Introduction and Speaker Background

Hi, everyone. Welcome to the Reversing Type 2 Diabetes Summit. I am your host, Doctor Beverly Yates, ND It's my distinct honor and privilege to interview Dr.

Orville Kolterman. He's a wonderful expert who has been a key part of the team at Pendulum, who's been developing these marvelous therapeutics that are probiotics based.

He's the chief medical officer at Pendulum since its launch. He's also an adjunct professor of medicine at the University of California, San Diego. He has successfully distinguished 40 year medical career, and during his 20 year tenure at Amylin, he served as a chief medical officer there, creating two of the first GLP-1l L drugs SYMLIN and BYETTA.

And we all know that these peptides that are so powerful are really making a difference for people who are just struggling, struggling, struggling with their blood sugar.

Before Amylin, Dr. Kolterman was the program directorof the General Clinical Research Center and medical Director of the Diabetes Center at the University of California Medical Center.

With that we say welcome to you. Dr. Kolterman. Thank you. Thank you for having me. It's really a pleasure to be here. I look forward to the discussion.

All right, great, great. So we're going to be talking about the gut microbiome and using that as a targeted tool for glucose management, and we're looking to control blood sugar.

I think people often don't connect the dots around the health of their gut and its microbiome and how profound it can affect blood sugar and glycemic control.

And we're going to definitely unpack that here in this discussion. Right. Look forward to it. Okay. So we all know that for a long time, for quite a number of years, that the access to the connection between the gut and the brain is well established.

Lots of research, lots of clinical experience and lots of lived experiences of people who've gotten better as a result of that work.

Gut Microbiome and Type 2 Diabetes

So how did you know to explore the gut for answers to metabolic diseaseslike type 2 diabetes? So the story begins with the becoming of busy with general or detailed genome sequencing becoming available or actually becoming cost effectively available.

With that academic investigator. Then lookI began looking at what was in what was in the gut, knowing that there at the outset that there was millions of bacteria in there.

But understanding whether they were the same in every individual and more importantly, whether there were any associations with, you know, disease states.

And so early on, those investigators began to notice that certain diseases were associated with specific, you know, profiles within the microbiome. And as it relates to type two diabetes and the metabolic syndrome, there were there was decreased diversity, which means that there weren't as many members of the community as as you saw in healthy individuals and also in in the particularly importance, there were two classes of bacterial functions that were

so that were sorely underrepresented in in those microbiomes, namely the ability to produce short chain fatty acids and then the other is to maintain know the gut barrier that keeps things within the gut lumen, the various toxins and what have you that, you know, evolve as food is digested and other events happen in the GI tract.

Number of those subset substances are toxins as they get into the bloodstream and they generate inflammatory processes. So it you know, there was a association, but that just represents at at the outset that's guilt by association.

So that doesn't prove causality. And so the next step was and as it relates to metabolic diseases, particularly type two diabetes, we were well positioned to delve into that because there are multiple well established well-characterized role models for the disease.

So these observations were taken into those role models. You know, I guess the most straightforward way to talk about it is that there were, you know, feces were or fecal samples were harvested from patients with type two diabetes and then transplanted into one of these rodent models and observed that even if you did the transplant into a healthy, normal mouse or rat, that that rodent, you know, eventually developed type two diabetes, obese insulin resistance and, you know, hyperglycemia, you know, and it was also in those models, it was demonstrated that if you took if you did a maneuver that restored the normal composition of the gut microbiome, that, you know, the disease went away, you could do that by transplanting fecal samples from unhealthy, lean, you know, human or, you know, the things that we associate, you know, in clinical practice that we tell our patients that they should be doing, or if they can do them, they will be beneficial in terms of managing the disease, namely, you know, increasing the fiber content, you know, of the diet.

So in these role models that was shown that if you put soluble fiber into the diet of the animal, that the microbiome won't be very back, you know, back to normal.

And the other thing was, is that if you did a transplant from a, you know, a healthy rat, you know, into the disease trap, you could also, you know, ameliorate the, you know, the disease.

Okay. Okay. So I've always thought those particular experiments and research has been fascinating to me, and I've heard of it being done for type two diabetes.

I have heard of it being done for obesity. And also when people have really, really nasty GI illnesses like say they have an infection with C difficile, you know, Clostridium difficile bacteria.

I think it was amazing that people came up with the idea of a fecal transplant.

Key Microbiome Dysfunctions

To me, a fecal transplant is not the most obvious therapy, but it has given some profound insights to the power of that gut microbiome for sure. That's that's absolutely the case. And, you know, we we now understand that there are these dysbiosis or abnormalities of the composition of the of the gut microbiome across a whole spectrum of diseases, you know, neurodegenerative diseases.

You know, Nash dappled, you know, the fatty steatosis or fatty liver disease, cardiovascular disease, you know, depression, you know and know know the list is just growing ever, ever growing, you know, even even today.

It is amazing how this this is growing and we're all working the work you're doing there. At the work I'm doing, our other colleagues are doing are all trying to turn this trend around.

Okay. So with that in mind, what are the two main dysfunctions that can occur in the gut microbiome of the peoplewho have type 2 diabetes? So the two two major dysfunctions are the production of short chain fatty acids.

Let me digress for just for just a moment. I mean, when I was in medical school, basically learned that the GI tract was sort of a tube through which to through which food passed and some of it was absorbed, but the fiber content

of the diet was largely absorbed and unaccounted for.

Well, it turns out that that fiber, when it reaches the colon, you know, is the foodstuff for a healthy microbiome. And the microbes, as they digest that fiber, they produce short chain fatty acids, acetate, propionate, and most importantly, you know, butyrate and these short chain fatty acids, you know, nourish the lining of the gut and help maintain that gut barrier that I mentioned, you know, a bit ago.

But they also can pass into the bloodstream and serve as messengers, you know, to the brain, to the heart, to various parts of the water, of the of the body.

And then reiterate also plays an important role in metabolic control by stimulating the secretion of the gut peptide, you know, glucagonlike Peptide-1 or GLP-1, which is a very hot topic in metabolism today, you know, given drugs like, you know, goby and other drugs that are getting really dramatic results.

JLP one secretion is known to be decreased in patients with type two diabetes, and so increasing the production of reiterate can help reverse that deficit.

The other major defect is what can be discussed under the umbrella of a leaky gut syndrome. So it mentioned how the short chain fatty acids or nutrients for the lining of the gut that keeps the the cells of the interstitial lining healthy.

But it also helps maintain the tight junctions between the interstitial cells, which is a major component of the system that blocks toxins from entering the bloodstream.

The second component of that is that on top of the the interstitial lining of the gut, there's a layer of abuse then that also serves as a as a as a barrier.

And in patients with type two diabetes, that mucin layer, you know, thins and in some cases that can almost be, you know, not nonexistent. And, you know, those can combine, you know, the setting of the music layer, the unhealthy lining cells in the loosening of the tight junctions, you know, while various toxins that enter the bloodstream.

And we now understand that those toxins create an inflammatory state almost anywhere that you want to look, you know, in the body.

Beneficial Bacteria and GLP-1

And, you know, in recent years, it's become it's become to be understood or has been demonstrated that there is inflammation in skeletal muscle and in adipose tissue, which is which is particularly important in type two diabetes, because it it may be the major driver of the insulin resistance that, you know, has been known to be associated with type two diabetes for some time.

So you need those functions to be present and robust in order to have have a healthy gut in the to avoid this leaky gut syndrome makes sense. It makes sense.

These things are all a partnership and they work together, that's for sure. And in some of us, that kind of basic health has been completely undermined.

So we can see now why people would have problems with their blood sugar regulation. Okay, so with this in mind, these two main dysfunctions that occur, are there specific bacteria that are decreased or missing in individuals with type two diabetes?

And if so, what made them go missing? So there are two strains of bacteria that are particularly important that are decreased or absent, sometimes absent in patients with type two diabetes.

One is there are multiple strains with they form a cluster of butyrate producing bacteria. We just talked about how

Butyrate is is important. So those strains particularly seem terrorism or Clostridium butyrate.

So being decreased or absence results in decreased butyrate production and then all of the things that reiterate does sort of fall in disrepair, in disrepair.

The other sort of hallmark strain is the strain Akkermansia leaves. And Ofelia, this is a bacteria that actually lives in this museum layer that I had described, and this bacteria was first described in 2004, and it's been fairly intensely studied since that point in time, and it's now known that it plays multiple important functions.

It actually eats it actually lives off of some layer. Now, that seems like a good dichotomy here. So we need a healthy mucin layer, but now we have an important bacteria that is eating the museum layer.

So how can that be? Well, it's becoming pretty clear that the way this works is that that bacteria eats damage. MUCIN It's mucin that is aged. It's it's been if you say, beaten up in the battle and so it clears out that damaged mucin.

And by so doing that actually stimulates the proliferation of goblet cells within the material lining these goblet cells are the cells that make mucin.

So you get an increase in the number of cells and you also get an increase in output of mucin. But you know why those cells? And that's is the way that the missing layer is replenished and maintained.

So after months you play a very important role in regulating that process. Cool. Super cool. Good to know. You know, it's interesting how important it is that the body have places and ways processes to regenerate and restore and I did not know that Mucin was impacted this way with the goblet cells.

And also that's that's a key piece of that journey to understand, particularly if you're a health professional, a medical colleague, etc.. So for those of you listening to this episode, you know, take notes because you might be getting some insights and information on how this all works that perhaps aren't common knowledge.

Okay. So with that in mind. There's one other thing to add about. Sure, Nancy, that I failed to mention, and that is is that it has been demonstrated to be a really powerful stimulant of GFP one secretion itself.

It actually secretes a peptide that stimulates the LP one secretion. There's another peptide that's part of its outer wall that when the outer wall breaks down, it's released that stimulates JLP one secretion and then it actually secretes one in the slice in the cytoplasm vesicles that can also stimulate job one's secretion.

That's great, powerful to know. And a lot of people are talking about the GLP one receptors, the actual biochemistry, the medications that impact it. And so now we have something that's more natural.

It also is clearly a powerful player there and it's just great to know. It's always interesting to me that some things are just like almost like a powerful intersection, a nexus of things in the body where we can affect that.

We can have marvelous change, positive change. Yeah, absolutely. So you also asked how how did the how did this go astray? How did go up with the rails?

Diet, Fiber, and Microbiome Recovery

Yeah well it the Western diet is is heavily implicated. You know in this. So if you think about what characterizes, you know, the western diet its rich in simple sugars it's deep it's depleted of complex carbohydrates and, you know, increased fat and protein.

So it basically is almost the ideal approach to starving, you know, the microbiome. And so that's starvation, setting a situation that that is set up leads to, you know, multiple bacteria sort of thing that help with this.

I'm not going to hang around here, you know, any any more. And they leave the community. And as they leave the community, you know, their function, you also leave with them and the microbiome is actually it's more than a village.

It's actually a well-integrated community where, you know, microbe A does its thing, but it produces products that help microbe either do its job or actually serve as nutrients from the microbiome.

And so you have to have all of the players present all of the functions represented to have a healthy microbiome. That totally makes sense. There's synergy here.

All right. So then is there evidence for the use of probiotics and prebiotics in glucose management in individuals with type two diabetes? Absolutely.

So it turns out that, you know, the sort of the time honored recommendations of dietitians like the patients with type two diabetes, one of the reasons why they are enjoying the success that they enjoy is that they replenish the fiber content of the diet.

So they're putting that putting the foodstuff back in to the you know, to the gut to feed, you know, a healthy, you know, your microbiome probiotics. You know, at Pendulum, we've formulated a live stream, you know, probiotic that also had a has a bit of a prebiotic inulin in it.

And in a controlled clinical study, we demonstrated that just simply adding that to the patient's daily life practices, you know, no other dietary modifications or anything, you know, result that.

So this study was done in patients who were treated with metformin that were not achieving the degree of control that, you know, that was desired. And when this probiotic that's now sold as pendulum glucose control was added into the into the regimen, it resulted in a mean reduction in A-1 C of a point 6%, 8.7%.

And also it achieves that primarily by reducing the surge in glucose that falls, you know, the ingestion of a meal, the so called postprandial spike and that and that spike was reduced by 33%.

And so, you know, that that resulted, you know, knocked on into the reduction in hemoglobin weren't seeing any improvement of the metabolic state of the patients.

Now this changes was associated with an increase in measurable butyrate within the stool and it also correlated to an increase in butyrate within the within plasma.

And when you look at the increase in butyrate in plasma and correlated with the change in hemoglobin A1 C, there was a direct correlation so that the greater the increase in butyrate, the greater the reduction in hemoglobin A1.

C, which, you know, does a very nice job of tying all the animal work related to type two diabetes together with for the scene in the clinic. And so it just reinforces the the importance of the reiterate pathway.

This all comes together, doesn't it? You know, the integrity of the gut and the gut sliming and all of the beautiful things that our digestive tract does for us are really critical to our health and for blood sugar regulation.

This is an important point that is I feel overlooked. And so I'm really glad we're doing this interview, that's for sure. People I'm hopeful are getting plenty of insights and maybe reaffirmation of the central role that the gut plays in determining blood sugar and metabolism.

That's a very, very important point, and it's something that didn't exist, knowledge that didn't exist when I was in medical school. Okay. So from a nutritional standpoint, is there anything that individuals with diabetes can do to improve the state of their gut microbiome?

So the important thing is to pay attention to the fiber content of the diet, particularly soluble fiber. So we're water

soluble fiber junk comes from fruits, particularly blueberry, strawberry, any any berry, you know, is good for your microbiome.

You know, vegetables such as broccoli, cauliflower, spinach, you know, beets or good are good sources, you know, as our whole grains, quinoa, chia seeds, you know, nuts, particularly almonds and walnuts are good sources.

Probiotic Support and Product Information

And then, you know, whole grain or as I say, a marine flying flours like whole wheat flour, you know, oatmeal or flour. You know, those things also have good fiber in them to to nourish the microbiome.

Okay. So it sounds like there's lots of opportunities to replenish and restore and help that gut to heal. So you think in today's world where many people have an amazing exposure to highly refined foods, ultra processed, low nutrient density, strange chemical additives to stimulate the appetite in tongue, etc.

But it's kind of an uphill battle from a nutritional standpoint to stay healthy and well and certainly to protect the integrity or restored of the gut microbiome.

So the products the pendulum has formulated are key to addressing that issue. Yeah. So I think one way of looking at what I've described here is that if you do the dietary practices, you know, you get benefit from it.

But that appears to be sort of half of the loaf. If you combine that with the probiotic, that that in and of itself helps put the healthy bacteria back into you know, the gut gut microbiome.

You know, you actually get nice synergy and you get, you know, a larger effect. Rate that's so good. You know, before we end our episode here, our interview, I'd like to know if there's a place where people can get more information about this tour.

Go to our Web site, which is pendulumlife all one word. pendulumlife.com. you can you know, the products are available there. But there's also a lot of good information about the science.

You know, there's a special landing page there for health care professionals where, you know, you can, you know, find your various white papers addressing various topics, you know, related to the you know, to the microbiome.

And also in interests of supporting the use of the products in your practices out there. I'm happy to share with you that if you go to that website and you look, you can establish the health care account which will unlock wholesale pricing for you.

And to benefit from that, you use a code, all capital letters, WSDR TALKS40, and that will qualify you for a 40% discount. If you'd like to try the products yourself, you can also use the code.

DRYATES for a 20% off of your membership. You know, order. Okay, great. So while we're here, I want to be sure we can capture this. So the website note number of websiteaddress is www.pendulumlife.com.

Right? So that's pendulumlife.com. Is that right? Correct. And if people want to have a wholesale account, could you please repeat what the code is for that for the discount doing this summit?

Sure. It's W as in Western S as in sand same D as in Dog R as in Roger T as in Tom A as in Alpha, L as in Lloyd, K as in Kansas S as in SAM 40 four zero.

Okay, great. It's all. It's all together. No spaces. No spaces. And it's all capital letters. Correct. Okay. And if someone wants to use the product personally, the code for that is all capital letters DR like the abbreviation for doctor.

So DRYATES, DRYATES, all capital letters. Correct? Perfect. Okay. All right. So, friends, as you watch this

episode, particularly our colleagues here, health professionals, please share this with others so they too can benefit and anyone who's watching is a member of the general public.

I'm sure there's some information we just shared here from Dr. Kolterman's insightsthat are probably news to you. Think about what's going to be supportive and help you in your health journey.

You're welcome to make use of these products and find out what the benefits could be for you. I think that as we go along, there'll be more in the way of personalized medicine with really specific targeted results, because we all know that people don't respond identically to everything in their environment and nutrition and stress and life and all these other things don't impact this the same way.

So as you put together, what's working for you, we invite you to be a part and you make use of the pendulum products.