Introduction and Doctor Singh's Background

Doctor. I don't like saying it's currently the chief medical officer at timeline, which is a company that develops next generation advanced nutritional products targeting improvements in mitochondria and muscle health.

He has a, medical degree, and completed residency in internal medicine, a PhD in immunology and has experience including work for top consumer health, including Nestlé health Science.

And a startup biotech companies a scientist in timeline. He's authored over 40 articles in, top peer reviewed scientific journals and has designed and led, over 50 randomized clinical trials, and, in nutrition.

His research over the past decade across multiple clinical trials in the post biotic you're within a and it's health benefits played to muscle health muscle strength in mitochondrial health.

So I'm really excited to have this conversation with Doctor Singh. So, doctor Singh, I'm so glad to chat with you again today. I thought we could start with a brief description of what is your Lithuania?

Because our audience may not be aware of that. Sure. Well, thanks, for the opportunity to speak again and talk about your litany. So your alternate is a gut microbiome derived metabolite.

In short, it's a post biotic. Erlotinib is produced when we are exposed to sort of the Mediterranean diet containing rich in antioxidants and polyphenols and a certain class of polyphenols that are rich in fruits and nuts like pomegranates, berries and nuts like beacons and walnuts.

So when you consume these, dietary, food items, you're exposed to allergies, tannins, and your gut microbiome then digests these larger tannins. And in certain cases where the gut microbiome is conducive, you release, your litany.

And so that's what essentially erlotinib is. So it's and this is a really important, concept for our listeners. We have it's two parts. We have to eat the right foods that have these polyphenols, antioxidants.

So the bacteria in your gut can further digest them. And one of the compounds you make is your litany. So you have to eat the right food, and you need to have the right microbes.

Got it? No. A lot of us have taken antibiotics early in life. I'm one of them. I had a lot of, tonsillitis when I was very young. Had my tonsils out. About age four.

And so I would be at risk of not having the right microbes. Correct? Absolutely correct. And and I'm also in the same camp as you early on in life. I grew up in India, and everything was, treated by antibiotics.

What Urolithin A Is and How It Is Made

And so what I think your gut microbiome, even though it is mighty liberal with your dietary habits, pretty much a lot of the good, I think, as I say, your mother's microbiome is laid out in, in the first thousand days of your life.

And with antibiotics, when you disrupted, you pretty much take away the good bugs out early on. And so what we see when we do studies in the French population, or we look at the American population, we see the highest incidence in European cultures where Mediterranean diet is prevalent.

We see about 3,040% in the US. We see about 10 to 15%. You're left in a naturally occurring and healthy individuals. And I've now gone to my home country, which is India.

And the instances even lower, 5 to 10%. So this is, an important come, compound for health, in in part because we haven't had, vaginal births that's declined early, and early antibiotics.

If you have a C-section, you get antibiotics at the C-section. And so, and then antibiotics often occur in the first, thousand days, first two and a half years of life after birth.

So if we are missing those bacteria that help us make your less than a. What do we missing out on? Is this an important compound? It is. So today it was actually discovered about 30 plus years back.

And it was for many, at least the first, ten, 15 years since its, identification. It was thought of as a metabolic, waste product, of the alleged tannin and the polyphenol metabolism.

About 15 years back, we started deconstructing the health benefits of, pomegranate. And we found that compared to the alleged tannins, this particular post biotic was, was very potent in terms that it was really renewing the healthspan of mitochondria.

And by that I mean, as we all age, our mitochondria get damaged. And this these damaged mitochondria accumulate. And so what we found was that this particular post biotic year lived, and they was rejuvenating the damaged mitochondria into healthy ones.

And so that particularly has immense health benefits. And again, for the listeners, you've heard me talk about the critical role our mitochondria have, in brain health.

When your mitochondria are not performing well, it will accelerate disability. It will accelerate, cognitive decline. Brain fog probably also accelerates, our problems with anxiety and depression.

So whatever we can do to support our mitochondria will support better brain health. It will help slow the accumulation of disability for all of us without mass.

So, I think we've made the case that you're listening is a really good compound to have. So how much should I take and how would I take it? This is something I rub on my skin.

I take it by mouth. Yeah. So, this is almost ten years of running randomized, placebo controlled trials. And one of the first trials we did was really do these, what we call those, escalation studies with your listeners.

So we started, with, two 50mg of your litany. We are an oral supplementation format in a, in a soft gel in a pill format. And then we kept going from two 50 milligram to 500 milligram in a gram.

And, and the first studies were really looking at older adults who were very sedentary. Their they were, almost frail. Their muscle, health was not very optimal.

And looking really with, with genomic technologies into the mitochondrial health inside the the skeletal muscle of these individuals. And so what we found was that at 500mg, you would start to get this improved mitochondrial signature coming in in the even the absence of diet or exercise that almost was identical to the signature regular exercise was inducing on things like mitochondrial health.

And so 500 milligram and a gram is the sweet spot. So that equates to two pills a day or four pills a day. Wow. Okay. So, is this the same whether I'm 40 or 60 or 70?

So aging definitely has an impact on as we were talking and mitochondrial health, you know, when you're, let's say, in the 60 plus population, we see that maybe even higher doses like a gram is having even bigger benefits.

So on muscle strength, endurance and insulin aging, as we call it, chronic inflammation. So 100mg the dose I recommend if you are fit person in your 40s and 50s and you're already doing diet, etc..

So that's the sweet spot. I would if you have issues with fatigue, etc. I would go a bit higher. Okay, now I'm getting a little more sensitive. I'll be 70 here, this fall.

So does that mean I should go to a gram or can I stay at my 500mg? It really depends. Doctor Walz on on, what? Where you think your health sort of, status.

As if you have a lot of energy at the end of the day and still don't, you know, you don't feel as fatigued as, then then 500 milligram is the right dose because that's the dose we know maintains healthy mitochondria.

Dosage, Age, and Mitochondrial Health

Already now, a gram is where if you have, if, you know, your blood work, if you know that you have things like C-reactive protein, which is a marker of inflammation already high up, or you have, difficulties recovering after a big bout of exercise, then I would take a gram.

Okay. So I'm feeling pretty good. I, I think I can say at 500mg, you know, I can still lift weights, carry 60 pounds without a problem. Go for a jog. So, thanks for that reassurance. Sure.

Okay, so, can we talk a little bit more about the connection between mitochondria, inflammation and aging? Because, you know, inflammation is something we're very worried about.

In the mouse world. Sure. So, you know, earlier it was thought and there are these well-described hallmarks of aging. And the two that are really, I would argue, even the centerpiece of that puzzle and connect all the other hallmarks.

One is mitochondrial dysfunction so damaged mitochondria as we age or stress mitochondria. And the second is chronic inflammation aka inflamed aging. So as we age our organs ourselves, they become stressed and they they become more reactive and they induce things, you know, growth factors that cause inflammation.

So what's the connection? I think this is really a new, exciting area in the field where we believe now that these damaged mitochondria, they're very leaky, their DNA, their mitochondrial DNA starts leaking out into the periphery.

And this becomes more like a danger signal for the immune system. And so this, this sort of damaged mitochondrial parts, they start stimulating the the immune system and causing inflammation.

So if you're able just like you know, a plumber to to stop the leak, these damaged mitochondria and they all get reassembled and renewed into healthy mitochondria.

Then there is less of the mitochondrial DNA leaking out and causing inflammation. And so in all the trials actually, we run where we see improved mitochondrial health, we always see a dampening of inflammation in every whether it's a young athlete or a middle aged, overweight, 40, 50 year old or a 70 plus older adult.

Okay. Now again, for the listeners, I'm going to, review this, make sure, I'm understanding it and getting clarity for everyone who when the molecules that should be inside the cell begin to leak to outside the cell, these molecules activate the, immune cells because they know that that shouldn't.

Those molecules shouldn't be free. Those immune cells will release other molecules that, that amplify this dangerous single, and bring in these immune cells to eat up the damaged cells because our immune system knows that damage is a problem if you, burn yourself, break, bone, tear your muscles to your ligaments.

There's these damaged molecules, and the immune cells comes in. It's up to damage and organizes the repair. If our cells are leaking, the molecules that should be on the inside to outside the cell, it begins that process to clean up the debris, which, you know, creates more damage for us.

That's the inflammation that doctor is talking about. And the older we get, we are more vulnerable to that. And I

think what I'm hearing, Doctor Singh tell us is that you're less in a is, turns out to be a very helpful compound for reducing that leakage.

And so, many of us know that, euthanizing is a good thing. And I'm hearing this and it correct me if you've got it wrong that you're Lithuania could be part of that euthanizing program.

Yeah, exactly. I think, so what happens is you're literally stimulates this process of my autophagy. Now, there are other months. Let's explain my ag because I don't think our listeners would know that one.

So let's explore the different ways you can improve mitochondrial health. First. One of course is is your diet if you eat, as we were talking about a very rich diet and antioxidants, polyphenols, it keeps your mitochondria healthy and less damage.

That's one exercise is probably the best mitochondrial, you know, stimulator out there. And it's a biogenesis stimulator meaning biogenesis is to lay it out is the creation of new, healthy mitochondria.

Now your cell only has a certain amount of real estate. And if with aging, what happens is that that real estate is filled up with damaged mitochondria or other damaged cellular organelles, and that cannot be recycled, and that's when the cell becomes senescent or when we, what we call it like a zombie like cell that is taking the nutrients, but not really, you know, providing you with good cellular health.

And that's when all the organelles we were talking about starts leaking. Now what is my autophagy. My topic is or autophagy. Let's start with autophagy is really the self-renewal capacity of the cell.

And my autophagy is in many ways a autophagy of the mitochondria, meaning you take your damaged mitochondria that have this sort of eat me or renew me signal, and you flush them out and they become the building blocks.

Inflammation, Aging, and Mitophagy

And so in many ways, by activating mitosis during this garbage renewal process, you know, think of your garbage disposal in your homes. If you have this sort of, you know, the bio ways that you can renew.

And that's exactly what our cells are doing. And so that's what we see with your litany, is we activate my autophagy. And that leads to more creation of new or healthy mitochondria.

Okay. For the listeners, let's see if I can, summarize this and you correct me. I've got it incorrect, doctor saying, so our cells are able to recognize these mitochondria are not performing well.

I bring in other parts of my cell. So like the lysosomes that come in, eat up the mitochondria, break it down to its constituent parts, and then the cell is able to use those constituent parts to make a, new, young, healthier mitochondria that is now functioning well, exactly.

Perfect. That's that's how it works. And exercise, fasting, all these are ways to to to to do that. And now there are nutrients like earlier today that allow you to stimulate mitosis.

You, Okay. So staying young, again, for the listeners, some key building blocks, a good healthy diet. I'd say probably avoiding sugar, white flour, eating these radical things known as vegetables, nuts, seeds, sufficient amount of, protein, or meat, if you're into legumes and rice, that would also we have another source of protein exercise.

Would be super helpful. Occasionally fasting. Is that a good thing? Yeah, I think the caloric restriction by about 16%. So, you know, all these, six or, you know, you're eating within a 6 or 8 hour window, these fasting protocols that have been shown to stimulate biogenesis.

So all of these things super helpful, in your life in a, again, and, let's do as you should know, I've been using your health in a, like, a, a lot. And, as I'm getting to, shall we say, a bit more mature, I now a very thrilled that I have a grandchild.

I want to be sure that I could, chase him, carry him. And so I'm lifting weights. You know, I'm running around now carrying 60 pounds, so I'll be ready.

As this fine young lad grows, if we want to age. Well, having healthy mitochondria is part of that, and having, a plan with great diet, exercise and fasting.

And I think your health in a, can be part of that plan to help you age. Really? Well. Now, what about, again, our. You know, my audience is multiple sclerosis and autoimmune patients.

Does your health in a hold promise for us beyond, you know, our goals of healthy aging? What about our disease activity? Yeah. So there's a lot of new, exciting and emerging research coming out.

And I'm a trained immunologist. And when I see the the dual pronged effect, the biological effect of this molecule and a the mitochondria rejuvenation and B inflammation, that actually tempted me to actually run, recently, a randomized clinical trial to study the effect of your litany on, on, on the immune system.

The trials on autoimmunity, etc. are a bit further out. So just to build on that, there is already pre-clinical work done in, models of multiple sclerosis.

Well, hang on, our audience won't know what pre-clinical means. Yeah, so let's separate it out. So let's talk about, the randomized clinical trial data.

This is unpublished. This will hopefully come out in, in the top, medical journal soon. This is where we gave you earlier today. And we we took a few blood draws, and we characterize the effect on the entire human immuno, meaning the entire immune cell, population, which is hundreds of different cell types.

What we found was that you earlier today was having, almost, of, of removal effect on immune aging, meaning as we age. And there's an organ in our body called the timers, from which these elite forces of the immune system come out, that what we call the T cells, they disappear and they can patrol, our, our bodies that.

Well. And so what we find is actually a lot of stem cell like, naive T cells coming back into the system, and they have more mitochondria that's, you know, these are these are new findings.

So what this may stop be for just a moment, for the listeners, once I pass it all past the age of 40, our immune cells become less and less effective.

It's a hallmark of aging. And so, you know, our hormones slowly decline, our stem cells decline, our immune cells decline. Which is why, as we age, there's higher rates of cancer, higher rates of infection.

It, comes back to this declining immune cell. The fancy word is immuno senescence. And so what Doctor Singh is observing is that if our immune cells are euthanized, that really has profound implications for our health and vitality, because that will lower.

That's sort of a bold claim, but I'm going to make it for you, Doctor Singh. It will lower our our susceptibility to infections and cancers if our immune cells are working better.

And I'll hand it back to you. Perfect. So, you know, now that we have this great set of new data and that is leading to more randomized trials, we are now engaging, as is Doctor Walz mentioned, as we age, the incidence of cancer goes up.

So we now engaged with the National Cancer Institute to study the effect of, you're letting a in in folks who have

cancer, but then beat it out. And how does the how does the boosting the mitochondria help in immune rejuvenation in that population?

We are also adding it on to there's a fascinating trial where it's being added to an immunotherapy protocol. Now, what does that mean is basically when you're diagnosed with cancer or you're given, basically, a drug that boosts your immune system, and that's what immunotherapy is.

Immune Rejuvenation and MS Research

And you're adding might appear to it to see if you can have a, sort of a synergistic effect. Now, back to your question. And our immunity, the trials have not started yet, but they are models.

And that's what I mean. Preclinical is the step before you go into randomized trials. There are models of multiple sclerosis. That are existing today.

These are called experimental autoimmune encephalomyelitis, which is a big word, but it's essentially a model of M. S. And in those models in in animals, in animals, you've got this.

Okay. Where there's myelin, degradation and damage. And so, what researchers have shown actually a fascinating paper in Lancet, in biomedicine came out showing that you're literally had a very potent anti inflammatory effect and even had a, effect on, on sort of the recovery of these symptoms of, this model of M. S.

and in this model. So we hope somebody translates it as a supplement. You can't really study it in a drug like indication. And that's one of the challenges we have today.

Right. So if you when you have a new exciting compound like you're with today, you end up having to make a decision. Are you going to go down the drug route, which is a much more expensive route?

Or are we going to go down the nutritional supplement route? You're not going to be cured is as to why timeline made the decision to go down the supplement route in terms of use, as opposed to the development of a drug.

Yeah. A this was, a natural compound that was very safe, that as we started discussing, about 30% of the individuals already are getting exposed, some very levels from the diet.

And so it was easy to, you know, it was easier to study its effects going in first into sort of the populations where we thought, people were already deficient in it.

So, you know, it's like studying vitamin C, for, for, for boosting your, your, your immunity against cold and infection. So that's where we thought it was easier to get into, but easier meaning in terms of it wasn't that easy, to be honest.

Now that I look after 15 years, we did we had to do the exact same safety and toxicology and, and get the FDA approval as a grass, what we call as a food supplement approval versus a drug where it would perhaps be a bit longer, as you were saying, and bit more expensive.

And you will have to narrow it down to a indication or a set of indications. So, yeah. Would you take a supplement that improves cellular health for everybody versus the narrow indication we decided early on in the supplement drug?

I'm so glad that you did, because it can have a much larger impact on the population. It's easier for people to access if if you go down the drug route, then it's going to be specific indication by specific indication.

And you need to have, a relationship with a physician that's going to be a much more expensive compound. So, you met I mean, what what if somebody had decided to go down with ascorbic acid as a drug, like, I mean, that would have, a, you know, that decision could have been made when ascorbic acid was first identified, which is, by

the way, vitamin C.

So how would people know if I have the correct bacteria to make erlotinib or if I'm one of those folks who, like you and me, don't have the correct bacteria on board.

So this is, easier to say, but it's been a project. I've spent long and long research hours working with my brilliant team of scientists here. The initial idea was, let's go identify the the gut bacteria that is making the conversion.

And perhaps there's also a potential to create a new probiotic that will allow you to to do the conversion. And so we actually did these studies where we saw that, there were like 10% of the adult population were these super producers.

And then there were the in between folks that were making some levels of your own today. And the 60, 70% were even if you gave them a six glasses of pure pomegranate juice or a bottle of not every day, they wouldn't.

And so we sequenced the gut microbiome. The the gut microbiome is very complex. It's like hundreds and thousands and millions, in fact, different bacterial species.

And and we found there was more Aquaman's, in the folks that, that were producing erlotinib, etc., etc. it was never easy to tease out that one particular, strain that was leading to the conversion.

So today I've developed a test, that can allow you to know if you're if you're naturally making it or not. And some very simple tests, a few, a break in your finger and few spots of blood on, on the, dry filter card, and you send it to a lab, and this is not yet commercial, but we are still validating the sensitivity of this as part of a clinical studies of folks listening in.

Can perhaps, try this test as part of, you know, experimental clinical study. If they want to know if they're making your lab today or not. Okay, so the listeners, this is not a test.

You could go to your medical doc and say, I want to know, how can I make this year a compound? Because it sounds interesting. Not yet available. Stay tuned.

Will, when it becomes available, doctor saying be sure to reach back out. We'll get you back on our podcast so we could talk about this. So right now, if you want to know for sure that you have your listener, the safest way to do that would be to take, some Muralitharan.

Anthony. By mouth. Are you the only company that makes that is manufacturing? You're looking this is a fascinating another fascinating twist. And, in the it's a story.

For 15 years we've been studying it, only after getting convinced 4 or 5 years back, we decided to launch it. And then, let's say the early adopters, folks like yourself who are convinced of the science, have been taking it.

Now, what we see happening is a lot of Chinese manufacturers coming in with me to copycat products in the market, and which is great because it's making the supplement even widely available.

But I think as we go on Amazon and look at the quality of these supplements, most of them don't have the, the purity of, you find probably 10 to 20% of products have some trace amounts of your earlier A and B, I would worry because these are not GMP and these are not.

Oh, we should explain to our, listeners what GMP means. Yeah. GMP means the so far our GMP is good manufacturing practice, meaning you have a, focus factory where you make in a very clean, sterile environment the molecule, and you make sure it's, you know, it's passing through multiple layers of quality and then the, the, you know, or the regulatory organizations also approve this.

So most of these sort of meta products wouldn't do that. And so I want to but yeah, I'm going to add in here that,

these meta products may not actually have any of the year lithium in the compound.

So, you want to if you're buying supplements, get them from a company that, you know, what the the label on the box says is in the compound really is in the compound.

Supplement Quality, Timing, and Where to Buy

Because there can be sort of a wild West where the label and the content in the actual supplement, the pill, doesn't match, that is, a worrisome sign.

And, I, you know, I'm very concerned that you take the time to verify the products that you're buying have been manufactured properly, and that the content in the supplement matches the label so that when it says you're taking your oath today, you really are taking your health in a as opposed to just some empty filler.

And it's safe for human consumption that has cleared all the microbiology, the heavy metal contamination, all that stuff. Because you know that that's the other the safety of I would really, as a physician myself, I would be very cautious of using, a non-branded product.

Yeah. Well, unfortunately we have seen, some of these natural, natural supplements coming from, Asia, that there is lead Mercury and other heavy metal contaminants. So, be very cautious with the source of your, supplements.

You don't inadvertently create harm for yourself. How how quickly would you anticipate people, would see an effect? So, Sarah, losers are like, okay, I want to give this a try.

I'm going to order some timeline. Should I what's the timeline that people could expect to see some response? And what kind of responses might they, observe there?

First I would like to say there's not a magic pill, so it's not like you take it, for a few days and you feel the effect. The earliest we see in in our randomized, placebo controlled trials, the, the mitochondrial held in the cellular health really sort of getting renewed and more or more energy, kind of setting is about a month.

So you need to take it for a month to, to have an impact at the cellular level. I recommend a minimum of two months. And that's when in clinical studies, we see an impact in something like VO2, we are to being a marker of how good your oxygen consumption rate of your body is.

And and that's where we also see older adults for example 70 plus have more endurance. If you start seeing the effects on on strength and inflammation.

So like the 2 to 4 months is where people can really see visual visible effects. But I would try it at least for a months, two months. You know, in my, clinical trials, we generally use a three month intervention.

So we get baseline assessments, do our intervention, whatever that might be, reassess at three months and then again at six months. Yeah. And I think in general, that's a, a good timeline.

So sometimes, you know, when people add a supplement, I invite you to take your little notebook, write out what, what symptom it is that you're trying to improve, whether it's your your mood, your mental clarity, your, reducing your fatigue, better stamina.

So write out what's the symptom you're trying to improve? How are you going to measure it? I like the medical symptoms questionnaire because you get a numbers score.

That's very handy. And you can get it by, sort of, organs system. You know, your head, your heart, your mind, your energy level. And so you have an overall total score and score by, general systems.

Do it at baseline. Start your supplement in this case timeline, and then, risk for yourself in three months. And then

you can look at the two scores and sometimes and this is sort of interesting, sometimes people feel like, you know, that didn't help one darn bit.

And so they stop, and when they stop it a couple of days later, they feel markedly worse. And that's when you're like, oh, maybe it was helpful and I should go back on it, because now that I'm not taking it, I can I'm aware that I don't feel as good.

A part of that, the reason that can happen is when we begin to feel better, the change comes on so slowly, so gradually, I become addicted to it. I can't perceive that I'm better, but when I stop it, I realize.

And I'm not feeling as good, in that, So that can be another clue. So I've given you a couple tools you could use, medical symptoms, questionnaire. Right.

Give yourself a numeric score at the baseline. Check it again in three months. See how you're feeling. If you're feeling like. Well, then help stop and then reassess.

And a couple days and, after and often, using this technique, people can sort out the supplements that are making a big difference. The actions that are making a big difference.

And over time, you can fine tune your self-care routine. Certainly. I have I have found that, the mighty pure, adds to my, strength and my stamina. And so I like it a lot.

It's been helpful for, my patients in terms of their energy and mental clarity as well. Now. As I get older, more mature, let's say I get into my 80s and I'm planning on getting into my is that's only ten years away.

Does does the dose change at all as we get more and more mature? To be honest, the oldest participant in the trials I've run has been, vivacious 89 year old lady who, even though it was a blinded trial, which means that she didn't know whether she was taking the placebo or the active, but she swore she was more active.

And the moment the four month period finished, just like you were saying, she felt the difference. You like I I'm sure I was on the active product because I'm feeling a low energy.

And I need your product. So. And the youngest we have had is is a 20 year old love, good athlete. And it's back to what we chatted earlier. It's really feeling if you're a bit more sore after exercise, if you feel a bit more brain fog or a little lack of cereal at the end of the day, then I would up the dose to a gram.

Okay. Well, you know, this has been just such a wonderful conversation. You know, that saying I'm looking at the time I realize that I should be wrapping this up.

Can you tell our listeners, who are probably really quite intrigued, how they would get this product, and how they would, find timeline, how they can go to, www.timeline.com and they can take a look at, the different, array of products.

We have the pills as we talked about, but we also have the, have the fruit flavored, the one limited flavored, fruit sachets. So which gives you that in one sachet the same dose and soon hopefully will launch gummies.

So then there will be an even bigger option, for, for, for the, for the listeners. And, yeah, they can learn more. It might appear.com about all the signs as well.

Okay. So again that's timeline one word.com. And the other the pure in my opinion.com. Yeah.com. Okay. Well thank you doctor Singh. This has been, really very enjoyable pleasure.

Thank you for having me. Doctor. Was.