A BACTERIA THAT GUARDS YOUR GUT LINING – COLLEEN CUTCLIFFE, PH.D. – #881

Dave Asprey:

You're listening to the Human Upgrade with Dave Asprey, formerly known as Bulletproof Radio. The show, not me. I was just formerly known as that heavy kid over there who's acting like a jerk because his brain doesn't work. But I fixed all that, and, well, that's probably why you're listening. Today we're going to talk about, well, one of the reasons that I probably was heavy, and that is gut bacteria.

You might have heard me talk about gut bacteria quite a lot on the show, because we have tens of thousands of species of this stuff that we're just figuring out what they do, and worst, We're just figuring out that they all talk to each other. So, you can say, this one does this and this one does this, but when you put them together, one plus one does not equal two. It equals either 1.5 or 2.5. In other words, systems biology in the gut is disrupting the big pharma model that we had that said one thing can only do one thing, which is pretty much BS. That's just not how it works. There is usually not a single cause. It's usually a systemic cause.

And today, we're going to talk about that with Colleen Cutcliffe, who is CEO and founder of Pendulum Therapeutics, and she's exploring some of the latest around kind of a famous gut bacteria. Just like recording artists, some of them are just like Sting, like, well, lactobacillus. Everyone's heard of lactobacillus. It's like the famous one. But then, there's all these other little things that'd be like Rage Against the Machine, before they sold out, I mean, and maybe like Eric Clapton, where everyone just loves him no matter what, no matter how much the Washington Post tries to cancel him. Those people just love Eric Clapton. So, there are gut bacteria like that.

And what we're looking at now is a new kind that you can combine that helps you to control your blood sugar. We talked about that in episode 767, Colleen and I did, because that's a specific gut bacteria that has an influence on blood sugar for type 2 diabetes. And since then, Colleen's done a lot of work on Akkermansia, something that you might have heard about, but only if you follow some of the more carnivore and some of the more paleo sites, but it turns out, this is a new up and coming rock star have got bacteria. Colleen, welcome to the show.

Colleen Cutcliffe, Ph.D.:

Thank you so much for having me, Dave.

Dave:

What does it feel like to be a manager for all these Rockstar gut bacteria?

Colleen:

Well, they are divas. You have to really coddle them, make sure you understand all their individual needs, and make sure that you are helping to cultivate them and grow them so they can become the Eric Clapton's and the things that we can't live without in our lives.

Dave:

You sound a lot like Shep Gordon, who was on a while back, who actually did manage like, all of the big names, like Janice Joplin, all the people you've ever heard of in some ways. But one of the things that I do want to just disclose, I take Pendulum every morning, because I know that controlling blood sugar is... I don't have type 2 diabetes, but I know that it's a fundamental part of my anti-aging strategy, but I feel like there's almost no upper limit to the number of probiotics that you conceivably could take, but

I'm looking to figure out which ones matter most and how to encourage their growth. And I think you've done phenomenal work on that stuff. What got you from your glucose control formula into looking at Akkermansia?

Colleen:

Well, first starting with glucose control, I think that's a really important thing to focus in on, all the health benefits. And actually, there's been some recent evidence coming out that going after these neurodegenerative diseases, things like Alzheimer's, that we've always thought about, how do you target the brain, might really have a strong relationship to glucose control. And in fact, some of the really big pharma companies are starting to invest in clinical trials, where they're using diabetes drugs to try to treat Alzheimer's disease.

And so, I think, when you think about the gut bacteria and its role in glucose control, it's just a big opportunity to bring back these bugs that we've always had and lost along the way, in order to help us metabolize sugars. And one of those important bugs is Akkermansia, and this strain has been studied for quite some time in the academic realm. Well, I say quite some time. Really, the last decade or so.

And what we're finding is that when you think about your gut lining, it's sort of like a fence. And so, when I first bought my house, I have this wooden fence in the backyard. It was beautiful, shiny. All the planks were really solid, kept all the bad stuff out and the good stuff in. And what happens over time is that, with weather and snow and rain, those planks can start to wear out and become thinner, and then sometimes fall down, and if you're not repairing those planks, you're going to end up with a really vulnerable system.

And so, your gut lining is just like that. It's like a fence. And so, what Akkermansia does for a living is, it's the guy that comes in and checks your fence, and makes sure that all of your planks are sturdy, and repaints things when it's needed, and puts new planks in when needed. And so, what we have discovered, we as sort of the entire scientific community, is that when you are low in Akkermansia, or some people have undetectable levels, it's missing, you have all kinds of problems.

And it starts, for us, it started with understanding its role in glucose control, but it goes a lot farther than that, Dave. It goes into inflammation, immune response, GI distress, and probably also is a big part of the gut-brain connection. And so, it's a really, really fundamental, keystone strain in our microbiome.

Dave:

So, what this stuff does is, it eats the mucus, that lines, the gut, right? And that's important. And I wanted to point out too, there are questions we're going to get into about fasting, about maybe if you have no mucus, what's it going to do long term fasting? The other thing though, this was only discovered in 2004. This is the year that smartphones came out. I had some weird HTC thing with a round thing on it. I've always been the guy who buys the latest smartphone. So, we didn't have them before that. This is a very, very new discovery in the history of biology. So, before that, every single recommendation ever made in medicine was ignoring the fact that there are bacteria that affect the lining of your gut, that keeps food and bacterial toxins out of your blood. So, all of the sudden, we have this new tool, and we've had it for less than 20 years, and we've learned a few things. What percentage of the things we need to know about Akkermansia do we know today?

Colleen:

Well, I would start by saying we've always had Akkermansia, we just didn't know about it.

Dave:

Of course.

Colleen:

It's only recently that we discovered its existence.

Dave:

It's always been there.

Colleen:

Yes.

Dave:

Just, but every recommendation we've ever made was, oh, yeah, that'll work, without knowing that it was in the system doing stuff that really mattered.

Colleen:

Exactly, exactly. Oh man, what do we know? We know almost nothing. As with any new emerging science or health field, we like to think we know a lot of stuff. And we're learning a ton, so we know a lot more than we did before, but I think there's still a world of things to learn, including in what circumstances is Akkermansia reducing your mucin layer, and in what circumstances is it increasing your mucin layer? Because it really is emerging as a regulator of that. And so, how does it interact with other strains? How does it sense or know what your mucin layer looks like? How does it know when you're changing your diet, just in a different environment, and how does it respond to that? And then, probably most importantly, how does it get depleted, and why does it get depleted?

Dave:

Are you more likely to have leaky gut if you don't have Akkermansia?

Colleen:

The idea of leaky gut is really, this is really centered around the gut lining, and an insufficient gut lining. And so, it's very much tied to the exact role of Akkermansia. And it has been shown that people who have IBS, GI issues, leaky gut, they are lower in Akkermansia levels. And you know, there's a variety of different microbiome testing labs out there right now, and what you'll find is that these microbiome testing groups are starting to call out Akkermansia as one of the keystone strains. And so, if you're low in Akkermansia, you can find that out by taking a microbiome test and then understand what your levels are.

Dave:

How easy is it to turn Akkermansia into a probiotic? I know there are some species that just die. Like you, you really can't take them. Where on the scale of, we should all be smearing this everywhere is this one?

Colleen:

Akkermansia is a diva. Akkermansia is very hard to grow, very hard to cultivate, and it starts from the fact that it is located in an anaerobic environment. So, where it's situated, there is no oxygen. So, first, you have to figure out, how do I manufacture something in an entirely closed system where not a single molecule of oxygen can get in? So, that's the first thing.

But the second thing to know about Akkermansia is, not only is it sitting in an anaerobic environment, it's actually housed right up against your gut lining. So, it lives on this muse and layer, and that means that it's not just living in a culture, like when you think about brewing beer. It's not living in a culture media like that. It's actually attached to something. And so, here in the US, you actually cannot grow a strain and sell a probiotic strain that has been grown in anything that has a meat-based product in it.

But your mucin layer is effectively a meat based product. So, how do you take this thing that grows in an anaerobic environment, attached to a meat byproduct, and try to grow it in a vegetable-based environment out here in the world, outside of our guts, where there's oxygen present? And that's made it really challenging to understand and how to grow Akkermansia. But once we figured out some of those key things on how to grow it, we've really been able to scale it up and include it in a variety of different settings, where we can now test what happens when you give Akkermansia back.

Dave:

So, it's pretty much the Rockstar that has to have the bowl full of green M&Ms. You know, it's the highest maintenance of them all.

Colleen:

The bowl full of green M&Ms, as well as the Doritos that are only when they're fully formed. No chips of Doritos, the whole Dorito, and the bubbly water, which was just infused with bubbles five seconds ago.

Dave:

I love it. So, it's very high maintenance, but you've managed to put it into capsules that are not oxygen-proof, clearly. So, how does that even happen? I'm kind of interested because before this, there wasn't a way to take this. Everyone talks about it and there's sort of saying, well, me, maybe it grows, or maybe you need a fecal transplant or something. This seems like a better way than a fecal transplant. That's not been high on my list of biohacks to try.

Colleen:

I think one of the beauties of being an inventor is you can think about what is the invention I would like to use, and I would not like to use a fecal microbiome transplant. So, we were definitely keen to figure out how do we get this thing into a pill format.

So, I think the biggest challenge is, you have to grow these things in the ways that I described, where it's anaerobic and you're compensating for the lack of a mucin layer in your manufacturing plant. But what we found is that after you grow these... So, it is like brewing beer. After you brew this thing, you can freeze dry it. So, if you have raisins and things like that, those are freeze dried fruits. So, we freeze dry it, and that gets it into a powder form.

Once it's freeze dried, it's actually in a much more dormant state, so now, it is not susceptible to oxygen, and now you can keep it. Actually, Akkermansia can be kept at room temperature. And so, you can now have it in a pill format that you can take with you, ingest it, and then when it gets into your GI tract, the capsule opens. So, these are enteric coated capsules that get through the stomach acid. And

so, when it gets to the GI, they'll dissolve, and now your Akkermansia can reconstitute and come to life in the environment in which it was intended to live. And so, the name of the game is the freeze drying process, and then using these special capsules in order to get them to where they need to reside in the GI tract.

Dave:

Okay. So, I'm imagining the lining of the gut. It's got its normal layers tissue, and then there's that layer of mucus or mucin. And what happens if it's too much? Because one of the things that they look for in fecal samples is mucus in the stools. So, how do you know you have the right amount? How do you know you don't have too much Akkermansia, that it's not causing problems?

Colleen:

Well, I think this is part of the unknown about Akkermansia's role. It is a regulator, which means that it has a sense of how much mucin is actually there. And so, what we're still trying to uncover are, what are the signaling pathways that let Akkermansia know, is it time to munch or not? So, you can have Akkermansia sitting there that's kind of inactive, and then you can and have a situation where it becomes activated, and now it's actually reducing the mucin layer. And that's really the science that we're trying to uncover.

Right now, it doesn't appear that having an excess of Akkermansia, or high levels of Akkermansia, is anything but healthy. So, when you look at healthy individuals, they have very, very high levels of Akkermansia, and when you look at people who are sick, and when I say sick, it's a variety of different things from metabolic syndrome to, if you want to consider aging an illness, to people with GI issues, they are lower in Akkermansia.

So, the short answer is we don't, but I would say, this is the thing about the microbiome that's very distinct from small molecule drugs. We naturally evolved with all these strains. So, we have natural ways to keep these things in check. And that's different from a small molecule drug, where you take this thing, it's totally formed to your body. Your body does not know how to metabolize it. And so, your microbiome being an ecosystem, we are a little bit relying on mother nature here and saying, there's a method to this ecosystem that keeps things from getting too out of control. And the only way things really get out of control, Dave, is when we do something like take an antibiotic. Otherwise, this is an ecosystem that thrives on its own.

Dave:

One of the things that you can take on the market today is called Mucinex, or Guaifenesin, which is a common over the counter pharmaceutical that makes mucus more liquid. And I know about this because it used to be a prescription drug, and it was the only thing that worked for me when I had serious toxic mold as a kid. So, I would get huge amounts of mucus in my sinuses, and probably also in my gut, just chronic inflammatory, things like that. And so, does taking something that is a mucus thinning agent, like an expectant, does that ruin your Akkermansia levels?

Colleen:

Well, the short answer is, I don't know. I haven't really looked at these studies in depth, but I would say this. It's one thing to take and have it get to the mucin layers in your head. It's an entirely another thing to try to get it to your GI tract. So, again, we go to great lengths to make sure that these strains get through the stomach acid and get released in the place where these strains are going to be activated. And so, I actually don't know the answer to the delivery question there, but since we've had to work so

hard to be deliberate about the delivery, I have to imagine that it's not accidentally going to get to your GI tract. But I don't know. I actually haven't looked at that data.

Dave:

Got it. I'm just thinking that if the mucus is thinner or thicker, it may have a substantial effect on how it grows, or it may be the thing that controls it. Or maybe the reason I had so much mucus was I had no Akkermansia, because I was taking antibiotics every month. And these are those things that just were not considered, even 20 years ago. We just didn't have much of an understanding of it. A few doctors were talking about it, but we didn't have the data, because we didn't have the technology to see it. How did you know to zoom in on Akkermansia, versus all of the other species that are out there?

Colleen:

Well, as we started all of our studies, it's really centered around mapping people's gut microbiomes. So, using DNA sequencing, metabolite screening, looking at all of the strains, as well as the small molecules that are being made in the microbiome. And we've always approached the microbiome, like a systems biology problem. And so, that's why we have people like Eric Schadt from Mount Sinai on our board.

It's really about how do you make a map of a perfect person's microbiome, and then understand, if I compare a healthy person to a person with a disease state, what is the difference in these maps, and if I push over here, what happens? So, it's almost like a trampoline, where if I jump on this part of the trampoline, how far away does the other guy have to be before they feel it?

And so, we're trying to understand how all this stuff is connected, and what we found was that people who are healthy have a ton of Akkermansia, and there are a variety of different disease states where people were low or entirely missing it. And so, at the same time, a bunch of academics were also publishing this same observation. So, when you see something like that, you just have to try to dig into it and understand, well, what is this thing doing, why are people missing it, and is it related to the disease?

Dave:

That makes sense. It's been frustrating for me, because I have spent, oh, at least $100,000 over the last couple decades on probiotics of all sorts of different flavors. And I didn't have a lot of results in the early days, and I've had much better results lately, and it's probably because I focus on making sure I take a prebiotic as well. And some of the things that you're doing, A, you have a species I couldn't have tried when I was really working on my gut, because we didn't know about it, and then it wasn't available commercially until very, very recently, you just came out with it. So, that would've been off the table, but even so, no one was really taking prebiotics. So, you guys use inulin or chicory root as a prebiotic for it. Can you talk about why that one, versus all the many other prebiotics, and just kind of define what the prebiotic is for people who don't know the difference between prebiotic, postbiotic, and probiotic?

Colleen:

Oh, boy. Yes. Let's define terms, and new terms are constantly being made up. So, the probiotic is the actual bacterial strain. The prebiotic is the food for the probiotic. So, that's the inulin, the fibers and things like that, that the strains eat. And the postbiotic is what the bacteria produce. So, in the case of Pendulum glucose control, the prebiotic is inulin, the probiotics are all the strains that are in the capsule, and the postbiotic is the butyrate that gets produced by those strains.

And so, the important thing to note is that we have actually tried to increase prebiotics through good nutrition. And so, prebiotics, you can actually get from your foods much more easily than you can get probiotics. And I think about the pairing of prebiotics and probiotics, or the pairing of nutrition with

food, nutrition with your microbiome, as fuel and an engine. So, if you're putting great fuel into your car, but you've got a crappy engine, you're really not going to have this humming car. What you need is both the great fuel, the great nutrition and prebiotics, and the great engine, the great microbiome with all of the bacteria that are helping you along the way.

And so, when you pair a prebiotic with a probiotic, you're actually bringing these two things together in order to have your car, or your body, really optimally performing. And the reason we chose inulin is because that is the prebiotic that best feeds the strains that are in our formulation, but there are a variety of other prebiotics that also help feed other beneficial strains.

Dave:

I finally arrived, after years of doing intermittent fasting and keto for longer or shorter periods. Longer periods appears to be bad for gut bacteria. Who would've thought? To where I do intermittent fasting most often with a prebiotic, so even though I'm fasting, my gut bacteria are still pretty happy. So, I think that's where we're going to end up, where you need a source of low toxin food for your gut bacteria, and you need a source of good quality fat and some good quality protein and aminos, and magically you can perform pretty well.

What I want to know though, is what happens when you have Akkermansia, and then you go on a long-term fast, or maybe even just a long-term carnivore diet, where there's no food for it whatsoever. There's no inulin, there only mucin. Is it going to eat all of the lining, all of the mucus that should be there? And then what happens? Do we know that's real? There's a lot of questions about that online right now.

Colleen:

Yeah. I think, well, I'll start by saying the science is early, and so we don't know. There's not a solid answer to that question. It's a great question. And the second thing I would say is, it's probably different from person to person, because it matters what ecosystem that you have in your microbiome. That's what sends messages to the different microbes. That's what triggers certain behaviors or non-behaviors.

And so, it's not about simply having the bacteria there. It's about what activates those bacteria to behave in certain ways. The different bacteria have the capability to operate at a high level, just like us. Operate at a high level, or operate at a Saturday morning kind of a level, for those of us who relax on Saturday mornings. And so, really what we're trying to understand is, when you go into fasting periods, or you change your diet, or you travel, or you're just in a totally different routine, how does that impact the ecosystem, and how does that impact the activity of these specific strains?

And again, I think when we are trying to understand Akkermansia in particular, it probably matters very much how much starting Akkermansia you have, what all is in your ecosystem, and how your body is responding to whatever the environmental change is, such as fasting. So, unfortunately, I don't have a straightforward answer for you, but the fact that you can test your Akkermansia levels, and the fact that you can alter them with prebiotics and taking Akkermansia probiotics directly, now allows you to start to experiment in what am I doing to my body, and what am I feeling as a result of this?

Dave:

There's an interesting kind of picture in my head about this mucus lining in the gut. So, it's easy to think of it kind of a layer of gloppy stuff, but it's actually more, think of it like a fingernail. It grows, and then some of it goes away, and then more of it grows. So, it's constantly excreted. And if you have lots of Akkermansia, Akkermansia makes you grow more of it. So, the mucus turnover is higher, which means any other crap that gets stuck in there, whether it's parasites or yeast or fungus, or whatever else could

stick to boogers, for lack of a scientific term, that stuff is going to get flushed off. That's kind of what mucus is there for, right? Same thing in your sinuses. If you have pollen or something, it gets flushed out by that.

So, it's doing that constantly. Akkermansia improves that, but when Akkermansia takes off the outer layers, it's turning into one of my favorite chemicals, butyrate, and it's one of my favorite chemicals mostly because my seventh grade sense of humor says, ha ha, I said butt. But realistically there... I just woke up. Realistically, butyrate has studies that show when you eat it directly, and it's a post biotic, you mentioned it earlier, it has anti-inflammatory effects in the brain. And when you eat it, it causes you to grow more butyrate-forming bacteria when they sense that it was in there. And of course, the real reason that's my favorite is that it's named after butter. It actually, that's where the name came from. They figured it out in butter.

And then when you make a bunch of it onboard in your gut, you have much less inflammation of the gut and much less inflammation systemically. So, I take a couple grams of it before I go to bed, and I likely have good bacteria that make it, and I take the Pendulum product. So, I probably have enough Akkermansia and probably have enough butyrate, but I feel a lot better than I used to, so, I think it all works. But how do I measure all that? Like, is my mucus turnover good enough?

Colleen:

Well, you can take a gut microbiome test to know what your levels of Akkermansia are, and that is sort of a starting piece of data that you would want to have. There are tests. So, there's a small molecule called zonulin, and that is a molecule that tells you the integrity of your gut lining. And so, this is a clinical diagnostic test you can get your doctor to prescribe for you or recommend for you, and then you would look at your zonulin levels.

So, there are not a lot of tests out there, because as you pointed out, this is all new science. And so, there are not great ways to, to know outside of getting a biopsy and actually looking at your mucin layer. But the two tests, I would say testing your Akkermansia levels, and then testing your zonulin levels, can start to give you some insight into how that's going.

Dave:

Zonulin is one of those things that gets raised when you eat wheat, whether or not you have IBS or celiac or anything else, right?

Colleen:

Well, I think, as with all of these tests, I think it's important to remember that the body is a dynamic system. So, I am never a fan of taking a test one time and saying, oh my gosh, this is the truth about where I am at. And so, you have to correct for that by taking tests over time and really understanding what your baseline is, so that you don't have these one offs. Because the issue with all these tests is that of course, to your point, your body responds to different things that you're doing, and so, you want to make sure that you're taking it over time. And when you do that, you're taking multiple time points of your zonulin levels, you'll start to understand what your baseline is, and whether certain things you're doing are causing it to go lower or higher.

Dave:

Okay, so it's relatively tough to test, but if someone has higher zonulin levels, they're much more likely to have leaky gut, regardless of their Akkermansia levels?

Colleen:

Oh man, you're asking all these hard questions that we don't know the answers to, but these are all the things that people are delving into and trying to understand the relationship between these different biomarkers and what's existing in your gut.

Dave:

I think Dr. Hyman and Dr. Gundry and Dr. Perlmutter and me, and probably Dr. Mercola would all say that that grains raise zonulin. Hope I'm not putting words in any of their mouths. I'm just thinking of people I know who I've interviewed, who are almost certainly on that, that it's a big sign you have leaky gut. If you have higher zonulin levels, you're going to have leaky gut. But maybe you could eat tons of wheat and tons of these other things that are bad for you, I would say, or at least non-optimal for you at their best, and maybe be totally fine if you have this super thick layer of mucus, just studded with Akkermansia. But I would say we don't know that yet. I'd love to be able to eat a bunch of stuff. So far, even though I take Pendulum, I haven't found that I can eat anything I want with no effects.

Colleen:

I can't believe that. We haven't made the magic pill that allows you to eat whatever you want.

Dave:

No. I tried drinking a can of paint and it totally, totally didn't work for me, and I'm like, what?

Colleen:

We're working on it. We're working on the paint metabolizing microbes.

Dave:

Well, the FDA said it was safe, and so did the EPA. It must have been safe, right? I trust those guys. They have my back.

Colleen:

We won't go into that.

Dave:

No, we don't, we don't have to. That's just my job, but we don't have to. I'm kidding. Speaking of that, when you have a gut bacteria that it is so powerful that it can actually make people more sensitive to their blood sugar, like they have to lower their meds, do people have to tell their doctor, or should they tell their doctor if they're taking Pendulum? Like, oh, I started a probiotic that might fix my metabolism. How often do you need to kind of report if you're taking blood pressure... sorry, not blood pressure, but blood sugar medication? Like if people are Metformin, do they need to say, hey, doc, I just went on Pendulum, or are they kind of separate?

Colleen:

They're absolutely related. And in fact, in our clinical trial that was published in BMJ, we showed that the efficacy of Pendulum glucose control was on top of Metformin. So, if you're on Metformin and you take Pendulum glucose control, it lowers your A1C even further. And so, it's important that your physician knows that. That's why your physician asks you in your intake form, hey, what other things are

you taking? Vitamin supplements. And so, it's important to share, what are all the things that you're taking. If you have the right doctor, they might even be able to make sense of what you're doing.

And you know, I just met a customer a couple of days ago who got told that they had an A1C of 10. They went into their doctor, they got this test result back, and she said, "I freaked out." That was her exact phrase. "I freaked out. I had this A1C of 10." And she had been on multiple medications. And after being on Pendulum glucose control, she's been on it for over a year now, she's been able to lower her A1C down to six and gotten off of her meds. She's basically on no medications right now. And she's obviously been working closely with her doctor. She's not a physician. And so, being able to titrate back these different...

And this is not the first. We hear this from many, many of our customers. This is part of the diabetes management plan. And so, if you don't tell your doctor all the things that you're doing to try to manage your blood sugar, you're leaving gaps out, and physiological changes, they don't really understand why. So, I think it's important. I think if you've got the right doctor, they're going to understand the microbiome and the benefit here, and then they're going to work with you to figure out what's the right dosing for you.

Dave:

It's the same thing. If you start intermittent fasting, doing high intensity interval exercise, getting quality sleep, and your blood sugar changes, and you're taking, especially some of the more harsh drugs, more aggressive than Metformin, you might actually have low blood sugar, and then you would want to tell your doctor. And if you have the right doctor, they're going to say, that's great. And if you have the wrong doctor, they're going to say, that can't happen, and therefore it didn't. And they're going to say, you're crazy. So, you can judge your doctor based on whether they believe you when you tell them what's going on with you.

Colleen:

When your doctor... If your doctor ever says you're crazy, I think that's when it's time to start a search for a new doctor.

Dave:

Yeah. You only need two words when the doctor says you're crazy, and those words are, you're fired. Unless it's a psychiatrist, in which case you might want to listen.

Colleen:

Fine. Very good. Yes, yes.

Dave:

Just saying. It depends on what kind of doctor you're going to. But I did say those words when a doctor told me vitamin C would kill me, many years ago. In fact, that was one of the things that launched me on the path of becoming the creator of biohacking. Just like, I have to do this myself. It turns out I didn't, I just didn't know how to find the right doctors. So, how many supplements do you take, Colleen?

Colleen:

Well, Dave, I only take one. It's Pendulum glucose control. No.

Dave:

Seriously?

Colleen:

No, that's not seriously true.

Dave:

Come on. That's like the biggest plug ever. That can be real.

Colleen:

Well, to be honest with you, I do think the goal is actually to be able to, as much as possible, get the different supplements you need through your diet and your nutrition. But of course, that's not always possible. And so, I take a few different things, and most of the things that I take are actually centered around be being a woman and cyclical hormonal behavior. And so, I think that I am very much a believer, and I would say the only reason that I'm such a believer is because my husband is a believer. And so, when your spouse tells you that they are seeing changes from the supplements you're taking it's got to be true.

Dave:

Got it. So, you're taking, what, 10 a day? 10 supplements?

Colleen:

No, it's seven or eight.

Dave:

Seven. Okay. There we go.

Colleen:

Yeah.

Dave:

So, you're getting up there. Now, here's the big question. How do you know what those do to your gut bacteria?

Colleen:

Well, one of the advantages of being in a gut microbiome company is being able to get tested. And so, I definitely am constantly. And I'm actually also trying all these different gut microbiome tests that are out there, to understand what data are they giving back to us. And I would say, everything can impact your gut microbiome. The most dramatic things are still, if you do a dietary change, when you travel, and of course, if you take an antibiotic. But there are other changes happening too, and I think understanding what those changes mean, well, we're just really at the beginnings of that.

Dave:

What's your favorite tests for Akkermansia? You're inspiring me to go out there and start pooping on little microscope slides.

Colleen:

Yes. Well, I would say, there are quite a few out there. Two that are particularly good at measuring Akkermansia are, one is from DSL. Now, that's a microbiome test that you can only really get through your doctor. And so, that one is quite accurate. They don't measure every strain, but Akkermansia is one of them, and the method that they use is qPCR, specifically targeting Akkermansia. So, it's quite good.

The other one is a company called Longevity, that was started by Chris Mason at Cornell and Joel Dudley at Mount Sinai. That test was actually recently acquired by Thorn. And so, it's the Thorn gut health test, and that one uses DNA sequencing to measure, and it does a good job of measuring Akkermansia. We've actually worked with both of these companies to verify that they can measure Akkermansia levels accurately, and those are the two that I would say, they're sort of the top of our list right now.

Dave:

Okay. That makes sense. And that's what you're using for patients. Well, you don't have patients because you're a PhD, but that's what the doctors you work with are using for patients, what you're seeing that your customers are using, and what you're using for research. Got it. We talked about Akkermansia eating mucus. We talked about it liking inulin available. If it has inulin, is it also going to be doing the mucus thing, or is it just going to eat the inulin?

Colleen:

Well, the amount of inulin that we have in the capsule is really not enough to sustain. It's really just there to jumpstart its activity as it's starting to get into the GI tract. But no, I mean, if you're eating a high inulin or high fiber diet, that's not going to reduce the activity of your Akkermansia. If anything, it's going to help more Akkermansia grow, so that you have higher levels.

And one other thing I will say about Akkermansia is that this mucin layer... And you said this, which is it's really about regulating that layer and constantly turning it over and flushing the system out. One of the other important things that people don't think very much about is all the receptors that are sitting in that mucin layer. And these receptors are basically the signal from the inside world of the gut microbiome to your bloodstream.

And so, there are very important, for example, G protein-coupled receptors that sit in this mucin layer that when you produce butyrate, butyrate binds to those, and it sends a signaling pathway out into your bloodstream. Or when you think about inflammatory responses, it sends a signal to your body to increase immune or inflammatory responses, which you can see through these markers.

And so, if the receptors are not localized in the right places, you're actually losing your signaling. And so, I think what we're going to find is that it's not just about the regulation of this mucin layer, but it's actually about these receptors and their localization and their concentrations, because those are the signaling things. Those are the things that are telling your body how to respond, and that's going to be actually a really important key here.

Dave:

Okay. I totally, totally believe you there. And I'm kind of leading into this. Okay, we want to encourage it to grow. You've kind of put in this super growth fuel, which is the inulin, so it's going to be present and

move into the mucus. We also, though, have a bunch of other polyphenols that feed it, and I want to test a theory with you.

Throughout human history, the first trading routes we had were for salt, and then after salt... And there's a whole interesting conversation we might be able to have about salt in the microbiome, but we won't go there. Because the next thing that we used on those trading routes was herbs and spices. And when you look at the amount of polyphenols compared to the amount of toxins in most herbs and some spices, you end up going, wow, these are like the densest vegetables on the planet. because you could have a piece of kale, which has a large anti-nutrient effect and a relatively small amount of polyphenols, whereas you could have a little shred of oregano that totally kicked its ass all up and down the street, and tasted better too.

So, I'm looking at what feeds Akkermansia, and we've got black currents, peppermint, chocolate, cloves, plums, apples, things like that.

Colleen:

Don't forget red wine.

Dave:

Oh, red wine, right. Okay. Does red wine... I mean, alcohol is bad for your gut bacteria, and it's bad for your sleep. Does red wine actually pencil out with Akkermansia, or is it just the polyphenols in red wine?

Colleen:

Source of polyphenols.

Dave:

Okay. But so I mean, if I took a shot of vodka and a capsule polyphenols, am I going to be better off?

Colleen:

You've been doing such good things for your body and your mental state.

Dave:

From a shot of vodka? It's like, what? But I'm just like, because some probiotics, or some microbiome components, they hate alcohol. So, everyone who's had a bender knows you wake up the next morning, and your gut's not that happy, right? Because alcohol is a bacterial toxin. That's why we clean our skin with it, right? So, how bad is alcohol for Akkermansia?

Colleen:

I do not think the direct study has been done to look at the effects of alcohol and Akkermansia. And I can tell you, as a bourbon lover myself, I will not be running that study. So, somebody else is going to have to run that.

Dave:

I love it. So, you're like, I'm just doing the bourbon. And the bourbon has some polyphenols in it. That's why it's got the colors. So, you're okay.

Colleen:

That's right. That's right. It's the most natural way.

Dave:

I love it. I actually like pizza too, because it's a vegetable, because it has tomatoes on it. I totally see your logic, yeah.

Colleen:

That's right, it is, if you've got vegetables on it.

Dave:

All right. What's next in the world of probiotics? You're at the very cutting edge with Akkermansia. It's neat to me that there are probiotics that you could not get, and actually new postbiotics on the market, that just were never available. We didn't understand the chemistry. So, you've got the glucose control, which is very well clinically studied. Enough that I'm like, okay, this part of my permanent stack, right? You've got the Akkermansia-specific formula that just came out. Actually, do I need to take them both? Because you have some Akkermansia glucose control. I should ask you that.

Colleen:

We have people who are taking both. I think my co-founder might be one of these people, and it's really about, it's about adding more Akkermansia. So essentially, if you took both products, you would be effectively doubling your dose of Akkermansia every day. And so, I think if you... Again, I'll come back to the test, just because it's important to be data driven. You get a test back that says you're really low in Akkermansia, and you want to double down and really increase how much you've got in there, you can take both. But it's the same dose that's actually in Pendulum glucose control, so if you're taking that, you are getting a good dose of Akkermansia daily.

Dave:

Okay, got it. So, people who have specific blood group concerns, which really, as an anti-aging guy, you always kind have some of them, but my blood sugar is very well controlled. It goes up after I eat carbs, and it goes right back down the way it's supposed to, right? And my fasting is somewhere around 87, which makes me happy.

Colleen:

Yeah.

Dave:

That's funny. Life Extension Foundation said that you should do that, starting in the '90s, they've been recommending it. That's one we've known for a while, but didn't have the ability to control it this way. So now, I'm going to continue doing my Pendulum. If I wanted to double down, I could, I probably would do the Akkermansia. And I'll experiment with that just over the next few months to see what happens, and if I get magic unicorn poop, then I'll know it's working. It is... Actually, how do I know? If my Akkermansia goes way up, I know I've got healthy Akkermansia. What am I going to feel?

Colleen:

I think there's a few things that you could feel. First of all, you might feel... If you've... Some people... I'm trying to think about how to... Some people, when they're in a heightened inflammatory state, they know it, they feel it. And it kind of comes in the form of things like grogginess, or sometimes bloating and things like that. And so, if you are somebody who's very hyper aware of your internal systems, you'll notice for sure, and you're keeping track of all of that. You might notice it in terms of things around metabolism. So, there have been quite a few studies around Akkermansia that we have not done, but other people have done, showing changes in obesity. And so, that's something that people could definitely be on the lookout for, as well. But I think...

Dave:

I love the way you said that, because you're not allowed to make medical claims. Did you guys see how sneaky she was? She did not make a medical claim. I make that really clear. I will tell you though, as someone who does not work for Pendulum, that it's shocking, if you have better blood sugar control, you'll probably lose weight if you need to. Like, oh my God, who would've ever imagined that? And you can get better blood sugar control via a variety of mechanisms, including better gut bacteria. Look. See what I did there? Wasn't that great?

Colleen:

That was beautiful. We're a duo, here. And thank you for recognizing that I've definitely been trained, wrist-slapped, shown an orange jumpsuit. So, I'm aware of what I'm not supposed to be saying.

Dave:

One of my favorite conversations ever, in terms of shockingness, was with a former government enforcer who said, oh, you've left the era of free speech. You're now in the era of controlled speech. And said it without feeling shame. I'm like, what? What is this? If you have a study, you should be able to say what the study said. So, I respect your skillful dancing around things that thou shalt not say, because I'm looking forward to there being a lot more things we aren't allowed to say coming up, here. So, well done telling us the science, which is fantastic.

Colleen:

Thank you. Well, so, I think the things to look forward to, and now I'm going to start to here share with you things that are on the horizon for us. I think...

Dave:

Yeah.

Colleen:

You mentioned polyphenols, and I think pairing Akkermansia with polyphenols, that's an obvious thing to put out there. And then, I think what you'll start to see coming out of us is more on these novel strains. And so, I'll just highlight a couple of these that people, they haven't quite come to light yet. Akkermansia is sort of the first child coming out. I think the, the future debuts include clostridium butyricum.

Dave:

Oh, awesome. I love the good clostridiums. No one knows about those. Yay.

Colleen:

Oh, yeah.

Of course you would.

Dave:

People are all down on the clostridiums. In fact, I'll tell you, when we went to go do preclinical testing, we had people turn us down. They said, oh, you've got a clostridium. No, I'm not testing that. And so, there are all these biases that people have, but not all clostridium are. And so, clostridium butyricum interestingly has been used in Japan for decades. It's kind of this little known secret that's been going on in Japan, and it has, they have shown improvements for irritable bowel syndrome, inflammatory bowel disease. But the concentrations that we are able to bring it out at are much, much higher and so clostridium butyricum, you're going to hear a lot more about that strain.

And then, another strain, which I think you'll hear first, and then you'll start to see it everywhere, like when you get a new car, all of a sudden that car is everywhere on the road, is eubacterium, or anaerobic bacterium hallii. So, anaerobic bacterium hallii is also a novel strain that you can't find on the market anywhere else, and also plays a role in metabolism. And this one is very, very early in research, but it is important for glucose control, and we'll start to learn a lot more about that strain and share that out with the world in the future.

I love it that you have a roadmap there that you can share, and there's probably some stuff that you can't share. I mean, I know that as an entrepreneur with multiple companies, someone's like, well, my product roadmap is confidential. But you're also a scientist, and this isn't, I don't want all the details, but I want listeners to understand, there's a whole bunch of bacteria that are missing from our guts because we've had a very weird view towards life. When we discovered antibiotics, we got this weird thing. Well, if something is good, more must be better, which is kind of the human trap. And it's true for fasting, for keto, for vegan, for exercise, all of this, oh, let's just do more.

So, right now we're coating our soil in antibiotics, and we've coated our bodies and our food in antibiotics, and our gut bacteria is paying the price. So, what we're doing now is understanding one at a time, these ones mattered a lot and most of us don't have them anymore. So, we're learning how to grow them, learning how to put them back. So, this is part of restoring life into the soil in our guts, which is also part of restoring life to the soil on the planet, because there's a, a cycle that happens here.

So, I would encourage you to try Akkermansia from Pendulum, see what it does for you. See if you notice the difference. We talked about brain fog and weight loss and glucose control and things like that. Or maybe you don't. You could also get tested for it. But as importantly, you've got to stop eating meat treated with antibiotics, because the reason you have to buy probiotics is because we put antibiotics on our food. That was wrong, and it is wrong, and we have to stop doing it.

So, let's fix the system that makes this necessary, and let's be grateful that there are companies like Pendulum doing real cutting edge stuff so that you know, oh, these are the good clostridiums, not the bad ones. And there are some really good ones that actually crowd out the bad ones that you could be taking right now if you're in the hospital, but they aren't giving to you unless you're in Japan.

So, there's all kinds of knowledge and goodness and amazing things happening right now, and I think the research you're doing around these novel things that are hard to do, that none of us really have, or don't have very much of, or we don't know about it, I think it's really valuable, and it's some of the most important biohacking happening right now. So, thank you for all the cool research you're doing at Pendulum. I really appreciate it, Colleen.

Colleen:

Thank you. And thank you for making the plug on all the things that we can be doing in our lives to help our gut microbiomes to maintain health. And it's really about diversity and an ecosystem that is thriving. And so, when we think about the microscopic things that we've been talking about here in your gut microbiome, it really expands out, even into society. What we've been doing with antibiotics is the equivalent of saying, in this community, there's a criminal, so I'm going to kill everybody in the community, and that's my solution. And that's what we've been doing. But the truth is that you've got one criminal and you've got 99... 9,999 great people. So, we're trying to figure out, how do we maintain that ecosystem and population of diverse, beneficial microbes, while eliminating that criminal, but being much more sophisticated about it.

Dave:

You know, it's a really good analogy, right? If you just assume everyone is equally suspect, and so therefore, it's just not worth the trouble to sort out the innocent from the guilty. That's not the kind of world that you want to live in, it if you're a bacteria, anyway, because they have a job to do in us. And, and that's fantastic.

I also want to thank you for sharing a discount with the Human Upgrade listeners. You guys, go to PendulumLife.com. Use code DAVEVIP, and they'll give you a big discount. And the idea here is that when people come on the show to share their newest research, but they're actually making stuff that you can use, I always ask to get a discount for you so that, well, this show has always got to be worth your time.

Any final thoughts on how to think about our gut bacteria? Things that come to mind for you that maybe most people have never thought about?

Colleen:

Yeah, well, first of all, I would tell you about that discount. I was told this discount that we're giving you is the biggest one that's out there, so...

Dave:

Oh, wow. Okay.

Colleen:

Yes.

Dave:

There you go. DAVEVIP. PendulumLife.com. All right, that's cool. I don't even know what it is. I just know that I ask my team, I'm like, guys, make sure that if we're going to talk about something new, that our listeners get it. The Upgrade Collective members always get a list of all these discounts. So, that's cool. In fact, they're asking me right now in our live studio audience, going, all right, can we do it, can we do it? So, yeah, guys, there's your code.

Colleen:

There's your code. Yeah. I think that the most important thing for people to know is we are doing things all the time that are changing our gut microbiome, and we don't even know it. And there are things happening to us all the time that are changing our gut microbiome, and we don't even know it. So, when

you change your diet, when you travel, when your circadian rhythm is different, day is night, night is day, we go through these time changes. All of those things, aging, menopause, menstrual cycles, all of these things are constantly changing our microbiome.

And I think the most important thing is awareness and knowing. When I was a kid, there was a commercial: Now you know, and knowing is half the battle. And that really is where we are with the microbiome. And so, being aware, understanding this is an important part of your health, knowing that if your doctor is telling you that they can't explain what's wrong with you, they're giving you all these drugs, there is an alternate entire system in your body, your gut microbiome, that you need to be looking to and forcing your healthcare provider and professionals to be looking at it with you.

Dave:

I'm looking forward to a world where we know what every bacteria does in our guts. We know what it eats. We know what it does in relation to all the other bacteria in our guts. And we can actually custom engineer ones to make whatever substances we want. So, we don't need chemicals anymore. You just take some onboard manufacturing things, and they do what they're needing to do in your body. That's how it was originally built, before we screwed it all up, and I think we can actually exceed our original design specs if we get this right, but it might take more than a couple years. It's a worthy task, and it's one that you've definitely undertaken. So, many, many thanks. I look forward to having you on, what, in about a year and you can tell me about the newest thing that's now possible that wasn't possible before? So, you're always welcome to come back. I always love being able to dig deep in gut bacteria with you.

Colleen:

Thank you so much, and I'm also happy to share all the latest and greatest in what we know and don't know.

Dave:

If you liked today's episode, you know what to do. Make sure that you have rapid mucus turnover on your gut lining. It's what all the cool kids are doing right now. And if you're done with that, you might as well leave a review for the show, and I always appreciate comments. DaveAspery.com/podcast. You can suggest guests. You can tell me what you like, what you don't like, and join our UpgradeCollective.com. if you'd like to be in the live studio audience and be a member of my mentorship group. I'll see you all in the next show.