Improve Your Healthspan with Mitophagy and Urolithin A Transcript

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Introduction to Dr. Singh and Urolithin A

Welcome back to the conversation. I'm Laura Frontiero. I'm your host of the Mitochondria Summit. And today I have a very esteemed guest with me, Dr. Anurag Singh, all the way from Switzerland.

Thank you so much for being here with us. Thanks, Laura. Pleasure's mine. Yeah, well, I think the pleasure is actually all mine, because I'm really excited about what you are going to be bringing to this summit and to these talks today.

But first, let's introduce you to our audience. You are an internal medicine doctor and immunologist. You're the chief medical officer at Timeline. And that company develops next generation advanced nutritional skin care products, targeting improvements in mitochondria and cellular health.

And they also produce oral products, which we'll be talking about some supplements today. You've authored over 40 articles for top science journals. You've been awarded more than 15 patents and you've designed and led over 50 randomized clinical trials.

And the work in the world that you have completed is significant of much of your research over the past decade has been on a post biotic molecule called Urolithin A and we're going to talk all about its health benefits today.

So so Dr. Singh, we're really going to jump into this. We're going to talk about where your life in a comes from, why it's good for us. You'll also help us link the connection with macro autophagy, dysbiosis and chronic inflammation.

All of which these three topics are being talked about on our summit. And you're finally going to unpack for us why our audience should be paying attention to your lithium in terms of longevity.

Because I know that our audience is really fascinated with extending their life span, internal, external. They want to look good. They want to feel good.

They want to be here on the planet, leaving a legacy for their family and spending time with their loved ones. So with all of that, let's jump right in.

Okay? Sure. Okay. So first off, all right, so let's unpack what this says. Mitochondrial function is what we're all about here. We know mitochondrial function is really important for cellular health and health span.

So can you first explain the connection there, mitochondrial function to cellular health and ultimately health span? Yes, sure. So the cellular health is the by energetics of cell, as is an absolute key pillar of, let's say, an organ.

And any organ that has a lot of mitochondria, such as the skeletal muscle or the heart or the brain is absolutely reliant on energy. Right? So when these origins, when mitochondria are not functioning well, your cells are not functioning well, and when your cells are not functioning well, your organ or tissue is not functioning well and as a result, you will have full body dysfunction, which means, for example, that the mitochondria and skeletal muscle are not well, then your muscle cells are not getting enough energy supply to power up the muscle cells, which means now you have mobility and fatigue problems and that kind of manifests to the whole body level as issues moving around and in general finishing your daily activities of living.

Mitochondrial Function and Cellular Health

So that's what is in essence cellular health is it's really a key foundation of your good health and health span. I always say to my patients that the end stage problem with mitochondria decline and cellular decline in mitochondrial decline, we have a word for mitochondrial decline.

It's called Alzheimer's. It's called heart disease. It's called cancer. So I see you nodding your head. Yes. So we're on the right direction there. So in terms of mattering for our health span and making sure that we live long, healthy lives, it sounds like if we ignore cellular health or mitochondrial function, we're never going to get there.

We're not going to reach that goal. You absolutely correct. I think mitochondrial dysfunction is that key hallmark of pillar of aging that connects actually all the dots that lead to Oregon dysfunction.

And so you were mentioning Alzheimer's disease and Parkinson's disease and even mobility issues such as frailty and sarcopenia. These are all pointing now all the research is pointing to mitochondrial dysfunction and cellular dysfunction in these tissues.

So absolutely. And I love how you said almost all the research is pointing to that. And this is what makes this summit so relevant in the conversation right now, because we're bringing the world's top researchers and leaders together to help people understand and break this down in a way that makes sense for people.

Instead of the high academic speak that we tune out, we can't understand. It's a foreign language academic speak. We're making this super simple. So as we talk about we're going to get into your life in a in a second.

But I think before we do that, what we need to unpack is mitophagy as a foundational process for health. So before we get into early athenry, you have to tell us what Mitophagy is and help us understand it so we can get into that discussion.

Sure. Yeah. Mitophagy is is a very well conserved anti-aging sort of pathway that is always happening at the background level. So what happens is as it's a form of autophagy, right?

So a lot of folks that you are in your audience may have heard this word autophagy, which is basically taking the cellular waste and clearing it up. Mitophagy is basically a autophagy of the cellular race inside mitochondria.

And what happens with aging and or age related processes in general is that mitophagy and autophagy in general starts declining. And so what you get is basically you think of, you know, the trash bin in your house that if it fills up and you're not cleaning it out, your house is not going to smell very well.

And that's exactly what's happening in these tissues in the cells. And the mitochondria are not feeling good. So over time and you're in this process of decline starts early on in the thirties and forties and accelerates really in the fifties, sixties and seventies.

And what happens is basically now with the increasing amount of mitochondria waste accumulating, a lot of mitochondria cannot produce energy properly.

And so these processes of cleaning the waste are slowing down. And that is what we call mitophagy in general. Okay. So now that we know what Mitophagy is and and we're here to talk about your role with an A, so can you explain what it is?

You're a lithium. What is this molecule and how did how was it discovered, too? I'd really like to know that. Sure. So we started gosh, almost a decade and a half back with the whole idea to bring sort of the biotech life science approach to to nutrition and really understand how certain natural compounds present in our diet could give a health benefit.

And so one of the key fruits we started to deconstruct was the pomegranate. And there had been a lot of studies around pomegranate, basically attributing the high pomegranate consumption was linked to better cognitive ability to better muscle performance.

What Mitophagy Is and Why It Matters

And so when we started deconstructing the pomegranate, we found there were hundreds of compounds and these

are composite. We often call this polyphenol.

So these are polyphenols such as alleged tannins in the pomegranate. And so these are present in our diets. The granite is a good source of these polyphenols, alleged tannins.

Then there's the nuts like walnuts and pecans and the berries. So we started looking into these compounds, and what we realized with the simple experiment we did was that it was not these compounds that were causing the health benefits, but actually the gut microbiome was actually taking these dietary precursors and causing a transformation and releasing what we now call as a post biotic, sort of in the field, another compound called a litany.

So this your litany is basically a gut microbiome derived metabolite that is produced when you're eating healthy foods and diet, such as unrelated nuts.

And this is the molecule that we found having great effects on mitochondria and mitophagy in general. Okay. So our audience, I think we have pretty savvy audience.

So they, they know that post biotics are important. Post biotic is something that your microbiome makes when you break down and ferment prebiotic foods.

So what I'm hearing you say is that this urethane is actually made inside your body by your microbiome, but it needs the raw ingredients of pomegranate specifically is where we get this from.

And this polyphenol that's inside of pomegranate becomes this amazing post biotic that helps fuel the intestinal cells, the healthy bacteria. But I'm sure there's more to it than that because this is a very special molecule.

Yeah. So there's, you know, the two key pillars needed to get your lab today is you need to be eating right. Right. So you need to be having a good, healthy eating behavior, eating a lot of fruits and nuts in your diet.

So that's one which we know a lot of people are not doing correctly. Yeah. The second is that you need to have a very healthy and very rich and diverse gut microbiome.

And so we have done studies around the world, we've looked at the friends, we have looked at the Canadians, we've looked at the Americans, and really the percentages vary.

But the highest we saw was in the French, about 30, 40% in the US and Canadians we saw only 10 to 20%. Well, holding adult population had the correct gut microbiome to produce your children.

And even if they did, the levels they made were what I as a clinician call as sub optimal or sub therapeutic. So they were not enough to give you sort of the the direct benefits that.

And so that's how we came up to giving a direct calibrated supplementation with the post biotic directly. So from reading between the lines, what I'm hearing is even if you ate pomegranates every day and probably most people are not going to do that, and you'll have to tell me what the ideal dose of a pomegranate or the ideal serving of a pomegranate is for this.

But even if you did it every day, unless your microbiome was robust, healthy, then you're probably not going to derive the benefits. Yeah. So a glass of pure 100% banga juice is about 4 minutes peeled and sort of crushed in a blender.

Discovery of Urolithin A from Pomegranate

So the partizan, the the polyphenols or the alleged tannins are in these white, you know, kind of covering around these red beautiful arrows in the in the fruit.

And so when you reign, the you need to write about four to get a glass of juice up to 40 to 50 emails. And so someone like me so I typically think I eat very good, healthy diet, but my body cannot make I just don't have the right gut microbiome.

So I can drink six glasses of pomegranate juice. My body still won't make enough. Or not even a trace of your litany. Yeah, yeah. So that's kind of the story.

And in people, what we see is about you need to drink about six glasses of juice to get to, let's say, the dose we are giving in a nutrition product. Right.

And then we're dealing with spikes in blood glucose levels and all kinds of problems if we're drinking six glasses of orange juice. So that's a problem. Do it.

It's a big problem. I think these glasses like 30 grams of sugar. So there you go. Yeah. Okay, so. So hear us. Everyone listening right now. The answer to your with an A in your body is not to go drink six glasses of pomegranate juice per day because you have, you know, some other problems that can occur if you spike up your blood sugar levels too high, which is going to be counterproductive to your longevity goals.

So can you share with us a little bit more about how we would get your life in a and know that there's some supplement development? Tell us more about this.

And I know you've done, you know, many studies on this. I'd like to dig into all the benefits once we put this postpartum in our body. But since we're talking about how to get it into our body, let's talk about supplement your lithium.

Yeah. So, you know, we have been studying this molecule now for a good ten out of ten years and we've published and name it all any top academic journal Nature.

So Science, we've published our extensive body of scientific evidence and clinical evidence in it now. So we have developed a whole range of products now that give you a very targeted dose of your litany.

So in our clinical study, we have seen benefits starting to happen on things like improving cellular mitochondrial health already at 500 milligrams of pure you earlier tonight dose.

And this translates if you get taken longer for about 2 to 4 months in terms of improved muscle strength. And then we have done what is called is absorption studies to see how much increased doses will give you better, higher bioavailability or better absorption.

And about a grams, about a thousand milligram is the top dose we see really in all these randomized clinical trials. So now we have a whole range of foods and supplement products of foods with fruit flavored like berry pomegranate flavored, ginger flavored products that give you a daily dose of 500 milligram that you can put in your daily lifestyle.

Smoothie six. And then a lot of people prefer to eat pop pills and take soft gels. And so we have a soft product and in addition we can talk about it.

We have also have now started developing skin care products that deliver this molecule topically. Yeah, I want to know all about this. So I want our I want our audience to understand why this should be a priority in supporting their mitochondrial health.

What are all the benefits they're going to get when they bring this in? And then how do they get it? Yeah. So I sort of zoom out into what all people probably are doing today to improve mitochondrial health, right?

So you can improve mitochondrial health from a sort of a scientific thought process through three different ways. One is what we call is biogenesis, which means, well, you create new healthy mitochondria, and so are compounds

like resveratrol or energy boosters that are known to do that.

Second way is to take your existing pool of functioning mitochondria and make them more efficient. And this is where compounds such as Coenzyme, Q10 and L-Carnitine come into play.

But the very unique molecule that this is, which is your alternate, is probably the only well-studied, natural and clinically proven mitophagy activator which takes the dysfunctional mitochondria claims about that then becomes the building blocks of the healthy, you know, the newer mitochondria.

So that's one thing to keep in mind the uniqueness of this sort of way to improve mitochondria. Unless you clean the waste, you really can boost the other functioning mitochondria.

And so yeah, go ahead.

How to Get Urolithin A and Effective Dosing

So I think that's really critical to to really pinpoint that if you don't clean out the mitochondrial waste, you won't be able to create new mitochondria, new, you know, more energy.

You won't be able to solve chronic health problems, you won't be able to recover from chronic health problems. Now there's different things we can do to support mitophagy.

Taking a polyphenol supplement is one way we can do that. Why would we want to focus on this when there's other ways we can promote mitochondria cleaning?

Yeah. So the two best known interventions out there today that induce mitophagy in a very robust way are regular aerobic exercise or even resistance exercise to a certain extent.

And second is calorie restriction or intermittent fasting, both of which have been extremely well documented and studied. But the issue with those interventions really is compliance, right?

Right. Complying to think of an older adult with energy issues as a doctor, as you going to put them on the three days per week of exercise training, they're going to do it for a while.

After a while, they're going to have certain compliance issues. Guilty. I'm guilty. Guilty as charged. Well, you're not older, but yes. And the calorie restriction is another one.

Overweight people who have a lot of mitochondrial dysfunction have similar issues. Right. You put them on a calorie restriction diet and the compliance rates are worse than 50%.

So I think there's a need. So diet and exercise, obviously are the two key pillars of health. And I think what I want our consumer and audience to take away is that there's a key third pillar of health, which is slow increasing, and erlotinib should be a key sort of element to promote that self-help.

Okay. So I'm really glad that we're talking about all of this because if I were queen of everything and if I were in control of everything, I would have everyone trying out some intermittent fasting, sticking with it, figuring out how to do that, because we know the research is solid, that this actually contributes to longevity.

I would have people exercising to their ability and building up on that, but since I can't be at every single one of my clients households all the time holding their hand and helping them do this and being, you know, accountable to themselves and things come up and life happens.

Then something like you're all within a makes this very simple and dare I say like a biohacking, right? It is a bio hack to make this easier. Now the term biohacking to me I have issues about biohacking because it feels like you're cheating the word hack sounds like you're cheating, but biohacking actually is not cheating.

Biohacking is bio elevating. It is improving your situation. So what I'm hearing is this is a really simple way to get this into your body, to get this support for mitophagy without having to rely on your accountability to do that exercise, to do the intermittent fasting all the time.

Yeah, extremely well. So to summarize, I think I see it more as bi optimization. Right, exactly. Exactly. Both your health and your house band, which obviously will then improve your lifespan in general.

And we started out actually studying 70, 75 year olds who were running marathons and comparing their sort of muscle and mitochondrial health with 70, 75 year olds who were very frail and sedentary.

And what we saw, we saw like a dysfunctional mitochondria and a defect in Mitophagy.

Benefits for Mitochondria, Exercise, and Recovery

And that's one of our first studies that we published in Nature Metabolism, because we actually then took those very frail, sedentary, older adults and we gave them four weeks of supplementation with a very targeted dose of 500 or a gram, fewer than ten.

And we were able to show in four weeks a similar signature in their muscles that we take chunks of muscle. And that's the muscle biopsies, and we start to look them under signatures with gene expression, etc..

But what we saw was basically an exercise like signature in these trials. And that long term, of course, has numerous health benefits. Well, so what my where my mind is going right now is the hamster wheel that people get on who have low energy and they have, you know, their muscle strength has declined, their energy is low.

And they just don't have the motivation or the drive or they can't find the, you know, the drive to keep up with an exercise routine. And they find it challenging to fast.

This is a really great way for people who have struggled up until now. If you're not a professional athlete or, you know, in really tiptop condition, this is also a way to get you this benefit without having to be on that wheel of giving up, giving up, giving up all the time because it's too hard.

Yeah. And that's the most obvious. You know, I'm a triallist, so I obviously have to design trials that have the best chance to show an effect. So you start with older adults with energy issues or mobility issues because you know, their mitochondria are not in the best shape or you work this none of the other trials we did was with overweight individuals who are quote unquote healthy, but, you know, very sedentary lifestyle, BMI for about 28, 29 and if you put them on a sort of a running real kind of experiment or illness on a treadmill, they don't last too long.

And we obviously showed effects there. But then, you know, the Holy Grail is and where the whole mitochondria feel is actually moving is even if elite athletes overtraining is inducing mitochondrial dysfunction.

If you're a healthy person, if you just get a flu or, you know, a cobra or whatever, and you're in the hospital for a few days, your muscles are already starting to have struggling issues in your mitochondria are going to be dysfunctional.

And so, you know, now are all our researchers now we actually just finished a trial and elite athletes were put on a three week overtraining kind of camp setting.

And you see that the mitochondria are struggling to cope up, their muscle recovery is struggling to cope up. So we all need support. And that's why I use the word by optimization. Yes.

And that was actually going to be my next question is, how would you use your litany with people who are fit and in shape and people who may even be more on the athletic side?

Because, you know, our range of audience viewers here is everyone from Chronic Fatigue Syndrome all the way

up to elite athletes who are looking to improve their performance.

So can you talk about how your Athena can be used in the person who does have good energy, who does have the ability to exercise and who might also exercise regularly?

Yeah. So, you know, we are running these trials and we also getting a lot of real world feedback and we have done other studies with Giving Your Lives and they might appear as it's trademarked in these settings is helping even augment the benefits of a regular exercise so or even augment the benefits of intermittent fasting.

So that's how I see, you know, sort of a double tool in your kit kit box kind of helping you achieve by optimization. And, you know, obviously somebody struggling with energy issues is the clear target.

But what we are seeing now is a lot of people who do sports are adopting or taking in the use of your religion as part of the daily regimen and why they're using it and the feedback that is coming.

It's really a muscle recovery. So when muscles are working over time, they get damaged. And so you accumulate a lot of lactate, you accumulate a lot of inflammation, which is all again pointing out we touched upon it or you touched upon the connections, inflammation and gut dysbiosis.

You know, in the end, what this molecule does or what you're seeing it do is that it even lowers or dampens inflammation just because now your mitochondria are in top shape to the kind of are able to your immune cells have a lot of mitochondria at your your heart cells have a lot of mitochondria.

And so, you know, that's that's where we are seeing the real life real world uses a lot of athletes who are doing bike races or weightlifting or rowing.

They're kind of using it as a recovery tool. Oh, excellent. Now, I'm sure in all your research, because you are such a prolific researcher, can you speak into using your life within a in terms of supporting people maybe with cancer or chronic neurodegenerative disorders or, you know, multiple sclerosis, Parkinson's, anything along those lines?

Can you can you tell us what you know about that? Yeah. So we, of course, have not done randomized trials in different all indications. You mentioned most of our trials have been in fatigued older adults or fatigued, overweight or and now we're moving to sort of the to recovery, you know, angle of research.

Now, what we have seen or what we have published or what our we are now seeing a lot of interest in the field from other top academics who are interested in the mitochondria space.

Potential Roles in Brain, Immune, and Cancer Research

The National Institute of Aging, actually the first one, about four or five years back, to come out with a big paper where they took a look at about 2000 natural compounds that could target reverse neurodegeneration via, of course, improving mitophagy.

And you're a legend, actually stood out at the top when they published this paper showing that even neuronal health could be improved by boosting mitophagy with this aging process.

There's another group that at the Buck Institute of Aging, which is really one of the top Centers for Aging, that's actually repeated the same experiment and showed the same data.

So we know brain cells have thousands of mitochondria and with aging, these are compromised. So we actually they and we are planning to run a big study with a group at Harvard, really looking at early cognitive decline biomarkers and good mental health in that aspect.

Back to your question, cancer, I'm trained immunologist. So I actually think this whole field of immune biology and immune metabolism has ignored the contribution of mitochondrial optimal mitochondrial health to optimal immune

health and we've all talked about immune health a lot in these last two, three years because of obvious reasons linked to COVID and and things like that.

But one of our collaborators just came out of the very big paper where he showed actually that the key immune cells are these cells that we call this T cells that always remember the signature of the virus, sort of bacteria.

You can supercharge these T cells taking that have been exposed to your liver. And so he's shown that even fighting cancer is improved in these models of of colorectal cancer.

And another group is showing that actually a post cancer recovery. So after you've gone through chemo radio on your recovery, know you're cancer free, you basically are coming out of the immune system and you're coming out with fatigue levels the highest.

So that's where also you're hallucinating. But these again, these are trials we're running actively right now. Wow. I can't wait to see the outcome of the trials.

How long do we have to wait? Well, research is two words. I always say re-insert. So you always have to, you know, keep building. You start somewhere.

So we show these great effects of your litany on improving muscle performance. And we, of course, have showed on mitochondrial and cellular health. Now we are getting into brain and and immune health.

And of course, we can talk about the skin health and the visual signs of aging where we think we can by delivering it right to the organ through topical skin.

We can really. Yeah. Let's, let's go there. So I know now I know you said that I was young and I would have you guess my age, but I am 50 and and so something is going right here for me.

I think I have some good genetics and some good healthy lifestyle. And one of the most and most prevalent questions that I get from my community and my clients is how do I slow down aging on the outside?

I mean, everybody wants to look good and feel good, right? They would love their energy like the outside of them to match the amazing energy they're feeling on the inside after they work through, you know, healing protocols.

So what do you have to say about looking good on the outside? Oh, again, it's very relevant. Part of the discussion we're having is there's a key component, and that's the energetics of your skin cells.

And that's, again, boils down to the mitochondrial health of the skin cells. And so we and others have looked at skin cells from different donors, 28 all the way to seventies.

And the older you are and the older you look at the skin cells of the skin biopsies, the signature is really of impaired mitochondrial health. And so the more wrinkles, sort of visual signs of aging are all sort of now the skin aging is has two components and what is called is intrinsic aging.

So that's where a lot of these processes where collagen breaks down and things like wrinkles start happening. But the second is extrinsic aging. So what with the harm from sort of the UV exposure over our lifespan, the pollutants in the air, you know, environmental pollutants they're having, they're kind of contributing 80% to that visual aging.

And this photo damage, along with the intrinsic aging, is really greatly accelerated. And so what we see in our studies now that these are still a of the press data, not we're trying to get this published.

Skin Health, Aging, and Topical Products

And really the talk from the College Journal is that year olds and they can actually had both an intrinsic and extrinsic aging via its effects on mitochondria and immune pathways.

That's incredible. I'm so excited. So it's going to battle. What I just heard you say is it's going to battle the 80% of aging that's caused by the environment.

You got it. I mean, take retinol, which is right now being used by almost every person for anti-wrinkle effects. Right. And it works on the intrinsic parts of the aging, you know, sort of rebuilding the college pathways.

But there's a lot of controversy and a lot of irritation. If you put retinol in, you go, you know, directly in the sun. It causes a lot of irritation.

So it's, you know, if you can have a new safe alternative that hits both extremes again and again, it's a game changer. Again. Is this product available yet for skin?

Yeah, we just launched it last month. And this is a very timely. Oh, it's very timely. We've been selling the oral products for about two years and we just launched the topical line prep side.

Tell us, where can we find it? Where can our audience get a hold of this. Yeah. So the company timeline, you can go to timeline nutrition dot com and you can see all the range of products on at rest Explorer, nutrition, the different food products, the dietary supplements and of course you'll see the skincare products on the website.

And if folks want to learn more about the signs, they can go to meitu pure dot com as well to learn more about the science. This is incredible. I know that we're going to get a flood of people checking you out.

So in the last couple moments that we have here, final thoughts from you. I mean, you've dedicated your life and your career to medicine, to research, to solving chronic health problems that seem like I feel like we've been so stagnant for so long and I feel like we are entering a an era of learning new, innovative, cutting edge ways to solve problems.

And you are one of those people who is at the forefront of it. And many people will come after you because you paved the way. So in our last moments here, in this vast knowledge that you have in the in the healing and natural medicine space, and you also come from this Western medicine's place as well.

So you bring this wealth of knowledge. What would you say to our audience in terms of living well and, you know, creating a long life worth living?

Final Thoughts on Longevity and Precision Nutrition

Yeah, I think I touched upon it. You know, I have a firm belief that there are three key pillars of health. You know, you of course, you always need to eat, right.

And, you know, diet and exercise are the two absolute key pillars of health and longevity. And oftentimes, you know, we get busy in our life and we can't really do justice to these pillars.

You know, I myself am what I call a weekend warrior. I like to run, but I only find the time on a weekend. So what can you do, you know, as a third pillar.

And that's where I think a lot of this biohacking or bi optimization tools come in. And and we certainly think the discovery we've made and studied for 15 years and we got ourselves convinced that for 30 years that this whole feel of silicon tradition and how you can boost cellular health as we all age that sick people are in this compound and we talked about it earlier tonight.

Thing is a key part of the puzzle and the future looks great because if we can figure out strategies to even optimize. So I think precision nutrition is a big area where you can really figure out and we are even developing now kits that people can hopefully buy in the future that will tell them if their bodies making this molecule or not and then they can, you know, titer and take the altered dose accordingly.

So that's how I see that evolution. Thank you so much for your words of wisdom and for being here and supporting, you know, this summit and educating our audience.

I'm really excited to hear feedback on the products. Once people get to train them out, myself included, I'll be getting that skin product now that it is available.

All right. Thanks for having me, Laura. Great piece of. Yeah, thank you, Doctor Singh. Take care. Bye now.