

Episode 135 Transcript

00:00:00:00 - 00:00:06:20

Dr. Jaclyn Smeaton

Well, we should definitely talk about this more. But maybe, like not when the cameras are rolling so our competitors don't hear the conversations that happened after we cut.

00:00:06:22 - 00:00:09:03

Dr. Kara Fitzgerald

You heard it here. Live. It's live.

00:00:09:05 - 00:00:34:21

Dr. Jaclyn Smeaton

Live. Welcome to the DUTCH Podcast, where we dive deep into the science of hormones, wellness and personalized health care. I'm doctor Jaclyn Smeaton, chief medical officer at DUTCH. Join us every Tuesday as we bring you expert insights, cutting edge research, and practical tips to help you take control of your health from the inside out. Whether you're a health care professional or simply looking to optimize your own well-being, we've got you covered.

00:00:34:23 - 00:00:56:04

Dr. Jaclyn Smeaton

The contents of this Podcast are for educational and informational purposes only. This information is not to be interpreted or mistaken for medical advice. Consult your health care provider for medical advice, diagnosis and treatment. Hi everybody and welcome. I'm so excited that you're joining us here for our first live Podcast from this year's A farm event at The Venetian in Las Vegas.

00:00:56:08 - 00:01:20:00

Dr. Jaclyn Smeaton

I'm Doctor Jaclyn Smeaton, your host of the DUTCH Podcast and chief medical officer at DUTCH. Today we're joined by our wonderful Mark Newman, founder and CEO of DUTCH. And our special guest today, Kara Fitzgerald. Doctor Kara Fitzgerald, and Kara, I have a copy of your book to show here. Kara is the author of *Younger*. You reduce your bio age and live longer and better and really your natural Catholic physician by background.

00:01:20:00 - 00:01:42:14

Dr. Jaclyn Smeaton

And I would just say a mover and shaker in this field, moving through clinical trials and really applying the foundational lifestyle techniques and targeted nutrition and seeing an amazing impact on age reversal in your patient population. We're going to talk about that. I don't want to jump into that. You know, Kara's also doctor Fitzgerald is also a renowned functional medicine clinician and researcher.

00:01:42:18 - 00:02:03:04

Dr. Jaclyn Smeaton

And younger you is not your only book, your author of several books and really leading as a pioneer in DNA methylation and biological age reversal, which is all the rage now, media in the rest of the world has caught up with the work that you did, but really doing those clinical trials, I can't wait to dive into. So welcome so much to the Podcast.

00:02:03:10 - 00:02:05:18

Dr. Kara Fitzgerald

It's great to be with you both. Of course.

00:02:05:20 - 00:02:14:18

Dr. Jaclyn Smeaton

Well, I want to start by talking about your primary research. Can you walk us through like what inspired you to conduct this clinical trial and kind of talk to us for a little bit about the trial?

00:02:14:19 - 00:02:41:13

Dr. Kara Fitzgerald

Awesome. Yeah, absolutely. And, we have a publication that came out based on that data, and we're working on a new one that came out this year. So let me just back to that. Thinking about epigenetics really started to, grab my, my, my brain. I want to say around 2013, it was a while ago, more and more papers were like, passing across my desk or at PDFs and,

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Dr. Kara Fitzgerald

So the so the question for me is always, how does functional medicine influence, you know, the physiology influence mechanism? I'm always thinking through the functional medicine lens. I'm always thinking about how I might apply this to my patients, you know, is what we're doing best practice, can we improve, etc., etc.. So

those questions as a, you know, as a clinician at heart, kind of lab geek slash clinician are always really top of mind for me.

00:03:06:09 - 00:03:33:08

Dr. Kara Fitzgerald

And so the epigenetic data early on was primarily in cancer. Cancer takes over gene expression. It hijacks the tumor microenvironment for its own nefarious. And so it will turn off protective genes, that keep cancer at bay. The tumor suppressor genes. And it will turn on oncogene. And this is primarily through, DNA methylation. So turning off a gene is hyper methyl.

00:03:33:10 - 00:03:56:15

Dr. Kara Fitzgerald

A methyl group goes on, you know, and multiple methyl groups will go will land on that gene, inhibit it from being expressed in the oncogene. The methyl groups are actually removed. And and then the cancer microenvironment is incredibly efficient. And it's real and it reliably occurs across cancer. So much so is you can measure that. You know if you've you've heard of the Grail Test, there's DNA methylation to look at.

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Dr. Kara Fitzgerald

Early evidence of cancer is you know, it's just being widely adopted now because it's just a reliable measure for many different tumor types. It's it's quite interesting. So the question at that time, for me, thinking about it through the lens of cancer, and others, you know, cardiovascular etc., biological age at that time was thought not to be.

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Dr. Kara Fitzgerald

It was was immutable. We didn't think we could change biological age as measured by the epigenetic clock. So back then we were really thinking about cancer. And a few other things. But, Romney, Hodgins, my, you know, the director of nutrition and and she's still with me. She and I started to dialog how we might interpret, you know, manipulating this using a functional medicine approach.

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Dr. Kara Fitzgerald

And so we designed to that we designed a dietary pattern. We and then just our best read on the literature at the time, a lot of it was, was was pre-clinical in animal

models. And so, but we figured out that a methyl donor dense dietary pattern, you know, lots of greens, lots, you know, folate rich nutrients, B12.

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Dr. Kara Fitzgerald

We had people consume liver, eggs, beets, etc. plus a huge complement of, nutrients that are dense in polyphenols, green tea, herbs and spices, berries, etc. this combination dietary pattern plus, you know, adequate fat, a good, you know, a decent chunk of protein, was the optimal for favorably changing gene expression in this way, we and then we include exercise.

00:05:29:01 - 00:06:03:23

Dr. Kara Fitzgerald

We included a meditation practice. And we wanted people to engage in good sleep. During the course of our study, it was an eight week intervention. The first publication showing the biological age can be reversed and came out during our study. We knew that we were going to look at that measure. We had the data to look at it, but I wasn't holding my breath that we the needle on it because it hadn't, you know, we didn't have any human data on that prior to, but when that study came out for me, you know, for the space where people are thinking about biological age, epigenetics and so forth, it was like times.

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Dr. Kara Fitzgerald

Yeah. And that was the trim, trial, the trim trial, Greg, phase work. So we were excited to look at it. And so we was the first question that we asked of the epigenetic data we had. And, you know, it was, I can't even tell you how exciting it was. The moment that, you know, my our biostatistician informed me that we had in our study group, reversed the biological age as compared to the control group by over three years.

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Dr. Kara Fitzgerald

You know, what time eight weeks time, using a diet and lifestyle intervention. I mean, we knew that we were onto something pretty special. It was the first of its kind to study.

00:06:40:03 - 00:07:00:20

Dr. Jaclyn Smeaton

Yeah, it was really the results were shocking as it's a reader not participating. Yeah.

Because it just goes to speak to. And that's something that I've always foundationally believed the impact of lifestyle on. That's right. And that's what was so profound about this. This is a lifestyle based intervention. It wasn't this targeted amazing new supplement. This is something that anybody could do.

00:07:00:21 - 00:07:23:00

Dr. Kara Fitzgerald

Yeah. As Dina Kaser, our fellow and said to me, get carrots is graphic medicine. You know it I it's true, it was true. And we were you know, at that time a lot of us were talking about nutrition, omics and, and we were throwing out the idea of epigenetics, but the data weren't there for us to really say that strongly.

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Dr. Kara Fitzgerald

And so just to be able to participate in creating new knowledge, to be able to participate in providing new knowledge to the, you know, to the scientific pool was incredibly, just incredibly, vanishingly gratifying. And it was, you know, it was pretty like career change.

00:07:39:12 - 00:07:40:03

Dr. Jaclyn Smeaton

Oh, I bet.

00:07:40:05 - 00:08:00:16

Dr. Kara Fitzgerald

After that it was unexpected. It got a lot of attention. And then we went on to, you know, write the book and, and we reproduced that in a smaller cohort of women. So the original study was limited to men. And then we published a follow up looking at women and saw actually better outcome. But it's not quite an apples to apples comparison.

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Dr. Kara Fitzgerald

The men with saliva and the women blood. So the the specimen was different but the women really did fabulous.

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Dr. Jaclyn Smeaton

Well tell us about the reason.

00:08:10:09 - 00:08:34:16

Dr. Kara Fitzgerald

The recent but so we went back in to tease out what elements if we could of inter the whole intervention seem to do the heavy lift on changing the Horvath clock, which is what we used, and it turned out to be those nutrients most dense in polyphenols. So the polyphenols and what's really cool about it is well, since that 2021 publication.

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Dr. Kara Fitzgerald

So there were, there was a scant amount of human data. But since then, the trajectory looking at, you know, diet, dietary interventions, dietary patterns and, and epigenetics and biological age, it's just a skyrocketed. And so it's very validating. It's very satisfying. Polyphenol dense dietary patterns like the Mediterranean and some with additional polyphenols added like we're just we're really being validated in our original findings.

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Dr. Kara Fitzgerald

And we went back and quantified the amount of polyphenols. You know, we using our best, you know, the best tools available to us. We didn't get specimen for those, but it's about three grams a day, just under three grams a day, which again, when you look in the literature is it's as dense in polyphenols as you know, as it comes.

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Mark Newman

And that was by way of supplement or no dietary.

00:09:22:18 - 00:09:23:23

Dr. Kara Fitzgerald

Yeah, dietary.

00:09:24:02 - 00:09:29:14

Dr. Jaclyn Smeaton

Can we roll it back a little bit. And for people who are maybe listening for the first time and new to this area, what is a polyphenol.

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Dr. Kara Fitzgerald

Yeah. So it's a it's a phytochemical. It's a it's, it's, it's what makes, you know, the it provides colors. You know, when you're eating your berries or you know, peppers etc.. You know, it's a, it's a phytochemical that is what we call a trophic meaning it does a lot of really cool stuff. You know, it's not our macros.

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Dr. Kara Fitzgerald

We don't it's not a sugar. It's not, you know, it's not a fat, a carb, a protein there. They're these really important plant compounds that are, associated with, just improving the hallmarks of aging. So the, the, the breakdown process that happens during the aging journey, they've, they've they've characterized like 12 major players. Polyphenols will will improve those.

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Dr. Kara Fitzgerald

They polyphenols tend to the microbiome. They tend to the mitochondria. They take care of, you know, gut health beyond the microbiome. They you know, they help with brain health. They're antioxidant. They're anti-inflammatory. They're anti-cancer. They're just profoundly atrophic and important. You know, it's why we eat, you know, these this these plant dense diets. It's I mean, you know, it's a prime reason, it's to really consume a lot of this, what I call as incredibly important information.

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Dr. Kara Fitzgerald

And I think the, the way these guys are working is, you know, the most upstream location is that they're changing expression. And then there's these downstream benefits, these profound, far reaching downstream benefits that were.

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Dr. Jaclyn Smeaton

Are there a couple that people might recognize and have.

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Dr. Kara Fitzgerald

Yeah. Yeah. There's a lot going. Listen, you're already eating a whole bunch of these polyphenols. You're already eating. We call them epi nutrients because they can change the epigenome. In the book, one of my favorite parts about the book is the appendix. It's the epi nutrient appendix. So you can go in there, you know, especially if you're somebody who hasn't sort of adopted a healthy dietary pattern.

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Dr. Kara Fitzgerald

But you could go in there with a highlighter and be like, oh, yeah, you thought, oh yeah, eat that. You know, I eat pepper. I put rosemary on my food. You know, I love time in my spaghetti sauce or spaghetti for the sauce for that matter. The lycopene in tomatoes. But really famous ones we know of course, are EGCG in green tea.

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Dr. Kara Fitzgerald

What else? The, the, curcumin in turmeric, rosemary acid and rosemary. I'm all in time. I mean, it's just kind of, kind of goes on and on. But resveratrol, you know, again, lycopene, sulforaphane as we were talking about earlier, is a real badass polyphenol. There's many, many of them.

00:12:08:18 - 00:12:25:17

Mark Newman

And the when you say polyphenol obviously poly meaning many or whatever. So the the action from those comes after those are broken down into their individual parts, which is just a great big mix of, of some known, some unknown compounds. Is that kind of the general way.

00:12:25:17 - 00:12:46:00

Dr. Kara Fitzgerald

Those were I would say, you know, that's awesome. And there's, you know, the it's not called the dark matter of nutrition for nothing. It's such a good it's such a good mark. Kind of a question. We don't have a lot of we're still wrapping our arms around understanding. So some compounds appear to really work their magic directly absorbed.

00:12:46:01 - 00:13:11:15

Dr. Kara Fitzgerald

Some compounds have to be absolutely transformed by the gastroinTestinal tract. And this is this. You know, the family of post biotic compounds, compounds work in concert, you know, and they're acted upon by the microbiome, sort of collectively. But we also know that there's awesome data on standalone compounds, like one of my favorites is your elephant. A it's a it's a post biotic compound coming from ellagic acid.

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Dr. Kara Fitzgerald

And some other players from like pomegranate, you know, some seeds, etc.. So, so the, the polyphenols are liberated when you eat pomegranate. And actually the white part is more dense. One of the, one of the doctors in my practice will eat like Snow White.

00:13:26:06 - 00:13:27:17

Dr. Jaclyn Smeaton
Well that's commitment.

00:13:27:20 - 00:13:59:22

Dr. Kara Fitzgerald
You know, that's that's a blend right. But there's it's still in the red, the yummy, juicy part of it. And if you have the correct microbiome, you can liberate those polyphenols directly in your allicin a and then it's absorbed. And then there's a ton of fabulous clinical data on it, you know, engaging. My top figure. So just helping with mitochondrial turnover and biogenesis and just, you know, lowering inflammatory markers, just even increasing the mass and sedentary individuals.

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Dr. Kara Fitzgerald
The benefit of this one post biotic compound are extraordinary, far reaching. But a lot of us don't have the appropriate microbiome to be able to me, and especially in the quantities that we need. But, you know, you can you can actually supplement with it. However, what I like to point out is this is one in a sea of the dark matter of nutrition.

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Dr. Kara Fitzgerald
There are many more to come. But I do think it illustrates nicely the exquisite power and importance of these players. We evolved, our bodies, evolved, ingesting this information, transforming it, using it like our genetic apparatus expects. This kind of information. And we've, you know, we've been away from it. And I think, you know, it accelerates aging. It causes the chronic diseases of aging, the litany of, of problems that we confront.

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Dr. Kara Fitzgerald
So polyphenols. I, I'm excited to see that we are able to tease out and identify those as doing the heavy lift. But we would still argue that you know, in the context of the

dietary pattern, you know, overall is, is is would be best practice.

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Dr. Jaclyn Smeaton

I'm not surprised to hear you say that because, you know, even when you think about that polyphenol rich diet, you're also getting fiber. And you're getting, you know, when you talk about the mechanisms required to use the polyphenols that they require a good microbiome. And there's other things that were not elucidated specifically in the study that almost support the use of the polyphenols.

00:15:25:06 - 00:15:27:07

Dr. Jaclyn Smeaton

It's a family. It's like a family adventure, you know.

00:15:27:07 - 00:15:48:11

Dr. Kara Fitzgerald

That's right. Yeah. Fiber is essential for a healthy microbiome. Yeah. All the the other elements in the plant compounds, you know, good fat, protein, adequate hydration, etc.. Yeah. Pulling out, you know, when we removed, pro-inflammatory. So it really sort of gives the runway and the space for these healthy nutrients to kind of do their.

00:15:48:13 - 00:16:11:07

Dr. Jaclyn Smeaton

Can we talk more about your elephant eggs? That's something that I think is really rising in popularity. And yeah, the study there's been interesting studies that have come out. Yes. On the supplement form of your elephant, a I'm sure you are more aware of them than I am. Can you speak a little bit to that of like what the data is showing when it's used as a dietary supplement compound, and how you would kind of compare that to the benefits of getting it through a whole food source.

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Dr. Kara Fitzgerald

Okay. Yeah, I can speak to the data. There's always more studies coming out in this arena. I mean, there's the, you know, the company that's producing your elephant. A they've just put a lot of intention and time and energy and, and money into researching it. And by the way, congratulations on your publications. Well, you guys, it's, you know, it's important.

00:16:33:00 - 00:17:06:09

Dr. Kara Fitzgerald

It's important. And it takes time and effort and all of that. And these guys have really, really made a commitment. I would say, you know, the studies that have really knocked my socks off around your life and I include, looking at sedentary older adults, improving, VO2 max in this population, so sedentary. So they're not exercising, only prescribing the euro within a one gram, and they increased, VO2 max by about 10% on average.

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Dr. Kara Fitzgerald

Not only is that massively, statistically significant, but if you look at a chart and look at VO2 max, associations with, age, that's about a VO2 max.

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Dr. Jaclyn Smeaton

That's a that's a breath measurement. Yes. And they use it for like metabolic rate measurement. Yeah.

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Dr. Kara Fitzgerald

It can.

00:17:22:01 - 00:17:22:16

Dr. Jaclyn Smeaton

Be. Yeah okay.

00:17:22:18 - 00:17:50:05

Dr. Kara Fitzgerald

And just and it's it's your it's your fitness your it's your respiratory fitness. And you know an important you know tracking with cardiovascular like it's a good longevity measure. And to be able to in sedentary non exercising it also improve it by by 10% to me is really incredibly profound. They increased muscle mass in sedentary adults. This you guys is a post by polyphenol count.

00:17:50:07 - 00:17:54:18

Dr. Kara Fitzgerald

You know we're not talking about some kind of a crazy drug or gene therapy.

00:17:54:18 - 00:17:55:12

Dr. Jaclyn Smeaton
Or something like.

00:17:55:12 - 00:18:27:05

Dr. Kara Fitzgerald
That. But it's like this compound from polyphenols. They've lowered, from pomegranate, they lowered crp, they lowered a whole selection of cytokines. They have cool epigenetic data that's prepublication. They've improved immune fitness. They improved, you know, the various T-cell ratios. They, and what else have they looked at? They're, they're if they haven't published, they're just about to publish an, a paper in elite athletes.

00:18:27:09 - 00:18:52:07

Dr. Kara Fitzgerald
So they're looking at different cohorts, but really pretty consistently, the data that they show, and they source it to its ability to engage in my tough AG, which then engage prompts vital biogenesis. So like this mitochondrial recycling phenomenon is, is kind of what they think is doing the heavy lift. I mean, I think it's, I think it's multifactorial.

00:18:52:12 - 00:18:58:19

Mark Newman
Is, that particular example in the ballpark of what you can get through dietary sources or they supplementing with.

00:18:58:22 - 00:18:59:21

Dr. Kara Fitzgerald
Their supplementing it.

00:18:59:21 - 00:19:02:18

Mark Newman
So with a lot like more than you can get from dietary.

00:19:02:18 - 00:19:22:14

Dr. Kara Fitzgerald
Yes. More than you could get. So they have a Test that they really need to make available to clinicians where you can see whether or not you're making your and I am a producer. I'm proud to produce there, but I'm not producing and say I need a t shirt, but I'm not making the quantity that they've been using in some of these

studies.

00:19:22:14 - 00:19:29:13

Mark Newman

I mean, multiple people with the same dietary intake will make kind of like the equal thing where some people make it and some people don't.

00:19:29:13 - 00:19:30:19

Dr. Kara Fitzgerald

That's exactly right. Because the.

00:19:30:19 - 00:19:31:12

Mark Newman

Microbiome.

00:19:31:15 - 00:20:06:07

Dr. Kara Fitzgerald

It's that's it's it's a it's a microbiome dependent compound. Yes. And there's a handful of different you're olefins. You're living a b perhaps the most important but yeah they're, they're working with what a, a super physiologic amount in the supplement. Okay. However there is data on your role within producers and good outcome, like they measured your olefins a, b, c I think in the direct study, which was a mediterranean, the direct plus was just a mediterranean dietary pattern plus additional polyphenols.

00:20:06:12 - 00:20:25:03

Dr. Kara Fitzgerald

And they were able to see that they increased them naturally just from the dietary pattern. And that was associated with some of the good outcomes in that particular study. So so you don't want to throw out the diet potential. Yeah. The challenge is, is that not all of us make it. So it would be nice to just like equal because he was another really important player.

00:20:25:03 - 00:20:30:03

Dr. Kara Fitzgerald

And and not a lot of us I don't I don't know that a lot of us make it. Yeah.

00:20:30:03 - 00:20:36:06

Mark Newman

And lab guy wants to know that's they look for that in urine, not in blood. Or is it in urine? They're looking for them.

00:20:36:11 - 00:20:39:23

Dr. Kara Fitzgerald

I think it's I but you're. Listen. You're listening. Yeah. Oh, yeah. Yeah.

00:20:39:23 - 00:20:41:01

Dr. Jaclyn Smeaton

Very interesting. Yeah.

00:20:41:03 - 00:21:01:03

Dr. Kara Fitzgerald

Urine. Thank you. I know what you're going with that. That's I really I know where you're going with the light bulb build on. That is a really good direction to take because it's an important tool to be able to be able to look at this, not just the your listeners, but the other post biotics like going back to equal like that would be just to have that kind of panel.

00:21:01:05 - 00:21:15:19

Dr. Kara Fitzgerald

You know, to see if we're making these, to see if we're making them in appropriate quantities to begin to tease out, you know, what polyphenols need to be transformed. You know, what need to be absorbed directly, I mean, and, and and then the absorption technique.

00:21:15:21 - 00:21:17:12

Dr. Jaclyn Smeaton

Yeah.

00:21:17:13 - 00:21:21:23

Dr. Kara Fitzgerald

You know, with curcumin, there's, there's different ways of optimized sorption.

00:21:22:01 - 00:21:29:06

Dr. Jaclyn Smeaton

Yeah. Well, we should definitely talk about this more, but maybe, like, not when the cameras are rolling. So our competitors don't hear the conversations that happened after we cut.

00:21:29:08 - 00:21:31:13

Dr. Kara Fitzgerald
I heard it here. Live it's live.

00:21:31:15 - 00:21:34:05

Dr. Jaclyn Smeaton
Live.

00:21:34:07 - 00:21:37:18

DUTCH Podcast
We'll be right back with more.

00:21:37:20 - 00:22:06:03

DUTCH Podcast
If you're already running DUTCH Tests in your practice or thinking about it, there's never been a better time to become an official DUTCH provider. Why? Because we go beyond lab Testing. Our provider community gets exclusive access to clinical education, in-depth report interpretation training, monthly case reviews, and one on one clinical support. Whether you're just getting started or looking to sharpen your functional hormone expertise, we give you the tools to grow.

00:22:06:05 - 00:22:14:03

DUTCH Podcast
Join thousands of providers already making a difference. There's a DUTCH Test.com today.

00:22:14:05 - 00:22:17:00

DUTCH Podcast
Welcome back to the DUTCH Podcast.

00:22:17:01 - 00:22:38:06

Dr. Jaclyn Smeaton
I'm going to develop the next panel. I want to talk a little bit about an element of the work that you did, because I think it's really interesting. You looked beyond nutritional data at stress and stress reduction in meditation. And guest mark, I'm hoping you can start, because I also think it's fascinating that we have HPA access as part of a panel that people think about for reproductive health.

00:22:38:07 - 00:22:48:21

Dr. Jaclyn Smeaton

Yeah. Can we start the conversation with you framing up why when you think about hormone health, HPA axis and adrenal function and cortisol are such an important part of that story.

00:22:48:23 - 00:22:49:22

Mark Newman

Just generally.

00:22:49:22 - 00:22:51:19

Dr. Jaclyn Smeaton

Yeah.

00:22:51:21 - 00:23:11:05

Mark Newman

Yeah. I mean, I think that's a pretty good foundational place to start. You're I mean, just thinking of reproduction. You know, if you're getting invaded by the Huns, it's not time to make a baby. So our bodies are our bodies are pretty smart that, when that's going on and you're in flight or flight and there's a whole bunch of stuff not going on.

00:23:11:07 - 00:23:38:08

Mark Newman

That obviously, if it's, prolonged, then you're not going to get good outcomes. And then we live in this over the history of the world. We live in such a weird space now, where literally nothing can happen and those systems can be turned on almost all the time. And by this silly world we live in, in terms of just what's going on between our ears that can create, fight or flight without the tiger chasing us around the room.

00:23:38:10 - 00:23:56:23

Mark Newman

So, you know, having knowing what's going on. And then when that happens, you know, then you can have a spectrum of that's happening and I'm functioning properly, meaning I'm running hot because, you know, lots of cortisol, lots of adrenaline, whatever. And then of course, fast forward when your body's like, okay, that's about it. Now, if we're going to shut that system down a little bit.

00:23:56:23 - 00:24:18:20

Mark Newman

So so depending on where you're at in that, in that kind of progression of being exposed to that in unhealthy ways for long periods of time. And then, you know, the consequence is kind of you're well aware, like roll off of that in many ways. And then you too, as doctors get to pick up the pieces, you know, decades later or, or whatever.

00:24:18:20 - 00:24:28:06

Mark Newman

But yeah, just the, the foundational thing that if it's off for prolonged periods of time, the, the consequences are, are many and pretty profound for lots of people.

00:24:28:06 - 00:24:42:13

Dr. Jaclyn Smeaton

So it blows my mind when you think about like, stress and cortisol in every system of the body has been researched and that it's impacted by cortisol. And then what about aging when it comes to aging? Have they looked at that and the impact of stress on.

00:24:42:15 - 00:25:04:15

Dr. Kara Fitzgerald

You know, it's such a it's I'm so glad that you brought it up. I, I you know, I have said often that, you know, stress cortisol is like gasoline on the fire. Like really it is. And what was super interesting to me was the clock that we used has a lot of these, what they call glucocorticoid response elements on it.

00:25:04:17 - 00:25:12:17

Dr. Kara Fitzgerald

So it's responding to that or it's responding to the dump of cortisol. And it's very much aging phenomenon.

00:25:12:17 - 00:25:24:17

Dr. Jaclyn Smeaton

So it's interesting that you say boring gasoline on the fire because I describe cortisol as a fire extinguisher. And like in its best form, in its healthiest state, it is. Yes. But then when you get too much fat. Yeah. Is that reverse effect?

00:25:24:20 - 00:25:50:18

Dr. Kara Fitzgerald

Yes. Yes. I think it is profoundly pro aging. But yeah, to your point, short term acute stress is one of the most powerful experiences. I'd like to undertake a good athletic event or be challenged in some kind of a short term kind of. You know, controlled, for

lack of a better word, manner. And it's incredibly, you know, nourishing, powerful and essential.

00:25:50:18 - 00:25:59:11

Dr. Kara Fitzgerald

And that's how we evolved. But then to your point, mark, when we're in fight or flight in our heads, you know, chronically, constantly. Yeah. It's profound.

00:25:59:13 - 00:26:08:22

Dr. Jaclyn Smeaton

Yeah. Are there other elements of like crossover with the hormone impact around like polyphenol intake?

00:26:09:00 - 00:26:39:04

Dr. Kara Fitzgerald

No doubt. I mean, for sure. There are just, you know, a number of really beautiful polyphenols that will help balance out the transition. I mean, I was just talking earlier, an earlier two group of people. I mean, we're here at the vineyard. I've been talking to a lot of colleagues. I mean, there was a time when women didn't experience the transition, like, as intensely and acutely like it was relatively uneventful.

00:26:39:04 - 00:27:19:14

Dr. Kara Fitzgerald

And it was probably. And I think there's other parts of the world where, you know, moving through menopause is not a is not the challenge that we experience here in this country and, you know, in other countries. And certainly part of that is the dietary pattern. I mean, we know, you know, the polyphenols from soy, the polyphenols from, from clover, you know, there's a whole host of polyphenols that will definitely help, you know, maintain an estrogen like environment or, you know, in other turn, in other time, actually help metabolize out and clean up estrogen.

00:27:19:16 - 00:27:31:11

Dr. Kara Fitzgerald

In premenopausal, estrogen excess or dominance patients. So yeah, there's no doubt polyphenols in the context of an overall healthy dietary.

00:27:31:13 - 00:27:35:12

Dr. Jaclyn Smeaton

Now you bring up a really interesting point about hormone metabolism.

00:27:35:13 - 00:27:36:07

Dr. Kara Fitzgerald

Yeah.

00:27:36:09 - 00:27:54:19

Dr. Jaclyn Smeaton

And one thing that I'd love us to cover today, maybe Marc, you can start us off, is that I think there's a lot of concern because we talk about methylation, we talk about estrogen metabolism, and we also talk about methylation. We talk about epigenetics. And I get asked a lot, is this the same methylation? Are they connected? Are they not connected?

00:27:55:00 - 00:27:59:17

Dr. Jaclyn Smeaton

Can you start, Marc, by talking a little bit about methylation in the context of estrogen.

00:27:59:18 - 00:28:25:01

Mark Newman

Sure. Yeah. We actually one of our I think our most recent publication actually was a case study of me, and, you know, we I pushed my Testosterone up, which made too much estrogen and it wasn't getting metabolized. So we used some nutraceuticals like them, and I think, to push it down that two hydroxy pathway. And then me being a genetic person who has the homologous Comt snips.

00:28:25:01 - 00:28:56:16

Mark Newman

So my methylation sucks. Yeah. Because I was loading up that two hydroxy, my methylation was even worse. And then and then we looked at tri methyl glycine like helped that. So there you have like nutrients that help methylation. In that particular case you have CMT, which is the enzyme that's going to push my two hydroxy that catcall to be methylated, which then at the same time, I presume that's going on with epinephrine and other things that are catcalls.

00:28:56:20 - 00:29:21:18

Mark Newman

So that world I live in, and it makes sense that there's a genetic component with an enzyme that's not, as I understand it, involved in the type of methylation you would talk about or epigenetics, but the nutrients and this is where my knowledge gets

super fuzzy. So epigenetic idiot in the room, that's me. Is the nutrients like magnesium and, you know, methyl donors or whatever things that are involved in the methylation of estrogen.

00:29:21:18 - 00:29:45:02

Mark Newman

So for people to use the DUTCH Test, the methylation is either going well or it's not going well. And if it's not, then they might want to encourage it. So it leads to these questions of like okay. At the same time, in a parallel universe, in that same body, there's methylation going on with epigenetics, which might be either high or low, potentially differently depending on whether it's a genetic source like for me or a nutrient source.

00:29:45:02 - 00:30:09:12

Mark Newman

So can you talk about where there's overlap between the two, like they're using the same co-factors whatever. But then different enzymes. So as we push like this is like a good question for our DUTCH people as we push methylation of estrogen metabolism, which we think of as being protective. And it is what are the potential consequences that we need to be thinking about with a methylation going on in the epigenetic world?

00:30:09:12 - 00:30:14:01

Dr. Kara Fitzgerald

Yeah, that's a great question mark. So.

00:30:14:03 - 00:30:36:00

Dr. Kara Fitzgerald

They're all relying on the universal methyl donor, you know, acid, DNA, steel, methionine they're all relying on it. So if we go back to the methylation cycle and you can see that the methylation cycle is wonky, maybe there's a high homocysteine. And I know we can measure you know, that's adenosine homocysteine. Yeah. We can we can dance around the methylation cycle with labs these days pretty pretty efficiently.

00:30:36:00 - 00:31:08:02

Dr. Kara Fitzgerald

Pretty well. So if that is not functioning, of course you're going to see problems, you know, metabolizing estrogens, methyl eating them appropriately. You'll see problems clearing out epinephrine. You we were talking offline. I think that there's a hierarchy.

So there's precious Sammy a pool. You know, when it's compromised there's going to be preference. And I would I would argue that, you know, something like epinephrine is going to, you know, get that precious pool.

00:31:08:07 - 00:31:11:13

Mark Newman

So methyl donors are universal. That's what those are working.

00:31:11:13 - 00:31:16:12

Dr. Jaclyn Smeaton

Everywhere because that's a compound. It's like a chemical compound. And if you add it to some other chemical structure.

00:31:16:15 - 00:31:21:20

Mark Newman

If you're in fight or flight, then those methyl donors presumably are getting snatched up.

00:31:21:23 - 00:31:38:00

Dr. Jaclyn Smeaton

Well, that's an interesting piece. Bringing it back to what you talked about of stress pouring the gasoline on aging. Because if we need those methyl donors for detoxification, and we need them for epigenetic expression to be optimized, and they're being dumped in stress at the stem, they're unavailable potentially.

00:31:38:04 - 00:32:13:05

Dr. Kara Fitzgerald

So if you're under consistent toxic burden, that's an awesome point. You know you're going to spend your methyl donors if that. So homocysteine, even, you know, outside of the methylation cycle is the 16 residue or glutathione. And so it's going to just drain it towards glutathione. If you're if you're detoxing really needing to, you know, to to grab that endogenous pool of glutathione and and that's, and that compound when it's used to detox is spent, you know, you're not recycling it like when you Bluetooth ion in a redox reaction where it can be like over and over and you're just spending it.

00:32:13:06 - 00:32:49:20

Dr. Kara Fitzgerald

So you could say that we're like our methylation cycle or our, you know, and then the, you know, the, the initial cycle, the Bluetooth ions and that synthetic pathway, taurine,

etc.. I mean, we're always, you know, grabbing it and it's probably it's going to be used preferentially for the most damaging. So I would start with epinephrine and then maybe that, you know, that mercury burden or whatever toxic compound that's going to be leaning on glutathione in some of the others, is probably going to go towards that estrogen is going to is like a, you know, sort of survival is at stake here.

00:32:49:20 - 00:33:19:02

Dr. Kara Fitzgerald

You know, maybe I mean, this could be a piece of the estrogen dominance or the real imbalance just because this you know, this limited pool is going elsewhere. And I think by and large, of course, it's going to alter gene expression. It's going to alter methylation and the AP and the epigenome, the availability of Sami to the, the, the DNA, the the DNA methyltransferase enzymes.

00:33:19:04 - 00:33:34:02

Dr. Kara Fitzgerald

So yeah, I mean, we would, we would add, I would say in the hierarchy that's probably, you know, less essential in some ways for survival than some of metabolizing out, you know, adrenaline metabolizing know toxins.

00:33:34:02 - 00:33:42:19

Mark Newman

And the consequence. Yeah. Under methylation in an epigenetic sense is what you're not turning on genes you want to turn like what is the consequence.

00:33:42:19 - 00:34:08:22

Dr. Kara Fitzgerald

Well I mean it would be I mean I, I think that it I you know, I think that it would be if you can't adequately methylation I mean, or if you're doing it sloppily, imbalanced methylation, imbalanced gene. Epigenetic methylation would be like pro aging. I mean, you can look at the chronic diseases of aging. You can look at cancer.

00:34:09:00 - 00:34:18:01

Dr. Kara Fitzgerald

It would be allowing those things like lowering the threshold, I would imagine, of really developing those things by not having an adequate pool.

00:34:18:02 - 00:34:19:12

Dr. Jaclyn Smeaton

I've got a great example of that.

00:34:19:14 - 00:34:40:08

Dr. Kara Fitzgerald

Let me just let me just say I want to hear that, but I just want to throw in before the train leaves the station that we, we do our our ability to methylation effectively the epigenetics, epigenetics declines with age. So that's known. But I want to just layer in is interesting point is that it actually becomes aberrant. It becomes imbalanced.

00:34:40:10 - 00:35:02:11

Dr. Kara Fitzgerald

So we've got we turn off genes that protect us. We hypermethylation them like predictably on the aging journey like those tumor suppressor talking about. So we'll take our, you know, our prisoner, our reserves, our, you know, cherished reserves of Sammy and we'll turn off genes that protect us, and we'll allow genes that can drive disease forward to be turned on.

00:35:02:11 - 00:35:10:10

Dr. Kara Fitzgerald

It's pretty crazy. Like if you look at the aging epigenome and side by side it with the tumor microenvironment, in some cases they look really similar.

00:35:10:12 - 00:35:27:13

Dr. Jaclyn Smeaton

Well, one of the things that just makes me think about the agouti mouse model. Yes. And you know what you're bringing up mark around. Like are there actually impacts of a deficiency in methyl donors. And that's been elucidated in animal research in a pretty interesting way. So yes, there's this mouse model that's used for epigenetic research called the agouti mouse.

00:35:27:15 - 00:35:50:18

Dr. Jaclyn Smeaton

The mouse looks like a normal healthy mouse under typical circumstances. And then it's just kind of bad phenotype is that it's yellow coated instead of brown and has heart disease, high cholesterol, basically the modern American. And they've done studies, for example, where the give the same mice are genetically identical. These mice get the same amount of chow. And they were pregnant is the one say that's coming to mind.

00:35:50:19 - 00:36:05:14

Dr. Jaclyn Smeaton

Is pregnant mice given the same amount of child, same quality, same nutrient density, same, you know, quantities of same macros. And they were also exposed to BPA. Then they looked at the offspring. One group of sorry, one group one was the.

00:36:05:17 - 00:36:07:09

Mark Newman

Only variable was BPA.

00:36:07:11 - 00:36:20:02

Dr. Jaclyn Smeaton

You know, they were both exposed to BPA. One of them had methyl donors in the diet added. So the only difference was one got methyl donors, which were I think folic acid. They've looked at that take B12.

00:36:20:04 - 00:36:20:23

Dr. Kara Fitzgerald

Choline.

00:36:21:01 - 00:36:44:08

Dr. Jaclyn Smeaton

Yeah. And and that's coming to mind for me. The one mother group got that. Then they looked at the offspring. And what they saw was that the BPA exposed offspring of the agouti mouse predominantly showed the unhealthy phenotype. The other parent offspring that got the methyl donors with the exact same nutritional environment their offspring had predominantly the healthy phenotype.

00:36:44:13 - 00:37:04:18

Dr. Jaclyn Smeaton

And those offspring it was 21 or 28 days after birth. This is a long time since up to this data, the offspring got the same feed, the same quantity, etc. so they've really made me think about our exposure as humans as well, and the importance of methyl donors in a preconception diet, which is kind of the lens that I view the world through because we are all exposed to toxins that we don't know about.

00:37:04:18 - 00:37:22:09

Dr. Jaclyn Smeaton

And I think the presence of methyl donors, when you think about things like

childhood obesity, there's food quality issues that tell part of the story. But then there's also elements where you see cases where it just doesn't make sense, and you see kids that have maybe in the same family, one of them struggles with weight and health, and the other one doesn't.

00:37:22:11 - 00:37:45:18

Dr. Jaclyn Smeaton

Well, you can look to in utero environment and methyl donors. And that preconception time is critical for epigenetic expression. So anyway, your conversation makes me think about that of there are studies, at least in animal models, I don't know, humans might be too complicated. You might know of some data, but where methyl donor presence or absence has made like a make or break piece of whether someone is really healthy or really, really ill.

00:37:46:00 - 00:38:14:23

Dr. Kara Fitzgerald

Yes. And let me say the reason that, the offspring did well under the circumstances with the BPA exposure is because the methyl donors hyper methylated and turned off the agouti, the specifically it did, it did it probably helped. It helped with clearing out the BPA, I'm sure, as well. But it shut that particular gene down. And when that gene is on, it's the obese blond, you know, type.

00:38:15:01 - 00:38:33:22

Dr. Kara Fitzgerald

So yeah, that's a that's a great example. And they've looked at that. They've the agouti mouse model has been investigated in a lot of different arenas. Genna Stein was actually beneficial in one of the studies. But the wild thing about that, the whole agouti mouse research, is that other scientists look around to see how many generations it would influence.

00:38:33:22 - 00:38:42:04

Dr. Kara Fitzgerald

So generation zero gets it, the pregnant mom gets it, and then they look at it through generations and I think up to six generations.

00:38:42:05 - 00:38:43:08

Dr. Jaclyn Smeaton

Or 7 in 1 study.

00:38:43:12 - 00:39:06:07

Dr. Kara Fitzgerald

Influence. So that baseline exposure to those methyl donor nutrients influence gene expression. Seven seven generations out in a mouse model. It's extraordinary. And we can see that. We can see that in human data as well. You know, in populations that have experienced starvation, you know, generation one, you can look out populations that experienced food adequacy or excess food.

00:39:06:07 - 00:39:26:06

Dr. Kara Fitzgerald

I mean, there's been some there is some human data on that, and there's some interesting data on quantity and exposure to B12 and Foley, you know, in utero and birth outcomes. Actually a U curve. And for about a Johns Hopkins, associating it with increased incidence of autism, possibly as well.

00:39:26:08 - 00:40:06:05

Dr. Jaclyn Smeaton

It brings me back to your kind of original. The original question we started this talk about, which was around the estrogen metabolism and looking at methylation. And it gets me thinking like your hierarchy concept is really interesting. And if we looked ever before at the patterns that we might see in a more toxic population or a more stressed population, because that what you're proposing, Kara, makes me think that if estrogen metabolism was not the primary, you know, place for methyl donors to go in the hierarchy, there could be other factors beyond, you know, just the adequacy of those donors that would affect methylation in our Test.

00:40:06:05 - 00:40:08:14

Dr. Kara Fitzgerald

Yeah. For yeah. Yeah. You could all the.

00:40:08:14 - 00:40:26:16

Mark Newman

Toxins have fennel groups and then you end up in that same need for methylation to get rid of whether it's, you know, benzene type compounds and all of those. One of the questions I've got that's related that I wonder if you could shed some light on is like, I'm a good example. I have this CMT defect.

00:40:26:16 - 00:41:06:15

Mark Newman

Right? So if I take methyl support, it gets better. It's hard to get it to really move the meter a lot. So if I just, narrowly focused on that and I overdo it and so I'm just methylation the crap out of other things potentially, I don't know. But my estrogen is still struggling. So if I'm over if I'm overdoing the solution to that problem by adding methyl donors into the mix, etc., etc., then if I then move my focus back to epigenetics and that world, and I've put my gas is maybe the wrong, analogy here, but if I, if I've done too much to push that, so what is the consequence potentially

00:41:06:15 - 00:41:13:13

Mark Newman

good question of excessive methylation on that front. Yeah. While I'm trying to affect something that's still struggling with under methylation.

00:41:13:14 - 00:41:38:07

Dr. Kara Fitzgerald

And the what would the solution. So there is there is literature out there, you know suggesting and this was another one of our original concerns and questions. You know, our field a while ago went through a phase of fairly aggressively prescribing method. Right. Oh yeah. Very high dose folate. Maybe it was folic acid. And then we started using, you know, bioidentical.

00:41:38:09 - 00:41:39:16

Dr. Jaclyn Smeaton

Grams of it, rams.

00:41:39:16 - 00:42:09:20

Dr. Kara Fitzgerald

And rams in very high dose B12 and not and that was a piece of our original research question like could you be pushing methylation aggressively forward. And I think that the answer is yeah I think it's possible. So going back to aberrant or imbalanced hypermethylation and going back these tumor suppressor genes that can get methylated and inhibited, or that John Hopkins paper where there was a U curve.

00:42:09:20 - 00:42:38:04

Dr. Kara Fitzgerald

So you know, higher levels of, of, of methyl donors in, the blood of the pregnant women had some negative outcome in offspring, as did deficiency. So the the literature is clear that insufficient methyl donors is a massive a problem for many. Sure. You know, in cancer being one of them for sure, like DNA repair and all of the

important thing methyl donors too.

00:42:38:06 - 00:43:07:21

Dr. Kara Fitzgerald

But access there is suggestion that it could also similarly play a role in driving forward some conditions in particular, you know, one that I talk about in the book is, you know, is cancer. And and perhaps a piece of the mechanism is through hyper methylated tumor suppressor genes that protect us. So I think there's reason to be cautious about these Uber high doses long term, like we were I think we were getting in uninformed habits back in the day.

00:43:07:21 - 00:43:30:10

Dr. Kara Fitzgerald

And I think we've have since become a little bit more measured. But we were going very aggressively. And there are. So I want to say there are times when we need to I mean, for instance, Reba, folate deficiency, you know, individuals require a higher dose, higher amount of a full in IC acid to really make sure there's adequate fully entering into the, you know, just getting across the blood brain barrier.

00:43:30:12 - 00:43:50:22

Dr. Kara Fitzgerald

There are there are appropriate reasons for using it. And we also want to think about, can we get this from food because you can eat all the folate. And we increased circulating methyl folate in our participants without giving them any significantly compared to control. So we know we can increase through diet. And there's no there is no negative outcome in the literature.

00:43:50:22 - 00:44:09:20

Dr. Kara Fitzgerald

You know, on eating too many, too many greens and jacking up your folate that way. So yes, if we have to go high dose. No, you know, we're using it for this reason. We're going this high, we're going to do it for this duration, and then we're going to try a taper if we can. So that's thing one to think about.

00:44:09:20 - 00:44:44:17

Dr. Kara Fitzgerald

So don't walk. So don't leave it. Don't get too scared about what I'm proposing here. And walk away from using methyl donors because they're of an essential they're essential tool in our toolkit. Absolutely essential. And you know, pregnancy to your

point is a is a huge one. The other piece that we learned extraordinarily, that's ridiculously interesting is that these polyphenols, they're not participating in the methylation cycle directly, but they seem to have a role in directing how methylation happens so that it happened in this clean, awesome, balanced way.

00:44:44:18 - 00:44:55:02

Dr. Kara Fitzgerald

In our study, for example, we didn't increase net methylation on the epigenome as compared to the control group, but we arranged it to a more youthful pattern.

00:44:55:02 - 00:44:57:07

Dr. Jaclyn Smeaton

Fabulous. Isn't that amazing to think about?

00:44:57:09 - 00:45:17:17

Dr. Kara Fitzgerald

Yes, and I think the secret sauce is a combination of methyl donors with polyphenols. So going back to your point mark where you're working on your your Comt and you're really wanting to improve estrogen metabolism, I think that that's awesome. I think you could do it through dietary pattern, with methyl donors on top of that and just, you know, and make sure you're consuming those polyphenols.

00:45:17:17 - 00:45:30:19

Dr. Kara Fitzgerald

So of change for me in this science and just thinking about it clinically has been if I'm going to prescribe somebody, you know, a fairly aggressive methyl donor protocol, I'm going to make, I think up with, with a nice mix of polyphenols.

00:45:30:23 - 00:45:46:18

Dr. Jaclyn Smeaton

That makes a lot of sense and like what you are reminding me of, just the elegance of the biology to be able to rearrange and, you know, the interaction that we have with food and with our environment that are so critical, you know, we only have about a couple of minutes left. I want to bring it back to your book again.

00:45:46:18 - 00:46:03:16

Dr. Jaclyn Smeaton

If you guys want to learn more, we'll put the link in show notes to get Doctor Kerry Fitzgerald's book *Younger You*. If you could give a couple of key clinical takeaways you

hope clinicians would get when they read your book, especially in context of DUTCH Testing, what are the things that you wish they would really take away?

00:46:03:18 - 00:46:46:04

Dr. Kara Fitzgerald

But, yeah, thanks. Thanks. That's a good question. So you are going to get a nice snapshot of methylation outside of the DNA, you know, using the DUTCH Test. I mean, and I think that it's absolutely essential to see that we're doing it cleanly. I would say that if you see imbalances, which is ridiculously common, you know, you may then turn the volume up and look at homocysteine and dance around the methylation cycle and infer that it is possible that epigenetic methyl at optimal, you know, given what you're picking up on the DUTCH.

00:46:46:09 - 00:47:15:12

Dr. Kara Fitzgerald

So I think the DUTCH could be a nice entry point for people who aren't thinking about epigenetics to think about it. We just talked about methyl donors, I am I supplementation is absolutely is is absolutely indicated in certain cases. But you can do the dietary pattern and increase methyl donors and improve outcome in the DUTCH Test. With we prescribe the younger you dietary pattern.

00:47:15:12 - 00:47:45:23

Dr. Kara Fitzgerald

We prescribe components of it to all of our patients. And we also obviously use the DUTCH, you know, with the vast majority of our patient population as well, with or without methyl donors. So we have data in both cohorts. And this will move the needle and help favorably augment, you know, some of the, some of the imbalances that we encounter on the DUTCH so we can use it, what would I say for so, so don't forget the power of the diet.

00:47:46:00 - 00:48:06:03

Dr. Kara Fitzgerald

I mean, it really works. We don't always have to immediately go to a supplement and start here. We can come back to here and move away from the supplements, perhaps sooner. So yeah, I would do it. And one and just since we are talking to clinicians, there's a section, there's a brief section in the book. We have much clinical experience doing this.

00:48:06:05 - 00:48:26:12

Dr. Kara Fitzgerald

So I included a table of modifying the younger you dietary components in Sibo, in, you know, in, in, in celiac if you're going to do it with an elimination diet, if you're if you want to keto lean. All right. The common kinds of conditions that are dietary patterns, I've been practice I covered in the book because we just have a lot of experience.

00:48:26:13 - 00:48:40:00

Dr. Jaclyn Smeaton

Wonderful. Doctor Fitzgerald, thank you for your commitment to functional medicine and the way that you advanced the field. It's inspiring and we're really lucky to have you as a, you know, part of our DUTCH family and also here on the Podcast today. So thank us.

00:48:40:01 - 00:48:42:06

Dr. Kara Fitzgerald

Thanks for having me both. Thanks, Kara.

00:48:42:08 - 00:48:46:00

Dr. Jaclyn Smeaton

Martin. So glad you should be on the Podcast more because it's really fun. Yeah.

00:48:46:02 - 00:48:47:03

Mark Newman

Yes, we can nerd out.

00:48:47:04 - 00:48:48:19

Dr. Kara Fitzgerald

I like it. Yeah. It's so.

00:48:48:19 - 00:48:51:06

Dr. Jaclyn Smeaton

Great.

00:48:51:08 - 00:49:04:00

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