Why You Start Losing Mitochondria At 21, And What Builds Them Back Transcript

(Transcripts are generated by AI and may contain errors)

Introduction and Guest Background

What we realized, finally, is that the mitochondria make this very specific steroid that is initiated through reactive oxygen species. The ROS is not bad for you.

If you have too much of it or too little of, it's bad. It's like water is no bad, but if you're too low water, too water could kill you, oxygen is bad but too oxygen and too can kill.

So again, remember homeostasis, it's the balance to the right amount of rust. Welcome to The TBD Fit Podcast on Dr. Talks. I'm your host, Daniel Keeley, and I will be guiding you through this wellness journey in terms of optimizing health and longevity where we unpack the science, the do's, and everything in between.

Come join us. Look forward to seeing you inside. Today, we're honored to welcome a visionary in the world of drug discovery, mitochondrial science, and metabolic innovation, Dr.

Sandeep Dugar, with more than 35 years of experience in small molecule drug psychology, neuromuscular disorders, cardiovascular health, inflammation, central nervous system conditions, and metabolic disease.

Dr. Dugar is one of the brightest scientific minds of our time. He's the co-inventor of Zedia and Viteron, has authored over 70 publications, holds over 100 patents, and has received prestigious honors, including 2005 National Inventor of the Year.

His latest mission-driven venture, Blue Oak Nutraceuticals, introduces a nutraceutical inspired by his 15 plus years of discovery of natural flavanols that mimics an endogenous steroid produced by mitochondria during exercise.

So this molecule supports mitochondrial biogenesis, mitochondrional density, and overall mitochondrical quality. We are definitely in for a treat today as we dive deep into the energy deficits and chronic conditions, mitochondrial collapse, aging, and how we can restore the Energy Currency that sustains life.

Welcome to the show. Thanks, Daniel. Wonderful to be here today. So what brought you to doing what you do today? Well, actually it was, you can say a happenstance or an accident that happened about 16 years ago.

when a colleague of mine who I worked with on this project, George Schreiner, and I looked at coming out of some clinical studies at UC San Diego from cardiologists.

And this was the time when antioxidants were the big rage. Antioxidants, everything, would do everything. But as I look at the data, I said, no, this is not an antioxidant.

There's something more happening here. So the clinicians had done some very good clinical studies published and that led to this whole idea. And unlike you, that was my first introduction to the mitochondria.

And I had no idea what I was looking at with that data. And then when I looked at it, it just became very, very clear that there's something amazing is what the data is showing us.

That led to this huge, big journey for me. Here we are today. It's been an amazing revelation about mitochondria. I hope that we touch on those points as we go.

Yeah, let's start with mitochondria. So maybe if you can paint a picture of kind of what is it, why is relevant, and why it's important. Simply put, no mitochondrial life.

How about that? People are publishing now that genes are not the blueprint of life, Genes can't make proteins

unless the mitochondria provide the energy for those proteins to be made.

The mitochondrion decide on what proteins be make. If you ask yourself the question that when you exercise or when do something, what initiates, how is that protein synthesis initiated?

When is it terminated? Who decides all that? That all process is controlled by the Mitochondria. And it came, it's the one came into our life, what, two and a half billion years ago to a process of endosymbiosis.

So mitochondria are a bacteria body. And what is fascinating is that every living creature, thing, species on planet earth have mitochondrion.

Why Mitochondria Matter

That includes plants. fish, animals, name it. If it's an oxygen consuming living thing, it will have mitochondria. So if you think about it, this is the fundamental particle or organelle that we share with everybody, every living being on planet Earth.

And it is one that is sentinel of our health. Every pathology, ever disease touches the mitochondrion. whether you have metabolic disorders, or you had neuromuscular disorder, Cut yourself or break a bone.

That gives your body an internal process of what a good colleague and friend of mine, Bob Navio at UC San Diego coined the word cellulogenesis. So our bodies have an innate capacity to heal themselves.

It's just that when the insult becomes chronic and continuous, you start to lose the capacity. To heal yourself. Now, what is the mitochondria? I mean, it has its own.

Oh, yeah. And it only comes from the mother, it replicates itself, It fixes itself. Without it, the cell cannot make mitochondria. If you were to take all the mitochondrial out of the cells, The cells have no capacity to make my mitochondrion.

The mitochondrid decide when to Make more of themselves. And if you think about this, every motion, even right now, as we are talking, we're shaking our head, um, We are thinking, were looking, Every action of our body requires mitochondrial energy.

Without this we wouldn't even be able to move. And it makes ATP. And it makes it instantaneously at that time of need at the tissue that needs it. And what is fascinating is that the product is ATP, but the reactants are two highly negatively charged molecules.

ADP and inorganic phosphate. And if I were to try to do that reaction in a lab, I couldn't do it. The energy required to that would just not be possible to make one.

Yet every cell in our body has the capability to made that in an instant. Just imagine what it does. It does a reaction that physically or energetically is almost impossible outside the mitochondria.

And it does it to the point where each cell in a highly active energy use situation, each sell can consume up to about a billion ATP, right? You have over a million trillion mitochondria in your body.

So just think about this, how important is it yet we have completely. kind of ignored it because it is the holistic system that, that it treats the whole body processes.

You know, in physics, they call the, you know the God's particle was the Higgs boson, right? I call mitochondria the god's particles for life. Without it ain't no, there's no life, so I could go on and so you can, see what we have learned, what I have learnt.

And what is fascinating is that the most natural way to make more mitochondria is exercise. Because that initiates

the energy demand, the mitochondrial sense it, and then they make mitochondrion within the cell without the self dividing that allows the cells to more energy.

What is known very clearly that at the bottom, exercise and nutrition are the two most validated processes for health span or whatever you want to call it, longevity or anything.

It's the key. But we keep going into the reductionist phenomena. right? Let's tweak one part, let's take the other part. But that's not going to help the whole system.

And that is why exercise and nutrition is so important. If you think about it, exercise produces the mitochondria, and nutritional is the fuel that your mitochondrion needs to provide ATP.

What do you think of in terms of nutrients also drive this process beyond just the exercise? So there are two complimentary things, right? Think about it, in your house you have a fireplace and now you need the wood to provide the heat, so the mitochondria are your fireplace.

Nutrients are the wood, and the type of nutrients makes a difference. So, for example, if you have all the firewood I can stack in your house, but if don't have a working fireplace, it's not going to do a whole lot of good.

At the same time, you can build all of the fireplace and not the right kind of wood. You're not gonna get the heat you want. So yes, you can take supplements.

A lot of these supplements, they promote mitochondrial function. But remember, starting age 21, your losing 10-15% of mitochondria every decade. That's aging, that's the natural process of aging.

So you've got to figure out how to stop that loss of Mitochondria. Now on top of that, the environment and the food you eat, processed food, sugars, Uh, the pollution, air are all stressors, right?

So our lifestyle, our diet is not helping. We don't exercise enough to replenish the mitochondria we're losing. That's not. So that is what I call is the energy deficit, energy crisis.

Your body is falling behind the eight ball. And as it falls behind further and further, as we age, we lose our skeletal muscle strength first. Right. because that's what you see.

Then your metabolic processes slow down. No matter what, you gain weight because you keep eating processed foods without the exercise. And then of course your genetics start to play a role, right?

Because you have other issues, pollutants in the air. So if you are given the opportunity to do this and you eat healthy and your exercise at the level you need to, you will have a better health, but we just don't.

And we can't, our modern lifestyle is antithetical to that whole system. We all love our donuts in the morning. That's the problem. Constantly in this fast food convenience based culture is only to our detriment naturally.

So in terms of, um, Nutrition for your mitochondria. Let's put it that way. What's best? All right. So eat proteins and fat, get rid of sugar, fiber. Okay.

I say to people, don't drink orange juice. Orange nature made for us to eat an orange, not drink it. Eat an apple, Don't Drink It. Because when you drink an Apple, you've gotten rid a lot of the other fibers and other components that is present in an We give our kids juice and we feel it's great.

Yeah. But what are we doing? We're just giving them a boot, a big load of fructose that the body absorbs very quickly. Now here's the interesting part that there's another bacteria system in your body that works in connection with the mitochondria and it is the microbiome.

Right? So imagine two bacterial systems are responsible for our health. Fascinating. The one in the gut, its only

purpose is to take the food you eat and convert it to the foods that the mitochondria can use.

But if you don't give it the right food, it's not going to give the good food to mitochondrion. So you have the microbiome, which is everywhere. You have a skin microbiomes, you got a gut microbiom, You got the mouth microbioms, and you know, have microbiomas for everything.

And what we do, and so if you eat an apple, you don't absorb all the fructose. But that fructose that is not absorbed is excellent for the microbiome, right?

It's food for them that creates the healthy microbiomes. And the microbial mitochondria axis, the connection, is very clear. So the kind of food you create is the right nutrients, creates a healthy microbio.

and your mitochondria with exercise are ready to receive this wonderful nutritious food and you stay healthy.

Exercise, Nutrition, and Energy Deficit

Of course, the issue comes in is that what if you can't exercise, right? There are issues, there are situations, and I respect that, that it's easy to say to everybody, go exercise two hours a day or two-hours every other day, or whatever.

That's modern lifestyle, that's the reality of art, but that does lead to the consequence we're seeing. Excessive obesity, metabolic disorder, mental health issues.

These are all deficits of energy. Looking at NAD and NAHDH and the ratio of NAAD to NNADH. So you mentioned nutrition, you mention juices. Because once people recognize how much sugar they're intaking, it is astounding.

It happens at the level of both the microbiome and the mitochondria. So, let's go a little bit into the myocondrial structure itself. The idea here is that the Mitochondria have two membranes.

Inside the inner membrane is what we call is the matrix. That's where the TCA cycle is. So that's what the nutrients go in. And that inner matrix also holds all the electron transport chains, okay?

And they quoncriste, which is these bends in the intermembrane where ETC5 sits that makes ATP. Right? So in this very simplistic one, ETC 1, 2, 3, 4, the primary role is to pump protons into this intermembrane space.

And we call it creates the proton motive force. That proton then comes through the ETSI-5 back. It's a rotor, and the ET-C5 as it rotates through that proton moving makes ATP by combining ADP to inorganic phosphate.

and that ATP is released out into the cytosol and used by the cells for energy. Now, of course, you can have primary mitochondrial mutations, because remember, as mitochondria multiply a lot on demand, so because it has a small genome, the degree of mutation can increase.

or they have a higher degree of mutation possibility in the mitochondrial genome. But when we're young and we are healthy, our health cells have respectable energy to get rid of these.

mitochondria, mutated mitochondrial. So even today, as we're talking, our cells are making mitochondrion, but we are healthy enough to get rid of these mutating.

But imagine that as the cellular energy goes down, the cell will decide to expend that energy to keep it alive and functioning and starts to let go of the mutated or dysfunctional mitochondria.

Okay, so the process of what we call mitophagy goes down. And as that mitaphaggy goes, down the dysfunction or damaged mitochondria accumulate, and they themselves release more and more of these things like reactive oxygen species, et cetera, that starts to become detrimental to the cell health, cellular health.

And this is what is called as heteroplasmy, where dysfunctional mitochondriacs continue to accumulate and then those cells become dysfunction and eventually die, right?

So the process is that the insults coming in to the cell, if, for example, you have excessive sugar in your diet, that sugar makes the mitochondrial more glycolytic, right, because it has sugar.

But your mitochondria are best functioning when the fuel is fat. It takes longer, but it is less harmful for the cell. So the diet as it goes in, because the whole idea of the TCA is for glucose to be converted to pyruvate and pyrovate enters the TC cycle.

Okay. And that whole process is what is responsible. too much pyruvate and the cells are not, the mitochondria is not doing it, it goes into lactic acid and that creates lactic acidosis.

Okay. So that your pH goes. It's a very dynamic complex phenomena that goes on between what's coming in, how the cell is processing it. On the other hand, glucose is also a critical nutrient, so it's not to say glucose it not a critically nutrient.

It's the fructose that's a problem, okay? If you have excessive fructose in your body, right? But when you refined sugar, it is 50% glucose, 50 % frucose.

But glucose in itself, for example, your brain primarily uses glucose because it needs high amounts of energy. And so the whole energy homeostasis or balance is between right amounts and right amounts of physical demand.

And what is fascinating is that we say, you know, with your brain, use your or lose your, right? Use it or loose it. Same thing goes with the mitochondria and your physical function.

Use or it lose it? If you are sedentary and you don't walk around, your cells will get rid of excess mitochondrion because it costs the cell energy to maintain more mitochondry.

So if your mitochondria are not working well, slowly your cells will get rid of the mitochondrion. So there's this whole dynamic process going on where the homeostasis and the balance happens within the cell.

And one of those examples I give people is, look at it, what's your basal body temperature, right? 98.4 degrees Fahrenheit, that's what most of our basally body temperatures is.

That's healthy. 0.6 degrees Fahrenheit up at 99 degrees, Fahrenheit, you're febrile. At 1.60 degrees above that, at 100 degrees you have a fever. That's not a big temperature variance.

So 1 point 6 degrees fahrenheit. And if I can say, and you add another thing about, global environmental health. When we talk about a one degree rise in temperature, just compare it to 1.6 degrees Fahrenheit, and our body is a fever.

One degree centigrade rise, in global temperature you're giving Earth a fevers. Just think about it. This is the whole total balance we have. So we're not detached from that.

All this is, a big systemic balance of homeostasis. Our health relies on it. Our help relies in this whole environment we live in. So it's as good for us to take care of our body and also as a good, for the environment, we're living because that will affect our bodies.

People don't realize that as these systems change, has the environmental changes and we living in it, it will effect our health. So even I, you know, as I said, mitochondria are the sentinel.

They sense everything we do, how much we sleep. If you don't sleep well enough, it affects your mitochondrion. Your thoughts, the stresses in your life affect the mitochondrial.

Everything boils down to mitochondria. So, as I said, because of mitochondrial we have life, and so we need to really have good nutrition and mitochondrion to sustain health.

It's about as simple, but also very complicated, given our modern lifestyle. That was a very elegant explanation of mitochondria and cellular metabolism.

So mitochondrion are never static. They're changing accordance to the cell in accordance, to restore homeostasis, they will fuse and divide and elongate and change function.

And when looking at, you know, the CDR or DAMPS and PAMPS, and nanolipids and nano particles and then nanoplastics now and all these different. danger signals that perturb the system very quickly in the kind of upregulation of this oxidative burden that now we're exposed to.

And so when you get into phase three, disease becomes so perverse and that's when things are stuck. The mitochondrial normal state is in this M2 here.

So when your phase 3, you're sick and we are all walking wounded. We all have the heightened toxic burden. Um, which yeah, damaging to the mitochondria, all of us then, as you said, you know, alters lactate into perubate.

And now you have high in, uh, in your lukins, IL-6 IL 10, L1 beta TNF alpha. Um. Then you. The cell danger response where it's just a plethora of different toxins and intoxicants and pathogens and infections and adjuvants decreasing complex four to make ATP.

You have the prevalence of heavy, heavy metals. So fructose, um. People think, okay, fruit, then is fruit bad for you? Should we monitor fruit content?

What is the? No, no, not fruit is not bad. For you, it's how you consume it. Right? Now, just imagine that you're not going to eat 100 apples a day. You can't, right?

And also when we have seasonal fruits, you eat them in season. Nature made these things to be seasonal, to So fructose, as I told you, is great for your microbiome, but also fructose we convert to fat, okay?

Just like bears do. We cannot metabolize frugtose. The only reason for fruktose is evolutionarily, it was there so that we could have that stored as fat for future use when we didn't have food, right?

Five thousand years ago, there was no refrigerators. We couldn't walk down at midnight and have a pint of ice cream. That's what we do. But it was made for evolutionary pathways.

So we're living in a body that is 10,000 years and is not modern technology. It has not evolved to modern technologies. Yes, please eat fruit. All I said was don't drink an orange.

Eat an Orange. that's What nature made it for because you get the fibers, you Get the other things with it, right? It's not processed. So, you know, evolutionarily, but also, I was just at the Cal Academy of Sciences, we're only, the homo sapiens are only about 200,000 years in existence.

I mean, we're like in a microsecond on the evolutionary time scale of the planet. But look at the impact we have created globally in 200,000. I means, it is incredible.

It is incredibly, but that impact is going to come back and haunt us. Yeah, because we're the only species now that just lives for ourselves. We have detached ourselves from nature.

Just imagine I was just in the Antarctic, you know, a month or so ago. I mean, we couldn't survive there for two days. I mean, so what I'm trying to say is that, well, these are, this is okay.

I am not trying say we should live outside our houses and live in trees and stuff like that.

Mitochondrial Structure and Dysfunction

But we need to really be really cool that look, you know, spend a little bit of time to exercise and spend little time, to make your meals correct. All right.

Eat what your body wants, not what you want or needs, but of course, given where we are the reality of the situation is, that is. in a hope, but the reality is that we still need to figure out how to function in the environment we have for ourselves and live as best as we can and address the posities of the deficits we've created.

Just as a segue to the part of the conversation, Anil, is that what intrigued me was that while everybody knew exercise is good for you, nobody will debate that if you exercised, it's going to be bad for your, and nobody would debate.

So the question became, and exercise makes new mitochondria, but how does it happen? And I went around and I asked the questions, nobody could tell me.

And, I said, here's one of the most fundamental things of human health, exercise based. The first thing exercise does is makes more mitochondrion. People say, well, exercises makes you lose weight.

How? Exercise makes more muscle. Well how? It all starts with the mitochondria. First thing that exercise does is makes the Mitochondria and then the my mitochondrion respond to the body's demand to make more muscles if you're lifting weights.

To make your heart function better because you are working better. So your heartbeat is lower. Your cognition is improved. All that is a consequence of that.

But the first thing is the So you had to ask the question, how does exercise make mitochondria? And nobody could tell me the answer. I went to PubMed and that was the part that made me really move forward to figure out how that happens.

And that's what we figured out. What we figure it out is what actually happens biochemically in your cells that tells the cell to make more mitochondia.

That learning, that discovery, Daniel, was to my mind was a game changer, because now you can have an intervention in a situation. So while we can talk about all the things we should be doing, but let's live in the real world, right?

And to the extent we and humans who really are in an energy deficit. That became my purpose because I'm a drug hunter at the end of the day, but I decided that this is what we can learn.

And by the way, I have to very much acknowledge all of my colleagues over the 16 years at various places, universities who worked with me. So I happen to be speaking about it, but I am not the only one.

This required a whole group of scientists and people who thought through this thing with me, okay, alongside me. And I thought with them. So as much as they contributed to my thinking, I contribute their thinking.

It was a work that required lot of good, smart people. So let me acknowledge all of them. I don't want to name them because we'll take a whole lot of time on doing that, but I want acknowledge their contribution to what I'm speaking to you about today.

And what we realized finally is that the mitochondria make this very specific steroid that is initiated through reactive oxygen species. The ROS is not bad for you.

If you have too much of it or too little of, it's bad. For you, right? It's like water is, not that for, you but if you're too, little water, too. Much water could kill you oxygen is.

Not bad, for. You, but too Little oxygen and too Much can kill, so I can't remember homeostasis. It is the balance. So the right amount of ROS is good for you.

So it's the same thing I tell people that, hey, if you go to the gym regularly, don't take antioxidants, please, because we have shown that when you up the mitochondrial level, the Mitochondria automatically make catalase superoxide dismutase.

The cells know how to protect themselves. You just have to give them the resources to do it, right? People say, well, I take exercise and I go antioxidant.

This literature there now says that if you say take vitamin E post exercise, actually it inhibits the benefit of exercise because you are inhibiting that specific signal for the cells to make mitochondria to more mitochondrion, yeah?

So it's again, and what that happened is that understanding of that mechanism led to what we have in apicaticin, which is the blue oak, is that it mimics that steroid.

It's found in cacao, and the Mayans introduced cacow to humans. In Mayan culture, this is 5,000 years ago, in the royal family, ate cacao extracts. It was bitter and they put chili in it.

I don't think you and I could even consume it, but they did it! But the royal family used it and the other group that were allowed to consume this concoction were the messengers, the messages that carried messages from village to village.

And that's when we all realized that the importance of that was endurance. They just didn't know how, they just did know what was doing it. That's what we figured out.

So the endurance, we have demonstrated that very clearly. The endurance of what the mitocatalyst E is. It enhances endurance because levels of mitochondria levels go up.

You have internal energy and capacity to sustain the exercise or the demand you're making on your body. And so the whole idea here is that this understanding of how biochemically the cells signal or the mitochondria signal the nucleus to make more mitochondrion without cell division is a resident on this steroid.

And then this steroids is released by the exercising cells into the general circulation we have detected in human blood. That is why when you exercise, your whole body feels good.

your brain feels good. Your brain is not running. You're brain's not lifting, but you feel good, and imagine people who exercise regularly, suddenly you don't go exercise for a week, you'll feel like something is missing, right?

A little bit. you know, on the edge. So, and we have shown that the levels of the steroid goes up in tissue beds like liver, kidney, brain post-exercise.

The whole system is upping its mitochondrial process just because you're running. It's amazing how the body is so geared to do this. This is triggering mitochondria biogenesis, similar in a way that exercise does.

Yeah, exactly. So this is the first molecule that I know of that mimics, replicates your natural process of mitochondrial biogenesis. This is all it does.

One thing I have to say, because it's been in human diet for thousands of years, and it is so safe that all is does is initiate the mitochondria biogensis and then the body does the rest.

And so now you can imagine that its application is widespread. And we have finished six studies. We're doing seven, eight more studies, everything from muscle steatosis to you know, frontal lobe dementia to primary mitochondrial myopathies to cardiovascular to metabolic issues, because they all affect the mitochondria.

And the argument we have is that if you up the metachondrial levels in these patients, how does the body respond? And what we are seeing is the bodies response by addressing those pathologies.

So remember, I told you that we haven't inherent capacity to heal ourselves. that we lose the energy, the bioenergetic to heal our body as we age through the other stressors and our genetics, et cetera.

If you can give the body back at, does the bottom respond? And so far our evidence is suggesting, yes, it does. And some of these studies are now happening through clinicians who are experts in their field.

I don't know if you know this, but the Expise Foundation, we were selected as one of the teams to study this for health span and longevity in that study starting at University of Glasgow.

So I think what is happening, and one thing is that we are very, very clear that want to continue to collect clinical data. on these things so that we're not simply saying, take this and hopefully you'll feel better.

Our purpose is to continue to understand that if you supplement mitochondria, that it is agnostic to the pathology. It doesn't matter what affects your body.

If you give the body the resources, it will try to fix itself. Perhaps the best it can do at this point is address progression. Or decline. Yes, progression of the disease.

Yeah, but we have seen in muscles, turned microscopy of muscles and this was done at UC San Diego, the muscle sarcomeres of patients who are in their 60s after three months look like muscles of people who would be in the 40s.

This is published data. I mean, this is not. And so, but the main intent right now is, not just reversal, the idea here is can we support patients with a very simple intervention?

And it can sit in the background of everything else you're doing, because all it is doing is upping your mitochondrial process. That's it. It is telling your body, hey, I just exercised, even though you didn't.

So there's a direct correlation with myocatalyst and the steroid function, and we have you know, studied both next to each other that says, okay, whatever the steroid does, the mitocatalyst does.

It's less potent, of course, mind you. And the steroids that we found is about the most potent stero- compound in your body that it's incredibly potent.

So you need very small amounts of it for it to function. That's why just a little bit of exercise does a lot of good. No. Let me unravel that for you.

Peptides are, again, nutrients. When you say AMP kinase is simply a signaling process for the mitochondria. So these I would classify as nutrients.

ROS, Homeostasis, and Chronic Disease

Some of these peptides break down into amino acids. Okay? First of all, they're injectables, all of them. They're not oral, okay? People are trying to come up with oral peptides, but then oral peptides will break down to the functional amino acids within it because the gut will destroy them, so you are in a way providing a lot of good amino acid as nutrients, right?

Number two, that for them to function, at the end, you still need the mitochondria. they can improve the Mitochondria you have, But they don't create the They can improve the function of your residual mitochondria for sure, but can they create more mitochondrion?

No. As far as I know, we're the only product that actually creates new mitochondrial naturally as if your body exercised, which is how your does it to begin with.

Hence the safety, but also in the peptides, there has been no really established clinical studies, right? These are a lot of studies that have come in and people are doing it and I'm sure they have benefit like NAD has a benefit, OQ10 has benefit.

Eating steak has the benefit eating an orange has benefits. I am not saying they are not beneficial, But they act mostly on the mitochondria you have and they make them function better.

But what if you don't have enough? Are you losing them? What is the name of the molecule as well? Yeah. Which one? The steroid? The steroid, I just call it by the chemical name.

It's 11-beta-hydroxypregnenolone. So we published that paper. We haven't named this like cortisol or estrogen. But it's just this, because we're the first ones.

I mean, if you go to PubMed, you'll still not find any biology, pharmacology, except for a couple of papers from us. And it is a flavanol naturally found in cacao, as you had mentioned.

If nature made it, it was okay. Man-made it stay away. That's my philosophy. Is this suggestive of people, you don't really need that this is a replacement for exercise?

Well, I wouldn't go, that's what people come down to, is it exercise. I would go down there that path because I think, remember your body makes it on demand.

So yes, it's not simply just you take this and everything will be okay. It will improve your function. We do have evidence that It prevents, and this is not the work done by us, it was done other people, that you have what is called as disuse atrophy.

If you don't use your muscles, you lose it. We have shown that this flavonol prevents dis-use-atrophy, so we've shown. That means if you stop exercising, the muscle loss is curtailed by the presence of this flavanol.

So we've shown that. So the question here comes in that, can it replace exercise? I wouldn't go that far, but what I would say that yes, it can definitely accentuate the exercise need.

Because as you get older, you need to do more and more, and you're not capable of doing it more. And it could be your lifestyle. But most of our focus right now is in the area of where you have a deficit of the mitochondria.

That's what we're focused on right now. That includes aging, mental health, neurodegenerative diseases, metabolic disorders, cardiovascular disorders et cetera.

So that's where we are focused. But the continuation to normal healthy people is clear because all of us have mitochondrial deficit. It's like most of have vitamin D deficiency too.

So if I understand this can arrest the deficit indefinitely, or is it short acting? If someone's not training during that duration, will this preserve the benefits in terms of the metabolic adaptation acquired from fitness?

How long can I preserve, arrest that deficit? So our data suggests that that. It would be true, but I cannot, we don't have enough longitudinal data to say how long it will go.

But it's like exercise, right? If you keep taking it, just like you'd keep exercising, it should continue to do the function. There's no reason why it shouldn't stop, because all you're doing is you giving the body the biochemical signal that it would get if you were to exercise.

See, if your exercise you'll make the steroid that gives the the signal. Now, if you're not exercising, and instead of making the steroid, you give the body the flavonal, the bodies still gets that same signal.

And that's what we are seeing. But in terms of patients, we have not seen what the logic. So most of our studies

have been where people have on it continuously, because the insult doesn't go away, right?

And the insert is, let's not talk about insult just as a disease. Insult is lack of exercise. That's also an insult to the party, If you think about it.

Right? Because exercise is essential for good health. And if you're not exercising, that is a quote unquote insult to the body. So my thought on that, is it should keep working as long as you keep taking it.

But we don't have the longitudinal data on patients that way, where we have taken them off of the, so that study was just done where, we did a 15 day study and we could very clearly see that the muscle atrophy was arrested.

How long- How are you testing the state of mitochondria? How can people learn about the health of their mitochondrion? That's a very good question. One of the things we're trying to do is develop a base to understand the levels of this steroid in your blood as an indicator of mitochondrial health.

That work is still in progress. Now, that would be the easiest way. You can look for markers. in your blood, but this is not so standard because see, not many people have had a mitochondrial biogenesis product to define a diagnostic, correct?

Because if you want to understand what mitochondria proteins you wanna study in the blood you need a tool that would initiate mitochondrian biogensis so you can see the effect.

But we are the first ones in that field. So we're working on it. So, we are looking at proteins like GDF15, citrate synthase, and others to see what acetylated proteins, to if you can reduce the redox.

But a lot of these are indirect markers. Because first of all, you don't want to have mitochondrial DNA in circulation. That's not a good thing. Okay, so mitochondria are best within the cell, not outside the cells.

Okay? So that presents a challenge. I mean, what we have done, our mitochondrial process is through muscle biopsies and electron microscopy. We can look at the mitochondrion levels, but you can't do that all the time.

So you are relegated to the secondary markers, which are direct mitochondry-related proteins that are in circulation. You can look at the redox status of the body.

You could look the other markers of citrate synthase and GDF-15. But one of direct readouts for mitochondria would be this steroid because mitochondrion make it.

If you have good mitochondrial levels, you should have a higher level of this steroids in your body But that would require us to develop a lot of background data to validate what those levels are and what they should be, right?

And that work is in progress and it'll take a while for us. But this could be the first direct marker of mitochondrial levels in your cell and their function because mitochondria directly will make it.

What we're discussing today, which is certainly very thought provoking, is where mitochondrion medicine is now arriving at, right? And kind of the frontier, which you're staying on that cutting edge.

So in terms of, let's say, mitochondrial medicine, it sounds like it really falls into that same foundation phi philosophy that that I've integrated, um, but you're, per my understanding, you are considering obviously ATP efficiency, edox balance, membrane integrity, circadian signaling, I would presume someone there.

And obviously, uh, recognize the impact of inflammation or, buffering against the inflammatory burden. So nutrition certainly matters. As you said, stress will impact the mitochondria.

I know we mentioned peptides, which we use very effectively, obviously. PQQ or CoQ10 NAD, which has been very much the latest craze. Yeah. So, you know, P Q Q, I'm not so sure about to tell you frankly.

Structurally, it worries me. There's very little, I don't know if there's any clinical data on PQQ. It's all preclinical data. I've not come across a clinical study about Pqq.

So I'm just fascinated why people would want to be doing that. Now CoQ10 is itself a part of the mitochondrial inner membrane, correct? NAD plus NNADH is part of the redox process, correct?

And they are part the mitochondrial function. Again, as I said before, the question is, yes, you can take CoQ10, but how much of it is such a big molecule?

How much if it goes through your gut, through the systems, and ends up in the inner membrane of is not clear to me, right? Because remember, these membranes, so it has to go through the plasma membrane, to the mitochondrial outer membrane through to inner membrane.

It has go to all your gut and the liver and everything along the way. So yes, clinical evidence and anecdotal tests, CoQ10 does something for sure, but I'm not so sure how much.

So because there's a shorter version called Idebinone, and people have studied Idaibinone for a long time, it's been done in clinical setting, then it is a smaller molecule than Coq10, But it has a very poor pharmacokinetics, right?

And if that has poor pharmacy kinetics the pharmacogenetics of Co Q10 is gonna be similar, if not worse. That's why IDebaNone has not really shown good clinical data outcome in clinical studies.

It has now. Now, some members, something happened with NAD, et cetera, and now they've come up with an MN, you know, another conversion of NADA, but you gotta take a lot of it and you've gotta really rely on the cellular machinery and again, not to sound kind of like a broken record, the mitochondrial function to be able to use it.

Right. But also remember redox balances, just saying that I'm going to. Use an antioxidants or address the oxidative challenges to the cell. Just do it, perhaps may not be the best way to think about cellular homeostasis.

Remember Ross is a very powerful signaling biochemical. The cells make it for a reason. If it was so bad, why would they make it? And part of the process is that the raws…

So remember one thing. So here are a couple of things I'll tell you. That mitochondria initiate all steroid synthesis. All of your steroids synthesis is initiated by the mitochondrion.

That includes testosterone. That include estrogen. The first step of cholesterol synthesis happens in the mitochondria.

Blue Oak, Cacao, and Mitochondrial Biogenesis

And that happens because of ROS. So people forget that ROS at the right balance is a very good thing, and the cellular machinery knows how to control it.

If it didn't, we would have cellular ROS damage from the day we were born. But that's not the case. The problem is we lose control of it because our intracellular machinery is falling apart.

And that machinery, is the mitochondria. When the Mitochondria can't make more of themselves, can fix themselves can get rid of the broken ones, ROS starts to take a bigger role.

of damage proportionality. But if we reverse that and allow the mitochondrial and intracellular processes to kick in, your Ross will be fine. So the idea here is we keep bringing things down to a reductionist idea.

Science says, let me look at this thing and find one thing, but they cannot differentiate causality and concept. Is the levels of ROS related to a cause?

Is it the causal or is it a consequential issue? It's very hard for science to do it. People will say, well, this protein has upregulated in cancer. Well, is up-regulating because it's trying to address the insult or it is the one that is causing this?

Very identical premise when we treat beta amyloid plaque with Alzheimer's medication, right? It's a huge misnomer, I think just up in evolutionary medicine, how we're just treating kind of the end stage is very reductionist, things are in isolation, nature doesn't work that way.

So Daniel, let me tell you a couple of things, right? And before we run out of time, number one, inflammation, mitochondrial control information. To this day, we do not have anything that addresses chronic inflammation.

And one of the things in Alzheimer's and everything is chronic information, in diabetes is, chronic, information all these chronic diseases cause chronic and we don't have a single idea of how to address chronic.

Can you believe it? Not one. And we take about inflammation as if it's one thing here. Inflammation is a systemic process and it is controlled by the mitochondria.

They initiate it. One tidbit around this is that, you know, why sleep is so important? Your brain is 2% of your body weight, uses 20% percent of its energy, okay?

Can you imagine when is the highest use of brain energy? When you're sleeping, your brain actually uses the most energy when you are sleeping. In your REM sleep is when your body is in paralysis.

Your brain lets go of your physical function because it is so focused. on its own bioenergetics. So our brain doesn't use more energy when we're awake or exercising.

It uses the most energy. When you're sleeping, it needs that energy resource to be able to do it. That's when you lay down your short term memory. And that's mental health.

Right. We no longer live in congruence with our biology. Why? Because we have blue lights. The industrial area that has allowed us to be more productive and perform better at the consequence of sleep and the detriment to our health, metabolically is the brain is physically repairing itself.

And yet we don't prioritize that. What time do you set your alarm to go to bed? It's very different philosophy. No, but the thing is, I go to the gym and I see these young guys exercising and between each set, take up their iPhone and look.

I actually went to one guy, finally the other. You know how much harm that causes to you when you go and you look at this screen with the blue light? There's a very clear correlation.

between this because your optic nerve is full of mitochondria. Imagine, as you and I are talking, it's processing everything we're seeing in an instant between colors and depth and expressions, and it is directly connected to the brain.

I said, you guys listen to good music and exercise. Why do you have to, between sets, pick up this phone? I just find it amazing, but you're absolutely right.

that these simple things, these simply things are affecting. We don't understand the damage that we're doing, especially in our youthful population, because now it's starting with children, right?

We just we don' recognize the long-term damage. We're aware of this short-term damage, but again, long- term, we're living kind of in this very large experiment.

So you said, you know, the intracellular damage which happens at the foundation of the mitochondria looking at homeostasis and ROS or reactive oxygen species.

It's interesting because you mentioned that all the time, people don't realize, right? Exercise drives a lot of stress. It regulates that heightened burden of reactive oxygen species, but we need that, right?

It's that trade-off. And so that's why people realize even nutraceuticals can be harmful, what drives dysfunction at the cellular level or the impacts of mitochondria.

So I call it the unlucky seven, which is parasite, virus, bacteria, fungal. Now we have environmental toxin, heavy metal, and trauma or stress. Is there any overlooking in my unlucky 7 that drives…

Yes. that upregulates inflammation that is now the consequence of unhealthy aging. I think you've touched on some of the major ones, and I thin malnutrition is one of key ones too.

What we eat has significant role. I mean, if you look at our grocery stores are 85% highly processed food. The fresh vegetables are in one aisle at the corner one place, in the next 15 aisles.

You know, and sometimes as scientists are thinking, I mean, yesterday I was watching a history channel where, you know Philip Morris, to reduce the irritation of the throat in their cigarettes, put in ethylene glycol in those cigarettes.

Now, ethlene, just imagine, imagine the consequences of that. So we often don't look at things in a broad systemic sense. We look and say, hey, if I do this, I mean, this is also the story in the pharma industry, which I've been part of.

But looking at it, we say hey here's one thing, let's define a drug and feed it. but we haven't moved the needle. You know, cancer still sits where it is, cardiovascular disease sits, where is.

So we continuously look for these simple answers rather than a systemic understanding of what is happening. Malnutrition is a huge, I don't talk about malnutrion as deficit of nutrition.

I think it's an abundance of bad things we eat every day, right? I mean, just imagine we take our kids to Little League and then when they're done, we give them sugar, water, and pizza.

I mean, what are we doing, right? And then they become obese and they don't function well, they are tired. Well, it's no surprise. It's not surprising.

And so to me, one thing that the Malkan has taught me is that, look, solutions can be simple if we are diligent, if are focused, nothing has proven better than nutrition and exercise to be the foundation of good health and longevity or healthspan.

Nothing. And which is not surprising, nutrition keeps your microbiome healthy, which provides the good food for your mitochondria that you generate through exercise.

It's nothing more complicated than that. And it is shown people that exercise have less cancer, live better. But if you look at it this way, go to some of the underdeveloped countries where people have lack of nutrition.

They're physically working, they're lean, healthy. What kills them is infection. Physiologically, they are very happy. So there is evidence in human history about good diet, not so ultra processed food and exercise.

Same foundation part. We don't know how to master the foundation and we're looking for the shortcut. Because we had a conversation with a nutritionist here the other day.

She was sitting in our office. I said, can you imagine that you see patients Right? You were talking about nutrition. And to me, I said, it's so simple.

If nature made it, It's okay. Man made, stay away. But we don't, we have to read the label. I had said there should

be no label, the ingredient is a label but we didn't even stop to think about these things.

if you look at some of the indigenous tribes, in Tanzania, prevalence of cardiovascular risk, heart attacks, diabetes, Alzheimer's does not exist. You said they die from infection.

The sad reality of that kind of environment. We are in an environment that is just crippling us internally. It is. I'd mentioned to you the Mayan culture, right?

When they were up there, there was really, and people have done these studies, they had no cardiovascular diseases, no metabolic disorders. The Mayans that moved down into the cities, the CVDs skyrocketed.

There's so much evidence around us. See, we are our own worst enemy that way. We want the privileges of modern technologies. But in some cases, I think science is looking at very myopic ideas.

It's missing the forest for the trees, right? It is saying, No, life ain't that simple. It's not that simply. How many conversations we have with people on nutrition and exercise, right?

It is not. Okay, you mentally don't feel, well, just take an SSRI. 76% of the approved drugs by the FDA are toxic. Because we say that efficacy is okay.

The safety is a collateral damage deal with it. Right, no one talks about the nutrient drug-induced depletions, the microbiome drug induced depleations, and the mitochondria drug, induced depletions.

We're not one cell, we are not on pathway, We are one organ, but that's how we're treating it at the end stage, that reductionist philosophy. Exactly, exactly.

And so to me, for the 16-year dynamic, what I've learned is that at, again, you know, tell me why. I mean, we are the mitochondria maniacs, mitochondriacs, right?

That to me, it eventually all boils down to the myocondria. Take good care of it, and it is geared to take, because remember, evolutionary, this is the reason we're here.

It is because of the metachondrium. We're not here because anything else, not because our genes. The intersection of the mitochondria and the microbiome.

And one of peptides too, which I didn't mention previously, is SS31, an inner mitochondrial membrane enhancer. The target is the inner… Oh, I know Hazel very well.

She's one the founders of SS 31. It started with her work at Cornell.

Testing Mitochondrial Health and Future Therapies

I knew stealth biotherapeutics very, well I interacted with many years ago. Yeah, so SS31 just got approved for bars and it's an injectable peptide and stabilizes the mitochondria.

It bends the electron transport chains the right way for it to make more ATP. The question still goes down, Daniel. What if you don't have? You're focusing nationally.

That's it. But it is a great science and actually I have a two-hour conversation with Hazel first week of January because we're really starting to think about it Because I'm trying to bring a lot of these people into my circuit, working with them to, bring their knowledge also.

Because these are the people who have thought about these problems in a more holistic, systemic way. Right? And that's what we need. We need people who are willing to go down a path.

I mean, what I learned about the mitochondria has taken me 16 years. It didn't happen over a year, but it led to the fact that if you believe what this is capable of doing, you've got down to, go to down the basics and discover it.

And you're absolutely correct. If science does it the right way, there is a better path forward with science. But we cannot be really stuck with the idea of finding reductionist solutions.

Methylene blue, obviously, that's quite ubiquitous now as well, which helps the mitochondria and feeds into complex four, can also be considered a very good methylater, free radical scavenger without creating more oxidations.

I have not really looked at it much in the sense of what it does in terms of mechanistically, to tell you frankly, I've not had the chance to really delve into it.

Now, see, one of the things that I'm also a chemist, whenever I see flat molecules, right? And they're small. I also think about what has been done in terms of their association with DNA.

and things like that. Maybe the studies have been done. So let me preface this with the idea that I don't know. But same thing that comes to my mind. This is merely my scientific mind with no data.

Things like PQQ and methylene blue, these are flat molecules. They can be intercalators. And so we don' know what the longitudinal outcomes are. It's been in human use long enough.

And, uh, so perhaps it's okay. Uh, but I couldn't tell you in real, with veracity about what it would do. The question remains, what if you don't have enough, which is really concerning or modern chemical soup that we reside in where the mitochondria take the biggest hit.

I appreciate the mini masterclass in mitochondrial maniacs. So you're, um, mitochondriacs, we're mitochondrionics. Everybody around me is now tired of me because that's all I keep talking about.

Okay, enough already. But hey, it's been an amazing learning for me about human function and animals and the world around us. That you see how nature has evolved to give us something that is so wonderful and capable that allows us to work.

I'm not saying forget everything. Just work to take care of your mitochondria. Everything else is great. Don't stop. Do whatever you want to do. All the supplements you wanna take.

But please make sure you get yourself. What I am going to toast to now is a healthy microbiome with healthy mitochondrion. Maybe I'll call it the mitobiome.

That's there you go. Yeah. And that's a phraseology even I use because it is fascinating. There's two beautiful bacteria bodies in our life and they keep us healthy and strong.

Take care of them. Microbiome by eating good food. mitochondria by X. Where can people learn more about Blue Oak Nutraceuticals? We're constantly working with clinicians.

We are listing them. As the trials complete, we'll publish them, you can go to blueonx.com. and that's where we will put everything out as we can. We are registered with the FDA, FDA knows about us, we are very, very clear that we make our product pharmaceutical grade.

As you mentioned, just because it grows in nature doesn't mean it does not contain negative things. And then, yeah, stay tuned. So please go there. There's info.

Ask us questions and communicate with us. But we are very dedicated to make sure that we're still very scientifically sound. that when we go out there and say something that there is clinical evidence we are gathering and working some of the leading clinicians and KOLs in the world and the country to really see how we can

continue to, you know.

gather the information, speak with folks such as yourselves to get the message out, right? They say, hey guys, and perhaps you're right, we have a product, We are a business, but we're also a public benefit corporation, Daniel.

That's why we are funded by ourselves, have no VC funding. And the idea was to make it affordable and accessible. We're developing programs so that we can make this more and more available.

that is our mission. We're not in it to simply say, hey, we're going to just… So, you know, the idea here is that if we can start to make people healthy, or at least contribute towards that, I think that's what our mission and goal is.

So we are social, impactful, mission-driven, and want to work with you and others to say how can we continue to learn more and more? At the end also, We are a business, so we want alive and not go bankrupt.

But at the same time, we will work with folks to continue. And no question, We will not entertain. We'll entertain all the questions that we want. You're providing a lot of value, you're staying at the cutting edge of science and research.

Our goal is to always serve as educators. Let's help our parents understand why we do what we, do when we. The last question that I end every episode with is if you could have one superpower, what would it be?

One superpower to disseminate the knowledge of mitochondria to everybody. You practice what you preach, right? You stand true to exactly what believe in.

I do believe it and it's our nature's gift to us. and this is it, this the reason why we are who we. This is the world around us the way it is. The diversity of species, the life and everything is energy.

And at the end, you know, often said, and even a quote ascribed to Einstein, at end it's all about energy and that's it. It's not about philosophy, it not physics, its about the energy, And the universe functions on it Imagine the two things the sun gives us is light energy and heat energy.

That's it. It's energy, and imagine if that light and the heat goes away, the energy source goes way. Life would vanish. Right? So, so just think about it, the whole entire universe.

I mean, you can, matter and energy cannot be destroyed. There's a constant amount. They can interconvert, but you cannot destroy it. That's how fundamental it is.

So everything else follows. Beautiful. Beautifully said. You said because the frequency of the sound waves, The decibels can change the bioenergetics of our brain.

I mean, it's amazing. To me, I'm just crazy. I can spend the entire day just keep going at it. People get tired of me. So I know you probably have other people to speak with.

Really thank you for taking the time for the conversation. You've been a very astute You know, person to talk about, you brought in some very diverse sets of topics in our short conversation that covered a lot of stuff.

So be well, have a great new year. For everyone tuning in and listening, please like, review and subscribe. Share this with anyone who you think can benefit with improving their mitochondrial health, their metabolic health.

Because certainly this is the core of our existence. Until next time, stay healthy, Stay wealthy, my friends. Thank you for tuning in to the TBD Fit Podcast on Dr.

Talks, where we unpack all things health and longevity. If you enjoy the show, like, review, and subscribe. This allows us to have a greater reach and help others on their health & wellness journey.