Announcer: Bulletproof Radio. A state of high performance.

Dave: You're listening to Bulletproof Radio with Dave Asprey. Today's cool fact of the day is it turns out it's not just your mom who passes along mitochondrial DNA. If you read my book Headstrong about mitochondria and how to turn on your brain, you learned what we all commonly believe, that mitochondria comes from mom.

Dave: Well, in some cases, you might have your dad's mitochondria. They're just not that common. So leave it to dads to break the rules in textbooks. Turns out fathers in three unrelated families have been documented to pass their mitochondria, those tiny little things we like to call energy factories found in cells, onto their children. And if you're familiar with lots of the stuff that I talk about, mitochondria do a lot more than make energy. They're actually the frontline environmental sensors, and as you're going to hear about in today's interview, they do more than that when it comes to interacting with your brain.

Dave: But scientists have long thought that kids just always got mitochondria exclusively from mothers, because mitochondria and sperm get destroyed during fertilization of the egg. And this happened because a mitochondrial disease researcher said, wait. How is this possible that we could have paternal DNA in a woman? And after they did a bunch of work on this stuff, they figured out that that woman's cells had some mitochondria from her mom and some from her dad. And they looked at the woman's brother who also had that thing, and they said, this can't be. So they asked a bunch of other researchers, and they found 17 people in the three families who had 24-76% of the mitochondria from their fathers.

Dave: And the net of all this for you is that if you wanted to blame everything on your mother, you can't anymore until you've done your mitochondrial DNA testing. All right. On that news, speaking of blaming things on your mother, you should check out Game Changers, my new book, if you haven't already. It just passed 100 five-star reviews on Amazon, hit the USA Today bestseller list, and people on social media are really talking about the 46 laws for people who want to perform better, some of which are mitochondrial laws, but many of which have to do with how you think, your stress, and how you respond to the way you were raised. Basically, it's the rule book based on what hundreds of game changers have done, how they prioritized things, so that you can prioritize what you work on first in the right way.

Dave: And what you're going to learn in today's interview is awesome, because you're going to find out that your mitochondria have a much heavier role to play in a lot of the things that you think are about the thoughts in your head, the voice in your head. My self position has always been that the evil little puppet masters behind your ego, and I think we're getting a little bit closer to saying maybe that theory is true. We'll find out in today's interview, which is going to be amazing.

Dave: It's going to be amazing because I'm a mitochondrial nerd. You might call me a mitochondriac. We had T-shirts like that at the Bulletproof Conference a few years ago. And today's expert who's on the show is a guy I've actually wanted to interview for a

long time, because he's written some papers that I read on PubMed that got me really, really excited. And yeah, you don't hear that a lot from people who aren't total nerds.

Dave: His name is Martin Picard. I already asked him, he's no relation to Jean Luc. And he's an assistant professor of behavioral medicine and psychiatry at Columbia University. And for the last 10 years, he's been studying mitochondria and worked with leading experts. I mean, the godfathers of mitochondria. Godmothers, do you call them? Anyway, of mitochondria research. And in 2015 at Columbia, he established the Mitochondria Signaling Laboratory, and they're figuring out how mind-body interactions work, including these unusual, novel principles that underlie your mitochondrial response to stress, how you maintain your health, and how subtle mitochondrial defects can affect yourselves and even your aging.

Dave: If you want to know exactly what's going on inside that biology of yours so that you can have better control of it, you better be paying attention to mitochondria, and here's a guy who's paid more attention to those little bastards than anyone else I know. Martin, welcome to the show.

Martin: Thank you, Dave. It's really a pleasure to be here.

Dave: All right, I've gotta ask you. Has anyone ever called mitochondria "little bastards" in your experience before?

Martin: No, I don't think so. I think that's the first time I've heard that.

Dave: All right. I want to know, Martin, how the heck did you get so interested in mitochondria, of all the things you could've done?

Martin: I was an undergrad student in physiology at McGill University in Montreal, and I really was hoping to understand, why is it that some people just stay healthy for a very long time, and some other people just tend to get sick all the time? And I knew, maybe from personal experience ... My mom was a nurse ... It seemed to matter how people felt, and that would influence their health and some physiological functions. We all have experience of feeling not so good and being more vulnerable to getting a cold, and there's actually really good research on that.

Dave: So when you feel stressed or anxious, you're more likely to get sick.

Martin: Correct.

Dave: Okay, good deal. And you wanted to figure out what the heck is going on there, why.

Martin: Yes. So as a physiology student, I thought, surely I'm going to learn about these things. Psychoneuroendocrinology, how the psychological factors affect the hormones and affect the body. And as I was a student, the fashion at that time was cellular physiology. So I learned all about the molecules and about different parts of the cells and genes, and

there was nothing about the psycho part of it, the psychology. So I thought that was a little disappointing.

Martin: Then towards the end of my degree, I was looking for ways to learn about these things, and then I studied integrative medicine, and then eventually landed on this professor in graduate school who was a mitochondrial expert. She had just been recruited through McGill University. Her name is [Tanya Tievocello 00:06:27], and she studied mitochondrial disease, and then she said, oh, why don't you come work with me? And I was always attracted to mitochondria, 'cause you heard about them as the powerhouse of the cell, and I felt like there might be more to it, and it'd be a useful track to follow.

Martin: So I was attracted to mitochondria initially with a visceral feeling, and then there was this opportunity to work with an expert.

Dave: Wait, don't visceral feelings come from mitochondria?

Martin: They might, they might. I don't think we know that for sure, but they might, yes.

Dave: I'm going to argue that we do know that for sure, just based on reductive logic, because ... Well, where do the electrons that drive the feelings come from? They're produced by mitochondria, right?

Martin: Correct.

Dave: So if you go down to the electron itself, those visceral feelings had to come from a mitochondria.

Martin: Yes. That's going deep very quickly, but indeed, you could argue, the reason we are alive and the reason we breathe is because of energy flow in the body, right?

Dave: Yes.

Martin: If you think about the fundamental difference between a living organism ... A living, thinking, feeling, conscious person and a cadaver, a dead body, the main difference is the flow of information. The molecular components of the body are exactly the same, but in the living, thinking, feeling, conscious person, these molecules are animated by the flow of energy. And a big part of that is going through mitochondria.

Martin: And if you want to convince yourself how important the flow of energy is to consciousness, just block the carotid arteries in the neck that go to the brain, and if you interrupt oxygen flow to mitochondria in the brain within, I don't know, 15 seconds? 10-15 seconds? Then you're out, consciousness is gone. So I think that tells us ... It's a loose argument, but it tells us something very profound, I think, about the link between energy, consciousness, and our experiences and how we experience the world.

Dave: What makes sense now is you mentioned that you studied integrative medicine or functional medicine as a part of your path. And a lot of times when people are doing

more university-focused research and they haven't studied some of the holistic sort of things, they're not going to have the view that you do, 'cause you did a paper with Dr. Epel, who's been on this show, Elissa Epel. We talked about stress and telomere lengthening as one of the things that makes you old.

Dave: You've done work on aging, and you're doing work on these feelings and emotions and how they come together, and looking at it from a single root cause, which is unusual in my experience with academia. You tend to focus on one stack, and so to say, I'm looking at this ... but you're looking at one cause that may be filtering out into many different things. Did you grow up with weird parents or something that made you multi-disciplinary like that?

Martin: I think my mom was definitely inclined to think outside the biomedical box, having training as a nurse and having direct personal experience with patients. And so maybe that was part of it. I tend to credit my mom for a lot of things, and maybe that's one of them.

Dave: Including your mitochondria.

Martin: Yeah, exactly.

Dave: Sorry. Just for people listening, I'm going to keep making mother mitochondria jokes all episode long, and you're just going to have to deal with it. Okay, keep going.

Martin: What was the question again?

Dave: I was just wondering, why do you have a lab, and you're looking at aging, you're looking at stress, you're looking at emotions, and you're looking at mitochondria. And this is out of the norm for the last ... I'm going to call it 200 years of academia, until you go back to the natural scientists, natural philosophers before that, where they had spiritual and emotion and a very, very bad chemistry all mixed together. But it's been separated out for at least 100 years, and here you are, talking about emotions and subcellular components. In the same sentence, you talk about aging, which hasn't been done before. And that's actually ... Dare I say game changing? I don't know what made you the guy to do that.

Martin: I'm not sure I have a good answer for that, but I think what we've become really good at as a scientific community and maybe as a population is reductionism. And we've developed all sorts of disciplines and all sorts of scientific tools and machines in the lab, which basically aim to break down very complex things into very small pieces that we can understand and grasp, and make ourselves believe that we understand how they work.

Martin: So that's the beauty of reductionism. We can take really complex things and think, yes, this is how it works. This little piece A leads to piece B, and then that leads to C and that leads to D, and then somehow that's part of this bigger complex experience. So I think we're really good at reductionism, and it has served us really would. If you look at the

engineering feats that are happening now, we can go to space, and we can make electric cars, and we're maybe on the verge of becoming a lot more sustainable as a society. Those are all, I think, products. And all of the medical advances and treatments that are available, they're products in large part of our reductionist approach to science.

Dave: Yeah, no doubt that works. Anyone who says reductionism isn't useful is not paying attention.

Martin: Correct.

Dave: But it does take something out. That's what reduction is.

Martin: Yes, exactly.

Dave: The word itself. But you're adding something back in, which is unusual.

Martin: Yes. Well, I think what my lab focuses on and what I see ... Everyone in this world can make a contribution in some way. I hope that what maybe our lab's contribution can be is to integrate things back together.

Martin: So we still use the tools of reductionism to understand different parts of the mitochondria and how they use the food that we eat, the oxygen that we breathe in, and transform that into energy, and then generate specific signals. But we try to see this in the context of the whole person. That's what we try to do, and I think having trained in integrative medicine might have helped, and during my undergrad, I was also part of a systems biology training program-

Dave: Of course.

Martin: ... computational systems biology, integrative mathematical approaches. And at the same time, I was part of a training program in psychosocial oncology, to try to understand the psychological and social aspects of cancer. So I guess all of these things together, it's like when you're raised ... In sensitive periods of develop, things can have a big influence, and maybe all of these things had an influence, and now have convinced me that really where things are at is in integration. So we try to integrate the subcellular organelle, mitochondria being an organelle level, with cellular level, and then the whole person, and then the person within the environment and its context. So I think it's really a movement towards integration that's the driving force.

Dave: You're one of the leading voices, you and Elissa and Doug Wallace, another major researcher who I think you studied with ... If you're listening to this show, you've probably never heard of any of these people. And we have a good number of academic researchers and medical professionals who listen to this show who might have heard of them. But these are the people who are breaking beliefs left and right, where we just didn't understand how important this one part of the cell was. In my own life, having weighed 300 pounds, having had, what, we'll say, no ability to measure my mitochondria function when I was 16, when I had arthritis in my knees and all this

obesity and all ... other than just to look and say, wow, that guy's mitochondria seems to be making an awful lot of inflammation, which means they're not making an awful lot of energy. That's called muffin top, in case you're wondering.

Dave: But that whole thing ... So I looked that way, and I could even draw causation from environmental toxins that lower mitochondrial function and things like that. But I don't have data, 'cause no one had data back then. However, everything that I've ever done that made me kick more ass at everything I do basically makes my mitochondria either stronger or more efficient. And that's the body of work most of biohacking is around, making those little bastards happier and faster, which makes you happier and faster. And that's why in my model of the world, there's a very clear line between mitochondria and the way you show up for your kids or your next meeting, and that's why I'm so excited both for this interview and just to share on Bulletproof Radio ... This is the stuff that changes your life fastest. Okay. I'll get off my soapbox and ask you an actual question.

Martin: Yes, Dave, actually ... You mentioned Doug Wallace, and I'd like to take a moment to just say how important Doug was for the field. In my development, but mainly for the field. I remember when I was a grad student and I was starting to learn about mitochondria and mitochondrial DNA ... 'Cause it's the only other part of the cell, other than the nucleus, to have its own DNA. And we could talk about evolution and where mitochondria come from and how they made us, complex multicellular life, possible for a long time. But Doug was really a pioneer in first identifying the maternal inheritance of mitochondrial DNA, and you addressed something at the onset that contradicts this. But for the most part-

Dave: He's still right. The fact that there's a few corner cases ... No, they come from your mom. Let's just be really clear. And Doug figured that out.

Martin: Yes, yes. And he did so much for the field. And I remember as a grad student, I was reading this ... I was on PubMed looking for articles that were relevant to what I was doing, and then I see this paper from Doug Wallace. It was mitochondria as chi. Chi, this Eastern-

Dave: He's right.

Martin: Traditional Chinese medicine concept. It's like, wow, yes. This is it. I need to do my postdoctoral training with this person. So that's actually what made me write an email to Doug Wallace and say, can I train with you? And it was ... He's a visionary.

Dave: Have you changed your life in the last 10 years because you know more than the average human, by orders of magnitude, about mitochondria? So given that you know more than I do, do you wake up every morning and do a mitochondrial meditation? Do you drink a mitochondrial soup? What has changed for you, given what you know, 'cause I know for you ... You have what you can publish in academia because you know. But I want to know, you're going to lay the odds for yourself. I don't know what you're doing that you haven't published that's for you.

Martin: I definitely, from the stuff we've discovered in the lab and ... It makes a really big impression to me to see mitochondria, because they're so beautiful. And we do a lot of microscopy work, so you actually see them move about in the cell. If you ask Google what do mitochondria look like, Google images, you get these images of bead-shaped little things, or peanut-shaped, or whatever your favorite shape is.

Martin: But if you actually look in a living cell, they're so beautiful, and they move about, and they can actually fuse with one another. It's called mitochondrial fusion. And long ones can actually fragment into small pieces. That's called mitochondrial fission. And seeing this, and also just the inside of mitochondria in the electron microscope, is just something I love. It makes an impression on me and reminds me how beautiful biology is, that these are important little creatures to nourish, and we're finding out, how do we nourish them? And I think you know quite a bit about that.

Martin: We know moving, being physically active, is probably the best thing you can do for your mitochondria. And being inactive for a very long time is not so good. So I try to live by that and be active. Eating too much is probably the second worst thing you can do for your mitochondria, and if you have the choice to be hungry or to be overfed, you should aim on the hungrier side. A lot of studies have shown this.

Dave: Yeah. So do you do intermittent fasting?

Martin: I have tried it, yes. And I don't do it as a regular thing, but I'm very mindful of not overeating, because it saturates the mitochondria, and for seem reason, it makes them fragment and probably not talk to each other so much.

Dave: It probably also matters what you're overeating, like a bowl of French fries versus a bowl of salad is probably going to have a different effect on fragmentation, but no one knows yet.

Martin: We know a lot of sugar is probably the worst thing that affects the mitochondria.

Dave: Yeah. How about alcohol? What does that do to mitochondria?

Martin: That's a great question, I don't know. Actually, there's some work being done by Yuri [Hanyasky 00:20:22] at Thomas Jefferson on this topic. It definitely affects them, but I don't know in what way.

Dave: 'Cause we know they can burn alcohol. In fact, they'll preferentially burn it to get it out of the system as a fuel source before they'll even burn sugar. But it doesn't mean it does good things to them when they burn it, and we know the aldehyde spike and the rest of the body and the liver and the gut, it's pretty bad for you. But I don't know the research either, so I'll have to follow up on that. Maybe that's another interview I could do.

Martin: Yeah.

Dave: All right. So sugar's bad. Okay. So you don't overeat, you make sure you move. Oh, by the way, I also agree with you on the movement, and I've got a couple papers, 20 minutes a day of walking is kind of necessary. But I'm lazy, so I stand on a whole body vibration platform called the Bulletproof Vibe. It vibrates 30 times a second, which is a frequency that they know causes regeneration. They used these for astronauts to recover.

Dave: So if I stand on that for five minutes, maybe 10, sometimes while I'm on the phone or something, I like to look at when you're culturing cells and you have those little things that are keeping the cells moving ... I'm just going to shake all my mitochondria a lot really fast, and get it done for the day. I have no idea if that actually works for mitochondria, but I feel better and I look better and I have less muffin top when I'm done.

Dave: All right. So movement, food. Those two are obvious. What else are you doing?

Martin: Well, something we're beginning to find is that how you feel might influence your mitochondria. And that taps into this area that's developing called mitochondrial psychobiology that's connecting the psychological part of who we are ... We do feel things, we do think about things, that affects us. And then the biology, those biological, molecular, cellular processes that are happening at the cellular live.

Martin: What we don't know a lot about is how those two things are connected. And the hypotheses we're exploring with some of our colleagues is that mitochondria is that interface between the psyche and the soma, the mind and the body. We've had some results ... A paper that was published earlier in 2018 showing that how people feel a few days before you take blood to measure mitochondrial functional capacity or mitochondrial health is actually correlated. So if people feel better, it looks like their mitochondria have a greater ability to make energy the day after. But if mitochondria, better mitochondrial function, doesn't predict how people feel in that study. So it actually is the first evidence that mood and psychological states might influence the mitochondria in that direction, not that the other direction isn't happening, but that study showed quite convincingly that there might be a link from the mind to the mitochondria.

Martin: So I try to do things that make me feel good. I try to focus on projects and hang out with people who are stimulating. And I don't know if that really does something to my mitochondria-

Dave: Probably.

Martin: But it keeps me motivated and inspired, and I think that's important.

Dave: It's funny. In Game Changers, my last book ... And yes, I'm plugging the book. If you haven't bought the book and you're listening to the show, come on. It's going to save you a lot of time to read the book. But one of the big three things that hundreds of people like you have done really big work in their field ... What they do is what you just

said. They find a way to be happy which causes their performance to improve, rather than the other way around. Oh, I achieved, therefore I'm happy ... I was happy, therefore I achieved. And achievement, as we've already established ... Well, it's driven by energy that has to come from somewhere. Eventually, it comes from your mitochondria, or maybe from sunlight if you're a plant.

Martin: That's funny you mentioned the plant. You know, mitochondria do chemically ... They do exactly the opposite of what plants do. So plants take water and they take the CO2, the carbon dioxide in the atmosphere, and they fixate the carbon and the hydrogen, and then they make sugar, they make starch, and in that process, release oxygen. And what do mitochondria consume?

Dave: Oxygen.

Martin: Oxygen and starch. Then what do they release as part of the Krebs cycle? This is the series of biochemical reactions inside the mitochondria ... They generate CO2 and they generate water.

Dave: Now, I'm going to hopefully blow your mind, which might be hard to do. I referenced either one or two papers from some researchers in Mexico who proved pretty convincingly that if you eat enough chlorophyll ... In other words, you're eating lots of green vegetables ... that up to 5% of your energy requirements can be met by your mitochondria using sunshine, not food. And they actually have some lab measurements in this, and that's referenced in Headstrong.

Dave: So I'm wondering if that old movie called Swamp Thing ... Maybe it was based on that corner case where, yes, a little bit is possible, kind of like having some of your father's mitochondrial DNA. It doesn't really happen very often, but it's possible. I think there's another little corner case for mitochondria like that. So I like the idea of being a breatharian and living off sunshine. I'm just not going to do that 'cause I've got other stuff to do.

Dave: By the way, if you're listening and it works for you and you actually have done it with cameras and observation and you can show that it works, I would love to see your evidence, because it'd be kind of cool to find a human that could do that.

Martin: Interesting.

Dave: Maybe there's one in India somewhere who has some good evidence. But anyway, I'm getting off track here.

Dave: So you've talked about how you feel. There's a supplement that I manufacture. It's called KetoPrime, and it's keto-succinic acid. So it's the last step of the Krebs cycle before you reinitiate with coenzyme A, which is basically coming from carbs that you eat, or from ketones. And when people take that, in two clinical studies, they showed that the compound in KetoPrime, the active ingredient, that keto-succinic acid ... that it treats the emotional symptoms of PMS.

Dave: Now, this is an interesting thing where you're feeling crappy and angry, you take something that increases your mitochondria's ability to make energy from food by priming the pump of the Krebs cycle, and magically, your emotional symptoms subside. So that would support your point that, well, maybe mitochondria are driving this happiness and maybe happiness is driving the mitochondria. I think there's something to that, 'cause I'm the same way. I know if there's a stack of mitochondrial enhancers that I take, when I take them, I'm happier, and if I take them when I'm cranky, I get less cranky. What mitochondrial enhancers do you use?

Martin: I don't use any mito enhancers other than-

Dave: You don't drink coffee? Come on.

Martin: I actually love the smell of coffee, but I can't do the taste. So I don't.

Dave: Oh man. Well, if you put enough sugar in there ... Oh, wait, that would defeat the purpose.

Martin: Yes, it does.

Dave: So, tea? You must use green tea or something.

Martin: Yeah, I drink tea.

Dave: That's a mitochondrial enhancer. You've got your polyphenols in there.

Martin: Yeah, that might very well.

Dave: All right. If I send you a stack of the mitochondrial enhancers that I use just to try them ... I'm not asking you to endorse or ever tell the world you did it, but if you would try them, I'll send them to you, because they might even fuel your research a little bit.

Martin: Wow.

Dave: You want me to send them your way? I will.

Martin: No, I don't think I would. I trust in the balance of the organism, and its ability to do things. So I try not to put other foreign things in my body. Maybe that's my philosophy.

Dave: Got it.

Martin: Yeah. And there are, I think, situations where these things can be useful, and you're talking about the link between mitochondria and how you feel and mood, and there's good research that coming out linking metabolism and mitochondrial metabolism and depression.

Dave: Interesting. So they're finding depressed people have lower mitochondrial function?

Martin: Yes, and there's a marker of mitochondrial function, specifically the ability to mitochondria to use lipids. So as we eat, we're not talking about the trans fats that are in fries, but the lipids that are in pretty much everything we eat. These are very healthy. Perhaps the healthiest lipids are the avocado and olive oil and these kinds of things. Mitochondria love these, and they're so good at eating lipids and burning lipids. It's probably the cleanest thing that the organism, that the mitochondria everywhere in the body can burn.

Martin: So what people have found, and a lot of that research is coming out of Bruce McEwen's lab at the Rockefeller University in New York City ... They're finding that a specific marker, it's call L-acetyl-carnitine, or L-car, is actually low in people with depression. And you can study these kind of processes in animal models, and if you take animals, rats or mice, that are depressed, they tend to have lower levels of this. And if you supplement them with L-acetyl-carnitine, then it actually relieves the depression and the depressive symptoms. And there are actually quite a few clinical trials now underway to look at this, which is supplementing something that is naturally in the body and that is deficient in states of depression, and maybe that reflects something at the level of mitochondria, mitochondrial dysfunction, and their inability to efficiently use lipids. And if you can restore this, maybe you can restore the ability of people to perceive the world in a positive way. So that connects mitochondria to how we see the world.

Dave: It's funny. Acetyl-L-carnitine, or L-acetyl-carnitine, either way is different ways of saying the same thing ... is a very common and well-known anti-aging compound going back at least 30 years, we started supplementing that. People are likely to live longer ... before we knew what it was doing for mitochondria, 'cause you could see it was doing something good, but we didn't understand all the pathways we know now. And now we're understanding, oh, it increases a cell's ability to burn fat, which is why maybe people who are going to be in ketosis, intentionally, nutritionally, the way I talk about it in the Bulletproof Diet, maybe going in and going out ... You want to make sure you have enough L-carnitine, which comes from eating from red meat or from supplementing. So having that steak might not be such a bad idea, at least if it's grass fed and doesn't contain antibiotics that also inhibit mitochondrial function.

Dave: Let's go there for a minute. Mitochondria, ancient bacteria. Antibiotics kill bacteria. What's your take on mitochondria and antibiotics?

Martin: There's a lot of good data that antibiotics can damage mitochondria. So I think we've overused antibiotics in different ways in medical practice. We're really good at drugging a lot of things, and sometimes maybe it's not necessary. So definitely, mitochondria are sensitive, nimble little organelles. And they're clearly sensitive to antibiotics. So there's clearly a connection there.

Dave: One of the things that I went through as I was writing my book Headstrong about mitochondria and the brain was, let's find a list of the things that are documented in medical or biological studies to inhibit mitochondrial function, and what would happen if we just did those less? Not in a, avoid them with perfection and be afraid of them, but if you have a choice, don't eat the trans fats that screw up your mitochondria, don't eat

tons of sugar, but also things like antidepressants. A lot of antidepressants really wreck mitochondrial function.

Dave: And so I'm saying, if you were to build a lifestyle around supporting the mitochondria on the supposition that, well, they'll support you back, you should do that. Have you looked at antidepressants or any other pharmaceuticals that might have negative effects on mitochondria and thus unforeseen but predictable effects on moods or energy levels?

Martin: We haven't directly in our research, but other people have. There's some people who believe that a lot of the side effects that antidepressants and other medications have could be because they're altering mitochondria in some way. And people have discovered that there are different receptors on the mitochondria, receptors for neurotransmitters like serotonin and receptors for all sorts of different hormones on the mitochondria, including the cannabinoid receptor that's a receptor for cannabinoids and THC.

Martin: So we know they're sensitive to a lot of things, and there's very little known, relatively speaking, about the effects of drugs and medication on the mitochondria. So there's definitely a need to know more about that.

Dave: You talked about mitochondrial signaling, and as I was digging through the research in a way different and nowhere near as in-depth as you do, it looks like there's certainly chemical signaling between mitochondria. There's actual fusion, where they stick together and swap some stuff, and then fission that you talked about before. There's also potentially some ... They're responsive to electromagnetic fields, and they're also responsive to light, and they generate light. So you believe that mitochondria are using anything besides chemical signaling and fusion and fission to do quorum sensing or any of the other things that mitochondria might do to work as a distributed network of a quadrillion nodes?

Martin: That's likely. I'm not aware of any good data. The biochemical community in general tends to focus on the chemical stuff, the stuff we can see or measure directly. The biophotons are ... photons emitted from living things, living organisms-

Dave: Those are real, though, in that biophotons do exist.

Martin: I do believe they exist, yes.

Dave: Okay, yeah.

Martin: But they're really hard to see.

Dave: But those are hardcore physicists detecting them with real equipment in real labs that aren't run by people wearing tin foil hats, so I'm pretty sure they're real. But if you said, Dave, there's absolutely no evidence those people aren't crack smokers, I would reconsider. You think it's likely, all right.

Martin: Yes, I think biophotons are definitely real. The research on it has been a little put to the side because people have a hard time, one, measuring them, and two, fitting that into the traditional concept ... Whatever paradigm a scientist is raised in is a really powerful thing, just like the environment we're raised in as a child. And how and why mitochondria would generate light signals is a little hard to fit into the traditional paradigm. So that makes these kinds of things hard to study and push forward, so there's not a lot of research about this, compared to the chemical signals that mitochondria generate. Same thing for electromagnetic fields, and there's pretty good data that electromagnetic fields generated from different sources, biological or non-biological, can affect cells and probably mitochondria. But again, there's very little known about this, which means probably we should study this more, because that would be transformational.

Dave: Yeah. I've seen enough data in each of those that I know something is going on there, but I would be the first to say, I don't know what. And my background is computer science, and I did a lot of work on cloud computing, the very first cloud computing and early internet stuff. I taught at the University of California, so I would consider myself well-grounded in network effects, network behavior. And I look at mitochondria as a giant network in the body, and that they all have to communicate. There's algorithms we're using in crypto that are very similar to what I believe are mitochondria using for quorum sensing. Quorum sensing is the idea, how do we know what we're going to do as a group here? It's like voting.

Dave: So if you look at, say, aliens who'd be studying the US in the late 1800s saying, look. They send signals via the Pony Express. So all you have to do is just intercept the stage coach, use your X-rays to read all the letters, and you know everything about these weird creatures on the planet ... So they get obsessed snail mail. And then the telegraph comes out, and there's this one weird pointy-eared alien that's like, but there's gotta be something else here, I can see these little electrical bursts! And they're like, shut up, haven't you read the letters? Seriously, the letters are where it's at.

Dave: So they keep sending letters, and to this day, they're probably looking at all this junk mail going, how do they get anything done with all this junk mail? But they haven't figured out that there's also another signaling network. And when we build the internet, we have ... The data flows here and there's a separate signaling network that controls the controllers for the data. There's actually three or four of them, depending on what topology you're going through and how urgent it is, whether everything's about to break. So the body has to work the same way, because that's how large-scale systems always work. So it's those other things that matter the most that I think we're missing.

Dave: Now here's a question for you. Given that crazy alien world I just painted there ... If you, as someone who's well-grounded in what you've looked at ... If you had to bet on one of those things we talked about outside of chemistry as being the most important one, where would you place your bet?

Martin: There has to be some form of non-molecular signaling. I don't know how far we are into deciphering the whole alphabet or the whole system the way we've decoded the genome, the ACTG, the letters and how that codes for proteins and so on. I'd say

electromagnetic field and light, a lot of things ... There's a lot of good physical reasons why you would want to communicate with photons and with electromagnetic fields. It's faster-

Dave: You look at light and EMF together.

Martin: Yeah, in a way, isn't light-

Dave: I agree, by the way.

Martin: Light is a form of electromagnetic field, and the same way that physical stuff is also, to some extent, the materialization of some electromagnetic field that's denser than the usual stuff. So that's hard to say. The data is a little skim to make a good prediction.

Dave: It is.

Martin: But I think we can confidently predict that there's more than what we know.

Dave: Oh, that's a very safe and very truthful way of putting it. The light one is very interesting. Whether the light, the biophotons that mitochondria generate are sending a signal that's received by other ones ... I would argue that Mother Nature wouldn't waste energy creating biophotons if they weren't of use. So they're either of use in the body or outside the body. So maybe there's some kind of insect, like a mosquito or something, that reads your biophotons and says you're going to be delicious. I have no idea.

Dave: But I do know that I've looked at all of the research on what different wavelengths of light do to the mitochondria and the melanopsin sensors in your eyes, and I've looked at melanopsin mitochondria with Dr. [inaudible 00:40:32] at the Salk Institute on a microscope. And one of my companies, TrueDark, makes glasses that filter out all of the types of light that we know affect the melanopsin centers, which are studied with external mitochondria, that control the timing system in the body, which also controls mitochondrial energy throughout the body.

Dave: So you put these glasses on, and it's like noise-canceling headphones for your eyes, and you really, really want to go to sleep. They solved jet lag for me. And it's all based on mitochondrial light biology with the skimp data we have, to the point where it's a patentable thing. But I know there's so much more, and no one's been able to insert a light sensor between two mitochondria and just listen for a photon that might come every five seconds. And I don't know if we'll ever be able to do that, but there has to be something going on there, because how else are they doing what they do?

Martin: Yeah. And following up on that, and I think you made a really good point about the network behavior of different elements of a system ... If you start really high up, you have humans that organize themselves into communities and people specialize, they do different things, and then through communication with each other, we can do amazing things. We can build buildings, we can build new companies, universities, and so on. And then we just get better. But through the interactions of the units, of the people.

Martin: And the same thing is true if you look inside a human body. You have different parts. There's a brain, there's a heart, there are lungs. By themselves, the brain doesn't do anything. The heart doesn't do anything, the liver doesn't do anything. But put them together, connect them through with a circulatory system of blood vessels and of nerves and everything, and then all of a sudden, there's beautiful life that emerges from this. And this is all thanks to the network connectivity between these different parts. We think the same thing is happening at the level of mitochondria.

Martin: And a cool example of that might be some very important hormones in the body that I think everyone has heard about. These are the sex hormones, testosterone, estrogen, and then the stress hormones, like cortisol. These hormones, all of them, are made inside the mitochondria.

Dave: That is something that I wrote about in Headstrong, and no one knows ... You're listening to this. It's not just your balls and other various sex organs making your testosterone. It is subcellular components distributed throughout your body, and you have more of those in your brain and your heart than anywhere else. Okay. So now we know mitochondria are making sex hormones and energy hormones. I don't remember, do they make thyroid hormone too, or do they just respond to it?

Martin: They respond to it. I don't know that thyroid is made in the mitochondria.

Dave: I don't believe it is, but I could be wrong. And the thyroid controls general energy levels in the body. But what tells the mitochondria, make more testosterone versus less?

Martin: That's a good question.

Dave: Nobody knows that I'm aware of. But if you can solve that problem, you're going to put a lot of drug companies out of business. But this is unlocking one of the basic keys to being human, is why do your subcellular components not do what you want them to do, not do what's in your best interest? They're doing it for a reason.

Martin: And thinking about it from an evolutionary perspective, why would you put such an important process that regulates sex, gender, the sex hormones and then the stress hormones that basically can wake you up in the morning ... That's part of what cortisol does ... to place these, through evolution ... Why would you place these in the mitochondria? So there's a really deep connection there between those large-scale, whole-body regulation of energy and physiological functions in the mitochondria. So if the mitochondria can't sustain the energy demand that would arise from developing and being masculine or feminine or responding to stress, you better not secrete those hormones. So there's gotta be a link there.

Martin: And interesting, is that mitochondria in the adrenal gland, for example, which are little glands on top of the kidneys, or mitochondria in the testes that would make the testosterone, or mitochondria in the ovaries that would make the estrogens ... So these mitochondria produce hormones, and then you have mitochondria in the brain that have receptors for these hormones. So you can see the whole organism as a network of

mitochondria communicating, with some mitochondria generating a signal, other mitochondria being the receiver of those signals. That's a bit of a mito-centric worldview, but to some extent, I think that makes a lot of sense biologically and conceptually.

Dave: It's the only thing I can find that matches everything I knew about both Eastern and Western practices, and also just as a design engineer, the reason the internet's built the way it is is so no one can break it. It's a highly distributed system that has emergent behaviors. So if you cut off part of the internet, the rest of it can live. But if the internet lived in one big computer underneath the NSA or the Pentagon or somewhere, you could blow up that computer, conceivably, and then take out all the internet across the world.

Dave: So DARPA, who created the internet, created it to be a fault-tolerant distributed system. And I think Mother Nature would follow a similar design algorithm and say, hey, what if your body was a fault-tolerant system, and not only that ... If you believe as I do that the mitochondria are the puppet masters, they're the ones that are telling your body what to do, they're the ones reading the environment on a second-by-second basis, they're the ones who are the gateways to epigenetics ... Well, if you're in charge, you wouldn't want to centralize control outside of something you control. So I think that they're doing that, because those little bastards don't want to let go. Make sense?

Martin: Yeah, I think so.

Dave: I could also just be crazy, but I don't think so.

Dave: When you put on your futurist hat, you have 10 years of really digging on these. You work with some of the best and brightest in the field of mitochondria. What do you think we're going to discover over the next 10 years? Where's the field going?

Martin: I think our understanding of biology and the role of energetics, bioenergetics, is going to expand such that we're forced to develop new approaches to study these processes, and maybe through integration ... We talked about reductionism and reduction versus integration, putting the pieces back together ... I think that's going to become more common, a more common thing to do in the sciences. And then eventually once we integrate things enough, and we have a perspective that's inspired by bioenergetic principles, we'll start to have therapies and approaches that we can use to sustain health. I think there's not enough thinking and research about that. What makes a person healthy, what sustains that? I know you've written a lot about that.

Martin: So not only to treat disease when the system has failed after years of dysregulation, but really understand those mechanisms of regulation, of health, and ways to promote that in a non-destructive and non-inhibitory way. I think in the biological sciences, we'll move more towards integration, and that will lead to new and better approaches to sustain people's health and to make people age better, and maybe also to promote human development, 'cause if people are healthier and happier, good things tend to happen. You have more energy to devote to creativity and developing greater things.

Dave: Can I test out one of my core behavioral theories on you? I want you to poke holes in it if it's wrong, 'cause you know a lot more about this stuff than I do. So I like to pretend I'm just a bacteria floating on the ocean. I do this a lot at night. I don't really. But if you pretend you don't have a lot of processing power, you don't have a lot of memory ... So you must repeat basic algorithms that are going to keep you alive. And the number one most important algorithm is, run away from, kill, or hide from scary things, 'cause they're going to eat you right now, and game over, you lost. So that would have to be weighted most heavily.

Dave: The second thing you'd have to do is eat everything, because if you don't eat everything, starvation will take you out within a day or a month or however long it takes your species to starve. The third thing you'd have to do is have sex with everything else, because if you don't reproduce the species, then it's game over in one generation. And this is the algorithm of life, whether you're a tree, whether you're a slug, or whether you're a human. And if you think about it, everything that you've ever done that you're ashamed of is one of those three behaviors, right? And they're all mitochondrial behaviors. It's that ingrained into us. There's a quadrillion plus of these little bastards telling us to run that program over and over, and when you repeat this a quadrillion times ...

Dave: I think that this is where all the bad stuff we do comes from. But the saving grace which you reminded me of with your comment is that there's a fourth F word, if we have fight, feed, and the other F word. The fourth one is friend. So what do bacteria do? They form biofilms. They specialize, they create a community, they support each other, and they therefore grow better as a species. And that's the other thing that humans do. We also form communities and friends and we support other people. But if you're constantly reacting to stress, you're starving, and you never get any, you're probably not going to be that friendly to the people around you. You're not going to make everything nice.

Dave: What this means, though, is that we are wired to be nice to other people when our basic needs are met. That's built in as our desire to protect ourselves. So a lot of my work, a lot of the reasons I do everything I'm doing in the world, are because of that fourth F. I think that's actually our core nature. Do you buy that?

Martin: I don't know. There's this ... I'm not sure if it's a debate, but whether we're the most evolved creature on the planet or not. In some ways, we're very destructive, and you could say, not so evolved. But in another, I think there is something in us that is more developed than in others, and I really think this could not have happened without mitochondria, and without the symbiosis.

Martin: And what makes us truly unique, I think, is the ability of ... maybe not the ability, but the ... whatever emerged from bringing this ancient oxygen-consuming bacteria with these other cells that couldn't use oxygen. And together, they're really created something that's entirely different. And by themselves, the little oxygen-consuming bacteria and the other cell that didn't have mitochondria and couldn't evolve complexity and multicellular life ... By themselves, I think they were these first three things that you mentioned. The fight, the feed, and the reproducing, ad libitum.

Martin: But I think when they came together, something very new, very different, happened. And I'm not sure exactly how consciousness fit into this, but it does, probably. And now we have the ability to not just be those three things and be driven by those three things, but actually use those things. So the image that comes to mind is the Maslow pyramid, where you have the basic need at the bottom, and only when you have these set, only when you're not hungry and you're sufficiently housed and all of that, you can develop the higher capacities. So we have those abilities.

Martin: I tend to put more weight on that, and I do agree that this ability that we have to connect with each other and to work as communities and to ... That's true at every level of biological organization. When things work together, they make bigger things possible. And I think somehow, the way we evolve and all of complex life forms evolve, arose from this union and this symbiosis of the mitochondria and the rest of the cell.

Martin: I see what you mean. I'm not sure I see this as a driver of human behavior, but I do think, yeah, there's more to us and it can become detracted when the mitochondria are not fed properly. So I would put basic energetic needs and the mitochondrial needs at the bottom of the pyramid.

Dave: Got it. I like that view.

Dave: And I've got one more question for you, Martin. I've been running an anti-aging nonprofit group for 20 years based on functional medicine and what they used to call orthomolecular medicine before that, and looking at all the things we can do to extend human life. And clearly, mitochondrial problems are at least one of the big five or seven theories of aging, if you look at it. And I have a number. I think it's achievable for me to live that long, assuming a truck doesn't fall out of the sky on me or something like that. And it's much larger than most people's number. How long do you think you can live if you do things right?

Martin: I'm not sure I'd have the same number for everyone.

Dave: I mean you.

Martin: Oh, me.

Dave: Yeah, it's going to be different for everyone, of course.

Martin: I don't know, 100 seems like a good number.

Dave: 100 seems like a number. So you don't aim high, 'cause there are people who have made 120 that we know of today, 122, at least.

Martin: Yeah.

Dave: So even with all your mitochondria knowledge, your ability to manipulate those things, whether it's with happiness or something else, and all the other stuff ... You're still sticking to about what we can do today? You must be 35-ish or something?

Martin: 33.

Dave: 33, okay. So then you've got another 65 years. You don't think any progress in your field is going to happen that's going to give you at least five years more than 100?

Martin: Well, I guess the average lifespan now is, what, 80-something in the US?

Dave: 87-ish, yeah.

Martin: And it's actually going down.

Dave: Right. But are you average? You're not average. Number one, you're on Bulletproof Radio, which makes you a game changer. I'm just kidding. But seriously, you're probably far from average. You're an academic, and those numbers include people who have no access to healthcare, people who are at many different levels of the socioeconomic spectrum, people who are in prison. That is an average average, so I would guess that you're probably a little above average, unless you do really dumb things like start smoking.

Martin: So 100 sounds like a good number, and maybe the reason I'm not aiming so high is because ... Well, first, I think it's a cool number.

Dave: It's got three digits.

Martin: If I make it to 100 ... I do believe in the cycle of life, and I'm not sure if I was to stick around for 200 years ... Even if I knew some things that were useful, I would tend to think that everything gets recycled. You see leaves on a tree ... A whole tree, they don't live forever. They do good things. I hope I can do good things and pass on good stuff to other people, and then leave some resources for younger crops.

Dave: Yeah. That's a beautiful answer. So you'll quit when you've stopped adding value. Me too, by the way. I just hope to be adding value for ... My number is 180.

Martin: 180, okay.

Dave: I'm just saying, look. We can do 120 today. And that's without any knowledge of mitochondrial biology or any of the other anti-aging technologies. And I just somehow believe that over the next 100 years, 120 years, if we can't get another 50% in the lifespan, over 120 years ... Look what we did 120 years ago. We didn't have antibiotics. We didn't even understand washing our hands before surgery 120 years ago. For God's sake, if we can't do better than that over the next 120 years, dammit, I'll be dead.

Dave: But anyway, that's why that number is ... 50% human progress, 50% I'm going to do the right things now, based on everything that we know, at least that I know that we know. And maybe I'm wrong, but I'm happy to die trying. And like you said, I'll get out of the way if I stop being useful.

Dave: Martin, thanks for your work. Thanks for being on the show. I think that you're working on one of the most fundamentally important pieces of what it is to be a human in your lab. It is really important work you're doing, and I just want to say, thanks for continuing to do the work and asking the really hard questions. I think you're going to uncover some things about the human condition that are not well-known, not well-understood, and will impact everyone who hears this interview.

Martin: Well, thank you. It's been real fun, and it's a fun journey. It's very stimulating, and I hope we learn something useful from it.

Dave: The odds are high. Your research is at picardlab.org, P-I-C-A-R-D lab dot org. And I don't think it's high volume website with caching and all, so if after the show, your website gets really slow for a day or two, that's all right. And if you guys Google Martin Picard mitochondria, you'll find all sorts of papers, including some of the most seminal ones in the field, including one of my favorites, which is called something like Stress: A Bioenergetic View of Mitochondria. I'm forgetting the name of the study now.

Martin: An Energetic View of Stress?

Dave: Thank you, An Energetic View of Stress. I knew you'd know it. And if you want to look at what stress is at a subcellular level, this guy knows, and it blows away the stuff that we've heard about stress from the other researchers, the stress that we were looking at from the top-down. This is bottom-up stress, what happens at the foundation of you. So this stuff matters, it matters greatly, and I'm so happy we got to talk about it and share it with hundreds of thousands of people.

Martin: Thank you.

Dave: If you liked today's episode, to do ... Go out there and upgrade your mitochondria. Go for a walk, take a cold shower, any of the other things I talk about ... Get a little sunshine. The stuff that makes you feel good, because if you believe that theory that we talked about on the show today, that when you take care of your mitochondria, you might be wired to be basically a nicer, kinder human being, I think is actually true ... And one of the things that nice, kind human beings always do is leave reviews for authors like me on Amazon. So if you liked any of my books, especially Game Changers, go to Amazon and just take 10 seconds to leave hopefully a five-star review so other people can find the book. I am watching those reviews every day, and I read what you type. So if my work has helped you, helped to change your life, let me know and let others know. Thank you.