

[176: Resiliency Radio with Dr. Jill: Interview with Dr. Kara Fitzgerald on Aging in Reverse](#)

Dr. Jill 00:12

Hello, everybody, and welcome to another episode of Resiliency Radio with Dr. Jill. Today I have a special guest and longtime friend, Dr. Kara Fitzgerald. I will introduce her in just a moment.

Dr. Jill 00:23

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Dr. Jill 00:46

Today we are going to talk about aging in reverse. You might think this is science fiction, but now we have so much science to back up not only testing and determining what our biological age is but also the practical interventions—some very, very practical things. We're going to dive into what you can do based on the science. What I love about Dr. Fitzgerald is that she is all about the science and the research. We're going to nerd out today, so stay tuned and hang on. Let me just introduce her and we'll jump right in.

Dr. Jill 01:18

Dr. Kara Fitzgerald received her Doctor of Naturopathic Medicine degree at the National University of Natural Medicine in Portland, Oregon. She completed the first Council on Naturopathic Medicine-accredited post-doctorate position in nutritional, biochemistry, and laboratory science at Metametrics Clinical Laboratory. You and I both know that was years ago. I remember your first lab book, which is one of your first or second publications. There were all those case studies, Kara, and you did such a great job. Way back in the beginning of functional medicine, all of us were trying to pave a new road. You were part of the *Case Studies in Integrative and Functional Medicine* as a contributing author and did *Laboratory Evaluations for Integrative and Functional Medicine*. Both of those were on my bookshelves in the beginning.

Dr. Jill 02:04

As I said, we've known each other for a long time, and I've had such great respect. You publish a lot of different things. You've been a research clinician for the Institute of Therapeutic Discovery. You've been on the faculty for IFM. And I could go on and on. Your website is DrKaraFitzgerald.com. At the end and in the show notes, we'll leave all the links to where to find you. But welcome to the show.

Dr. Kara Fitzgerald 02:24

Thank you! Yes, it's going way back. I appreciate the shout-out for that *Case Studies* book. It was a pretty intense journey, but it was so awesome to write down what we do. Really, how do we practice this system's medicine called functional medicine? I still appreciate it, even though it's over 10 years old.

Dr. Jill 02:49

I do, too. And it's so relevant. You and I have been practicing [medicine]; we've been doing it for so long that it starts to come naturally. But when someone's first learning, there's no textbook for what we do. As I'm even training my clinic nurse practitioner, oftentimes she's like, "Where do I find this information?" I'm like, "I can tell you, but I don't know that there's a reference in a textbook about how to exactly approach it." And of course, we are all creating more and more pathways and case studies. And I think now, 10 or 20 years later, there's so much more out there. But still, it's really interesting when someone observes you in clinical practice or observes me, because there are not 20 textbooks out there that document it. So I really do appreciate that.

Dr. Jill 03:33

First of all, let's start with a little bit of the story about Dr. Kara. How did you get into functional medicine? Have you always wanted to be a doctor? Tell us more about your journey to where you're at now.

Dr. Kara Fitzgerald 03:47

I was thinking about medicine, conventional MD, and psychology. And take these together. As I was getting ready for my next move, doing my various graduate entrance exams, I was sitting with it. I was working in a health food store at the time in the supplement section. I also developed chronic fatigue. I had a lot going on. I was burning the candle at both ends and ended up developing classic chronic

fatigue. But all of these balls were happening in my life. My landlady at the time sent me to her physician, who turned out to be a naturopathic doctor. I had fatigue. I went to all sorts of standard medical doctors.

Dr. Kara Fitzgerald 04:37

One guy was sophisticated enough to prescribe B vitamins. I remember it being really interesting to me to get B vitamins in that classic orange bottle. But nothing got me better. They didn't find anything. So she sent me to her doctor, who turned out to be a naturopathic physician. He got me better quickly and pretty simply with some basic botanicals. He didn't strongarm me with diet. I was young at the time, and I don't know how much I would have done, but he made some suggestions to improve it. He gave me some Coq10 and a handful of combination botanicals. Before long, I was absolutely better. I was pretty blown away by that.

Dr. Kara Fitzgerald 05:23

After that experience with my first naturopath, being in a health food store, and being exposed to supplements, I found myself getting excited about the mechanisms. We would get white papers all the time. I remember that there was a popular book, *Fats That Heal, Fats That Kill*. You remember the book. It was famous. It was a long time ago, but it was famous. I was learning about omega-3 fatty acids, eicosanoids, and all of this. I was really excited about it. That informed my decision when it came time to decide on medical schools; it just made sense for me to become a naturopathic physician as I did my research. My training was extraordinary. All of it was inspirational and satisfying.

Dr. Kara Fitzgerald 06:21

I did have a penchant for biochemistry. I was in the Pacific Northwest. I was able to see Jeff Bland lecture routinely. He was lecturing a lot at that time, specifically in the Pacific Northwest. I ended up getting a postdoctoral position in a lab, as you know. That's probably around the time that we met when I was there under the direction of Richard Lord, who's a highly regarded nutritional biochemist. It was like dream after dream after dream came true. I started to speak. I had opportunities to do a really heavy, heavy drill down into the research, writing laboratory evaluations in integrative and functional medicine, as you mentioned. Our laboratory textbook was a huge part of my postdoctorate work.

Dr. Kara Fitzgerald 07:09

And then after that was the *Case Studies* book. In the *Case Studies* book, since we were writing in the functional medicine model, we were using the matrix, timeline, etc. "The Matrix: Antecedents, Triggers, and Mediators." At the time, that's what they had. That was the tool they had [inaudible] timeline out. David Jones, who was the chief medical officer and co-founder of IFM, started to mentor me. He didn't know who I was; I was just a young upstart at the time I was writing the book. But he wanted to keep an eye on this person who was going to be publishing something using the functional medicine structure. I just consider myself so blessed to have these weekly meetings, week in and week out, with David Jones. We would talk a little bit about what I was doing in the book. And mostly he would just, I don't know, give me sort of like zen transmission of information in functional medicine. It was just extraordinary. At the end of that, he asked me to join the faculty at IFM. I think that was my proving ground. But what a blessed career to start in that juicy way that felt designed beyond anything I could have, beyond my wildest dreams.

Dr. Jill 08:27

Right. I love it. And yet, in that, I see that your brilliance is that curiosity, that is the mark of genius, that "I want to know more. What's the mechanism?" And one thing I love about what you brought to our field is that I remember that lab textbook so well. Even on my shelves now, there's still nothing out there like that. I love to dive in and look at the pathways and figure out what the testing might show. And at the core, for those of us who really, really love functional medicine, we have to love biochemistry because it's all about going back to what we were taught peripherally in medical school. But most of us forgot and never really used that. And now we're going back to really, really diving in. I think those of us like you and me who really, really love what we do get fascinated by these pathways, right?

Dr. Kara Fitzgerald 09:12

Yes. They have so much more meaning when you look at them through the lens of functional medicine and nutrition. They become so much more meaningful than just memorizing pathways because you have to spit them out on your exam.

Dr. Jill 09:28

I always have such a deep respect for naturopathic medicine because you have paved the way with basically nutritional biochemistry in your field compared to us allopathic nutrition-poor physicians who have very little training. I'm sure you

know this, Kara, but my training in medical school was about six weeks of TPN, which is IV nutrition after surgery. And that was almost it. So everything else has been much, much on my own. And hopefully, now they're starting to incorporate a little bit more, but it's amazing how little nutrition the average doctor understands.

Dr. Kara Fitzgerald 10:03

I know. It's astonishing. And I do think the field is changing. I think that it's expanding. But yes. It's mind-blowing that it was not important or relevant.

Dr. Jill 10:15

So let's talk about this new thing. First of all, for those who aren't aware, I want to pave the groundwork [about] what this is. But you have a new article and you have lots of stuff you've published on your website and in podcasts about studies and information using epigenetic modeling for biological clocks. What does that mean? Tell us a little bit about that.

Dr. Kara Fitzgerald 10:35

Yes, sure. And just to bridge it with my background, I think being in an early Omics Lab where we were doing these broad investigations into fatty acids, amino acids, and organic acids was a good foundation for me to eventually, in my career, want to do this deep dive into epigenetics and just make it possible for me to think about it. [The prefix] epi- [means] above; genetics are genes. And this is studying the biochemical marks that influence what genes are on and what genes are off.

Dr. Kara Fitzgerald 11:10

And just a little bit of background: We thought that we were going to have the Rosetta Stone for all diseases when we mapped out the genome in the early 2000s. We thought that would be our answer. And it turned out that it wasn't, of course. Our genes aren't our destiny at all! That leapfrogged us into the era of epigenetics: What influences what genes are on and off? And that's the environment. There is a heritable portion that we can talk about. But really, by and large, it's our choices day in and day out: What we're eating, doing, saying, being, and breathing. All of this interconnection experience of being in the environment or exposure is what dictates whether we age well and live long or succumb to the plethora of chronic diseases. So this is the field of epigenetics. And it's just getting bigger, bolder, and brighter all of the time. We can really look at gene expression. Do you want me to give you a little background on how I got into it? Should I?

Dr. Jill 12:16

Yes.

Dr. Kara Fitzgerald 12:17

It was probably around 2013–15 that the papers on epigenetics were crossing my desk. At that time, the bulk of the research was on cancer, and still a lot of it is. Cancer very efficiently takes over gene expression from us. The tumor microenvironment will turn genes on that it wants on for survival and turn genes off that it wants off. Very predictably, very reliably, we can test reliably for cancer by looking at these different patterns of epigenetic marks. It's just really powerful and really predictive.

Dr. Kara Fitzgerald 13:00

It's funny; I was in clinic practice at the time. I think I had a journal club. I found myself—this is ironic, it's so ironic—[saying something] like, "Oh, God, I need to do this!" I knew that it was important, but I was a little bit reluctant to drill down into the complete rebuilding of my brain to dive into it and understand it. Believe it or not, there was a little bit of reluctance from this person, who's so eager for mechanisms. I think these papers were in a language just sufficiently different from where I had been so deeply trained, even though it was an extension of where I came from. I remember that little bit of inertia that I experienced. Sometimes I wonder if it's because, at some level, I knew it was going to completely change my career.

Dr. Jill 13:51

I was going to say, "hijack everything."

Dr. Kara Fitzgerald 13:55

Yes. It was going to just take me over. But as I dug into the science, the overarching question for me was, "What are we doing in functional medicine?" There was no doubt in my mind that we were changing gene expression. Was it all good? Was there a possibility that we might—with our heavy focus on methylation, our heavy reliance on methyl donors, and so forth—be doing something we don't want to do, because we haven't had these tools to look at it that carefully yet? It was potent enough for me to decide, with my strong nutrition team here, that we could design a diet and lifestyle program. And it started as a diet.

Dr. Kara Fitzgerald 14:43

There's no doubt that methyl donors are important: B12, folate, choline, betaine, etc. We need to be bathed in them. And as we get older, we need more. There's some suggestion that when we take them in isolation, as vitamins, there could be in certain situations—I talk about in the book that we can talk about more—that we want to be a little bit more nuanced or careful. Diet, however, is all beneficial. There are some neutral papers. But really, by and large, eating loads of greens is never a bad thing. Eating some liver, having eggs, and consuming lots of methyl donors in a diet is nothing but beneficial. That was our first piece of information. Let's build this methyl donor-dense diet.

Dr. Kara Fitzgerald 15:33

The second cool understanding from the literature was that these beautiful polyphenol compounds that we use every day, day in and day out, all of us know they're healthy. They have long-time use histories in traditional medicine around the world—things like green tea, curcumin, turmeric, resveratrol, luteolin, quercetin, and on and on. These guys seem to influence DNA methylation potently, but not by making methyl donors in the methylation cycle, not by producing S_AMe, but by directing how methylation is happening on the genome.

Dr. Kara Fitzgerald 16:12

Most of the research at the time of my first read in this was in cell studies, and there were some in animals. Sulforaphane was a really cool one. But these polyphenols and these phytochemicals had very important roles to play. Plus, we know that they're anti-inflammatory, anti-cancer, antioxidant, and on and on. So we wanted to combine the dietary pattern with these two components and then have it keto-leaning. We had good fats in it. We just layered everything into it that we knew would be smart.

Dr. Kara Fitzgerald 16:53

Then we looked at the literature on exercise, sleep, meditation, and so forth, and we saw that all of them act similarly. When we look at gene expression, epigenetics, and DNA methylation in particular, all of them behave like food—like kale. They all can help shape gene expression in this optimal way. So we put together our diet and lifestyle program. It was very exciting. And then we started to use it here in the

clinic. We wanted to research it immediately, but at the time of development, there were no epigenetic tests like we have available now—[none] at all—outside of the research setting. We were blessed with an unrestricted grant.

Dr. Jill 17:35

Like clinical [inaudible] in the beginning, right?

Dr. Kara Fitzgerald 17:39

Yes. Then we got to research it. We started to use it here in our practice all the time. We saw great outcomes with it. We saw homocysteine drop—a classic marker of methylation. We saw that we could change it with this diet and lifestyle intervention. We saw that we could drop inflammation. We saw that people would feel better. We saw that it was providing benefits to our patients. But are we actually changing gene expression? Are we changing epigenetics?—which is our hypothesis. This is what we think we're doing. We released it on white paper and just made it available to you guys, our colleagues.

Dr. Jill 18:14

And is that on your website?

Dr. Kara Fitzgerald 18:18

Now it's the book. Now you can get *Younger You*. The book is a much more involved conversation. But back in the day, we had the white paper that we released.

Dr. Jill 18:29

If you're listening, stay tuned. We'll have links to *Younger You*. I just want to make sure. Everybody who's listening is like, "Where can we get this information?"

Dr. Kara Fitzgerald 18:37

Yes. And the book is in plain language. It's easy to read. We used it here, but we wanted to research it. And then there was this cool turn of events where we were given an unrestricted grant to study this by Metagenics. I was friends with the then-CEO, Brent Eck. He and I were talking about the power of methyl donors in the era of being able to see gene expression. I remember very vividly, Jill, that we were sitting on the floor at the IFM conference when it was in San Diego. At the annual conference, we were sitting on the floor out by the registration, just very humbly, deep in conversation on this. He offered to let us embark on researching it.

At the time, I was like, "Geez, maybe it'll be \$10,000." Six figures later, we did it. When we embarked on this, reversing biological age was not thought to be possible.

Dr. Kara Fitzgerald 19:47

We started our IRB. We started the research back in 2017, and we launched our study. Our study ran through 2018 and 2019. At that time, biological age reversal was believed not to be possible. In fact, the guy who arguably started this whole biological age conversation, who developed the first clock, Steve Horvath, then out of UCLA, now he's at Altos Lab—actually, I think he's still at both—Jeff Bezos lab. He developed the first clock. He's on record saying many times that he did not think that we could reverse biological age as measured by DNA methylation patterns.

Dr. Kara Fitzgerald 20:30

When we were midway into our study, the first publication came out. There were two, one looking at low vitamin D [levels] in obese African Americans. When they repleted vitamin D levels, their biological age reversed. They had the biological age measurement and they were able to turn it back by almost two years over a 16-week study, I think.

Dr. Kara Fitzgerald 20:50

Then there was the TRIM study, which was a year-long study using growth hormone, DHEA, vitamin D, and metformin. And that intervention—which Steve Horvath, the clock developer, was an author of—turned back biological age by over two and a half years. I remember when that came out; it was such a huge deal. I was paying very careful attention to epigenetics at the time and that study came out and it was like time stood still in the scientific community.

Dr. Jill 21:19

It was like, "Okay, it's possible."

Dr. Kara Fitzgerald 21:21

Yes, it was a big deal. We knew we had the information; we measured the DNA methylome to look. That was one of the first things that we wanted to look at. We're still mining our data. But I remember the day that our biostatistician told me conclusively that, as compared to controls, study subjects got over three years younger. It was big. It was a big moment.

Dr. Jill (pre-recording) 21:56

Hey, everybody. I just stopped by to let you know that my new book, *Unexpected: Finding Resilience through Functional Medicine, Science, and Faith*, is now available for order wherever you purchase books. In this book, I share my own journey of overcoming a life-threatening illness and the tools, tips, tricks, hope, and resilience I found along the way. This book includes practical advice for things like cancer and Crohn's disease and other autoimmune conditions, infections like Lyme or Epstein-Barr, and mold- and biotoxin-related illnesses. What I really hope is that as you read this book, you find transformational wisdom for health and healing. If you want to get your own copy, stop by ReadUnexpected.com. There, you can also collect your free bonuses. So grab your copy today and begin your own transformational journey through functional medicine and finding resilience.

Dr. Jill 22:52

In *Younger You*, you outlined this. And we don't have to go into all that, but give us just a little bit of a glimpse. You talk about diet. What are the core principles of diet? And then what would you say are the top three, four, or five things—maybe sleep—that do move the needle?

Dr. Kara Fitzgerald 23:09

Yes, it's such a good question. I think every fork full of food should be packed with epinutrients, period. We should always be eating methyl donors and what we call methylation adaptogens—those polyphenols I mentioned earlier, or phytochemicals. That information taken together is incredibly important. Also, [being] exposed to good fats [is important]. We don't want it laden with sugar. We want to minimize chemicals.

Dr. Kara Fitzgerald 23:45

In our study, we didn't require organic. Otherwise, we would have had to provide food and we didn't have the income for that. I'm glad that we didn't, because I think that's important information that you can do it [even] if you can't afford organic. But we want to minimize the chemicals and exposures. We want good fat. We don't want sugar. We don't want a lot of foods that are going to kick in high-glycemic cycling. It was keto-leaning. It was anti-inflammatory and hypoallergenic. It has all of the hallmarks of a solid dietary eating pattern, probably more strict than all of us

need to be all of the time. It was only an eight-week intervention. Some people were like, "Oh, my God, I can't do this forever."

Dr. Jill 24:28

That's impressive. You can make a change in eight weeks. For example, it is likely gluten-free, dairy-free, mostly sugar-free, and refined carbohydrate-free. Then, fat-wise, are you giving them fish oil? Are you doing no canola and no processed seed oils? Are there any specifics on fat?

Dr. Kara Fitzgerald 24:50

The specifics were olive oil. You could do some coconut oil if you were inclined. We wanted them to eat fatty fish. That was a routine requirement. We primarily added fats that we wanted them to consume.

Dr. Jill 25:06

Perfect.

Dr. Kara Fitzgerald 25:11

You got it. Those dietary principles are really beneficial.

Dr. Jill 25:14

Yes, those things are universal. And plants are part of that. I use all spectrums of diets, but at the core, we must have these phytonutrients to influence our genome. Were there any criteria for hours of sleep, activity, or meditation that were required?

Dr. Kara Fitzgerald 25:31

Yes. Then let's circle back, and I want to just give you my thoughts on the multiple things that were the heavy lifters. We wanted people to move five days a week. They needed to engage in exercise for at least half an hour, at least five days a week, with a perceived exertion of 60–80% of their maximum—whatever they thought was 60%. [It was based on] what they thought. It's interesting because that's an accurate tool. People tend to know what 60% is for them. We specifically kept it simple and used that, and they could do whatever they wanted to, whatever made them happy. [At] 60%, you can still talk. You can still carry on a conversation. Maybe you're walking, or you're walking with your friends, or you're on the phone. At 80%, you're

still able to talk, but you're breathing heavier, you're perspiring, and so forth. That was the criterion there.

Dr. Kara Fitzgerald 26:31

In the book, I write about a little more involved exercise pattern—high intensity and resistance training and all of that. Those things are important. But this is the fundamental entry into lifestyle change. Let's keep it simple. Let's do something that you love to do. In fact, do whatever you want to do as long as you hit these targets.

Dr. Jill 26:51

What I love about that is that so often people are overwhelmed, so they don't do it right. I just want to pause there and say that this is doable. You made it [inaudible] to do this. And then we can figure out all the details, but that was really important.

Dr. Kara Fitzgerald 27:03

Yes. Just join the conversation. Let's start the party. Let's keep it simple. My mom is a gardener. That's her thing, and she walks around her block. She lives in a really nice neighborhood. They've got great sidewalks, and that's her thing. I love riding my bike and talking on the phone. I can get a good workout and still catch up with my girlfriends or sometimes even attend a meeting—whatever works for us.

Dr. Kara Fitzgerald 27:29

Sleep is essential. From the data on sleep in humans and animals—which at the time was mostly in animals—we could see that insomnia damages gene expression. It damages the DNA methylation of neurons and gene expression associated with neuronal development—immediately. One poor night of sleep deprivation has been shown to be damaging. Now we can see in humans that not sleeping well is a pro-aging phenomenon—no great surprise there. You are accelerating your aging, and then, of course, you're at risk when you're not sleeping for all the chronic diseases of aging, which are all associated with accelerated aging. Sleeping is essential. We wanted people to get at least seven hours.

Dr. Kara Fitzgerald 28:17

Part of our program required our participants to meet with a nutritionist once a week. We would ask them about their quality of sleep and brainstorm with them on

sleep hygiene tips, making sure they're getting enough runway to get enough sleep. If you go to bed too late and you have a [set] time you have to get up, you're not going to get enough sleep, period. Those basic sleep hygiene tips—figuring out whatever pattern you need—were helpful, I think, for our participants.

Dr. Kara Fitzgerald 28:48

Sleep, exercise, and yes, to your point, meditation. I think stress is gasoline on the fire of aging. I think it's incredibly potent. In the clock that we used in our study, a full 25% of it is associated with glucocorticoid response elements. In other words, it's changed by the cortisol response and the stress response.

Dr. Jill 29:09

I was just going to ask if there was evidence of cortisol's effect on epigenetics. When we look back, even for transgenerational epigenetics and Holocaust survivors, that's where I'm like, "Cortisol absolutely affects expression." You're saying the studies show that corticosteroids do affect it negatively if it's too high.

Dr. Kara Fitzgerald 29:32

Yes. I think so. We can see 25% of it. There's no other variable that influences this particular clock as potently. I think that suggests that stress is this extraordinarily huge, perhaps underappreciated variable. It's such a big deal. And it's an interesting conversation around Holocaust survivors. We can see that in the offspring of the World Trade Center [victims]. That was a single event. The Holocaust was longer, but you can see these inherited stress patterns.

Dr. Kara Fitzgerald 30:17

Meditation. We prescribed a twice-daily breathing exercise, [which is] very simple, called the Relaxation Response by a guy named Herbert Benson, who was at Harvard in the '70s studying meditation. But he wanted to take the woo-woo out, so he called it the Relaxation Response. Especially in the '70s.

Dr. Kara Fitzgerald 30:39

We gave two supplements. We did a probiotic, *Lactobacillus plantarium*. We chose that one specifically because there's some evidence that it can help produce folate—bacterial, microbiome-derived folate. It can help with that in the presence of adequate PABA, or B-vitamin PABA. And we did, Jill, increase circulating folate in our population significantly as compared to controls—without any folate in sight,

just food and the supplement. Then we gave an additional greens powder. This is evidence of my being very bullish on these important polyphenols. We gave them another dose, even though the dietary pattern is about seven to nine cups of veggies a day. You're going to be eating a lot of veggies during the eight weeks—make no mistake. We layered some more in.

Dr. Jill 31:29

Nice. I love that because that's so critical. This is all in your book, *Younger You*. But of all of the factors that add to the positive outcome, what about the elephant in the room—the environmental toxic load? I doubt that it was easy in eight weeks to study that, but I would just like, outside the study, your comments on what you see. Environmental toxic load, molds, metals, parabens, phthalates, pesticides, all these things—are there any studies out there that show a specific aging propensity for these chemicals or things? Any thoughts on that?

Dr. Kara Fitzgerald 32:09

I'm sure that there are. I want to say that there have been investigations looking at the urban environment versus the suburban environment. In fact, I think that was a recent publication [about] exposure to pollutants in the urban environment. Certainly, we know smoking is going to push biological age forward. We know without question that those toxicants disrupt gene expressions, specifically DNA methylation, but they get in and mess with epigenetic expression via a variety of mechanisms.

Dr. Kara Fitzgerald 32:48

There was a disturbing study looking at exposure to DDT and other chemicals in generation zero mice and tracking the damage through generations in the sperm of generations two, three, and four, and it went multiple generations out. And actually, the influence got worse over time. It was potentiated in this one study. But yes, there's more and more evidence linking the damage of these environmental toxicants.

Dr. Kara Fitzgerald 33:31

Moshe Szyf was a mentor in our study. He's a highly regarded epigeneticist at McGill University. And the fact is that it doesn't take a lot to influence gene expression. We're not looking at EPA levels of [inaudible] compounds or huge

occupational exposures when people worked in felt factories or whatever. Multiple low-dose synergistic exposures are wreaking havoc. Not necessarily directly damaging the DNA, although that obviously happens, but wreaking havoc with gene expression via DNA methylation. So yes, I think there's plenty of evidence and papers coming out all the time.

Dr. Jill 34:21

And especially in the field of cancer, we know these toxicants have a huge effect. And that's all about methylation—over-methylation, under-methylation, and everything in between. I love that you mentioned that. Traditional toxicology, as you and I know, has this nice curve. There's a chemical level where 50% or greater of the population is affected. But as you and I are talking, when we've learned about the research on endocrine disruptors, this happens with a very hormetic effect. It's almost like two stages of those chemicals where they can have a very low-dose synergistic effect. When they are combined, it is sometimes more toxic. I don't know if I can quote the study to prove this, but I'm guessing that these synergistic, hormetic, low levels in combination are probably a lot more damaging to the DNA.

Dr. Kara Fitzgerald 35:09

We can certainly say that they're influencing the course of all of the diseases. That's how we are exposed. I will say, interestingly, that I see really high levels of mercury these days and people attempting to buy really clean fish. I think some of our classically clean, wild-caught fish are no longer so clean. I am seeing higher burdens of certain toxins, especially mercury. But I think in general, all of us are experiencing the synergistic interaction of low-dose multiple compounds.

Dr. Jill 35:49

We're swimming in it, right? You can't avoid that.

Dr. Kara Fitzgerald 35:53

One of the cool things—let me just say this really heartening thing—is that this diet, by its nature, cleans us up from those compounds. It's dense with cruciferous veggies. It's dense with compounds that can reverse some of the damage. There's a really cool toxicologist at the University of Kentucky, Bernhard Hennig. I hope I have him on my podcast one of these days. His work looks at how you can offset the damage of these toxins through nutrition.

Dr. Kara Fitzgerald 36:31

PCBs come to mind. It was a study that he looked at. PCBs will drive the arachidonic acid-eicosanoid cascade. They'll turn up all of the enzymes involved in pushing forward one of the most aggressive forms of inflammation that we experience in our body. You can turn that off if you're eating adequate omega-3 fatty acids or having some of the really important polyphenols. So a healthy diet all of the time is one of our most essential defenses.

Dr. Jill 37:01

Yes. I love that you say that because I always say: Clean air, clean water, clean food. All these fancy supplements, these fancy programs, and these fancy biohacking things are great, but you can do 80% of the work if you really focus on breathing clean air, drinking clean water, and eating clean food. And that's kind of what you're saying as well.

Dr. Kara Fitzgerald 37:19

Yes. That's right. Absolutely.

Dr. Jill 37:26

So the last few minutes here. Two things I want to talk about. One is that there are a lot of tests coming out and now we can test our biological age. What are your thoughts on testing? It feels like it's exponentially increased—the companies that are doing it. Tell us just a little bit for the person who doesn't know anything about this: What would the tests do? And tell us a little bit about your thoughts on that.

Dr. Kara Fitzgerald 37:51

I'm very excited. It's a little crazy out there right now. There are a lot of companies coming out with a lot of biological age clocks. But it's really exciting. The winners will rise to the top, so we'll see the tests that are the best. They're measuring epigenetic expression, specifically patterns of DNA methylation that are associated with biological aging in some shape or form. There are clocks that are perhaps looking more at physical fitness than biological aging. They're measuring different aspects of physiology and function.

Dr. Kara Fitzgerald 38:33

The clock that we used was a first-generation clock. They're now into the third, maybe even fourth, generation of clocks. We used the Horvath original multi-tissue

clock, which I think is still a good, solid clock. It functions in any specimen. We used saliva. We didn't know back then that there were going to be other clocks. We didn't know that biological aging was going to be a big deal. We used saliva and that was the only clock that was reliable for us at the time. I still think it's a solid workhorse clock, measuring a general pattern of biological age. It's able to be used in any tissue. I like the pace of aging clock. I think that there's some good science.

Dr. Kara Fitzgerald 39:21

What I would say to people listening is that whatever lab you go to, I think we want to work with a company whose clock has been published in the literature. They're using it in research. Ideally, the components of the clock—the measured CpG sites and the methylation sites—are known so that other labs can try it and see its reliability, and we know how they trained and developed the clock. I think those things are important. The more open people are with that knowledge, I think, the better. I still think there are some good-quality clocks that are proprietary. I actually do. I really do. But I err on the side of keeping science open. We're currently using the pace of aging for our research. It's a pretty affordable tool and it's got a bunch of studies behind it.

Dr. Jill 40:24

Amazing. I'm assuming you've had your biological age tested.

Dr. Kara Fitzgerald 40:29

Yes, for sure.

Dr. Jill 40:29

You were happy with the outcome.

Dr. Kara Fitzgerald 40:31

Yes. I am happy. In my pace of aging—the DunedinPACE of aging—if you're aging at a rate of one, you're consistent with your chronological age. If you're greater than one, you're over, and if you're under, that's better. My DunedinPACE of aging, I think, is—I have to look at it; it's been a while—between 0.7 and 0.8, I think.

Dr. Jill 40:58

Beautiful! I think I'm right there with you on that. I was like: "Yay! I'm doing the right stuff."

Dr. Kara Fitzgerald 41:04

Yes. I know that it does change with exposures. It's probably a good idea for those of us who are healthy to do it annually and make sure we're reasonably dialed in. [We can try] doing the pace of aging. We can still get the Horvath and we can get other clocks. But yes, I think it's a useful tool to do.

Dr. Jill 41:31

I do, too. There's more information in your book, *Younger You*, but one comment I'd love to make is that I had cancer at 25, massive chemotherapy, and massive toxicity exposure. So I've done a lot of work. I want to say that out loud because even though my biological age is a little bit better than the average, potentially, I feel like it gives hope to those who are in crisis and maybe have had mold exposure or maybe have had cancer like myself. If I can do it, the average person... And I've had a lot of hits to my genome and to my epigenetic [inaudible]. And I thought that was really encouraging because I would expect that with all that my body has been through in my life—all the chemicals, chemo, and everything [else]—it might not be that way. And it's in a good place, which is encouraging.

Dr. Kara Fitzgerald 42:15

That's awesome.

Dr. Jill 42:16

Yes. And I'm sure you've seen that too, because I feel like there is power even after 30, 40, and 50 as we make those changes. A lot of this stuff can really transform our health.

Dr. Kara Fitzgerald 42:27

One hundred percent. In fact, there's cool research on exercise that I'd love to put out there that shows we do better epigenetically the older we are. So there's really no time like the present to start.

Dr. Jill 42:40

No age is too late to start. Okay, last bit before we let people know where they can find you. There are so many things on the horizon, like peptides, biohacking, and vagal nerve stimulators. I could just name a hundred different things. What would

be one or two things that you see as bigger versus diet that could be on the potential horizon for epigenetic aging?

Dr. Kara Fitzgerald 43:08

Probably rapamycin. I think the research in animals is pretty solid on rapamycin being beneficial at a lower dose than we use in transplant patients. What else? I think that's just nearing primetime for us. It'll be interesting to see Nir Barzilai's work on metformin—what that says and who's appropriate. We know that metformin is damaging to mitochondrial health in some of us, but for some of us, it may actually extend life. There is a population for whom metformin is probably bioage reversing and we just need to tease that out.

Dr. Kara Fitzgerald 44:03

A friend and colleague of mine, Sergey Young, talks about the longevity bridge. Right now, we know it's all of the things that we advocate in functional medicine. There's probably a place for stem cells and exposomes. We know plasma exchange is probably important. These are some radical, expensive interventions that we could do right now that are gaining some evidence behind them.

Dr. Kara Fitzgerald 44:32

But the diet and lifestyle, clean living—everything that we advocate is foundational and essential, [along with] some of these other ones, [such as] rapamycin, etc. We are reversing biological age aggressively in cell models, tissue models, and animal models pretty extraordinarily. Over in Altos Lab, Vittorio Sebastiano is a Stanford scientist who's nearing FDA approval for a phase 1 study in humans using Yamanaka factors, which are transcription factors that will significantly change epigenetics towards a younger, more youthful pattern.

Dr. Kara Fitzgerald 45:14

I do believe that probably the root cause or the foundational aging phenomenon is happening in the epigenome. So putting at least a chunk of our attention there, I think, when we address all of the various hallmarks—inflammation, mitochondrial health, cellular senescence, the microbiome, etc.—is essential. But it does seem like the business end of the aging phenomenon is right there in epigenetics. I think that we need to be paying attention there. But they're doing some pretty wild stuff in animal models and cell models. In 10–20 years, we'll be playing around with aging in

a way that, when we started our journeys, we never thought possible. It was totally science fiction. But we are sitting on the precipice of some pretty extraordinary changes, I think.

Dr. Jill 46:10

Well, we'll stay tuned. And what's great about you is that you always put out great articles, blogs, and podcasts. If they want to stay tuned with this, where can people get your book? Where can they find you?

Dr. Kara Fitzgerald 46:21

Younger You is available wherever books are sold. It's that bright yellow one over there. DrKaraFitzgerald.com is my website. I also have a podcast. You can find it any place where podcasts are. We've got blogs. We've got newsletters and all sorts of stuff coming out. We're having these more cutting-edge conversations on my podcast more and more. I'm just really excited about them. So if you want to go on this journey with me, that would be the place to go.

Dr. Jill 46:54

Yes. A shout-out to her podcast because you really do bring great people and experts on. And the level of science is phenomenal, so keep up the great work, Dr. Kara!

Dr. Kara Fitzgerald 47:06

You know what? Let me just say one more thing. We have groups. For people who want to join us, do the program with us, and contribute to the research, [visit] DrKaraFitzgerald.com.

Dr. Jill 47:18

Perfect. Awesome. And anywhere you're listening, you can find this in the show notes. Dr. Kara, thank you for all the work you've done over the years. Thank you for coming on today. We really appreciate it!

Dr. Kara Fitzgerald 47:27

Yes, it was great to see you, Jill!