Introduction to Dr. Kara Fitzgerald

Welcome to this episode of the Reverse Alzheimer's Summit. I'm so excited to introduce you to my friend and colleague, Doctor Kara Fitzgerald. She's the first ever recipient of the Emerging Leadership Award from the Personalized Lifestyle Medicine Institute.

In recognition of her work on DNA methylation. She received her doctorate in Natural Catholic medicine from the National University of Natural Medicine.

She lectures globally on functional medicine, is on the faculty of the Institute for Functional Medicine as an, and is an IFM certified practitioner with a clinical practice in Newtown, Connecticut.

She runs the Functional Medicine Clinic Immersion program for professionals and host of podcasts, New Frontiers in Functional Medicine. Doctor Fitzgerald is also actively engaged in clinical clinical research on the DNA methylation, using a diet and lifestyle intervention developed in her practice.

Her first study was published in the journal aging. She's published a consumer book, Younger View, and an application based program three. Based on that study.

She lives with her daughter in Connecticut. Carol, welcome. It's great to be here with you, Heather. I can't wait to dive in. I know, so I was telling you that I was as I was reading through your materials, I was just so excited to see that one of the things that you suggest to help with aging is cuddling.

Yeah. So tell me how I mean, where that comes from. It surprised me and it brought a smile to my face. And I was telling you that it's one of the things that I recommend to my patients.

So tell me how it ended up on your list. Yeah. So I love to sort of joke about how the, you know, we didn't include cuddling as one of the variables that we measured in our study.

I mean, it's really funny because we did a control a randomized control trial. So, you know, group A, no cuddling, no cuddling for eight weeks, and then group B, you guys need to cuddle in this structured, measurable way.

I just find that so funny. But no. So we so we didn't research it. But two things that we thought, in hindsight and actually in our app that you mentioned will bring some of these things in our community, the importance of community and longevity that's been demonstrated clearly.

And cuddling, like both of them, are huge. And so we're building this community component into the app. And our app is actually we're continuing to research our, our program.

And as you know, as I'm suggesting here, refining it. So cuddling has, longevity promoting, features to it. Beyond what I'll be able to say. I mean, we could we could write a whole book on it, I think.

But, the two top things that come to my mind are, cuddling and the decrease in glucocorticoid.

Why Cuddling Matters for Longevity

So the decrease in stress hormones, sort of the balancing of this hyper, Type-A driven sort of affect. You can wind back with some cuddling, with some connection, and it doesn't have to be a human, a spouse, a significant other.

It can be a pet. It can be, you know, just a loved one of any shape or form. So on the clock that we used in our study, the 2013 Horvath Biological clock.

And I know we're going to talk about this in a minute and define it, but it measures how fast our bodies are aging our biological age. A full 25% of this clock is influenced by glucocorticoid response.

And for me, as I wrote in the book, it's like gasoline stress is gasoline on the fire of aging. And that is just one example. Like this clock is locked in to the stress response.

There's no other variable that shows up. You know, with that extent of involvement in the aging clock in stress is just a big player. And then we can look at stress across the board, you know, early life stress, you know, stress changes that can be inherited across generations.

And you can see that they just promote, aging. And they, they promote all of the chronic diseases of aging, including Alzheimer's and dementia. So the stress phenomena is massive.

And anything we can do to change that is, is extremely important. And we can change it at the level of gene expression. The other piece with cuddling, which I know you likely tell your, your patients, is the whole oxytocin release.

And, oxytocin is a longevity hormone. And so we've seen there there are studies showing an oxytocin association with longevity, like with more muscle mass.

And with you know, important components of, you know, healthy longevity, health, health span and lifespan. There are certain conditions that can be, associated with hypermethylation of the oxytocin receptor.

So what that means in plain English is that, we don't get a oxytocin response in the same way we should. So it's not a genetic mutation of the oxytocin gene.

It's a thing. But the gene is inhibited at the level of epigenetics, which again, we're going to define again. So our thinking is that employing components of the study that we we're going to dive into, will could help I shouldn't say Will, but could help shift methylation of the all important oxytocin hormone, the feel good hormone.

So, you know, for that reason, I think cuddling would have been a nice variable to measure in our study, but not realistic. That's so yeah, I don't know how we we can't control for it though.

So you describe basically two different types of aging. So I think in our minds, most of us go into this aging topic, like when we're thinking about getting older and think, oh, there's nothing we can do about it.

I've been on this planet for this many years, and that's just the way it is. I can't go back and be any younger, but your book is called younger. You.

So tell us what you mean by that and go into the differences between biological age and chronological age. Sure. Yeah, absolutely. So chronological age is the number of birthdays we've celebrated, the number of trips around the sun.

And, you know, despite the fact that my sister says, you know, every year that she's 29 again, she in fact is not we can't change our chronological age.

And scientists really today say, you know, it's not the most important number by a long shot. Your chronological age is not your, you know, your destiny, your health, destiny.

It doesn't speak to how long and well you're going to live. It's your biological age or how fast your body is actually aging. That's where the rubber meets the road.

We've all seen people who are, you know, the same age as ourselves. And, they don't look like us, you know, either they look a whole lot older and a whole more, you know, a lot more, you know, damaged, perhaps, or just a lot, you know, a lot of changes of aging are present on them.

Or perhaps they look wildly young and amazingly youthful and our, you know, living in a really powerful space, these people clearly demonstrate different biological ages.

And what's pretty cool about science these days is that we're able to measure with increasing reliability, this process, this biological age. And I would imagine that in the not so distant future, this is a number we're all going to know.

You know, you go and you get your chem screen or your CBC, you're going to also get your biological age. You're going to probably care more. It's going to have more meaning for you.

You know that you're 50, but your bio age is 40.

Biological Age vs. Chronological Age

I mean, you're doing you're doing things right. And so you'll have this tool, you know, to, you know, base some of your life choices in the, in the plan you might design with your physician on.

I think it'll just become standard of care. In fact, probably at some point we'll have wearables like, I've got my aura ring on that, you know, that might give us snapshots into bio age, you know, and what's good for us in the immediate.

I think that's probably where we're headed. And I think it'll be really exciting. So biological age measures how fast our body is aging. The way that that is done is by looking at gene expression.

And this is called the field of epigenetics. So epi above genetics the gene. So we're not looking at our genetics. We're not looking at our DNA but we're looking at the biochemical marks that regulate what genes are on and what genes are off.

And let me just stop there, Heather, and see if you've got any, you know, defining questions in that. Yeah. Well, I think what I want to talk a little bit more about is unraveling how we measure this rate.

So if we know how to measure biological age, we count the trips around the sun, celebrate each year, and then hopefully. And then when we talk about kind of a biologic, sorry, that's chronological chronological age.

I'm saying well known biological age. So when I think there's still some discussion in the field, if I understand it correctly, that methylation is DNA with methylation is one way to look at that.

But like telomeres were very popular for a long time is another way to look at that. And I think there's several other ways that we can assess, like how old, our system is.

But why why did you choose DNA methylation? And then please describe the Horvath clock and who he is, and give us a little bit of context about how we're measuring this.

Sure. So, the so telomeres are sort of looking at the caps of DNA and these predictably get shorter after cell division, cell division after cell division after cell division.

And they've been associated with aging. They are not they've been demonstrated to not be as reliable as we once thought. In fact, you can actually measure telomere changes using DNA methylation pattern.

So you can look at the telomere genes and look at and look at methylation patterns on that specific telomere gene, and have a more reliable tool of what's happening at the level of telomeres.

So it's just kind of interesting. But DNA methylation biological age clocks have supplanted, I think, telomeres, although it doesn't mean that we're throwing them out there.

They're they're likely they will be in a useful biomarker. And we're just kind of rethinking whether or not they're the biological age. Tool we once thought that they were, especially interestingly enough that you can get a better job looking at the methylation pattern on the telomere gene versus looking at telomeres directly.

So I think there's there's just changes a front. This is a rapidly, rapidly evolving field. I should actually say that like the clock that we used in our study, is the flagship 2013 clock.

And there are we're up to three generations later. So we used a first generation clock and we're already up to third generation clock. So it's a such an evolving field.

There are biomarker collections that different scientists have pulled together to look at like standard biomarkers. And, and describe these as biological age clocks as well.

I don't know that they're I think that they're useful and, I think that they're important. I can say specifically, standard biomarkers used, in an AI model.

So, so, so plugged into artificial intelligence and sort of crunched with chronological age. Formed the basis of a methylation clock. So again, using these bio age markers plus chronological age, we're, we're used to train a DNA methylation clock called the fino age clock.

And but this DNA methylation clock actually outperformed these biomarkers. So it was more predictive of healthspan and lifespan, you know, morbidity and mortality.

So isn't that fascinating? So that's the other thing is like, what exactly does this biological age mean? Is it is it the length of time between now and when we're predicted to die or when we're predicted to have a good question?

Yeah yeah yeah yeah. So yes, yes. To both of those. And it depends on what clock you're using. So more so so for instance there's a clock called Grimm Age.

And just as the name implies, it's predictive of time of death, amazingly enough. So, whereas the, you know, age as the name implies, phenotype. This is more predictive of, morbidity, you know, so, so, healthspan.

And, and, and, you know, the robustness or lack thereof of healthspan, whereas the Horvath clock that we used in our original study is trained against chronological age.

So it, it, is much more correlative of, chronological age than telomeres, like, far more reliable. But it's not a 1 to 1 relationship. So if it were 100% predictive of chronological age it would only be useful for that.

So there's this wiggle room within this clock that, that actually is more predictive of morbidity and mortality than your actual chronological age. Does that does that all make sense?

Yeah. Yeah. And there and we're now looking at clocks that will measure age of various tissue like brain, mitochondria, immune system.

How DNA Methylation Clocks Measure Aging

So it's just it's, it's, it's an extraordinarily rapid, evolving and interesting field. We are so as we're into our second study, we are using a next generation clock that seems that's more predictive of healthspan.

So it's a little bit more malleable than the Horvath clock we used in our original study. So I want to go into the design of your study and what people can be doing today to reduce their biological age.

But before we go there, I wanted to just talk about kind of like setting the context, like you're looking into aging. And because for so long we've accepted aging as inevitable and something we really can't do anything about.

There hasn't been a whole lot of emphasis on it. And yet Dimension Aging have this huge intersection, right? The National Institutes on Aging, part of one of the institutes out of the NIH, the the National Institute for health, two thirds of their budget goes into Alzheimer's and dementia.

I mean, this is just a radical number of dollars that are being spent on understanding dementia. And yet it's taken at like two thirds of aging. You mean dementia?

Not really. Right. And like the overlap, it's like maybe if what we were looking at was aging, then by default we would be preventing dementia. Exactly. Yeah. That's that's yeah.

Yeah. That's right. I'm glad you agree. Because I'm kind of like I think this is backwards. We're like right at the final steps instead of looking at like what's the number one?

The root cause. Right. The root cause of doctors. Right. The I mean really the root cause of dementia, you know, Alzheimer, cancer, diabetes, cardiovascular disease, the root cause of these is aging.

You know, in fact, a really interesting and crazy statistic. But it kind of gives perspective is that, you know, what's the bigger risk factor for lung cancer?

Let me ask you, pop question what's the bigger risk factor smoking or aging. But I have to say aging now. But I would have said smoking 100%. Smoking.

Yeah of course. Yeah. No it's aging. It's aging. So the breakdown of the lung tissue over the long haul increases vulnerability to lung cancer. More so, you know, more profoundly than than smoking itself.

Yeah, I, I 100% agree with you. And I think that the paradigm is changing. So now that we, we're, we're starting to build these rather extraordinary tools to be able to measure aging, we can begin and they're sensitive because otherwise you can't really research aging in humans because we live a long time.

I mean, it's just, it it's just prohibitive to be able to it pull together, you know, reliable studies. We just can't get them. But now that we've got this sweet, you know, this building, this suite of surrogate markers for aging, these clocks and and and they're really more than surrogate markers.

So I want to circle back to that. They actually aging appears to actually happen at the level of gene expression. So if you want to talk. So again going back to the root cause of aging, it may just be, you know, sitting right there in the epigenome.

And I'm going to park that put a pin in it and we can come back to it. Well, this I think the one you just mentioned, it's hard to measure this in humans because we live so long.

And so, yeah, we have to be waiting decades to get we need or. Yes. So we need to take measures so we can do reasonable length studies. That's right. Right.

But there's a lot of information that comes out of labs like David Sinclair's where what they're looking at yeast and mice and, and other things that procreate quicker and die quicker and faster.

And those things can be applied at some level to what's going on in humans. So yes, you can definitely translate some of it to an extent. But we need to you can't 100% translate it like just no, there's just no way.

And we shouldn't kid ourselves to say that we can look at the rapamycin data or some of the other really impressive data, or the Yamanaka factor data and say, oh yeah, we can do that in humans.

No way. You can't translate that into humans at this point in time, those are just those are preclinical studies. Okay. So cynical study. Yeah, but but but we have learned a lot.

I want to say that we have learned a lot, though, from those guys and I and going to Sinclair's lab in particular, they've shown that aging happens in the epigenome and specifically, I think in DNA methylation and demethylation.

So they've driven aging forward in an animal model. Via disordered epigenetics, and then they've reversed it using something called Yamanaka factors, which are transcription factors.

So these guys turn on, they change gene expression. And so they alter epigenetics, these transcription factors, so what they're starting to show is that age aging is happening in the epigenome.

And I just think it's profound, you know, we've had these ideas that aging is, you know, increased free radical activity, increased exposure to toxins, like it's, you know, it's just breakdown of, you know, our ability to efficiently fold protein.

It's damage to DNA. You know, it's it's more mutations like we have all these pillars or hallmarks of aging. But we're starting to see that perhaps up above these downstream effects is this change to gene expression. So so we've got these clocks that are measuring changes to gene expression.

And they're doing that specifically via DNA methylation. But in fact maybe these clocks are more than just a surrogate marker of aging. Maybe these clocks are reflective of aging.

We don't know that answer. And it's probably beyond just the clocks. But it's ridiculously compelling, you know, that this might be like, you know, the root.

I just think it's extraordinary. It's so interesting, so fascinating and such exciting stuff. So tell us why you designed your trial. How many people are in it? What did they do?

Yeah. So I want to just give you a little bit of the backstory because I think it's just interesting, like, how the heck did I end up designing, methylation diet and lifestyle study, you know, or, or or program back in 2016, we, we, we published an e-book on the methyl diet and lifestyle, the Methylation Diet lifestyle.

This was before for any human trials looking at biological age clocks had ever. Yeah. Come, come to pass. And it was you know before understanding what we do from Sinclair's lab, we started to think about it.

In about 2013, I was reading the literature on cancer epigenetics, and it was a game changer for me as a physician in clinical practice. So cancer takes over, cancer hijacks epigenetic expression, so it takes over gene expression very efficiently.

The tumor microenvironment takes over from US what genes are on and off to drive its own life. So it turns off genes that protect us from cancer. It turns on genes that cause cancer.

That's what happened. So it's been a route that's been very well defined. And that was our entry into that.

Aging, Dementia, and the Epigenome

And I want to say that this change, this abnormal gene expression phenomena that's been so well defined in cancer appears to be happening in the other chronic diseases.

So you see this abnormal change happening at the level of a genetic expression. I didn't know this back in 2013. I was simply aware of what was happening in cancer.

And it occurred to me. So we're seeing increased and decreased methylation, what they call in science aberrant methylation, aberrant DNA, abnormal DNA methylation is happening.

Some genes are way on and that means they don't have a lot of methylation groups on them because the methyl groups block gene expression. You know, just think of them as a bunch of cars parked in the parking lot.

You can't get out. So when they sit on the gene, the gene's not able to open and be, you know, transcribed, or conversely, there's no methyl groups or very few, then that gene can be turned on, opened up and turned on.

So I was looking at it through the through the lens of cancer and decided that, well, in reading the literature, and it was apparent to me that the safest way that we could move forward with this information in functional medicine, where we're treating methyl, you know, we're thinking about methylation all the time.

We're measuring homocysteine and other intermediates in the methylation cycle. We're giving loads of B vitamins and, you know, choline and betaine and so on and so forth, where we are very savvy around methylation.

And it occurred to me that the safest way to do this, given the research on, on cancer would be through a diet. We could you can bathe the body in, methyl donor rich foods.

So folate rich foods, choline, B12 and so forth, all of these nutrients you can within the food matrix, within a whole food diet, you can just load them on.

And there is no negative outcome there. In fact, they're protective. You know, there's no study out there showing that greens cause cancer. So we started this program anchored in diet, and then we expanded from there and saw the influence of exercise of of quality sleep, of meditation, the all of these, these sort of upstream influences on DNA methylation as well.

So we're moving outside of manipulating the methylation cycle itself to variables that are upstream and influencing favorably. Methylation. The other piece of information that we learned, that was a huge for me was, phytochemicals, plant polyphenols seem to drive traffic off where methylation happens on DNA.

And our study appears to corroborate that. So our participants, our participants DNA was rearranged in such a way as to DNA expression. Excuse me. So their methylation patterns were rearranged in such a way as to, appear younger.

So we didn't net increased methylation in our participants. We did measure that. And there was no net increase in methylation, but there was a rearrangement of gene expression towards a more youthful, pattern, which to me is extraordinary.

So we poured in the methyl donors and we gave all of these plant chemicals to sort of direct where it was happening. At least, you know, that's that's my hypothesis.

That's what I think happened. And then on top of that exercise, which really kind of acts like a phytochemical, it sort of acts like a polyphenol. When you look at DNA expression, DNA expression, and DNA methylation, it's exercise is amazing.

But taken all together, we sort of rearranged towards a more youthful pattern. So how did you design the trial? What did it look like? Yeah. Yeah, yeah.

So, so yeah, I'm jumping around a little bit. So this is what we created in our office and then, and we used it for quite a few years. We anticipated we were changing gene expression.

We wanted to study it, though, but at that time, you know, there were and still really to this day, it's we don't have access to a lot of, assays. At that time, there were none, available to us in clinical practice where we could measure DNA methylation.

And we were given an unrestricted grant through metagenomics. They covered the funding of our study without, dictating, either ownership of the findings or the design, which, you know, is extraordinary.

And I'm just beyond deeply grateful to them as a company and to Brant, their, you know, visionary CEO for for supporting us. I mean, these were many conversations that I had with Brant on, what I was learning, you know, and

he was as riveted by it as I was.

So he allowed us to study it. We did it through Helfgott Research Institute. I don't know where you went to school, but it's my alma mater, National University of Natural Medicine.

You know, Ryan Bradley is the director there, and they're just a great clinical research center. I mean, they're just really doing top tier work, and I'm so thrilled it was Brant X idea from a genetics that we work with, with Ryan and and team over there.

And I couldn't be happier. I think they designed a really high quality study for us. The intervention was eight weeks. So again, diet, a modest exercise prescription, nothing too crazy, 30 minutes minimum, five days a week.

Perceived exertion of 60 to 80% of max.

Designing the Methylation Diet and Lifestyle Trial

So this could be, you know, walking. This could be gardening. This could be a little, you know, an easy bike ride, etc. nothing too crazy. And that was by design.

We wanted people to be sleeping well. And so, you know, we supported them with sleep hygiene, chips, etc. a basic meditation program. We wanted them to do twice daily, a minimum of ten minutes, use twice per day using the relaxation response by Herbert Benson.

This is a tool that's been used in, you know, many, many trials over the years. What else did we do with them? We had they took a probiotic, Lactobacillus plantarum.

There's some evidence that Lactobacillus plantarum may help increase. Microbiome production of folate. And we did significantly increase circulating folate in our, in our participants.

And we also gave them a greens powder. So another constant hit of these all important, phytonutrients that I've mentioned a couple of times, extremely important, was the fact that our study population met with a nutritionist.

They were required to meet with a trained nutritionist, somebody from our team, at least weekly for the first month to make sure that they had the basics of the diet down.

Now, this wasn't a cheerleading session. We actually had to have an IRB approved script. It was really dry. And, you know, Ryan Bradley, he was like, he's so he's a stickler for making sure all your eyes and T's are very correctly dotted and crossed.

So our nutrition team were not doing motivational interviewing with our population. They were just confirming that they, you know, do you have questions or don't you have questions.

And then they would also, you know, just make sure they were getting exercise in and you know, brainstorm on, on, on, on sleep hygiene and so forth. I do think given the complexity of this multi modal modal intervention, that our, nutrition team was the difference between success and failure.

Otherwise, I mean, it's it is an involved protocol. And I knew I had one shot. I mean, where are you going to get, you know, six, six figures, you know, get gifted to you basically for something like this.

And so I really wanted to, do the best I possibly could with, with this opportunity. Yeah. So incredible. So just so listeners know, I also have been working with Ryan Bradley on our clinical trials here in my office, where we took 25 participants through, the, our approach to, cognitive decline and reversing that.

And so we'll publish our results in the next six months or so. But Kerry and I have been on this. I've been behind her. I've been trying to catch up, but not running fast enough.

So she has. She and Ryan work together to publish your paper in aging and get this done. And all through my trial, I was scared. Oh, yeah, and Kerry's trial, they did such a great job of keeping participants engaged through this and that.

So we'll have to use what we learned from that trial. So yeah, our participants benefited from so much of what you guys learned. Awesome. Oh geez. That's great to know.

Yeah. Wow. I am so thrilled to know that. Yeah I mean, Ryan was like, you know, we're going to study you guys and actually executing this trial because it's very involved.

Yeah. And, I think he was dubious that we'd be able to pull it off, to be honest. I mean, I like that. Yeah, yeah, yeah, it's fun to kind of be showing him what's possible, but yeah, you guys did it first.

So then what did you find and how many people were in the trial? So it was a pilot study. There were 18 people in the treatment group and then 20 controls.

So 38 total. We found a handful of things, of course, most what kind of got us a ton of attention right out the gate was as compared to our control group, who received no intervention.

Our study participants got over three years younger, as measured by, you know, DNA methylation, again, using the flagship Horvath clock. The within group comparison.

So so looking at the study participants themselves at baseline, and then at the end of the eight weeks they got two years younger. So, so both within and control group comparison showed some impressive, changes there.

We actually. Yeah. Yeah. And this is like me being sort of a stickler, but we actually redid our calculation where we included the eight weeks as 1/16 of a year.

We didn't publish this in our study. But when we included the eight weeks, we achieved, we were almost out statistical significance originally with the within group comparison at a point, zero six.

But when we included that little chunk of time, in the study, we actually achieved, significance at.04 and it was over two years younger. So both measurements showed a, significant biological age reduction.

We also showed that our study participants were increased circulating for folate. As I mentioned before. Their LDL cholesterol dropped, their triglycerides drop, their total cholesterol also dropped.

And I want to underscore because people always, always ask me, in fact, I was just doing having a really fun conversation over at the Cleveland Clinic Center for Functional Medicine with those, doctors and, and providers.

They are. And they said, well, did you measure CRP and did you measure insulin? And did you measure, you know, other markers and, you know, did you see big jumps there?

And I want to we didn't do a lot of other standard biochemistry. And in hindsight, I probably would, but we used healthy participants. It took us, we had to use a rolling enrollment.

It took us a while to recruit a really healthy cohort. So no blood sugar wasn't elevated at start. Homocysteine was not elevated. HNC was not elevated. These were healthy guys.

So we didn't see, changes in those numbers. Interesting. Interesting. Okay, so and I think that's also really important here because. Right. If you're talking to somebody who's not healthy, you get even more of a change.

That's right, that's right. And that's been demonstrated. Yeah. So if you take diabetes for example, or are you guys using biological age. Are you looking at DNA methylation in your population?

We didn't no, not in our trial I just for patients sometimes if they're interested. But we didn't use them in trial, although I talked to those guys recently and it's like when we do our follow up, you'll do it.

And if you've banked specimen, did you bank specimen for a chance? No. Okay, okay, I understand. Well, you know, and Dale brothers and is going to be looking at DNA methylation and I hope to, just consult with those guys on that.

That's very exciting. Them. I'm really glad they're doing it. And I think I think we're just going to be using it as a tool, especially in the, in the research setting because we have so, so, so much to learn.

And I can actually remind me, tell you about some of our other findings outside of the biological clock, which I think are as interesting and as important.

Anyway, what was I what was I just saying? When we digressed? Oh, there's so much here to talk about. Well, you know what other things I want to get into for sure, is.

I mean, you already mentioned this intergenerational. Wait. I came back and the train reentered the station. So we were talking about accelerated aging when you have a chronic condition.

And yes, in fact, that is the case. So all of these chronic diseases are both accelerating at the biological age is accelerating. And when you turn around the condition, you can see a deceleration.

And I think that's been best characterized in in diabetics where they're, 6 to 9 years older biologically than their healthy counterparts. Now within an eight week time frame, will we see more of a bio age change or does it take longer?

I mean, I think that that's something that has, yet to be demonstrated. Yeah. For future trials. Yeah. So I do want to talk about this kind of intergenerational impact.

So whether it's trauma or what you were exposed to in utero, how what you eat, if you're, you know, a of procreating age, right. If you're in that age group, how what you're eating even before you're pregnant or before you are procreating, how that can have an impact on your offspring's genetic expression.

So tell us about what we know there. Because I think some of us kind of intuit this and I there was data out of highly stressed populations that shows that three and four generations later there's an impact.

But tell us kind of how that that applies here in your work. Well, what do I want to say? I get into it in the book, I get into it in the book. So what would I say?

Like, you know, we were looking at post conception. We're looking at middle aged guys, and changing DNA, you know, expression in this population. I mean, you know, each cell division is another generation.

You can think of it that way. So when we put time in and this is an important understanding, because when we put time into our good health habits, it's, it's going to spread to more cells with more and more cell division.

So you can you can just look within your own self and your own many generations of cells to see that in an investment and consistent investment is going to yield best results.

So we know that, you know, one meditation actually can show favorable changes to DNA methylation. But people who are practice meditators are biologically younger.

Likewise, we can see that in four hours time, of exposure to pollutants, you will see negative DNA methylation changes.

Trial Results and Biological Age Reduction

Conversely, if you're around this or, you know, more so if you're around if you're around a toxic exposure for long term, you'll see, further, damage to DNA methylation and gene expression.

So heritability in humans, there's a there's a good body of literature showing heritability in, animal studies. So, the very famous turtle and Waterland agouti mice study they gave to pregnant agouti mice.

So these mice are blond and they're very distinct. They're obese and blond. These mice, you see them once, and you'll never forget what an agouti mouse looks like.

That agouti gene is on an expression and making them blond and obese and also vulnerable to, you know, cardiovascular disease, etc., etc. in this in this mouse model, Waterland in journal showed in the actually the most cited his paper in the history of all science.

Their paper, their 2003 seminal paper showed that giving the pregnant Down's, methyl donor. So B12, folate, choline inhibited hyper methylated the agouti gene.

And they gave birth to a goody mice that were they call them pseudo a goodie because that gene was hyper methylated and therefore they were brown, wild type, slender.

Actually it was around it was a continuum of that. But they changed very visually. They changed phenotypic expression. And and they showed this actually they didn't conduct the studies, but other labs conducted longevity on the influence of this generation zero, methyl donor exposure and showed five generations out.

So five generations, generation zero pregnant Down's received these methyl donors and five generations out there influencing methylation of the agouti gene.

I mean, is that crazy? If that doesn't show, you suggest how powerful our nutrients are in this era of being able to look at gene expression and measure it.

Oh my goodness, humans, we've got some interesting data. We've got cohorts like Dutch Hunger, Winter and Overclocks. And these were generation. These were, populations that either had, profound food scarcity, as was the case with Dutch Hunger winter.

So this was World War two. They were, isolated by Germany and they were starving. Some of them women who were pregnant in during that time gave birth to offspring who had higher risk of really what we see as diseases of overconsumption.

So cardiovascular disease, obesity, diabetes, etc.. I think schizophrenia as well. The and different from siblings who were, who were either born then or born later.

So they had to be within this, exposure to the, to the caloric, the profound caloric deficit. It altered their gene expression towards something what we that we call the thrifty epi genotype.

So every calorie is really hung on to you now in the over cohort. What's really interesting about these guys is they just kept copious records. And so some farming seasons were lush with lots of food and other farming seasons.

There was a deficit. They weren't starving, but there was less availability. So they so showed similar negative outcomes with overconsumption. But interestingly, they showed beneficial outcome with less consumption.

So not starvation but a little bit. You know, you're not you're not picking out all the time either. What's what's circling back to your question, what I think is extraordinary is that they showed the benefit of this lower intake of food in prepubescent boys.

So prepubescent boys, they're engaging in spermatogenesis like they're they're sort of defining apart genetically what's happening. On on during the spermatogenesis journey, this pre-adolescent journey.

And that influences their later offspring through multiple generations. I mean, so when we talk about preparing, when we talk about thinking about eating for our genes, there's really no time and no sex like that.

You know, men are in this and we, you know, so we can see that, you know, adequate nourishment with what we call epi nutrients or the nutrients that influence gene expression and decent lifestyle factors, I think can influence at any time.

And it can be surprising we in the book, we include a preconception and pregnancy program. So what we think are the smart nutrients and we've got amazing data.

And this is for men and women. I just I can't underscore enough. This is where the rubber meets the road for men. So if you think it's all on women and during pregnancy, you know, you're you're simply mistaken.

We see the heritability of stress, you know, from both sexes, and, and, you know, likewise with exposure to nutrients or nutrient deficits influencing, you know, both sexes and offspring.

So we included that information in what we thought would be, a healthy program with our, in our younger you book. And we also write about grow baby health.

I want to give them a shout out. Lesley Stone and her daughter Emily, run a program called Grow Baby Health, and they're engaged in research, and they use our methylation diet and lifestyle program, with their pre-conception program.

And their birth outcomes are absolutely extraordinary. So they published on a, on a, on a cohort of 200. And they've got like zero incidence, I think, in their population of autism, you know, very low allergy rates, you know, preeclampsia, virtually nonexistence, gestational diabetes, you know, like non-existent.

I mean, their birth outcomes are extraordinary. Wow. Wow. Yeah. And it would be interesting actually to track that through the generations through the Jenner.

Yeah, absolutely. So this is I think just to underscore your point, right. Like there's no time that this isn't a good idea. It's going to wait until you have dementia or you don't have to wait until someone in your family has dementia.

Even though this is the reverse Alzheimer's Summit. This is really great information for yes for the anyone yes. Is concerned about the effects of aging or the risks associated with aging.

And I mean, just to go beyond that, our, our, our DNA methylation gene expression is doing stuff at every life stage.

Intergenerational Effects of Diet and Stress

So an important, really sticky point that Davidson Clare made on my podcast was that, you know, DNA methylation in embryogenesis, in pregnancy, in early infancy is just wild.

It's just, I mean, so the fate of all our pluripotent stem cells, if you're thinking, you know, when you're when we're an embryo, you know, when we're negative age, is defined by methylation and demethylation.

So it's, it's it's wildly important that we are consuming enough methyl donors. So we're not thinking about aging. We're just thinking about development.

And likewise, you know, newborns early infancy, infancy, toddlerhood. It's an a time of extraordinarily, robust development. And DNA methylation needs to be happening really pristinely.

And we can see negative fallout when it's not. And they these are the developmental delayed. So they're actually aging more slowly. And in this cohort, it's, you know, in this young group it's unhealthy.

So DNA methylation is playing a fundamental role in directing developmental traffic. I think throughout the lifespan. And, you know, there are different time points where I think we understand it a little better.

And these radical changes happening early on are as, powerful, and important and impactful as aging. So, so actually to state Sinclair, he put it in the opposite.

That changes to DNA methylation that are happening with aging are as potent as what's happening very early on. So there is no time like the present to be eating for gene expression.

I would say that that's what we can conclude. And if we are doing that and adopting some of these habits early on, then yes, I think that we can influence the aging journey.

And also keep our healthspan, and lifespan, you know, robust. So this is great because I often will have conversations with people saying autism is just the flip side of the Alzheimer's coin, right?

Like when we're talking about brain health, there's very similar things going on in the developmental stage. One is and the other is just as in the aging stage.

So this is speaking exactly to make sense what we're seeing clinically. Yeah. So I want people to have really great takeaways to be able to take, take this incredible information and put it into practice.

Yeah. What foods and simple swaps in the daily routine can add years to our healthspan. So not just our lifespan, but to our health. That's a it's such a good question.

And as you know, we're going to be giving people, a freebie of what our diet is. I would love it. I mean, I if you want the rubber meets the road, grab our book, grab the book.

Younger you because it's all in here in the in the, in the, the pregnant the the program for pre-conception and pregnancy is in there. And then the program that people can transition to after they finish this intensive is in there.

But important foods. So what not to eat. And I know, Heather, you talk about this and I'm sure a lot of the other people you're interviewing talk about this.

We don't want a lot of garbage like the standard American diet is not going to allow you to live long and prosper, period. It just isn't. So we want to move away from sugar.

We employ gentle, time restricted eating. This diet is higher. In fat. It's for the eight week time period. It's grain free, it's legume free, and it's dairy free.

You can transition back into those foods after you're off, but maybe a little bit more modest. I'm not anti legume at all. I think that there are longevity food, but just within the eight weeks we pull people off of it.

So what not to eat has is as important as what to eat your methyl donor rich foods. So simple swaps have some green tea green or this is a this is actually what we call a methylation adaptogen.

So this is the phytochemical I was talking about. The catechins in green tea are wildly important for gene expression, and we know they're also important for cognitive health and, inflammation etc..

So have some green tea. Coffee is okay. Coffee has some important phytochemicals in it. So you don't have to kick coffee to the curb. But, you know, switch your afternoon coffee out for a nice strongly brewed green tea.

Have a piece of liver, folks, if you're open to it. Liver is a methyl donor in a food matrix. I can't even tell you how extraordinary it is if you're willing to eat it.

I will admit I don't cook yet, and I have in the book there's a bunch of, recommendations for liver capsules if you're

open to doing that. Mushrooms. Can I stop you on liver?

Because I've never eat liver. You've never had liver? I've never had any. That's so funny. Even thinking about it. And then when I think about taking capsules, I'm afraid it's like.

And even when I think about eating liver, like, where was that animal raised? Because liver, it's going to concentrate nutrients, but it's also going to concentrate toxins.

Yes, they will. Let's break down like when you say liver. What do you mean how do you do it? Let me tell you. So yes. So you want to get clean source liver? Clearly.

And it seems to me that the most pristine we can get is from New Zealand. And it's available. And it's not. It's not wildly expensive. So you can do that. That's what I do.

And I want to say, Heather, you should know this as an anti. Actually, maybe you do. Now, I don't want to. I just find it so funny. You've never had liver.

You didn't grow up in the in the Midwest. So I'm just saying, it's it's where, it's what we prescribed back in the day for pernicious anemia for, you know, peripheral neuropathy for, you know, macro cystic macro psychosis, etc., etc..

I mean, it's what we were using before we synthesized B vitamins. So now we can give B vitamins. It's really high isolated doses. And arguably there are smart reasons that we want to take it in that food matrix.

And I talk about some of those in the book. So you get choline, folate, you get a day's worth of B12 in a serving in a serving of liver, all of these guys, plus minerals and so forth.

But but indeed, you're 100% correct that you need to get it really clean source. And we can I mean, that was funny enough. That was one of the conversations that nutritionists would have with the team, like the, the, the study cohort, like, where are they sourcing their clean liver?

And in Portland, Oregon, they're they're it was not difficult here in Connecticut. I think it's also not difficult, but perhaps a little bit harder. But some parts of the world that you find clean liver at the butcher and then what you just, like, fry it up.

Like how do you make. Because we her. Well, you know, one of the guys in the study loved making what he called the new chicken McNugget. So he would he would sort of bred it.

And I think he used a little bit of almond flour or something like that and fry it. And he absolutely loved it. Famously, since you're since you haven't had liver, where did you grow up?

I think I grew up on a walk, so like, I've eaten, I have heart, but I have. Or like like tuna heart fresh out of the ocean. So I've seen plenty of weird. Okay, okay.

You brought me to the table. Well, you know what? I think organ meats in general are really dense with those nutrients. I guess if you had grown up in Alaska with the Inuit, you would have probably had polar bear liver.

Maybe. Perhaps a little bit of that. We have an awesome paté. So probably the easiest way to eat liver, at least for me, is just a really nice paté.

And you can put that on, you know, a cracker that's legal, like a seed based cracker. Or you can put it on a celery stick or something like that. I it's just really delicious and flavorful.

We have kids, like, have no problem consuming liver in this in this really beautiful form. I grew up eating liverwurst, which is sort of like a poor man's paté and, you know, loved it with mayonnaise.

But but, you know, again, I don't, I don't I don't cook it either. I'm not going to tell a lie. So unless I, I can buy some prepared, clean source, liver product, which I can I can actually get some nice paté around here.

I just take it in caps. Got it. Okay. That's super helpful. Okay, then. You said mushrooms. We can move on. Yeah, mushrooms for sure. So mushrooms are really rich in choline.

And that's an incredibly important methyl donor. They're rich in a host of other really important nutrients as well including some folate. But, particularly shiitake mushrooms but enoki and my talki so really important good players if you can eat eggs if you're not allergic, I know it's a common allergen.

Or if you're a vegan, obviously you're not going to be eating these. By the way folks, yes, we do have a vegan vegetarian version of the diet, but we didn't study that version.

So it's there and it's available and we'll be collecting data on it in our new cohort in the app, but we don't have publications.

Foods That Support Healthy Methylation

But if you don't eat animal products at all, you can still do this program. We lean heavily on legumes and beans and stuff like that. Yeah. So mushrooms super important.

Your greens, we we we we list spinach and in our dynamic dozen list. But really, you know, any of those super nutrient dense, fresh greens. What else do we like?

I said, eggs, eggs. You know, just a superfood. What else do we have in there? Seeds. So seeds. Another really important player. And then you want good fats actually, in the seed arena, pumpkin seeds, sunflower seeds, omega three fats.

So if you can do a fatty salmon, you know, that's going to be an important, metal or epi nutrient, as well. And let me actually let me just add in the book we have there are many, many epi nutrients.

So if somebody was listening to this and going, you I don't like any of those foods which I hear from people or somebody emailed me not too long ago and said, I can't eat any of those.

I mean, she could she she had some, she had a bunch of different sensitivities. Yes. Like just she was really hit with pretty profound sensitivities and allergies.

There's a 30 page nutrient appendix in the book, food sources of the epi nutrients that we found in the literature. So there are a lot of foods out there that are, you know, epigenetic, active.

There are a lot any of us could go into the back. The most finicky, the most sensitive individual could go into the nutrient appendix and highlight all sorts of stuff, that they're either already eating.

So you could go back there and look and see what are you already doing. Right? And then you can look and see what what you can add. So if you need to enter into this conversation gently, I would say start at the nutrient appendix and see what you're doing right and see what you can add in.

And but if you were ready to be all in, you know, obviously I'm going to encourage all of us to do our eight week program as we as we used it in our study.

So helpful, super, super helpful. And so then I do you also like suggest variability right. Like eating with the seasons or do you guys get into that at all.

Not in our study. No we didn't. It has to be broadly accessible. So you can create something that you make unavailable to, you know, somebody who might be a little bit more in a food desert or somebody who doesn't have

the funding to access organic.

And we and we really wanted to be mindful of that. So, it's it we got our findings without, requiring organic, without eating for the seasons. Clearly, if we want to engage in some of those practices, we may, ditch the needle a little bit more, but we didn't study it.

Again, just with the intention of, you know, can we make this available to anyone, the masses that need it? Yeah. So let's talk a little bit more about some of the lifestyle practices that were in there.

You talked about some meditation, exercise and really the diet. It feels like the foundation. But there were other pieces as well. And do we kind of. Yeah.

In the sense I'm, I'm a complex systems thinker. Right. So I'm like, no, we want to do it all. Like, why would we do it? So reduction. Yes. And I think that we need to reject that at this stage.

So it's not just when I look at one food or it's not just about diet, it's about everything. But do you kind of have a sense of like how much was the diet, how much was the meditation or the stress?

How much? Like you said, 25% of your biological age clock is just glucocorticoids. So that's a heavy lift, right? Like that means like maybe we should put stress first, not the diet first.

But for somebody who's just kind of entering into this, what's what's the best, easiest entry point. So yeah, you know, it's funny because I've talked to other people, who have different opinions.

I am with you. And maybe it's our naturopathic background that we're like, yeah, the diet had to be doing the heavy lifting or certainly it's complex.

And you know, every nutrient on your for it can be in for information for gene expression like it's so powerful and all of the things that you're not putting in your mouth or how you're structuring your eating program is so, so, so significant.

So I, I agree with you that I think the diet is doing the heavy lift. But man, reading the science on stress, like you just said, you can see stress inherited through the generations.

I mean, it's extra ordinary, but I want to point out that it's the minority. So when we think about PTSD, the minority of individuals will actually have a true PTSD response.

So you can have a very stressful event, but it's going to be a at an actual small minority of individuals who are going to sort of change gene expression.

So wait, wait, we don't all have PTSD right now. Technically. Technically, yeah. You know, technically, no, we don't. Thank God, you know? Thank God. All right.

I think that's important. I think we, I think we tend to almost over diagnose PTSD and, I think that it's helpful to know, that it's perhaps not as widespread.

However, total life stress will influence gene expression as well, you know, stressful events or, you know, lack of I'm thinking of in infants, but also the, the famous animal studies from OSHA Saff, who was our study advisor, an author on the paper.

But, you know, one of the highest regarded epi geneticists is out of McGill University. He did these early studies looking at, maternal grooming of, in mice and the pups of the grooming the pups and, those that didn't receive it had a lower stress threshold.

So their, their epigenetics were found to create a stress response at a, at a much less stress exposure. And we see

that similarly in infants who lack counseling.

So going back to your original cuddling point, there you can see, you can see cuddling as almost a well, causing the lack of cuddling, causing a developmental delay phenomena in, in humans.

So stress is a big, big deal, I guess is my point. Stress is a big deal. But it looks like we can change things. I mean, it looks like we can change gene expression through things that distress us again, coming back to the idea that one yoga event or one meditation event, even one exercise event, can favorably change gene expression.

But then when you engage in something habitually, you know, you can it can spread like wildfire, can influence, have more impactful influences when you continue to practice.

So, you know, people who meditate are younger, biologically younger, sleep, you know, likewise, people who sleep well have a lower risk of all the chronic diseases of aging.

We see really negative. We see a pro aging phenomena in people who don't sleep. Well, you see changes. True. Neuronal pathways, like, pretty profoundly in animal models, who aren't, you know, with, with, with insomnia or not even insomnia, just one sleepless event, you know, can change things in a, in an animal model.

I mean, it can change it in my model, right? Like, I yeah, I across the world and I'm jetlagged and I think we can all relate to that. That's exactly right.

In fact, when I remember like it's a I'll never forget presenting this slide in Ireland, some years ago before we did our study. Yeah. And being like, I'm so jetlagged, you guys, I could barely get these words out.

So I'm experiencing this damage. I don't know that it's as far reaching and as a as it is in the animal model for us to just have one lousy night's sleep, but, it adds up, you know, if we continue not to be able to sleep well.

So to to your, to your point, these are all incredibly impactful, activities. I mean, they're incredibly impactful lifestyle habits. And, you know, okay, so you're eating a pristine diet, but you're just wildly stressed out, or you're always sitting in your desk day in and day out and stressed out, you know, without any exercise. I mean.

Lifestyle Habits, Stress, and Meditation

You know, is that person going to be protected from a heart attack because, you know, they eat wild, caught salmon, but they're living, you know, a really difficult life, I don't know.

Right? Right. And for people who are in stressful events that maybe they don't have a lot of control over, yes. Maybe circling back to your point of us all having PTSD.

Yeah. Right. That making sure that there are coping strategies and support that you have in place hopefully before that comes up. But things like meditation, which you included, can you talk a little bit more about the meditation that you guys included and how you chose that one?

Yeah, so this is going back to Ryan Bradley. It was his idea that we use Herbert Benson because it's so it's because he, you know, he was a Harvard, scientist who was studying the benefits of meditation, like one of the first guys.

And this was a basic program that he developed. It's super easy and turnkey. Anyone can do it. The instructions are in the book. The instructions are also on the paper, which is available.

It's open source journal, so anybody can get it and see what we were doing. It's just a simple it's a, it's a breathing exercise to elicit what he calls the relaxation response.

It has been studied as a standalone intervention in one using a using a different clock than the Horvath clock. But it

was shown in healthy population to, lower biological age.

So it as a standalone intervention was was was was shown to lower biology in a in a healthy cohort. They also used it in a in a in a cohort of heart disease patients.

And it didn't reverse bio age just in that one particular study. I think it you know, the take home is, is that we just need more research. But that gives an idea of how impactful meditation is.

It's so exciting because when you start to think about like, wow, if we can show that one thing can change it, then when we start stacking these things on top of each other, the potential benefit is just so much bigger.

And, and so many people are suffering unnecessarily. I think that's what gets me up in the morning. Right? It's like, yeah, just thinking about all of the people who are suffering today that didn't need to if they had the right information and the right resources, and to put these things in into practice a little sooner.

And so just make it. I mean, that's why we're here, right, is to make sure that people are, information. They can start making these great decisions and prevent and even reverse these complex chronic diseases that come with aging.

Yes. That's right. I mean, in our population, we looked at middle aged men. These guys were 50 between 50 and 72. So we didn't look any younger. We were able to show improvement.

You know, right in the heart of when age related decline is kicking in and we were able to do it. I think the massive take home and promise also the responsibility of us being in this omics area where we can measure, you know, gene expression is that our genes are not our fate.

You know, our genes do not dictate our fate. And I'm sure that you talk about this, you know, given the close association of the E4, allele in Alzheimer's we have there are things that we can do even if we have these genes.

So in this era, what appears to be the far more potent variable is those lifestyle choices that we make day in and day out. And we're really in the driver's seat of gene expression.

And so it's up to us to choose that we're the ones who get to choose quality of life. You know, one of the statistics I cite early in the book is that our final 16 years in this country, our final 16 years are spent with at least one and often more often than not, actually, multiple significant illnesses.

So, you know, just think about that. Multiple conditions, all of our savings, our kids inheritance is going towards, you know, complex care, pharma, hospitalization, etc., etc.

all of you know, we, we just we don't think about what's going to happen, until it's upon us. And yet we need to be thinking about it now and changing it.

You know, I also start cite some economics early on in the book, the potential cost savings for focusing on aging and putting some effort into improving healthspan.

It's just astronomical. It's absolutely 100% astronomical. And as you said in the very beginning, if we look at aging and slowing aging down itself and instead of siloing out, you know, Alzheimer and then, you know, Parkinson and then cardiovascular disease and diabetes and cancer stem siloing everything out in the National Institutes of Health and, you know, funneling billions of dollars into each of these isolated entities.

Let's look at aging as a whole and how we can slow that down. And, you know, the the economic, the the, the, the, the savings and suffering, the economics of it.

I mean, it's just I just don't I don't think we can overstate the potential benefits. Yeah. So compelling. And also just like, why are we not already doing this a little bit.

Well, I think a piece of it is that we haven't had Heather, the kind of the tools that we are moving towards now. And I think, you know, Sinclair's lab like, you know, identifying the aging might be happening right here in the methylation or in the epigenome.

And, I mean, I think we're at a confluence of events today that's really shining light on where we need to be putting our energy. And hopefully science will just, you know, in the government, in funding, etc., will just follow up with focus here.

Well, that is a hopeful message. And also for those of you who cannot see this, who are just listening, Kara's skin is a testament to how well this is.

So I think that I read somewhere that you're 54. Is that right? Yeah, actually, look at five now. 29. Yeah. Right. So I'm going to start eating liver today.

And, and for it's so funny. Yeah, I, if I didn't already drink green tea and, you know, lots of broccoli, then I would start that as well today. But, yeah, you're, you're the best spokesperson for this.

Because you clearly you're living it. And so thank you for sharing all of this incredible, helpful, empowering information with our listeners. I know that this is just insanely valuable and also so simple and straightforward.

And, and I hope that all of our listeners will get started and eat a little bit more of these great foods that you talked about a little bit more, maybe meditate and exercise starting today.

Thank you. So much. I want to make sure everybody knows. I know you've talked about younger you the book, but I want to make sure everyone knows how to, get the app.

Everything else that you didn't. Yeah. Just go over to younger you program.com and you'll find all things the book. They're younger you in the app. Younger you program.com app and book. Are there.

You can also go to my website if you're interested in our clinic, our blog, our podcast etc. etc.. And that's just Dr. Cara Fitzgerald doctor care if it's gerald.com.

Excellent. Kara, thank you so much for joining me today. It's been an absolute pleasure. Yeah. Likewise. Heather, I'm so glad to have this time to talk to you.