## Introduction to Postbiotics

Welcome to another fabulous interview as part of the MS and Autoimmune Summit. I'm Doctor Wahls, your host, and this is Doctor Singh. Now, doctor Singh is a MD, PhD, and chief medical officer at timeline, a leading research on mitochondrial health and vitality.

He does clinical trials, immunology and a post body nutrition science. And during our conversation, we'll explain what post biotics are, because that may be a new term for all of you.

So why don't we start with that? Help people understand the difference between probiotic symbiotic and post biotic. Right. So traditionally people know pre or probiotics or even symbiotic.

So prebiotics is the things like fiber the dietary fiber we eat in our diet. This is sort of the food that our gut bacteria, which we call as probiotics, need to to sort of utilize the energy.

And so a lot of times when we are taking antibiotics or not eating the right diet, the healthy gut bacteria go away. And so you need to replenish them.

That's the field of probiotics. Sometimes people use the word syn biotics which is combinations of pre and pro to sort of nourish an ideal gut microbiome.

Post biotics is is the area where I have worked for 15 years. I believe the gut microbiome is like a polypharmacy releasing many beneficial gut metabolites.

And so it's essentially what the probiotics do with the food, the prebiotics. And they release these nutrients that are beneficial for us, the human host.

So that's what we label as post biotics. And these can be short chain fatty acids. These can be, some of vitamins that are also made by the gut bacteria and can be gut metabolites, like earlier today.

Okay. So I don't want to talk about mitochondria. And how you're looked in a is a really potent compound for our mitochondria. So maybe we should start with what are how do mitochondria impact our health and vitality. Yes.

Great question. So mitochondria. Everybody's heard about it in their textbooks. You know they are the powerhouses of the cell. They are basically the batteries.

If I had to make an analogy, you know, everybody knows the cell phone and the battery when things are green and your cell phone, that's when your mitochondria, the batteries of our cell, are healthy.

When it becomes red and low in energy. That's kind of the aging and the sort of the impact aging as in mitochondria where they stop producing energy. And so a lot of times older adults or people in their 50s, 60, 70 start have low energy and fatigue levels.

## Mitochondria, Energy, and Aging

And so mitochondria, essentially the power grid, the sort of, you know, the batteries of our cell that keep us every time you get up from a chair or you think clearly that's mitochondrial health.

Yeah. You know, and again, for people with M. S. and autoimmune disease, the, declining energy from our mitochondria are part of what is causing that slow, progressive, gradual worsening in the absence of relapses.

Yeah, but we have this slow worsening. It's because the mitochondria can't make enough energy, enough ATP to nourish the neurons, the brain cells, the spinal cord, the cranial nerves.

And we have more fatigue, more brain fog and more anxiety, more depression. And we notice that walking is getting a little bit harder. It may be getting a little bit harder to open the jars and to, do some of the fine motor tasks of getting dressed and managing your buttons, for example.

Yeah. So now we're going to come back to this very interesting molecule. You're listening. How did you guys discover that? You know, like every big discovery in research, it took time.

It took many, many years. We started with this, you know, ideology that will bring the sort of the biotech standard of research to nutrition and discover new molecules, much like it's done in the farm, or the or the drug sector.

And so we started looking at pomegranates and berries and nuts, everything that was associated with sort of health and vitality and long life and different cultures and in a lot of studies, also a mediterranean diet, etc..

So we sourced pomegranates and berries from different, parts of the world and in for example, a pomegranate. There are 4000 bioactive compounds, and we didn't really know whether you needed all of them together or certain of them in certain concentration.

So we kind of went by literature initially we purified these polyphenol components called Elijah tannins or Punic l'agence. These are polyphenols that are kind of layer antioxidants.

And we started doing studies and what we found was and that there was a certain in models where there was more conducive to erlotinib production, which is this gut metabolite.

That's where we were seeing the beneficial effects. So we purified the the pure molecule. And we started giving this molecule to different, aging models.

And we realized that it was not really the dietary precursors, the polyphenols and the antioxidants, but was really this post biotic gut metabolite. Earlier today, we saw almost a 4,050% life extension in lower species where a lot of the early discoveries in aging and longevity are.

And then in older rodent models, we started seeing almost upwards of, 40, 50% increase in endurance. And now we can talk about the randomized trials we've done over the last ten years.

We see similar benefits in muscle in mitochondrial health. Okay. So for the listeners we're talking about lower species. I think you're talking what. Worms and flies.

Yeah.

## Discovery of Urolithin A from Pomegranates

Worms and flies is where typically all aging discoveries happen. And then they progress to a bigger species, typically, rodents and mice, rats. And then they go to, to obviously the big species, which is us humans that you need to study in placebo randomized clinical trial.

Okay. And so we've gotten around studying us big species, humans. And what are you finding there? Yeah. So we found that, the first trials actually looked at, what is the right dose?

So we looked at different doses and we, we looked at sedentary older people. These are folks in their 65, 75 age range. And they don't move around the don't eat well.

And when I went in and I, I can do a procedure called muscle biopsy. That's how a lot of muscle diseases are even identified. I can run a what we call a transcriptomic profile.

Every gene that is expressed in the muscle of all the people who cannot walk very well, that was shot down was mitochondrial gene. So we supplemented these folks with different doses.

And we found the sweet spot of your litany is around 500mg to a gram. And that's in about a month. We started seeing increase in mitochondrial expression.

There's a gene we look at called PGC one alpha, which is a master transcription. Let's say master regulator mitochondrial expression. We started seeing 20% increases in PGC one alpha.

And then in longer trials down after we have seen about a 10 to 15% increase in muscle strength, similar levels in endurance and really a blunting of inflammation, whole body inflammation.

So these are some of the trials we've done. Okay. Super exciting. So frail elderly folks we are improving their gene expression. What do we what does it show up in their life.

Did you see changes in muscle strength. Oh yeah. Yes. Sure. So I mean, typically you lose 10% muscle strength every ten years of, you know, starting in late 30s or early 40s.

And so, the muscle strength improvements were in these 67 year olds, almost like 10% over four months. So if they took it the the in a randomized, placebo controlled trial, if you had 30 older adults taking a placebo and 30 older adults taking, a gram of neural nets in a resigned without changing diet or exercise levels, a 10 to 15% improvement in muscle, lower body muscle strength.

Okay, now for the public, that's a really big deal. Muscle strength. We have more and more awareness that muscle is vitality the older we get. Maintaining muscles is just so important for for everyone.

Who's listening here? It will make the difference in. Are you able to stay home? Do you need assisted living care? Will you need nursing home care? Can you get off up off the toilet?

Can you walk, around your home? Can you walk and get your groceries? Muscle strength. So, so important. And so this really sounds like a marvelous, marvelous support for people who are old and healthy.

## Human Trials on Muscle Strength and Endurance

But even more important, for people who have a chronic neurodegenerative problem, such as multiple sclerosis or an autoimmune disease with a neurologic symptoms, we want to take care of our mitochondria, we want to take care of our muscles.

So and I'm going to be curious, have you done your lesson a plus strength training? Have you ever done that trial yet? Yes, we just published it in sports medicine actually.

And and so the trial was done not in older adults and exercise, but actually at a prominent it was a third party driven trial where a prominent sports researcher came to me a few years back and said, Anurag, I want a doctor saying, I want to test if this is going to have an effect on top of a regular exercise regimen and so these middle distance runners that we took, a cohort of middle distance runners, were training for different competitions like ten kilometer or half a marathon.

And we looked at to see if, over a period of a few months, adding your alternate a gram would have augmented benefits. And what we noticed was that even in this very fit population, we saw about a 5 to 7% increase in VO2 max, which is the volume of oxygen your body can produce.

So it's kind of a de facto measure of mitochondrial health. We saw lower inflammation in these athletes, and we saw less muscle damage. And the way we look at those markers, gold creatine kinase, which means your muscle is getting damages that train.

So yes, it can give a better, augmented effect. We have done this also in, different animal models in older, rodents. And we have seen an augmentation of both, exercise regimens and caloric restriction effects. Okay.

So a great add on because I hope hopefully everyone who's listening to this knows how important it is to include strength training in your self-care routine.

Adding in your listening can, sounds like be a reasonable way to further augment the benefit of your strength training. Yeah, and that's what the data is showing.

We still need to run this in, for example, recovering older adults from hip surgery or post rehabilitation. These are the trials we are planning to run.

But at least in both the resistance and endurance trained athletic individuals, it had an augmented effect on top, with your alternate supplementation.

And then as we get older, and it's sort of shocking this immune aging begins in our eyes. So since I'm 70, my immune system, you expect to be really quite mature in the aging process.

Does your Athena impact that immune aging? This is, I believe, a super fascinating field right now in the field of, both immunology and mitochondrial medicine.

And I call it immuno metabolism. I'm a trained immunologist. And in all the trials I was describing before on muscle strength or endurance, the underlying effect we always saw was dampening inflammation.

So when you look at something called C-reactive protein, which is a very general marker of inflammation, it would always be blunted in older adults with aging, it goes up with, being overweight, it goes up or even an athlete, it goes up because of the overtraining.

All these trials, we saw a blunting of the immune response, or the potent inflammatory response. And so we did a trial with, with a group in, in the US called the Buck Institute of Aging, where we took two cohorts of folks.

We took 55 year olds who were placebo, were given a placebo, and another cohort of 50, 55 year olds who were given, might appear earlier to supplementation.

The gram for four weeks. And we took small blood draws and using a technique called flow cytometry, which allows us to look at different immune cell populations.

What we saw was these T cells in our bodies that are called cytotoxic T cells or CD8 T cells. They kind of re re came back. So with aging what happens is a few things happen.

It's to the immune response. We lose this organ called the thymus. And so the body can really produce new T cells. So you're left with the bank of a reservoir of T cells that you have.

The second is a body is get inflamed. And third is the immune cells lose the energy to fight, things like infections or autoimmune antigens. And so we saw that the these T cells, these naive T cells came back.

## Immune Rejuvenation and Longevity Markers

We saw lower inflammation. And we saw that there was about 20% more mitochondria, the all the immune cells of the body. So these are the findings we just published in Nature Aging.

You know, again, for all of us, the aging of our immune cells is part of why we don't have so many relapses when we go look. But it's also why we have more infections, more cancer.

And, you know, that steadily increases the older we are. What I'm hearing you tell me, doctor saying is that we can

slow that aging process. So this is at least for our immune cells.

So I'm probably, going to be more effective at preventing cancers, more effective at reducing my infection risk. That's exactly. And I do believe that before all the other big organs and start declining, I do think the immune system is like the special forces that are patrolling all our organs, and they're sentinels and they are the first brick to fall in when they lose energy to survey.

That's when our immunity happens. That's when cancer rates go up, and that's when we start even getting infection. So I do believe if you can fix your immune system early on, you can actually prevent a lot of the chronic ailments that come down.

So that takes us into the longevity field. We have this radical idea that we can slow aging. And I know some scientists are now having this radical idea that we can reverse aging.

You know, clinically, I can sometimes see I help people fix their diet, exercise ways. We laugh, we call them youth, and then we can usually see visually that the person's looking younger and more vital.

What are you seeing with the longevity markers when you're testing your Letha now? Yeah. So we look at a constellation. I don't think today there's one gold standard marker to to that we can say, this is it.

So we, we see a lot of mitochondrial rejuvenation happening, so we can take blood cells and look at the amount of mitochondria and how the mitochondria are producing energy that we can measure.

Very, and we see about a 20, 25% improvement with with general cellular health. I talked about the lowering of inflammation. But what we've been using is, is these epigenetic age or DNA methylation patterns quite a bit.

And we do see a lot of these clocks like, and this may be a bit new for your audience, but there are all these aging clocks. So the the most valid one is something called Green Maid or you grandma's, we see about, you know, half to a year reduction in the biological age of the cells and in these people.

I do think longevity is not about just reversing aging, but being functionally better. And that's why we do functional readouts like, you know, making people can people a lot better.

Can they get up from a chair better and do they have better strength? And I do think we are seeing about a five, ten year age reversal in terms of that functionality in these people.

Now, again, for the audience, this is really important because while we can scientists, we can talk about our our interest in molecular markers that we see interesting genetic changes, that we see you as the person, well, you want to be able to do is get up off the toilet easily.

You were able to climb stairs easily. Yeah. You want to be able to walk through the grocery store picking up your food easily to, stand to make your meals.

And these are the things that we can lose when we become frail. And if I just heard you correctly, doctor, saying you were able to show, in addition to the interesting biological markers that that, we scientists really like to track, we're able to show the concrete task of daily life that we need to do those the things that improve.

And that is what really matters to all of us. Again, everyone who's listening, it's the task of daily life that we want to stop from going, you know, deteriorating.

And ideally we want to have, steadily improve. Exactly. So what we should be talking about, of course, is parent tradition, a strength training program.

You could ask for referral to physical therapy to evaluate your strength, your balance, and help have them help design a strength training program for you at home.

Sufficient protein, of course. And then where would your Lithuania fit into this? Improve self-care? I think it's amazing advice that you just gave it.

I see it as three pillars. I see it as as the diet and sort of watch what you eat and how much you eat kind of pillar, which is absolutely in your hands.

And the second is the physical activity levels. You know, the more you move, the more you train strength train, the more I mean, that's the best mitochondrial medicine we have, right?

A lot of times compliance becomes an issue with the first and second pillar. And that's where I see him, sort of a maintenance third pillar with really targeted nutrition.

And that's where I believe safe and clinically validated natural compounds such as your litany or even there are others like, you know, CoQ10, etc., that really fall in that third pillar bucket that can help maintain whatever benefits you're getting from the other two pillars.

Okay. Now some of our listeners might be thinking, well, I eat a lot of berries. I like pomegranates, I have pomegranate juice, or I eat pomegranates every day.

Could my bacteria make the your litany from all those berries that I'm eating? In the pomegranates? Well, if you're lucky and blessed one. Yes. For sure.

I've done studies now and looked at thousands of people around the world. The highest prevalence of, producers in that, what I call blessed people are natural producers of this molecule.

## Daily Function, Dosing, and Maintenance

They are eating a lot of fermented foods, and they're eating a lot of berries and walnuts, and they are often found in, in the Mediterranean area. So if I go to a study in Italy or France, I see 30 to 40%, healthy adults having some level of you're letting in their blood.

I have done studies in the United States and Canada. The incidence is 10%. And I think it's really how the gut microbiome has evolved. Either we are not eating the right diets.

Not everybody is eating a bowl of berries and nuts every day, or the processed foods. And the antibiotic use has got rid of the good, healthy gut bacteria.

So we see very low incidences of or prevalence of zero left in a production in, in sort of the United States or Canada or even in my home country, India is almost 5 to 10%.

But in Japan and places like Italy and France, where a lot of fermented foods are eaten, the incidences is a bit higher. And you do need to. Yes, the natural way is the right way.

If you can eat better diet and fermented foods and produce it naturally, I would encourage it. But 80% of the world's population in average doesn't produce this molecule, and so you need to supplement it.

Okay, so if I happen to be one of the blessed people who can can make my own year later, now I do I create any harm by taking supplemental cure? No, no.

So I actually have, invented a test with a with a dried blood spot. So just a little finger prick and you spot a few drops of blood, and we can tell you if you're a natural producer or not.

And irrespective of what the starting base is, whether you are or you are not a producer, we see you bring everybody to the same level. So that's what a calibrated dosing and targeted supplementation can do.

If you give juice to 100 people, only 2,030% people will make it and they'll make it in a very low to very high range. And not everybody will get a therapeutic benefit from it.

Supplementation overrides that short, you know, that very good. Yeah. No, is just something I have to take a couple times a day. Once a day, once a week, once a month, I think in the clinical trials.

And what I recommend is, take it in, in first thing in the morning, because if you're fasting overnight, autophagy or, you know, this molecule works by getting sort of this targeted autophagy in mitochondrial might haffajee, it works the best first thing in the morning.

And the best day you're seeing is at least couple of months. And so taking it at least for 2 to 4 months is is needed to sort of recycle the damaged mitochondria out into healthier ones and get that functional benefit that I was talking about.

And is something then that you take for 4 to 5 months and then you're done, like, okay, I've renewed my mitochondria now, I don't I don't need to keep it up.

Or is this something that is better to just maintained? So the longest trials, Doctor Wells we've done is four months. So you're doing the six month, a year long trial and then seeing also what happens when people moving off the product.

I do know the biology very well. And it's the same pathways in mitochondria that exercise stimulates. And so it's like exercise. If you train for something for four months, you will probably have the benefits for for another couple of months.

But then it's, you know, kind of lose your endurance capacities. I do think you mitochondria need to be harnessed and revamped every now and then. So even at least give it 2 to 4 months, then see if the benefits preserve.

If not you can go to a lower dose or you can bring it back in. So I'm a little confused here. I want to be sure I've got this. Yep. I want to be sure that you're doing it for months.

For sure. Yes. And then you could evaluate. Do I continue indefinitely? Part of me thinks, you know, if I, if I stop my strength training, I know that my muscles will begin to atrophy if I'm not doing my regular endurance training, my cardiac output, in stamina will decline.

Decline. So I'm thinking, well, maybe I need a benefit from a higher dose at first four months. I wonder if long term. Because I want to have healthy, vigorous mitochondria forever.

That did there should just keep this going or perhaps modestly reduce my dose and keep. So that's what I was suggesting.

## Future Research and Where to Learn More

Go in a gram for a four months, see the benefits, and then you can go to a maintenance dose of 500 milligram. And the reason I don't want to fully commit to lifelong being on the supplement is a I'm an evidence based person.

So we are still running the one year long trials, etc.. I know I have solid multiple trial date up to four months and then I can stake my reputation on that.

So you know, that's what I recommend. But that's the example. You nailed it beautifully that you know you will lose the benefits if you stop exercising.

And that's what I think will happen with this. Yeah. The size is really important. We know if you stop exercising, your muscles will deteriorate, your endurance will deteriorate.

And so I'm thinking, at least for me, I've been taking your lesson today. I prefer to continue on this, lower, more modest dose because my goal is to thrive to 120.

You know, I need good, healthy, vigorous by 200 to achieve that goal. Awesome. Now, what's next? The upcoming research for your lips. And, so two streams of research we are very excited about.

One is taking the immune findings we have to the next level. So we are going after older adults 70 plus. We we are going to try and replicate the findings that we saw with the sort of the immune rejuvenation in the 50 year olds.

Can we replicate that with the €70? And the little difference in that study? We are about to start is we're going to actually do like a pneumococcal vaccine, challenge to see if older adults, give a better immune response to that, that pneumococcal vaccine response.

So that's one trial we're doing another trial in cancer patients who are on Keytruda, which is an immune checkpoint drug, which basically works for a while.

And then then the immune cells fatigue out. And so we want to see if by fixing the mitochondria, you can deliver a sort of a two pronged punch with with the erlotinib supplementation.

We are also looking at brain. Does this molecule get in the brain and have, big effects on the brain. So these are some of the new, we are doing. Well, that is super exciting.

I look forward to hearing the results of those studies. That will be very exciting and hopefully we'll be back next year to hear the progress you're making.

Absolutely. Thanks for having me, doctor. Well, now, where do people find your your alternate product. Yeah. So they can go on the, on the website called www.timeline.com.

They'll see all kinds of products. We just don't have pills. We have gummies, we have, powders and whatever fits with people's lifestyle. And if they want to learn more about the science they can go to w w w dot Meitu pure.com, which is all in one resource on Europe Latin science.

Okay so timeline.com and mightypure.com. Perfect. Thank you so much. This has been a wonderful conversation. Amazing. Thank you for having me doctor Wells.