



THE

FATIGUE

SUPER

CONFERENCE

DNA Methylation and why your genes matter

Guest: Dr Kara Fitzgerald

Alex: Welcome to ‘The Fatigue Super Conference’ and my guest for this conversation is Dr Kara Fitzgerald and I’m excited to be getting into DNA methylation and understanding particularly how that is a key part of the jigsaw for people with the whole different range of fatigue related conditions.

To give a bit of background and context on Kara, Kara Fitzgerald completed her post doctorate training in Nutritional Biochemistry and Laboratory Science under the direction of Richard Lord PhD at Metamatrix Laboratory, now Genova Diagnostics that many people will know. Her residency was completed at Progressive Medical Centre in Atlanta, Georgia, Dr Fitzgerald co-authored and edited ‘Case Studies in Integrative and Functional Medicine’, was a contributing author to ‘Laboratory Evaluations for Integrative and Functional Medicine’ and The Institute for Functional Medicines textbook for functional medicine.

She has been published in numerous peer review journals and blogs regularly for professionals and consumers and is on the faculty if the IFM and maintains a functional medicine practice in Sandy Hook Connecticut.

Dr Fitzgerald welcome, thank you for spending some time with us today.

Dr Fitzgerald: Absolutely, my pleasure.

Alex: So I’m always curious with people that have gone deep into this world what’s been the personal calling. You were saying to me before we started recording that you were inspired by one of the kind of, I don’t know if you’d call it Godfather’s or Grandfather’s of the industry, Dr Jeffrey Bland when you were an undergrad.

So just tell us a bit about how that inspired you to want to work in this area?

Dr Fitzgerald: Well it was actually past undergrad I was already in med school when I saw him lecture. Nutritional Biochemistry resonates with some

of us, you know I've met colleagues in the field for whom they hear the pieces of the puzzle put together in kind of the biochemical structure. It's a framework for practicing systems medicine, for the jigsaw medicine, the term that you guys are using, and it just really deeply resonated with me as a solid tool and framework from which I could come and kind of figure stuff out, help people to get better.

Of course anybody's who heard Jeff Bland speak, especially when you're a student like I was, you know maybe every tenth word I understood but certainly his brilliance was apparent and how he elevates flavonoids, the tools that he uses in botanical medicine and nutraceutical medicine and how he locks it in biochemically just resonated with me. Then I had an opportunity to do a post doc in Nutritional Biochemistry at the lab and jumped all over it and I've loved it, never a dull moment.

Alex: I always think people which spend a long time working at the labs get a really deep insight because as a practitioner one does a different test in different places but when you're seeing those tests day in day out and you're figuring out how the concrete picture meets, I just think that gives a really deep insight.

Dr Fitzgerald: I appreciate it. It's very rich, it was just a great time for me and I have since tried to recreate it in my clinical practice here in Sandy Hook. Well actually we're virtual, we've got a virtual footprint, not dissimilar to yours. We have clinicians tracking with us, we have a clinic emergent programme. There are two physicians here and there are a couple of folks running the practice here, brick and mortar, in Connecticut, but then the rest of the team is elsewhere.

So we do everything on zoom, it sounds like what you guys do a lot of too, so we've invited clinicians in to come track with us and we've built out a journal club and we have a nutrition residency programme. So long story short is that I've just created this amazing team of curious, passionate human beings and we converge in the virtual space a lot and help our patients get better and participate in our mission and vision of moving functional medicine as the dominant medical paradigm. You know just really trying to change the trajectory of the disease paradigm in the world. So I'm sure we share a lot there.

Alex: Yeah I think so, I think it's very, very cool. Let's get a bit into the topic we're going to talk about today which is DNA methylation and maybe for those that are kind of thinking what the heck is DNA methylations, maybe give a bit of context of that but also why it's so important to the fatigue population?

Dr Fitzgerald: Absolutely. So DNA methylation, a lot of people have heard of methylation, there's a methylation cycle in the body that's happening, buzzing all the time in really virtually every cell in the body making a carbon with three hydrogens. That's just one of the most fundamental molecules in the body that when placed on a different molecule or taken off a different molecule can really change the behaviour of said molecule.

So we can make neurotransmitters for instance, we can metabolise neurotransmitters, you know thinking about fatigue patients of course we're going to make adrenalin and noradrenalin, you know synthesized dopamine. So a lot of our neurotransmitters are produced and metabolized via methylation.

We detox compounds, we clean our bodies up, methylation plays a big role there. The methylation cycle interfaces with something called the sulfuration cycle and the big player produced in that cycle is glutathione, you know our main endogenous antioxidant. I'm sure the folks in your world out thinking quite a bit about increasing glutathione and you have to have healthy methylation, you have to have active methylation to be doing it. Methylation is involved in not only making DNA but regulating DNA in immune cell synthesis and regulation, in neurons, in neurogenesis, in maintenance. It's such a fundamental compound this carbon with three hydrogens, it infiltrates everything.

So our conversation today, we sometimes in my world talking about this will distinguish from biochemical methylation, which is detoxification making and detoxification neurotransmitters, etc., and then genetic methylation. Sort of these two worlds, it's a false distinction but it just helps us wrap our hands around what's a complex concept. So in DNA methylation specifically methyl groups are placed on our DNA and when a sufficient amount of methyl groups are on a particular gene it shuts that gene down from expressing. You know conversely we can have regions of our DNA that are not methylated, so it's hyper methylated when something's got a lot of methyl groups on and it shuts down or hypo methylated when it's under methylated and that gene is turned on.

So we use this to regulate genetic expression. This is where the environment interfaces with gene expression, what's going on. DNA methylation is a huge, huge piece of it, I bet you can get Alex, that there's all sort of opportunities for negative environmental influences to alter gene expression and one of the big places would be right there. I want to say one more thing and then I'm going to stop. These epigenetics, it's called epigenetics, these epigenetic methylation patterns are actually heritable. So what you have right now you could pass down to your offspring, are you biased towards health or are you biased

towards disease. I mean it's really kind of as simple as that and there's interesting research demonstrating this. Lots of animal studies demonstrating this heritable aspect of DNA methylation and then there's something called, for people who want to look at long term human studies, there's something called 'The Dutch Hunger Winter', where during World War II the people in the Netherlands were starved for a period of time. Women who were pregnant actually handed down epigenetic patterns to their offspring that carried forward through generations, so yeah increased risk of obesity and cardiovascular.

Alex: That's fascinating, wow.

Dr Fitzgerald: So it's heritable within generational but also in the generation of cell turnover in our body. So we're cleaning and changing epigenetic expression all of the time.

Alex: I want to come back to that a bit more in a bit because that's super fascinating.

Dr Fitzgerald: Yeah I kind of just unpacked a lot there but yeah go ahead.

Alex: So just to help people get a bit more of a handle on this what are some of the clinical issues which you would say are associated with methylation imbalances?

Dr Fitzgerald: Yeah OK. So what aren't I would actually put it like that (laughs). I can give you a little bit of the background, I don't want to be too alarmist, but there are two reasons that it became so interesting to me. One is that in functional medicine we're always thinking about methylation. We tend to be thinking about what I call biochemical methylation where we're wanting to detox and we're supporting methylation that way or neurotransmitter synthesis or you know just tending to our central nervous system and thinking about methylation there.

Oh actually of course the other huge issue is Single Nucleotide Polymorphism so anyone can send off some saliva and have back a whole lot of methylation genetic data and decide that they're not good at methylation because they've got maybe an MTHFR polymorphism or something along those lines. People can become really anxious and there's a lot of content on the Internet talking about these massive methylation protocols that people should adopt. Sort of anchored in taking a lot of B12 and folate or you know in addition butane or certain immune acids. There's a host of nutrients involved in the methylation cycle so all sorts of protocols will just really ramp it up.

That doesn't take the DNA methylation, this genetic methylation, really into consideration. So the massive aha for me as a physician was when I started to read the data and most of the signs in DNA methylation comes from cancer research and we know in cancer research that methylation is really imbalanced there. Good tumor suppressor genes can be hyper methylated and shut down, sort of bad onco genes that promote cancer can be hypo methylated and turned on. So we can have this really skewed picture of methylation expression that allows for the pathogenesis, the promotion of cancer and there's just a ton of research out there on that.

So I think when I started to metabolize it some years back that stopped me in my tracks, me actually and the Director of my nutrition programmes Romali Hodges, it kind of stopped us and we really sat down and started combing through the literature and then we developed this whole methylation diet and lifestyle programme that we're going to talk about here in a few minutes. In fact we're researching it, so its proof of concept right now we're actually in the middle, towards the end of a big epigenetics study. So we're looking at methylation changes in this programme.

So cancer was where a lot of the research first came out but you can see it in any chronic condition, I mean even in acute conditions, and you could see sort of biases or vulnerabilities inherited. Cancer, cardiovascular disease, autoimmunity, certainly ME/CFS, really kind of you name it, allergic disease, schizophrenia, PTSD, alteration to the stress response can be inherited and can be based on these epigenetic changes, autism. So it's really kind of what isn't influenced by this.

Alex: Yeah it's super fascinating and one of the things that historically as I mentioned to you before we started recording I had ME/Chronic Fatigue as a teenager and one of the leftover pieces of that was always having sensitivities in terms of digestion and having to learn how to manage that in the right way.

It's fascinating my wife and I have three daughters and all three daughters had dairy intolerance from birth and all three daughters had silent reflux. The first one it took us a long time to realise it, with the others obviously we were quicker to see it, but there are certain things like that where you really start to see that can't be coincidence, right. You have three kids that end up with that level of, and we're talking about severe like proper intolerance.

Dr Fitzgerald: Isn't that fascinating and it's like nowhere else in either side of your family and then boom. And it's interesting because we always tend to look at the woman and the woman's health whilst she's pregnant and pre-conception and all of that, we put a lot on the woman. But let me tell you men do not escape, I mean this is seriously where the rubber meets the road with

men's health. I mean this is a really cool way to think about pre-conception and planning, just optimising your wellness, those are good thoughts.

Alex: So there's the kind of understanding that this is something that's going on, then of course we get into well what do we do about it and diet and lifestyle is the approach that you guys have been pioneering in terms of working with methylation.

So tell us a little bit about the story of how you saw the potential for that and became interested in that as a way to start to alter and change some of this?

Dr Fitzgerald: Yeah so again it goes back to our read in the literature, is it possible that I am as a physician could I be injuring any of my patients by pushing methylation to aggressively, by loading folks up on too many methyl donors. I just wanted to be mindful of that so we backed way up and cast a wider net, how can we influence methylation beyond just getting into the methylation cycle and throwing a lot of butane at folks and a lot of B12, a lot of folate and its associated nutrients. What else can we do?

Well it turns out a lot. It's really rather mind blowing how we can very safely and in this really elegant upstream systems way, very healthfully, influence methylation and I'll talk to you about a handful of the ideas that we pulled out of the literature. One would be reducing our stress response, I mean just very simply, well first of all you and I were talking earlier and we'll circle back to this, about the stress assault in utero exposure, adult, you know childhood exposure, that stress assault, you know that constant barrage of cortisol etc. can have some really pretty negative methylation altering properties to it. So working on stress or just the fact that you have to metabolise adrenalin all the time and you're going to use that methyl group, you're going to take that precious methyl group from other jobs and it's going to be just moving out your adrenalin all of the time. So just focusing on stress is a huge area to clean it up and it's extraordinary.

Our microbiome plays a massive role in epigenetic regulation, massive, actually in multiple ways. So we know a good healthy microbiome is going to make a lot of nutrients that are essential for good function, one of them being folate. So our folate reservoir can come from a healthy gut but also a lot of the compounds that our microbiome produce can just directly alter the behaviour of DNA methylation. So a healthy gut.

Looking at certain nutrients and compounds that we're ingesting, maybe the medications we're taking, are they causing us to kind of sop up our methyl donors. Toxins not surprisingly can damage DNA directly, can damage the

epigenome, can sort of utilize all of our methyl donors. And our diet, are we actually getting enough methyl donors in our diet.

Let's see what else did we look at that was really powerful. I think mitochondrial health, which I know you guys are thinking about all of the time, the nutrients, the compounds that are produced in the mitochondria in just the course of business in generating ATP are essential for healthy methylation. So we methylate and then we actively de-methylate if we want to change the expression, turn a gene on or turn a gene off, we can de-methylate, sort of clean it up. Some of those de-methylating nutrients come directly from mitochondria, so we want good healthy robust mitochondria to be able to get in there. So those are just a handful of things, you can see we can cast a wide net and we can augment DNA methylation.

Alex: One of the things I think is fascinating as you talk about it is it makes me realise you've kind of got these potential downward spirals or upward spirals that you deplete and that takes some out and that impacts the function which then depletes more. So when someone gets into a kind of illness cycle that it's almost like the weaker the system becomes that actually the more they're likely to express the negative parts of their DNA and that then weakens the system further. I guess it's the same thing on the healing path, right that you start to feed in a positive cycle?

Dr Fitzgerald: Yeah I think that's exactly right. So there's a continuum of change, it can be heritable so the changes to the epigenome can be very long lasting and they can also be rapid but in general I would think about it like we know from animal studies that one high sugar meal will actually have epigenetic changes long after blood sugar goes normal. So if you decide to go out and have a handful of cupcakes and you know a few chocolate bars or whatever, and think OK I'm going to have really bad blood sugar the next day or I'm going to feel lousy the next day but then I'll recover and I'll be fine, the fact of the matter is when we look at epigenetic changes, those changes go on actually for much longer.

Another area that I neglected to mention is sleep. Bad sleep can really kick your epigenetic butt as it were. So you're right these are lasting changes and then when you start to kind of alter them you can induce the same kind of speed forward cleansing cycle of lasting changes.

Alex: I know that you guys are doing an RCT on epigenetics and methylation at the moment. I would be curious just to hear more about that?

Dr Fitzgerald: So we're using our diet and lifestyle programme. We're putting people in a methylation rich diet, so all of the nutrients have been calculated

to supply optimal amounts of folate and B12 and all of the elements, you know, magnesium, zinc, etc., butane. It's also what we call a methylation adaptogen rich diet as well and that was one of our really cool aha things that I've alluded to but let me just kind of bring in. So we hyper methylate and shut down a gene and then we can clean that up, remove those methylation groups and actually turn the gene back on. So we want our tumor suppressor genes to be on, we want our inflammatory genes to be off, we want our anti inflammatory genes to be on, etc.

So there's a whole lot of sophisticated balance happening and there are a group of compounds we're calling methylation adaptogens that seem to have kind of this ability to sort of finesse things and probably a lot of them have fabulous science behind them and this is probably why they're so beloved and they're so time honoured. A methylation adaptogen that we're all consuming all the time is curcumin or green tea, luteolin, lycopene, rosmarinic acid from rosemary. A lot of these beautiful flavonoids actually can finesse methylation and kind of get in there and help with that sophisticated regulation. When we put this high methylation adaptogen aspect of the diet in with a lot of methyl donors on the diet we think we've got a pretty nice combination.

Incidentally, let me just say, there is no research suggesting that high methyl donor rich diet would push forward any disease condition like cancer, where there is some suggestion that supplementing at certain times with folic acid for instance, could move cancer forward. So food safe.

Alex: Yes and say a bit more about adaptogens because part of what's fascinating is the way that they can, I'm going to use the wrong language here, but they can increase or decrease in terms of, there's something that I think is biologically fascinating about that. It can be very to think about the body as being like a car that has a bunch of functional pieces that it's like you put this in and that happens and that happens but there's a wisdom and intelligence, a responsiveness, so it's fascinating.

Dr Fitzgerald: It's pretty extraordinary and the science is still emerging. By in large what we know about these methylation adaptogens, ECGC, curcumin, etc. is that they actually inhibit DNA methylation so they have an inhibitory effect at certain regions of the epigenome, it's not global. So there's a whole lot of de-methylating drugs, maybe not a whole lot but there's a whole collection. Mostly used in cancer where they globally shut down methylation and you can imagine that's going to shut down a lot of good stuff and be associated with the side effects. But these methylation adaptogens seem to kind of go where the body needs and help de-methylate genes that we really need on. Like again our tumor suppressing genes, that's where a lot of the science has been.

Then additionally there's some cool research suggesting that in some cases they might be actually promoting methylation on genes we want shut off while also releasing the methyl donors, pulling the methyl groups off of genes we want on. So the sophistication of these flavonoids extends far beyond what we could manufacture ourselves and perhaps part of it is just the property of eating the full food and there's a reason why a lot of these methylation adaptogens have been time honoured in traditional diets, the world over.

Alex: Yeah it's fascinating when you start to go into these kinds of things and you realise the depth. It's like often these things to the surface look relatively simple, like if you just get your head around the science and I love it when you get into these areas where it's kind of like we know something miraculous is happening but we don't know why, we can't just recreate it. It shows in a sense the innate wisdom of the body to do these incredibly kind of complicated, intricate processes.

Dr Fitzgerald: It's exactly right; it's like the sophisticated body wisdom. Let me put these ingredients in, way up stream, let go of wanting to push reactions forward, I mean coming from a biochemical background in a lab I really was interested in using high dose supplements, and I still do. I actually still do in my practice but I'm a lot more mindful now about having an end point and incorporating this broader thinking and just really relying on this sophisticated compliment of micro nutrients in a bite of salad for instance. Like yeah it is so beyond what we can manufacture.

I just wanted to mention too the other areas of the study that we're looking at, include exercise. So exercise again major either friend or foe in methylation, are we overdoing it, are we not doing it, or do we have a balanced exercise programme for us. Balanced exercise is amazing in its ability to just really favourably augment DNA methylation.

Alex: That's a really super interesting point because I think one of the things that can be a challenge for people with fatigue, particularly if they're at the more moderate to kind of severe end of that experience, is that they're unable to exercise or the exercise that they can do may be gentle yoga or it may be going for a 10 minute slow walk. I think it can be easy for someone to think well that doesn't count or that's not really exercise and in particular people that are getting into detox work they can think well I need to sweat and then they end up crashing their system by pushing it too hard.

So what you're saying is really interesting, that the point here is about balance and that balance point can change based upon someone's capacity and whereabouts they are in their energy cycle.

Dr Fitzgerald: That's exactly right, you said it better than I could, that's exactly right, and you know eventually we're going to be able to measure epigenetic changes like this more routinely so you'll see what's going on then that patient can feel validated rather than stressing themselves out which isn't going to be helpful that they can only get off the couch and walk and get themselves a glass of water or something like that. If they're really debilitated, that's OK, that's where they're at and they will evolve beyond that.

We're also looking at sleep, were tracking sleep and we're having our folks participate in a meditation programme and we're giving them two supplements. We're not giving them methyl donors as you might think, we're doing a probiotic that may increase folate, we're actually measuring different folate structures. We're measuring homocystein, we're measuring s-adenosyl methionine, we're measuring a bunch of things in addition to the DNA methylation sites. So a probiotic and then a methylation adaptogen concentrated, basically a greens food just loaded with really fabulous organic polyphenols that we're thinking will behave as a methylation adaptogen. So yeah it's kind of a systems lifestyle approach.

Alex: What sort of dietary changes are they making as part of it?

Dr Fitzgerald: OK. So again all of those flavonoids that I mentioned they're doing, it's a low glycemic/lower carb, not super high protein, there's a smidge of caloric restriction involved in it. We want people if they're willing to, to get in there and eat some liver (laughs) not everybody's willing to. Liver is an amazing methylation super food we'd call it because it's got B12.

Alex: Sorry to interrupt you but anyone that went to state school, I get that you call it your public school in the US, in the UK certainly when I was there kind of 1985 – 1995 will remember school lunches and liver. It used to be one of the most unpopular lunches of the month, it was up there with rice pudding and semolina and these kind of miserable kinds of foods.

Dr Fitzgerald: Oh that's so funny.

Alex: But you kind of come to realise many years later that actually how good that was.

Dr Fitzgerald: Yeah. You know when you look at the really, really old research on iron deficiency, anemia, on macrocytic anemia and B12, the research back in the 40's/30's and so forth they're all just giving everybody these liver concentrates. Loads of liver, yeah it was like the elixir food back in the day. But you know what I don't love liver, I mean I like pate. Actually so I don't forget on our website, which is drkarafitzgerald.com, we have a whole recipes

tab ad you'll see everything that's a methylation approved diet recipe will be labeled as such as we've got a really good pate recipe over there for people who want to venture over into liver.

But that's not it. You don't have to do liver if you don't like liver, in fact if you're vegan or if you're vegetarian or if you're on a restricted diet like you're on a FODMAP diet or you're on something for ulcerative colitis, or you've got particular food allergies or sensitivities you can fold the methylation diet and lifestyle principles real easy into any baseline prescription. As you can imagine it's loaded with greens, if you can do eggs we definitely want you to because choline in eggs is just a beautiful methyl donor. What else do we have, nuts and seeds, we want magnesium, we want zinc, shitake mushrooms interestingly, they've got all sorts of beautiful properties, including they're a methylation adaptogen. Again foods high in D, foods high in A, both especially A we can get from liver, those appear to have methylation adaptogen properties. So beyond the flavonoids or the polyphenols there are some vitamins that have research on them that appear to be adaptogenic as well.

Alex: So it sounds like it's a little bit less about taking foods out, there may be some of that, but it's more about emphasizing certain foods within the diet?

Dr Fitzgerald: Yeah that's right. We've got a few iterations of the programme, so I would say we want to keep it low glycemic, we want the carbs to be a little bit lower, most folks in our practice are gluten and dairy free at a minimum, we see a lot of people with pretty serious allergies and sensitivities so that piece you can manage and then yeah you can layer. Really most importantly is that you can layer these methylation diet and lifestyle principles into whatever you're doing.

Alex: I'm curious as to some of the clinical stories of how this goes. So someone comes in with fatigue and let's say they're kind of moderate on that spectrum, they're not kind of housebound/bedbound but they're also really not functioning, like it's having a significant impact on their life. Going down this path what would be a typical clinical picture of how you would hope or expect to see that unfold?

Dr Fitzgerald: Like how we might enact the MDL programme?

Alex: Yeah.

Dr Fitzgerald: Well I would say again that the person who comes to us with fatigue, I mean we're doing functional medicine so fatigue, chronic fatigue can have any number of underlying etiologies and you just really have to carefully tease it out. At our clinic we cast a pretty wide net regarding laboratory

analysis to just identify those underpinnings. Are we looking at an infectious cause, are we looking at microbiome involvement, are we looking at mitochondriopathy are we looking at thyroid HPA dysfunction, are we looking at all of the above. I would say as often as not we're looking at pieces of all of those and it's full systems approaches required. So that would be our first step. Really nailing down, in the IFM we use a tool called 'the matrix', which helps us really map out systems picture and identify where we need to go into first.

Certainly we see lots of immune dysfunction, lots of gut dysfunction and lots of mitochondrial issues. Actually yeah I would say those are the biggest three and then after that maybe we're looking at communication and HPA disruption. Although you know what as I'm saying this out loud I'm like we see toxins as well, don't we.

Similar to what you guys are doing at your clinic we'll just map it out and we'll begin to piece it together. So methylation imbalances are de rigor, we always identify them. There isn't a fatigue based condition that will not require some of this thinking. Do we put them 100% on, we've got what we call the methylation intensive, 'the methylation diet and lifestyle intensive' and then we have the layered. So are we going to just immediately put them on the whole intensive, sometimes we do that, probably more often in my practice we're layering it on because we're doing some sort of a therapeutic elimination as well. Does that make sense?

Alex: Yeah absolutely and I think it's that combined approach of the different pieces of the jigsaw but obviously you have this specific focus, which I think helps see things through a certain lens.

It would be interesting also to understand a bit more about, I'd like to come back to mitochondrial function in a minute, but a bit more about why DNA methylation is so important in M/Chronic Fatigue specifically and I know that there's some research that you were mentioning, before we started recording, about that.

Dr Fitzgerald: Yeah there is some interesting research. So it's an emerging area of research, I pulled up a handful of studies looking at it. All of us as we age we methylate actually more poorly, I would say. In general ageing is this global hypo methylation process, that means if we looked at all of our DNA we would see less methylation than we do on somebody young. That's why you see homocysteine, if people are familiar with that, you commonly see homocysteine rise that's a pretty good surrogate marker of global DNA methylation status. It's not perfect but it's pretty good.

So you can see that in ME/CFS folks perhaps a little bit more accelerated, actually you can see it in autism, there's a number of chronic conditions for which you can see this sort of accelerated global hypo methylation patter. But what's interesting is that there's these discreet pockets of hyper methylation, or what they call differential methylation, so you compare it to a healthy group of people and the CFS folks they've got different patterns, patterns that don't match. Those patterns can be associated with genes that are involved with inflammation and one of the interesting things for me was seeing that glucocorticoid methylation pattern, so on the glucocorticoid genes you can see the kind of disruption there and there's a lot of pretty interesting research actually by a guy out of McGill University, a scientist out of McGill, whose one of the premier epigeneticists in the world, his name is Dr Mose Chef.

He's really looked carefully at these differential methylation patterns on glucocorticoid receptors and he started in animals and what he showed was that when he looked at mice sort of the maternal grooming habits of the mum to pups would dictate later response to stress. So these momma mice that were really loving and good to their pups would build more resilient adult mice later on, they would be able to handle stress and then just conversely those that weren't their stress threshold was much lower. Those were really strong epigenetic patterns that were actually heritable, so they're pretty built in.

Then he started to look at humans, and he's actually shown a lot of really interesting stuff with regard to humans and one of the most fascinating pieces, the years of research that he's been doing with his team at McGill, is this ice storm that happened, tracking offspring out of this ice storm. So up in Montreal there was a massive winter ice storm that really kind of shut the town down in the 90's and it shut it down for, I want to say a week, I mean it wasn't forever but it was a good jolt to the system, and they tracked women who were pregnant during that time, they've tracked offspring and they've seen a higher incidence of autism as well as allergic disease in this population. Regardless of whether it was a physical stress response or just the stress of maybe having a difficult time getting food and having the environment really cold and just the anxiety of being in that as well as the mental and emotional response. So they looked at emotional and physical stress and saw a similar imbalance on the epigenome of these offspring.

Alex: That is so fascinating, it's amazing.

Dr Fitzgerald: It is yeah and you can see these same patterns, these differential patterns of imbalance in PTSD or just folks who have a higher total life stress experience, there's been research on it. So particularly in the population you're working with I couldn't underscore more the importance of that psychology piece that you're doing. It's a big deal and my pretty cursory

look on the science around it and it is new just underscored how incredibly important it is. Not only is it important but something that you just want to engage in for a while. I wouldn't necessarily go one distress sort of appointment and learn a rudimentary technique and then just kind of move on, if I was struggling with ME/CFS I would get in there and just kind of hang with this for the distance because there's some deep changing or restructuring that needs to happen.

Alex: Yeah, often the way I think about it is if someone has spent a lifetime, for example, unbalancing their microbiome its not a case of taking a couple of probiotics and it gets fixed, it's a case of fundamentally changing the culture of what's happening and the same is true with psycho-emotional patterning. You spend a lifetime wiring things up, you don't just do a couple of techniques once or twice and expect it to change. You have to rewire the system and if that's just calming the system down that goes through a series of stages and its like if someone moves too fast too quickly it just pops back because the bodies trying to find the homeostatic balance and it thought the imbalance was balance. So yeah you have to train that but that research is fascinating, it's really cool.

Dr Fitzgerald: It is fascinating I mean I think this is going to validate a lot of what we've known. I mean we're going to be able to look at it and in fact after Mose Chef is doing such cool extraordinary work, like if a Mom is pregnant and she's experience some kind of stressor lets test the offspring immediately and begin to augment it. In his mind this methylation and diet programme actually he's really interested in our study would this be an intervention or can we do short sort of aggressive intervention with methyl donors. Would this be a time if we identify these changes early that we get in there and get busy with different methyl donors like s-adenosyl methionine or B12 again or folate etc. you know for a short aggressive intervention where we get in and change baseline and then we do this longer sort of lifestyle work.

Alex: Yeah that makes absolute sense. I'm a little mindful of time but I just want to ask a little bit around the role of mitochondrial health and methylation because obviously for anywhere on the spectrum of fatigue, be it just kind of low energy or it be severe ME/Chronic Fatigue, mitochondrial function's obviously an important part of that jigsaw.

Dr Fitzgerald: I know it really is. I mean to have the healthy methylation cycle, so to have good biochemical methylation where you're making your neurotransmitters, making your white blood cells, you know detoxing etc. etc. All the myriad ways biochemical methylation is happening just to make the methyl donor to produce glutathione and antioxidant, just that fundamental cycle requires a lot of energy, it just requires good mitochondrial function. But

then really interesting to me and sort of a deeper dive is this idea that the intermediates in the kreb cycle, so the kreb cycle is one of the, well anybody whose done any training in medicine to an extent you need biochemistry and of course you'll learn about the kreb cycle, maybe you have as an undergrad. It's the way that we pass electrons onto the electron transfer train, ultimately it's like the first step in ATP synthesis, so it's turning our food into energy. It's hugely fundamentally important, if we don't have functional kreb cycle we're not going to be making any energy.

But these intermediates are actually involved in cleaning up the DNA methylation pattern, so turning things off and just helping us get a fresh start with DNA methylation pattern. So it's just another way that we need to support mitochondrial health big time.

Alex: This is super fascinating and I have to say you're doing a fantastic job of making something that could be very complicated very accessible so thank you. I'm mindful of time, for people that want to find out more about you and your work what would be the best place, obviously your website's a great resource, but yeah say a bit more about what 's on offer and people can find out.

Dr Fitzgerald: So if you're a professional and you're interested in learning about the content we've got directed towards professionals you can go to drkarafitzgerald.com but we also have drkfeducation.com, which we'll talk about some of the educational offerings that we have for professionals. And if you go to my website drkarafitzgerald.com you can get over to kfeducaiton.com. So there's a whole section for professionals where there are professional blogs and I have a podcast, in fact Dr Mose Chef is on my podcast, Randy Jirtle whose another amazing epigeneticist I have an interview with him, so there's a whole bunch of really cool stuff.

If you're a regular person and you like a little bit more professional level content check the out I think you'll enjoy them. We've got the recipe page as I was telling you about where you can get all sorts of free recipes that are what we would consider methylation super recipes. There's a store over there where you can get our Methylation Diet and Lifestyle book, again that's really kind of written for professionals but there's a ton of recipes in there. We've got our everyday methylation cookbook that you can just download as an eBook so if you want more than what we've got for free on the recipe page you can grab that book.

We've got a couple of webinars, a webinar package where we delivered this content to the Cleveland Clinic and that's available for purchase. So there's actually a ton of stuff, you can just go to the search and type on methylation.

Alex: Fantastic. Dr Fitzgerald thank you very much, its been fascinating and I really appreciate your time, thank you.

Dr Fitzgerald: Absolutely, my pleasure.