks on other cells throughout your body, depending on what it is.

By the way, guys, lectins, which you've heard me talk about for 10 years, they also stick to polysaccharides in your immune system. So polysaccharides are not good or bad. They're just everywhere. They think it was the sugar gunk on cells till they figured out, "Oh, that's your immune system." But a lipopolysaccharide the lipo, lets it get through the gut and the polysaccharide lets it get there and bad bacteria make this and I believe they have a direct, toxic effect on the lumen and the gut itself. So they're one, they're the third major damager on this little treadmill that we're constantly damaging and regrowing as it moves through. Does that make sense?

Kiran:

Well that makes sense. And in fact, most... And here's the crazy thing in all of those three damage roads that we talked about the pathways to damage we talked about LPS is actually a component of all of those, because in any case where there's damage to the lining, whether it's inflammatory or physical damage, LPS is being released because there's always microbial damage as well to the system. And when LPS is released it more than fivefold amplifies the inflammatory response to that area, because what your immune is system has learned over time is when it sees LPS, it thinks there are damaging microbes coming in or present. And so LPS is so important for the immune system to keep track of that the immune system produces a protein called LBP, which is LPS binding protein. And that LBP is constantly swimming around in your circulation, looking for LPS.

And so if you allow LPS to leak through and LPS levels in the serum and circulation increase, LBP is going to find it, bind it, take it to your macrophage or your dendritic cell and tell the macrophage and dendritic cell, "Holy, we've got a massive blood infection going on." That's what your body thinks when LPS comes in. It thinks you're undergoing sepsis. And so the inflammatory response that the immune system has in response to that LPS detection and binding is the same inflammatory response as you get when you have blood poisoning or sepsis. So it's really, really significant and that can occur in any local area. So it can occur right in your gut lining and continue damage your gut lining, or LPS as pervasive as it is, can enter in, make it to places like the hypothalamus in your brain, the amygdala in the brain, into your joints, into your heart, into your pericardium, all these areas where it drives damage by inflammation. Wow.

Dave:

And it's so you guys see this, the lipopolysaccharides from bad bacteria in your gut, they're causing damage to the gut on top of whatever weird foods you're eating and other things that you might be allergic to. Okay, so we've done all that and then once this gets through it's wreaking havoc, and it is a direct cause of brain fog, not the only cause, but a direct cause. It is probably a trigger for Alzheimer's. You think that's likely?

Kiran:

Well, so a confirmatory study on that in 2017 published showing that the foundation for the beta plaquing in the brain of Alzheimer's patients is start it by gut derived lipopolysaccharides.

Dave:

Yes.

Kiran:

So they can enrich them in the perinuclear region of the brain. They find that in Alzheimer's patients, they tend to have high levels of LPS in the brain from the gut and then that triggers the inflammatory damage to the brain and leads to the beta plaquing yeah. It's a driver of Alzheimer's and here's the crazy thing, not only is it a driver of Alzheimer's it's also a driver of Parkinson's the other one we don't want to get as we age.

Dave:

And ALS almost certainly.

Kiran:

Yep.

Dave:

Right. By the way I know about that. Because if you guys read Headstrong, most of research on enhancing mitochondrial function and reusing inflammation in the brain is done on those three conditions. So I read stupid amounts of papers to figure out how the rest of us who don't have those, can have better brains now as well as not get those later, because brain fogs sucks. I had it for way too long.

Kiran:

Absolutely. Yeah. And the LPS can get into areas of the brain that it interrupt with synaptic signaling. It can interfere and it does interfere with dopamine and serotonin binding in the brain. So you start getting anxiety, depression. It actually will get into this area called a dorsal vagal complex, which is in the stem of the brain, which actually interferes with signaling from the brain to the gut, which means that your bowels become constipated because the peristaltic movement signals don't go through. It gets into the pancreas and causes damage to the islet cells. It is the most pervasive toxin we have to deal with and it's an endotoxin, which is a key because we can't get away from it. Endo meaning it's made from within. Different from an exotoxin like if our house has mold, we can burn that house down and move away hopefully. But an endotoxin you can't get away from it. It's always there.

Dave:

There. You can't just eat Habanero's, which is the internal burning equivalent.

Kiran:

You could, but that can actually lead to a little bit more LPS in the system.

Dave:

More, not less.

Kiran:

Exactly.

Dave:

And unfortunately those really delicious spicy foods tend to poke holes in the lining of the gut which lets LPS through more effectively.

Kiran:

That's right. Yep. And another area, another route for LPS to get in is dirty mouths.

Dave:

Okay. I wanted to ask you this.

Kiran:

Yeah.

Dave:

Okay. This is such a fun question. You mentioned earlier that in Japan that people have oftentimes got bacteria that let them eat seaweed. And in fact, I think I mentioned that one in my books a long time ago too, because what you eat does that. In a recent interview with Trina, we talked about oral care and I asked her straight up, "Does that mean that you should make out with people of good teeth so that you'll get their healthy oral microbiome?" Because your mouth is the beginning of your gut.

Kiran:

Totally. Yeah.

Dave:

So talk to me about whether we should be kissing our friends from Japan so that we can digest seaweed or whether that's a more invasive medical procedure?

Kiran:

I think if you have a friend from Japan who has a healthy oral microbiome, for sure. I think there's no risk in... Well maybe a risk for them. But there are certain tribes, for example, in New Zealand, there are people that are well known to have microbes in the, in the mouth that completely prevent carry formation and high levels of plaque formation and prevent gum disease and gum bleeding all from

the microbes that you have in your mouth. Now we also know from studies that leaky gut action and the movement of LPS will actually drive gum disease because LPS from the gut will move through circulation. We know we have a lot of circulation capillaries in the gums. So once LPS gets into the gums, into the gingival cavities in the gums, it'll actually cause an inflammation which will change the types of microbes that are living in your gum tissue and it'll favor organisms that create more gingivitis. So stopping LPS from the gut and then in the mouth can be hugely important. But I think somebody has a really healthy mouth making out with is always a good idea. Just from a scientific perspective.

Dave:

All right. You heard it here. Should you make a out with people who have a healthy mouth? The answer is yes from a research microbiologist. Now I wanted to have you on, cause you've done all these clinical studies. Clearly, you know how to think about stuff, which is why I like talking with you and you work with Just Thrive on unusual probiotics. Now we've gone through the three major punches that your gut takes and clearly maybe eat less stuff that's shredding your gut and reduce polysaccharides which we're going to get into in a minute here as well as dealing with some food allergy response type of things. So let's start with just your overall take on okay. How of those three things that are causing damage, which is the one that we can mitigate most easily and how do you like to do that using the tools that you have with Just Thrive or anywhere else?

Kiran:

Yeah. So in fact, when we did our first clinical trial on this, we made it a really difficult challenge. So what we did is we took individuals that had bad leaky gut, and then we fed them things like a fast food breakfast. And then we fed them things like microwave pizza from the gas station and then measured their endotoxin level in circulation. And then of course looked at all of the inflammatory markers that increase on top of that. So what we saw is that they were profoundly affected by those foods. In some cases, and you mentioned this earlier that a single meal, we could measure that inflammatory response up for to two weeks. So it was really profound. And so we said, "Okay, can we then fix their gut to a point where that same offending food would then no longer have an endotoxic response?"

And so that was the whole premise of the study. And so we did 30 days of the spore based probiotics. And then when we repeated this study, we saw in the vast majority of the treatment group, a complete blunting of the endotoxic response even though we're feeding them that same offending food. So the conclusion to that for me is that the human system is pretty resilient. We can deal with a lot of stuff given that we are in the right homeostatic condition. And so we were able to repair some of the imbalance of microbes within the gut in that 30 day period. We were able to increase buterate production. We know that the spores increase buterate production by about 50% and buterate's really important for healing the gut lining. We also know that spores increase the expression of tight junction proteins. Those are the proteins that seal up the spaces in between the gut lining cells.

So we were able to shore up some of the defenses within the gut and the ability to repair and once we were able to do that, even that really offending food did not create leaky gut. so if you did that and on top of that, you cleaned up your diet to a certain degree, you eliminated foods that you knew you were sensitive to, that you tend to get a response to, or you reduce them at least and then you try to increase diversity of actual real foods that are not packaged, not processed and so on. You did that on top of taking the probiotic, you'd do wonders for your gut.

Dave:

Can you guys imagine which probiotic I take every single day? Yes I actually take the Just Thrive probiotic every day. It's not the only one I take just to be super clear. I take some other very highly specialized ones, including funny enough, one from Japan. But not the kissing one. And what I find those that this one is table six, because I'm aware of the research on that. But when people hear spores, they usually think of mold and this is not at all related to that. Can you talk about what a spore forming probiotic does versus a different one?

Kiran:

Yeah. And to me, I absolutely love these spores. That's the microbiology nerd in me. If you think about the life cycle of the cell. So when it's not in the spore form, it looks like a lot of other bacteria. It's vulnerable to heat moisture pressure and so on, acid and all that. But these organisms, what has happened to them is they've developed this capability of also existing outside of the body. Early on in our conversation, we talked about how the vast of microbes in the gut cannot exist outside of the body, but they ended up with this capability of covering themselves in a protein calcified armor-like coating. If they're going to leave the body that way they can exist in the outside world, that's not their ideal environment for indefinite amounts of time and then reenter into the body through consumption, make it past the stomach acid and the biosalts because of that coat and then go back into their normal vegetative state once they enter into the intestines.

And the spore form is thought to be one of the criteria that's required for microbes that could have seeded the earth with building blocks of cells. So that whole idea of panspermia. I think we might have talked about that last time, but this spore forming bacteria is absolutely unique and different than anything else.

Dave:

In fact, I remember this well, because we came up with a title for the podcast. It was something like Armor Plated Probiotics From Outer Space or something, which was also one of my favorite titles. So that panspermia idea is super... It makes people very mad, like "Don't you know?" And then they tell you a theory that is impossible to prove about where life came from. You're like, "No, I don't know that, but I like all of these theories and that one's cool. Because it involves comets and stuff."

Kiran:

Totally.

Dave:

So we use these spore forming things mostly because they don't die when they're in pills and because they don't die when they see the acid that you may or may not have in your stomach.

Kiran:

Right.

Dave:

Right. I say may not because you could have low acid. Oh wait, does that happen? As we age to everyone? Yeah, it does. So we'll maybe talk about acid later, but I want to go deeper with you on what else is happening in the gut here. So you did a study that said, "Wow, the gut is less leaky from these probiotics and they make more of this anti-inflammatory compound." So think of that as a rapid healing

salve that you would put on onto something to make it heal faster. That's buterate or butyric acid. And if you guys are long time listeners, what is one of the reasons I like grass fed butter? Because it contains butyric acid and the two studies show eating butyric acid has additional benefits different than making it in the gut itself. So my question for you is, okay, I'm taking probiotics. I'm taking actually the Just Thrive spore forming probiotics very specifically. And we have the study to say they make more butyric acid, but I have to feed them something.

Kiran:

Mm-hmm (affirmative). Right.

Dave:

So what would I feed them? What do they like to eat the most to grow?

Kiran:

So in fact they can convert protein, even, into buterate, which is unique and interesting. But mostly it's it's carbohydrates or fiber really and oligosaccharides. And oligosaccharides are unique because oligosaccharides were the first food for our microbiome. Mother's milk contains 200 different types of oligosaccharides. So those are really unique quintessential prebiotics for the microbes in your gut and many of them are highly complex where very limited groups of microbes can actually break them down and be because of that, they feed certain groups of bacteria, especially the buterate and short chain fatty acid producing bacteria, including the spores. So the spores love their oligosaccharides they love the proteins. They will metabolize the proteins as well and they can metabolize fat to some degree as well

Dave:

Now. Oh, that's interesting. I didn't realize that they were fat metabolizers, the species in Just Thrive. Is it all here? I think got four species in there.

Kiran:

[inaudible 00:45:01].

Dave:

They're all spore formers. Yep. And is one of them more of the fat eater because it's hard to get fat eating probiotics. Most of the time fat kills probiotics.

Kiran:

Right. Yeah. So the bacillus subtilis is a pretty robust organism and it's highly adaptive. It can metabolize almost any carbon sources and it can do that with fats to a small degree as well.

Dave:

It's almost like these tentacled aliens quad billions of years ago, by the way, I made that up, nano engineered these little things to eat almost anything and make other stuff totally out of it who would've ever thought.

Kiran:

And through our course of evolution, we came to depend on that other stuff that they make. We built our system based on their capabilities as little production factory of things. Yeah. So it's really fascinating.

Dave:

Okay, so I'm taking these and you talked about oligosaccharides now just thrive has... I think it's in your prebiotic.

Kiran:

Yeah.

Dave:

I take that stuff, I don't want to say every single day I take it most days when I travel. I probably don't. But when I'm at home, I usually do. That's the fruity flavored one. Yeah. And so that's got oligosaccharides and then I take... And it's also got some other prebiotics and it, and it's a relatively small dose and then I take 20, 30 grams of bulk soluble fiber. And I put one together for Bulletproof and it's primarily acacia gum and all of that. But it does something different than what the oligosaccharides do. And the oligosaccharides you design those for, is this for making more mucus in the gut lining? Is this for reducing IGGI? I'm not sure the mechanism action other than I'm feeding the bacteria that I get from you guys that have all the studies behind them. So what else is going on with those ingredient in the Just Thrive prebiotic fruity stuff? I forget what it's called. I could go grab my thing of it, but-

Kiran:

I think it's called maybe prebiotic. Just Thrive Prebiotic, maybe?

Dave:

Yeah that's it. It says that right on the front. Yeah. All right. Keep talking. I'm going to grab it. Talk about that for a second.

Kiran:

Okay. So yeah. So the prebiotic, the really important aspect of that is we all it a precision prebiotic. Now the reason for that is we wanted to take oligosaccharides-

Dave:

All right.

Kiran:

Yeah. You found it?

Dave:

There I found it. It's Precision Prebiotic.

Kiran:

Uh-huh (affirmative). There you go.

Dave:

It's the precision thing. That's pretty cool. And now we can look, it's actually, all... [crosstalk 00:47:28] Galactooligosaccharides fructooligosaccharides in xylooligosaccharides. So there's nothing but oligosaccharides in it. I look at that as an add on to the other stuff. Now, Mr. Microbiologist, are those heat stable? Can I put them in hot water? Will they still work?

Kiran:

You can, yeah. You absolutely can.

Dave:

They taste gross in coffee, sorry guys. Fruity coffee doesn't do it for me.

Kiran:

It doesn't at all. No. But you can make jello out of them if you would like jello. But you can put them in smoothies for sure. But the idea behind the precision part of the prebiotic is more and more of these studies are coming out, showing that certain spe-

Kiran:

... Is more and more of these studies are coming out, showing that certain species within the microbiome are considered to be keystone species, because they're really important in holding up the rest of the structure and function of the microbiome, or they've been shown to be really, really protective against large categories of diseases, like that one I talked about earlier, Faecalibacterium prausnitzii that protects against everything under the inflammatory bowel disease spectrum. And then there's other ones like Akkermansia muciniphila, which protect against metabolic syndrome, so it's inversely correlated with metabolic syndrome. Then there's Bifidobacterium longum, which protects against all kinds of cognitive emotional damage and so on that happens to the brain. And what we were looking for was oligosaccharides that had unique enough structures, that they would specifically feed those keystone species, in addition to the spores.

So, what we've done is we've actually published now, I think, two studies showing that when you add in the prebiotic with the spores, you not only more than double the effect of the spores let's take butyrate for example, you take butyrate production from 50% increase over baseline to 150% increase over baseline, so you're almost tripling the amount of butyrate, you're increasing diversity in the microbiome, and you increase the growth of all of these keystone species that are extremely important for overall health and wellness, which also improves our ability to repair after damage, so that combination of the probiotic prebiotic is absolutely critical for overall gut health.

Dave:

Okay. I found that by taking bulk prebiotic soluble fiber, I quadrupled the number of species in my gut. Despite eating unreasonable amounts of vegetables, my diversity was not bad but you want to have a broad diversity of gut bacteria. And a lot of people say this, "You should eat a wide variety, as many different foods as you can." And I want to ask you this, because I've never asked anyone this, but it seems like your gut bacteria change over the course of one or two or three days based on what you eat, right?

Kiran:

It does.

Dave:

If every day you eat some different random God damn food, how is your gut bacteria ever going to catch up? That seems like bad advice. And throughout all of history, did you eat 47 different greens on any one day? No, you ate whatever the heck was growing near you in that season for that two weeks before something else grew.

Kiran:

Right.

Dave:

So, are we really doing a favor by saying eat a wide variety of plants to feed your gut bacteria versus eat a lot of prebiotic fiber and eat a few plants for roughage?

Kiran:

So, the fiber part is the most critical part, right? That's the part that's really going to move the needle on the diversity in the gut. And we see that when we look at tribes like the Papua New Guinea tribes or the Hadzabe Tribe in Tanzania, they tend to have really massive diversity, three, four times the diversity of the Western population and a lot of that comes from the roots and tubers that they eat. So they don't eat a massive variety of roots and tubers, they eat four or five staple roots and tubers, but they're eating a lot of that root and tuber.

And so, they tend to have really high levels of keystone species, very high levels of short-chain fatty acid production and then they have all of these gut brain protective mechanisms that we don't have anymore, that we've lost over time. So yes, I would say the fiber is the biggest part of it, right? So if you can get it from a bar or drink and you can get a good variety and dose of fiber, that's a fantastic thing and you add in a precision prebiotic and you're targeting the keystone species, you're doing already more for your gut than the vast majority of people will do.

Dave:

That, and I'm definitely making sure that I kiss all of my healthiest friends.

Kiran:

Exactly. You can't forget the oral microbiome, it's for health and science. You just have to, right?

Dave:

I was talking with Dr. Mercola.

Kiran:

Yeah.

Dave:

I got to see him, because he was speaking at the conference and he was talking about how he noticed changes in his gut bacteria from... Am I allowed to say this? By the way, guys, how many times in the

history of Bulletproof Radio have you heard me say, "Am I allowed to say this?" That's because there is rampant censorship going on right now. There's a hashtag about the immune system and if you mention it, it gets blocked and they shadow ban your account on Instagram, so I'm being very careful.

And by the way, t.me/aspreyofficial, that would be my Telegram account where I actually post stuff that's a little bit more truthful and transparent, so all right, I just got all distracted by what I was going to say there, because I'm like, "Can I say this?" See, this is the pernicious thing happening in science right now where you're going, "Oh, can I talk about science or not?" So, where was I?

Kiran:

Mercola?

Dave:

Ah, he said that when he did a specific treatment from a guy named Frank Shallenberger, who was a major source of information for my book on... That was in my anti-aging book, who's a father of ozone therapy, which is still legal to talk about this week. And he recommended nebulizing, see the pause I put in there, so that the AI things will spell it wrong. I'm not even kidding. I'm doing this as we go on.

Kiran:

Interesting.

Dave:

Yeah, a medical ingredient, which is called hydrogen peroxide, and you might have seen some of my posts about that before they got taken down by authorities who didn't like them, but anyway, you can put that stuff in a nebulizer and you can breathe it and it changes your lung biome. And he noticed changes in his lung biome from doing that and probably also in his nasal biome, which you also, by the way, guys, can get if you do the, I called it the Bulletproof sinus rinse way back in the day, it's on daveasprey.com now. But basically changing the nasal bacteria and the lung bacteria was having profound effects on his gut bacteria. What is going on with that, why would breathing something that changes your lung bacteria change your gut bacteria?

Kiran:

Yeah, so there is something called the gut-lung axis, which is really interesting. And as it turns out, the microbes in the lung have a mechanism to talk to the microbes in the gut. And that's actually a really important part of a lung infectious process, right? So, let's say you get a virus that enters into your lung and it starts causing an infection in your lung. The first thing to notice the presence of that virus are the microbes in your lungs. So, if you have the right type of microbes in your lungs, they will notice the presence of that virus and they will actually send a message to the microbes in your gut that are sitting on all the immune tissue in your gut and say, "Hey, there's a virus in the lungs. We need you to recruit the immune system to come to this area."

And so, then the microbes in the gut will send signals to move the immune system, to recruit it to come to the lungs, because here's the interesting thing about that whole system, we've created this unique default, because we don't actually want the immune system constantly active in the lungs, because we're constantly breathing in things from the outside environment and if the immune system is responding to everything that we breathe in, we're going to have severe asthma all the way down to

chronic respiratory disease and all kinds of things, so we don't want the immune system always active in the lungs.

What we want is the immune system sitting by and ready and then a signal to be given to them when they need to get to the lungs. And as it turns out, that signal comes from bacteria in the lungs, talking to bacteria in the gut and then bacteria in the gut sending the immune cells to the lungs when there's an infection. So, if you change the microbes in your lungs, you can influence the microbes that are in your gut and vice versa. And of course, that kind of change that he's talking about can occur, another simple way of changing the microbes in your lungs, is to stop mouth breathing, so people who-

Dave:

You guys heard this on here before? So, keep going, I love this, yeah.

Kiran:

Right? It's so simple. And so, even things like taping and so on that people do, because as we breathe all of this gram-negative bacteria in our mouth, our mouth is loaded with microbes and if you're not kissing your Japanese friend, it may be bad microbes, so you're breathing all of these microbes into your lungs all the time and causing a dysbiosis in the lungs. And that's likely why we have such an epidemic of asthma in our country, that's one of the drivers of that.

Dave:

There's something else that we've got to bring up, because it's so complex, because of all these different systems cross talking all the same time, we have a big problem with environmental toxic mold.

Kiran:

Yeah.

Dave:

And when bacteria is exposed to the mycotoxins from toxic mold, so these are basically penicillin or any one of the other antibiotics that mold makes, the bacteria freak out and they make a biofilm.

Kiran:

Yeah.

Dave:

And the biofilm makes a lot of LPS, because it's stress, it's like, "Let me pump about some toxins." So, one of the symptoms of breathing toxic mold in a home, and this is a well documented symptom that you have to treat if you're a mold physician like Anne Shippy, who's been on the show, or Jill Carnahan or others who focus on that space, is that you end up getting this film in the sinuses that produces LPS right next to the brain and you get brain fog, you can treat mold in the body, but if you don't treat the bacteria, you have an issue. I think we're getting lung biofilm from toxic mold homes. Am I crazy?

Kiran:

No, not at all. I mean, the lung has a mucosal lining, so that's exactly similar to the upper respiratory tract, the airways, the gut, all of that has a mucosal lining, so not at all. Yeah, there's biofilms there. And here's the other thing about the mold toxicity, is that there are pathogens that have learned to work

with mold to together form a stronger team than just the mold itself or the pathogen itself, so some of those pathogens are like staphylococcus areus or streptococcus, they tend to work well with mold and they will actually form biofilms that both hold the mold and the bacteria together to try to protect it from other microbes and the immune system as well. So, when you're exposed to lots of toxic mold and mold toxins itself, you're going to actually get other secondary bacterial pathogens also growing within the system, which just amplifies the problem significantly.

Dave:

Another thing that happens with toxic mold and certainly happens very reliably with some species of mold in my case. And yes, guys, I have it dialed down to different flavors of molds because, well, I pay attention. The first night, if I'm exposed to really bad stuff, I got weird dreams and a nose bleed, okay, and there's different explanations, I'm not going to get into on this for why those happen. But then the next day like, oh, something really bad is happening in my gut and then I'm going to have [inaudible 00:59:21] digestion for a week. And the third or fourth day, I'm going to have really bad eruptions on my skin, like subterranean pimples that take a long time to heal. And of course, all of this time, I grow a set of man boobs and I have love handles, which is systemic inflammation, right?

Kiran:

Yeah.

Dave:

But why does it feel like the lining of my gut is likely shedding when I'm exposed to mold like that? What is going on physiologically? Do you have a good map of that?

Kiran:

Yeah, absolutely. So, when you start getting dysbiosis, which is an imbalance of microbes and you start getting mold overgrowth or you're starting to get inflammation that's driving opportunistic pathogen overgrowth, so there are lots of opportunistic pathogens sitting around in your body that have learned to look for inflammatory or stress signals as the cue to turn on their virulence factors. That's their opportunity to take over when the system was in a compromised state.

And so, what tends to happen when you get that kind of toxicity, is you start getting an overgrowth of opportunistic organisms and one of the ways that those opportunistic organisms survive, is to try to go deeper into your mucosal lining in your gut. So, you've got this thick mucosal lining in your gut, most of the microbes are sitting on the outer surface of it and then the inner surface of it, which is the closest to the intestinal lining of the gut, needs to be relatively sterile, they can't be a lot of microbes there. So what these opportunistic organisms are doing, they're making enzymes to eat away at your mucus lining, so they can go deeper into the mucus lining, thereby by protecting themselves. So then you start getting this liquidation, if you will, and a sloughing off of that top layer of mucus, so you may be able to notice that when you go to the bathroom, for example, that may be something that occurs.

Dave:

Yeah, in fact, a good test with microscopy of fecal matters, is always going to look for mucus, because if you have mucus in there, you got a problem. And of course, there's mucus present at that time, but not usually the rest of the time.

Kiran:

Right, that's exactly, and you see that with parasitic infections, worm infections, all kinds of things, you see that mucus layer coming out and sometimes there may be some blood associated with that mucus as well, because now you've actually caused damage to the tissue that's sitting under the mucus layer itself.

Dave:

One of the things that has always intrigued me, is the studies, I think I wrote about these in The Bulletproof Diet, about germ-free mice, these are mice raised with no gut bacteria. And they're like super mice, they can do whatever they want and they're like the honey badgers of mice until you put them in a place with bacteria and then they do give a, you know what. So, what is up? Can I be a germ-free mouse? We already live in bubbles thanks to government stuff and I mean, is there a benefit to that, what would happen to your immune system if you didn't have a microbiome?

Kiran:

In fact, studies on germ-free mice have really revealed the relationship between the microbiome and the immune system. And there's one study I talk about a lot that was published in March 2020, where they took these mice and they refer to them as gnotobiotic mice as well in some papers. So, they take these mice that have all of the faculties of a healthy mouse, meaning they have a full immune system, all the T-cells, B-cells, macrophages, all the immune tissue and all that, but they have no microbes in them. And so, then they infect this mouse with a virus and what they find is that the mouse's dendritic cells and macrophages and all that sit there and just watch the whole cells getting infected. They don't respond to the presence of the infectious virus at all.

And then when they implant in a microbiome, all of a sudden you get the response, so they've been measuring that to see what is that related to. Yeah, and as it turns out, it's the microbes within the microbiome that are providing the signal for the immune system to respond to the presence of something, so they create, what we call, the threshold tone of the immune system's need to respond. So, the reason for that, is similar to the lung thing that I talked about earlier, where we need to have a certain degree of tolerance to the environment that we live in, right? So, the big part of it is we want our immune system to respond when it needs to respond, but the biggest issue is we don't want it responding when it shouldn't respond, because having the immune system responding too much is equally a big of a problem as not responding.

And so, it's the microbes that dictate to the immune system what is really a problem and when it needs to respond to something. And when a viral infection comes in and you have a healthy microbiome, the first thing the microbes in that region release is interferon gamma. And once interferon gamma is released, then the dendritic cells and macrophages go, "Oh, shit, there's an infection. All right, let's go." If they don't see that interferon gamma signal, they don't respond. They'll sit there and let the host get infected, so that's so interesting when you look at it.

Dave:

Wow. It is quite fascinating and I'm sure people listening is going, "That was enough science that I don't know what to do. I don't want to get sick. I want to have a healthy layer of mucus in my gut. I want to have the good guys growing. I don't want the bad guys to grow. I don't want LPS." And frankly, it tends to be a little bit overwhelming. And, guys, you could spend your entire career in microbiology and still not know everything to do. Is that a true statement?

Kiran:

100%, yeah. 100%.

Dave:

So, the first thing to understand is, it is a complex self-managing system. Your whole body is, in fact, the entire planet is one of those things, so that's why, when I started this definition, change the environment around you and inside out of you to have full control of your own biology, that's the definition of bio hacking.

Kiran:

Yeah.

Dave:

So, we have wizards of poop, I don't know, wizards of gut bacteria on here, but there's a lot we don't know, so what we're doing here is recognizing that this system is mostly a black box. And as a hacker, a black box is a system and you don't know what's in there, because you're trying to break in, so all you can do is push on it and send a signal and see what comes out. And eventually, you realize if I do these five things, even if I don't know the guts, it'll do what I want it to do, right?

Kiran:

Yeah.

Dave:

But you don't know which of those five things in combination, but you know if you don't do all five or maybe you only do four, and this is what bio hacking is, so you're massaging and manipulating a system without knowing exactly where and how it's going to go in order to get the direction that you want. And that's where we are, but we know so much more now than when I was trying to solve this problem. I didn't know there's an environmental component and I'm eating tons of kale and tons of whole grains, because they told me whole foods were good for me. And let's throw out the obvious stuff that we know is garbage, but everything else, it's okay to not know everything. It's okay to not do everything, but you have to do enough that like, "Oh wow, I have the symptoms of less inflammation and a gut that works." Okay, what are those symptoms and how do I measure them?

Kiran:

Yeah, so the biggest things for people is really their daily, kind of how they feel in their digestive system. So, people have gotten very accustomed to the idea that discomfort in the digestive tract is normal, so they're like, "Ah, I'm fine. I get some bloat. I get a little loose bowel here and there, I get cramping, but that's normal. That's just how my gut has always been." And one of the things that I want people to really understand is that you don't have to feel that way. And of course, you have one big night, you're going to go out and party and drink and hang out, yes, you might feel that way. If you travel overseas periodically, you're going to feel that way. But that's not normal to feel that way throughout your existence.

Also, things like energy levels, ability to sleep, rashes that pop up on your skin, sensitivity to things like your environmental allergies, food sensitivities, all of these things are a symptom of all of this dysfunction and inflammation going on in your gut. And one big one is anxiety and lack of stress management, because the gut is really the core of the HPA activation cycle, right? So, that's the stress

management cycle that we have within the system. So, all of these things put together should dictate to you that, "Okay, something at the core is going wrong and even though these are some of the things I feel and they're not that severe, this is the same pathology that leads to long term significant issues." So, you feel it as tiredness, anxiety and all that, way before you feel it as Crohn's disease, so that's the pathway of it.

Dave:

Wow. What about labs? Okay, so I'm sitting around going, "All right, I'm going to invest in getting some data to see if my gut healing protocols, whether taking the probiotic, the Just Thrive or taking prebiotics, the oligosaccharides that you guys make or bulk prebiotic fiber and maybe something like the inner fuel stuff that I put together for Bulletproof." You're going to do that, you're going to eat bone broth, whatever, like there's countless stuff you could do.

Kiran:

Right.

Dave:

You do all that, you're saying, "All right, maybe you got your before, but you definitely want to get your after." Number one lab I should order?

Kiran:

Yeah, so we'll break it down into two categories of labs. So, number one labs, if you're looking at microbiome changes, there are a number of stool tests out there, so we work with one called BiomeFX, which is a whole genome sequencing one that gives you a lot of insight into it, but really where the rubber hits the road is what's happening in your blood, because whatever's happening in your gut is translating to impact in your blood, in your circulation. In fact, at any given time, about 50% of the molecules floating around in your blood, come from your gut microbiome in some way or the other. So, I would do your standard blood panel tests, looking at things like inflammatory mediators, because at the end of the day, all of this dysfunction leads to inflammation and it's inflammation that drives all of these issues. Inflammation is the biggest driver of aging. Inflammation is the biggest driver of most chronic illnesses.

Dave:

Yes.

Kiran:

Inflammation is the biggest driver of dysfunction in the brain, in the organ systems, in the heart, in the skin, everything else. So if you're looking for the endpoint, that's really important, I would look at inflammation. And there's so many ways of looking at inflammation, so there's so many types of tests you can do. Your doctor can do very cheap ones like CRP, or you can do very-

Dave:

All right.

Kiran:

Right, just hs-CRP, just a simple one.

Dave:

There you go guys, for 10 years, who's been telling you three lab tests you need? Homocystine, which is the genetic methylation problem, c-reactive protein, because you might have an infection problem, and I don't care if it's your root canals, whether it's your gum disease or it's something going out with your dysbiosis, it's something that's likely growing in there. And then LP PLA too, because everyone told you to be afraid of cholesterol and if that's a problem, that will tell you it's a problem. So, you could do a CRP test and say, "I fixed my gut, my CRP went down, hurray." But if you do a CRP test and your CRP levels are the same, but you feel like your gut's fixed, because you feel better and you don't clear the room every time after you eat, and so, maybe something else is keeping CRP up. Is there a marker maybe of LPA that you might have for LPS in the blood?

Kiran:

Yeah, so you cannot do a commercial LPS test. There isn't one out there. There's research tools for studying LPS. Now, some labs like Cyrex Labs, for example, will do an LBP test, that's that LPS binding protein that I talked about.

Dave:

Yes.

Kiran:

If you have a lot of LPS, you're going to have elevated LBP as well. So, they'll do an immunological assay for LBP levels. That's another thing you can look at, but once LPS is in your system and when it causes damage, it's elevating really key cytokines, so there's three that we use as surrogate markers for LPS damage in the body. One of the cytokines is called interleukin-6, the other one's called interleukin-1 beta, and then the third one is called soluble CD14.

Dave:

Okay.

Kiran:

Yeah, if you do any of those, you're getting real-

Kiran:

Oh!

Dave:

Okay!

Kiran:

Yeah, if you do any of those, you're getting a real clue into the cellular level inflammatory damage that's occurring in your body.

Dave:

Now, this is so weird because there's a really popular virus right now. It's like the Rihanna of viruses and we no longer speak its name.

Kiran:

Right.

Dave:

Because it is anointed as the virus to end all viruses. And if you guys don't know what I'm talking about, it's also named after a beer.

Kiran:

Right.

Dave:

Was that a chronic beer you were drinking right there?

Kiran:

I wish...

Dave:

It's a Topo Chico.

Kiran:

Yeah! I love that part. It's so good.

Dave:

I must've been confused. I don't know why that came to mind, but you guys know what I'm talking about here. Right? Some kind of magic virus.

Kiran:

Uh-hmmm.

Dave:

Anyway, what does it do when you get an inflammatory cytokines storm? IL-6.

Kiran:

Uh-hmmm.

Dave:

The one that you just talked about? The same one that your got bacteria raises.

Kiran:

Yep.

Dave:

Right?

Kiran:

And one, and here's a couple other things IL-6 does, right? So IL-6 triggers at HPA access. So when you have a high levels IL-6, it's constantly triggering the hypothalamic pituitary adrenal axis causing more and more release of cortisol. IL-6 also causes the reduction in what we call glucocorticoid receptors, which are supposed to bind the cortisol and reduce the amount in circulation and thereby triggering a feedback loop to reduce inflammation. So IL-6 screws up that whole system of cortisol management. IL-6 in this two big studies called the Boston Dublin study that was done at the end of 2020, where they were looking at thousands of patients that suffered from this Rihanna of viruses. And they were looking at what biomarker that they could use to predict these most severe responses to this virus infection. And what they found was that there was one thing, and that was serum IL-6 levels. If your IL-6 levels were high, when you got infected, then your risk for hospitalization and even death was way higher than if it wasn't right? And this is a massive study...

Dave:

Okay.

Kiran:

...between a research Institute in Boston and one in Dublin, and they work together on it. It was so clear. The data is right there.

Dave:

Guys in the fourth week of the current... Am I allowed to say, it's it rhymes with slam demic? I don't want anything to be censored here, but in the fourth week of this, I wrote a comprehensive paper about how to manage IL-6 because it's common in a few people in the upgrade collective probably saw it. I received this mystical warning letter about how that wasn't okay. And if you guys Google around you'll you might be able to find copies of it floating in circulation. And if you're following me on telegram, you might find a version of it there. That'll be going up is probably already up, but that's t.me/aspirinofficial is the URL for that. But is it a safe thing to say that if people have lower, but normal IL-6 levels, they're less likely to die of all causes?

Kiran:

Absolutely all cause mortality, for sure. Because elevated IL-6 is present in the vast majority of chronic illnesses, right? It's no secret. It's like the mother of inflammatory cytokines, right? Because IL-6...

Dave:

Yes!

Kiran:

... not only by itself is an inflammatory cytokine, but it triggers the release of dozens of other inflammatory cytokines in very specific tissues.

Dave:

Yep!

Kiran:

And that's been a target for us. So in at least four of our published studies, we measure IL-6 reduction. And what we see with the spore based probiotics that we can bring down and create healthy IL-6 levels.

Dave:

So, it's almost like if we reduce IL-6 reduce systemic inflammation and almost every one of the practices that I've been teaching you guys in the upgrade collective and listeners and on the blog for 10 years, at some level of we did studies is going to reduce IL-6. I don't think we have a study of mouth taping and IL-6, if you had to bet, would you bet that it reduces IL-6?

Kiran:

Oh! Totally. Yeah.

Dave:

Okay.

Kiran:

Absolutely!

Dave:

And by the way, if you're saying IL-6, the donuts are on IL-6. No, it's I, as in igloo, L as in love and six as in, after five, but before seven.

Kiran:

Okay!

Dave:

There you go.

Kiran:

And it's a cheap test. I mean, any lab can do IL-6 testing in your, in your system. So it's great to keep an eye...

Dave:

Okay.

Kiran:

...on your IL-6.

Dave:

Now, I'm going to add another thing in here that makes a little bit more complex. The other major issue is histamine...

Kiran:

Uh-hmmm.

Dave:

Right. In people with long, what's that thing called long rhymes with ROVID. But that one, they have histamine intolerance and mast cell over-activation issues. And when histamine has a mass cell, or I don't know when LPs hits a mass cell, if you're allergic to LPs, what we talked about earlier, mast cells degranulate and when they degranulate, they release heparin, which causes blood thinning, those nosebleeds I talked about before, but they also released about a hundred other really nasty compounds that wreak havoc, because they're, oh my God, there's a bad bacteria right here. Let me just nuke it.

Kiran:

Yeah.

Dave:

So you ended up getting these really bad things throughout the body. Hives would be an example of that. So if we were to look at the effect of gut bacteria and histamine, you guys remember that chapter in the Bulletproof Diet, it was there. So what have you seen from spore forming bacteria? The ones that the just thrive ones that I do take...

Kiran:

Uh-hmmmm.

Dave:

...full disclosure, whatever there, what have you seen around histamine prevention? Cause some bacteria make histamine, some eat histamine.

Kiran:

Uh-hmmm.

Dave:

What's the story with spore bacteria in histamine?

Kiran:

So spores are interesting. They've been shown to be able to metabolize histamine, which has an interesting effect that they have. Within the gut now in our clinical trials, we haven't looked at the histamine response yet. But when you look at the mechanism surrounding histamine response, right? So when you look at activation of things like granular sites and so on, what we tend to see is an inflammatory pathology that is reduced as it would relate to reducing kind of histamine tarring type of inflammatory signaling from the gut microbiome. So even though we haven't studied histamine specifically, my guess would be that we would have a measurable impact on people with elevated and intolerance levels to histamine self.

Dave:

Okay. So convincing evidence, but we don't know that it's going to calm mass cells. But...

Kiran:

Right.

Dave:

What I know about mast cells is about every six to nine months, they get rebuilt or...

Kiran:

Uh-hmmm.

Dave:

...refreshed or renewed. They die and get replaced like most cells in the body.

Kiran:

Yep.

Dave:

So if you can go six to nine months with less activation, the new ones who come up are likely to be less pissed off. And over time you can reduce your sensitivity.

Kiran:

Yep.

Dave:

So perhaps fixing your gut and then going over the course of a couple of years, it can take a while to heal some of these things. You can probably get less activation. And that's certainly something that I'd be looking at if I had long throw of it...

Kiran:

Uh-hmmmm.

Dave:

...or something like that.

Kiran:

Right. Absolutely. Yeah. And now we also know there is some evidence showing that when you have low diversity in your microbiome and you've got microbiome and thereby you have low levels of things like secretory IGA, and so on you will actually get more mast cell recruitment to the lining of the gut than you would if you had high diversity. Right? So, that's one of the defense mechanisms that the body puts in place. It goes, hey, we have low levels of secretory IGA. It's hard for us to defend this very crowded gate, if you will call the intestinal lining. So we're going to recruit other immune cells to the area to help protect. And you start getting lots of mast cell recruitment to the gut lining. Once you get mast whole recruitment to the gut lining, they're going to rear their ugly head. They're going to do their job,

whether they come in contact with things, right? So that's another role in which like the microbiome can drive things like allergies and hypersensitivity responses and all that just by bringing these mast cells to that area.

Dave:

I think one of the reasons my gut lining would degranulate or would shed was because of mast cell degranulation. When I would get exposed to mold triggers, broad spectrum, histamine, activation...

Kiran:

Uh-hmmmm.

Dave:

...and vessels throughout. And so the gut lining is studied with us, cause my IL-6 levels were too high and you could see why my life kind of sucked back then and all the brain fog that comes from it. And you can see why a lot of the stuff that I arrived at in the Bulletproof Diet has stood the test of time.

Kiran:

Right.

Dave:

Right? The higher quantities of vegetables, fixing the gut college and all this stuff as a bio hacker. I can't tell you which one did it because it wasn't just one,

Kiran:

Uh-hmmmm.

Dave:

It goes back to that black box, the systems' biology thing like that. And I really appreciate the work that you're doing because you're actually opening up the edges of the black box. So you're peeking in there and you're going to be able to tell me, take more of this one less of that one, pushing this button is way more likely to work than the one that I stumbled onto when I was desperate and spent stupid amounts of money, fixing it.

Kiran:

Totally.

Dave:

Right.

Kiran:

Totally.

Dave:

And I think you're doing great work with just thrive. I, like I said, I do use both the precision prebiotic. It's different than the prebiotics that I've put together. It's fact there's no ingredient overlap at all. I don't think at least no active ingredient overlap.

Kiran:

No. And yours are fibers, which are great. So the combination, again, that's a...

Dave:

Yeah.

Kiran:

...doing a couple of different a few different things together. The combo would be quite powerful.

Dave:

Yeah. And in cold water, yours tastes way better and it makes us better too. So it's like, it's the fruity flavor thing you put with ice. And it's funny.

Kiran:

Right.

Dave:

And then I do every morning I take the just thrive probiotics and I take them with my Bulletproof Coffee. Right. And I do that because they don't care.

Kiran:

Right.

Dave:

They're the one probiotics, like I don't care. And there's usually prebiotics in there anyway.

Kiran:

Uh-hmmm.

Dave:

But warm or hot coffee and fat, especially MCT oil is likely to harm most probiotics. You have to take them ahead of time and let them get into the gut. I don't worry about it with the just thrive. So...

Kiran:

Right.

Dave:

...that's my practice in the morning. I think it's a good idea. So that said, thank you for doing this work. I would love to have you back on some time. We'll talk about maybe brains in particular.

Kiran:

Cool. Yeah!

Dave:

There's some stuff around dendritic sprouting.

Kiran:

Yeah!

Dave:

Which is one of my fetishes actually dendritic sprouting is microbiology.

Kiran:

Keep on signing stuff.

Dave:

All right. It's always a pleasure to get a chance to throw out with, to chat with you.

Kiran:

Yeah.

Dave:

And I would just say guys, if you're looking at this going, my brain just exploded. I don't know what to do. Remember that part about do stuff that makes you feel better. There's no perfection possible here because we don't know what perfect is. Okay. You could play with this for the rest of your life and always get a little bit better. And maybe that just is fun. I kind of think that stuff is fun. I'm going to be playing with this for the rest of my life.

Cause what else are you going to do? But you don't have to be a highly functional human being if you're desperate, like I was. And you're like, I'm tired of being fat. I'm tired of being tired. I want my energy back. That is a much lower bar than being perfect way lower. So don't stress. You don't need more cortisol in IL-6, right? You just don't try this stuff. See what works, cut out these stuff. The sandpaper against your treadmill might be a first step, right? Yeah. Some probiotics would be a good idea that just thrive stuff with those species is very well studied by this man. So I find that highly credible, right? And then you can look at their immune support. There's an IgG product which I have used. And then there's a thing for mucosal barrier strengths...

Kiran:

Uh-hmmm.

Dave:

...called just thrive, gut fortify.

Kiran:

Yep.

Dave:

And then of course we talked about the precision prebiotic. For me, I always do the probiotics. I usually do the prebiotic and I have bottles of gut fortify and ultimate IgG. And I take those some days, not other days, I don't take almost any supplement every day, except for the basics like magnesium and ADK. But all of these are in my rotation and some of them more frequent than others. So if you're on a budget, like I think I'd start with the probiotics. Is that what you would recommend...

Kiran:

A hundred percent.

Dave:

...as well as that kind of less important?

Kiran:

Yeah. A hundred percent start with the probiotic that's foundational. Right. That's important. And then everything else will just be really positive hat on to it, but do the probiotic is that's the key.

Dave:

Okay.

Kiran:

Yep.

Dave:

So Kiran, thank you for that.

Kiran:

Yep.

Dave:

And I always good. There is a deal. I never, I know. I always asked for one, but just thrive health.com. Use code Asprey. You guys are given listeners 15% off and guys here's the deal. I want you to be healthier. I want you to actually get paid money to be healthier right now. I don't know how to do that. So I would like you to get healthier for free and I can help you do that. Like get better sleep intermittent, fasting cost less than breakfast, but there are some things like getting probiotics. It actually does take money, but at least you save 15%. So it's my job to find the stuff that's most likely to work. So you don't meander a path of years and hundreds of thousand dollars. The way I did, I think this way passes the sniff test and the usage test after years of me using it. So there you go. Just thrive. health.com. Use code Asprey.

Any final words for our listeners? Oh, I forgot to ask for questions. Shoot. Do you guys need questions? I don't see any major questions here. Oh, Patricia has her hand up. I think we have to, we have to take at least one question from...

Kiran:

All right. Let's do it. Let's watch...

Dave:

...the character. I've been trying to ask them

Kiran:

...over there. So we have to ask.

Dave:

All right. Patricia, your hand is up. What do you have to say?

Patricia:

So the historical information that we got was we were supposed to have 10 to 14 different strains of bacteria, ideally 20 to 30 see a fews. You want it to have enteric coating so that it didn't break down in the stomach, but in the small intestine. And then the more research came out about to create diversity about the probiotics, et cetera, that four or five strains of bacillus from bacteria. So is that just an evolution? And then obviously those strains are much more Hardy, so they don't break down in the stomach. So we not ever take a probiotic with all the other different strains in it that aren't present in a a spore biotic.

Kiran:

Yeah, no, I'm happy to answer the question and I think Dave put some of these ideas in a very elegant manner, meaning if it makes you feel good and it makes you feel better, then you could certainly take it, right. There's no really hard and fast rules here. Like I would never come on and say, never take this kind of probiotic because we don't know everything. Right. So, but we do know that the spore based probiotics do some very particular functions within the gut that are really foundationally important for a healthy gut and things like, resolving the leakiness in the gut, improving the butyrate production, modulating some of the microbes in the microbiome to improve diversity and so on. Those are critical functions that these spore based probiotics do that are really important for overall health.

Now I cannot say that your other 15 strain probiotic does nothing for you. Right? I don't know that. I don't know what's happening in your gut and I don't know what product you're taking. So if it helps you, you feel like it does help you then by all means, continue to take it. But yes, we have evolved pass a lot of those kind of initial ideas of what makes a good probiotic, a good probiotic. And we touched on that earlier, how the technology to understand the microbiome has evolved leaps and bounds in the last, just you've been four or five years, let alone 10 years ago.

So our ability to understand the impact probiotics have in the gut have dramatically changed in the last few years than it was 10 years ago. So certainly some of those ideas are definitely old ideas. The whole like 17 strains, 15 strains, 50 billion CFU, a hundred billion CFU. Those are just kind of arbitrary numbers that were set up as guesses. And now we can test those theories and those ideas much better. And we come to know that, those are really kind of arbitrary, arbitrary parameters that were set up. So absolutely take care, take the spores. You can rotate them with the other thing, the other probiotic, if that's making you, if that feels good. I don't see a big issue with that.

Patricia:

Would you, do you recommend taking them with food or without?

Kiran:

The spores you always take with food. Yeah.

Dave:

And, but Patricia, I have spent probably $200,000 on probiotics over the course of my life, trying to fix my gut. And I have been largely disappointed because, oh, here's the study. This one's going to work, but they don't grow unless you have the right stuff there. And like you said earlier, you take them at the wrong time. Oh, I took them with food. My stomach acid came out, they'd killed my $5 a pill probiotic from whatever research lab.

Kiran:

Uh-hmmm.

Dave:

So I would say the prebiotic side of the conversation plus armor plated probiotics, it is a really good idea.

Kiran:

Uh-hmmm.

Dave:

And the prebiotics from even with a handful of probiotics that I take on occasion until I started really upping my prebiotics, I just didn't have the number of species or the mix of species that I wanted. And so that was part of the journey that I took in superhuman was documenting that in showing the difference in...

Kiran:

Uh-hmmm.

Dave:

...diversity there, the diversity didn't come from eating more types of foods than diversity came from eating more of the stuff that good bacteria grow on. So I think play around with it in this such profound advice. Like if it works, you may find one that eats histamine or one that makes glutathione and go, wow, this is so cool. I know I took it for a month and it changed everything. Right? And you and I might not even know what those are?

Kiran:

Uh-hmmm.

Dave:

So it's okay to play around. But if you're not feeding them with the substrate, my experience has been, I wasted a lot of money until I understood that I needed to feed them the right way. Does that match what you've seen as a microbiologist?

Kiran:

A 100%? Yeah. Because again, a lot of the functionality of these bacteria are dependent on their source of fuel to be able to metabolize things and produce things and so on. So if they're not getting their fibers and their prebiotics in there to do their metabolic magic that they do, then they're not really functional in the system. Right. So they're, they're starving themselves. So yeah, absolutely. I think that's a really critical point with the prebiotics and the fiber.

Dave:

Awesome. Well guys, thank you for, or, well, Patricia, thank you for the questions and upgrade collective. Thank you for being on this is one of those information packed. Awesome interviews. And thank you for the extra time as well Kiran.

Kiran:

Of course!

Dave:

It's always fun to talk to a really smart guy who has done the clinical studies and to have you poke holes, not in my gut lining, but in my line of thinking. So it can be more teachable for everyone. Thanks again.

Kiran:

Thank you Dave.

Dave:

Guys just thrive health.com, use code Asprey. Give this stuff a try. See if it works. If it doesn't don't do it anywhere. There you go.

Kiran:

Thank you.