Introduction to Tom Dal and His Research Background

I have a speech today on the Telomere Summit. Doctor Tom Dal, who is, medical and surgical ophthalmologist and practiced for over 40 years in clinical epidemiology.

He maintains a clinical appointment at the University of Wisconsin, Madison and is a member of its I. Its McPherson Research Institute. He has also worked as a physician scientist conducting clinical trials.

Since 2000, he has had a research interest in the role of infection, specifically Mycobacterium tuberculosis or Map, in a broad range of human inflammatory diseases.

Also, he has studied clinical applications arising from telomere biology and telomerase is work testing an oral telomerase activator in age macular for age related macular degeneration has led to interest by the National Institute.

Welcome, Tom, to the, Telomere Summit. And, I'm really excited to speak to you. I remember when your study came out in 2016. We had a brief conversation in Las Vegas about it, but I've got, all sorts of questions, and I'm looking forward to this conversation.

Great. Well, thank you. I'm pleased to be here with you, Joe. So how does not the mouse become interested in such diverse things as, infectious disease and telomeres?

Certainly. On the surface, it would seem, incongruous. I have a background in microbiology, however, and, certainly the, the, infectious trigger for a number of autoimmune diseases is a bit in my wheelhouse.

The beauty of ophthalmology, at least as I practice it, was caring for, people primarily with age related problems. I was a cataract and coma surgeon, but that doesn't mean I didn't see every sort of, age related disorder.

Even before, the individuals, received the Nobel Prize for, telomere. Telomerase, identification. I had an interest in that. And, certainly, as it relates to, macular degeneration, a number of the early studies were done with, retinal pigment epithelium and, and, telomere attrition, you know, in, that cell culture.

So that's been a, a starting point here for my interest in, you know, telomeres and telomerase. Yeah. I was in preparing for this and the reading for the, a lot around the literature bit.

I was, I learned I didn't know before that the, rpe, the retinal pigment epithelium is the most highly, metabolic, metabolically active tissue in the body.

And so that starts as a stress right there. Lots of oxidative stress, telomere attrition, etc.. So, yeah, it seems like it's a pretty interesting model for what's going on in the, in, in aging and in the retina.

The, the pigment epithelium has an enormous job to do. There's 150 million photo receptors. And, the, molecular biology of vision, is such where these, photoreceptors shed their outer segment and as part of vision.

And, the pigment epithelium then has a job to do, and that's to consume and recycle, these leftovers of vision. And, so each, each retinal pigment epithelial cell may have to ingest and recycle 60,000 older segments, a day, for homeostasis.

Why Telomeres and Macular Degeneration Became a Focus

So, with, the amount of energy that comes into the central retina, the macula area, there's, lots of light energy and,

lots of oxidative stress. So, so these cells, have, big job to do and, not unlike, the cells of the rest of us.

They can run out of gas a bit as we get older. Yeah. I mean, the eye is not really a specialized area, but I was struck, by another paper that I was looking at where they.

It's really a kind of another validation of the hallmarks of aging, where you have, you know, oxidative stress, mitochondrial dysfunction and then you have ultra protein status.

The, you know, the if they stop doing their job to be able to clean up the, the, you know, the, the debris, which I guess ends up being Druse and, they, you know, they get this same thing as sort of amyloid being deposited in the brain.

And senescence is, is all part of that. And of course, telomeres are, you know, major regulators of senescence, both through replicative senescence, but also through the, oxidative stress causing shortening the telomeres.

And and so, I guess, you know, that would I guess that sort of was the lead up to what made you decide to, to do this study that you ended up with the 2016 paper went to tell us a little bit about that.

Yeah. So, understanding, that, the early changes of macular degeneration are a result of the, in effect of taking out the garbage function, if you will, of the retinal pigment epithelium.

So understanding that, we thought, well, let's, let's look at, basically function macular function and see if people who have the early changes, because actually do come in and sit in the chair and have your vision, checked is not a very good, not very representative of, of the state of your, macula early on.

You can have normal vision and, and still have a mild team and moderate changes. And so, so we thought, well, let's let's identify people who have, the early changes, the Drews and again, these are these deposits that are left over because, the inability to consume, these leftover products.

And so these deposits are the first sign and, of, of early macular degeneration. Macular degeneration is, aggregated into early, intermediate and late.

And, most people will know today individuals having shots in their eye, for late macular degeneration and, another, descriptive way of speaking of macular degeneration is dry or wet.

If there as part of the problem, a, abnormal blood vessel growing and leaking from under the retina, that's a wet degeneration. The shots actually make those blood vessels shrink away and actually can have a, fairly good, result.

Yeah, it needs repeated shots. Unfortunately. But it can have a, relatively good result in what historically was a terrible situation. So, so, most people, however, don't get to that.

Most people just have the early and moderate changes. It can have some distortion or blurring, but it's a, it's a progressive disease as it rarely stays that the early it, progresses with time.

And so, even though there was the, vitamins you'll see on, television advertised for antioxidant vitamins, primarily, and they're all the same formulation that came from the, age related eye disease study number two, the era two formula.

And those products are and preserve vision eye caps and, ocuvite all the same formulation. And those actually were used and that showed in an enormous, study, that it, slowed down the progression from, from early to intermediate macular degeneration.

So enormous numbers of people are taking these as well. They should we looked at, again, a different approach for this. And that is the, turning back the clock, if you will, about, the, pigment epithelium to see if they can perform

the function better and that be, revealed, then the improve function, for the macula.

Yeah. So, that would be rather than just slow it down, actually, you know, hitting the process of senescence within the cell by turning on telomerase.

So why did you describe what the study was and, who the patients were and what the outcome was? Yeah. So in our study, it was a relatively small study.

We had less than 40 people. It was double blinded. It was, randomized and, to be eligible for the study, people had to have one or both eyes with, early macular degeneration reflected as drusy.

We had a few people who, the second I had, wet macular degeneration, so, but but they, as you might imagine, were quite interested in being in the study with, fellow II having early macular degeneration.

So, so for those people, they were randomized. They had a, an A or B arm and, and so, we, we, introduced the participants to a, a functional test and it's, it's called the Myo machine macular integrity assessment.

And most physicians, very familiar with, perimeter, visual field testing.

The 2016 Macular Degeneration Telomerase Study

And this is, perimeter of just the center, ten degrees. So just the macular area. So 61 spots are tested, and, and the beauty of the instrument itself is that when you've had one test, it registers your retina.

So you come back and the place that tested number six or whatever, that's always going to be that spot. Okay. And this, this instrument makes adjustments 25 times a second.

So as you move your eye, the machines right with you. So, so anyhow, it's a, it's a it's a beautiful instrument for our purposes. So, what we did is we tested the, threshold, sensitivity and these 61 locations.

And, and this is after the patients had, had two, preliminary tests with the machine to to be introduced to the instrument. And so at, the we had at the start of the, before starting the, study products and then at six months and then again for the year.

And so, at six months, we were pretty sure we knew and pretty excited about knowing, that one of the arms seemed to be getting better. And, compared to the other arm and, and indeed, the year, that, the difference between the two, held and and the, the, the, product that turned out to be the placebo product, that, arm of the study actually got slightly worse.

So the spread widened just a little bit at a year. And so, we did have, we reported one, adverse effect. And it turned out a person had temporal arteritis, had an optic neuritis from that.

Happily, it was in her it she was, one of the individuals with only one eye in the study and the eye that previously had had a wet degeneration. This was the eye that had the problem.

And at the end of the study, when we were unmasked, we realized that person was in the placebo group. So. So, really, we reported them? No, adverse reactions.

So that, in a nutshell, was our study and that, I saw many of the people over the, a few years afterwards and, and people who, typically we would look in and see, confluent Druse on this would be, not just a few Drazen, but lots of Druse and and, in our mind, we would say the natural history of this is not good.

Okay. And for a person to come in and first of all, again, as I mentioned, that's occasionally you can have remarkably good measured vision on a chart, but still have this potential problem.

And so one of the individuals, have 20, 25 vision, good vision, confluent Druse and and amazingly, several years later, still 2025 vision and a similar, micro perimeter, to the end of the study.

So, so, I know that's incidental, really not related to the, the study itself, but, it's a supportive for sure. And I'm anxious for the National Institute to do, the large study.

Yeah. So you mentioned, when we were talking before that there when I remember hearing that there was a lot of interest, the company sciences was approached, to use to 65, you know, a larger study to, to see if this could be replicated in, you know, in the larger study.

But I guess that got, derailed, through what we were talking about earlier. Yes. The, the individual who, is the author for the, all the, Irish Eye related, age related eye disease study, the Aarons, studies.

Emily Chu, she assigned an individual to do the large study. That would basically, carry forward of what we had done. And unfortunately, the individual had a heart attack and died.

And so as far as I know, that's still on the back burner. So I'm hoping they, and and, you know, there's a reason I'm hopeful they do it. And that is, there's there is no other treatment, you know, and, you know, you can feel comfortable that you're taking the, antioxidant vitamins, but, certainly, there's no opportunity, that, to actually have an improvement.

So, you know, so it was, 265, twice a day, just for our listeners. The dosing was 250 twice a day or two. That's exactly right. 252 once a day. And, I guess I always think about aging as being, you know, a very slow process, and it seems like macular degeneration.

Oh, that's a good question. What percentage of people end up getting macular degeneration if they don't sort of die of something else? Is it is it sort of like an end stage of of. Hi.

It's just somebody of, aging or and somebody dies or something else before it gets really bad. Or is it more, specific subsets are there, you know. Well, is certainly this is a population related, story.

In America, we live a little longer or, we, perhaps it's our Western diet and this sort of thing. Course, it predisposes a bit to this. There is a genetic component as well for this, but for the most part, you know, as far as, severe vision loss, it's one of the primary causes in the Western world.

And as far as, you know, just the plain incidence is fairly high. The good thing, as many people, go along merrily, for years and sometimes decades, with normal recorded vision and maybe normal subjective vision as well, until things, you know, progress.

So, I guess the reason I, one of the reasons I, as I lecture a lot about 65 and its effects and measure telomere length. And so when a lot of doctors come up to me and, you know, tell me about their experiences with it, and I can talk about this in my own experience as well with my patients, is they're saying that some patients are reporting improvements in their vision.

And these are people without at least without known macular degeneration. Is there an aging of the retina phenomenon that takes place prior to macular degeneration?

That might be the, the sort of the same mechanism might be causing this improvement in vision because it's apparently it is, you know, not presbyopia, although that's also been reported.

But the myopia that they're seeing some improvement in, in their prescriptions for that or just some also, they talk about sort of just better sort of color vision and, and things.

I wonder if you, you know, whether that could be from improvements in, telomerase activation or telomere length. Yeah, it would be speculative for me to say about everything except, presbyopia and that we did try, the, double

blind, placebo controlled group for presbyopia, 1 to 65 as well.

And we didn't I, I had heard the, you know, the individual, testimonials, about that. But, you know, we didn't show an improvement in, in Presby, you know, over it was in you were looking at these same individuals or you did another.

No, no, no, these this would be normal, healthy, people who need reading glasses. So you did that and you didn't. You didn't publish or you did publish it.

We did not publish it. Right. And how were they? These would be people, from 50 to 70 years old. Okay.

Eye Health, Aging, and Practical Ophthalmology Advice

And, but, yeah, it's funny because I have, one patient, actually two patients that showed pre and post documented eye exams with some, improvement. It wasn't massive, but a pretty significant reduction in their prescription, after being on to 65, you know, who knows what else cleaned up their diets?

I don't know, because, you know, those sorts of things that people do is not super controlled. Trial. But it's, again, it's sort of one of those, I like to think about all the organ systems of having a program of aging that's pre-clinical. So, certainly I believe that as well.

And, I guess within the I that's the speculation that it's, not just replicative senescence, but potentially that it's, about protecting from oxidative stress, these sort of non-canonical actions of, tert, the telomerase, reverse transcriptase, turning on the mitochondria and increasing mitochondria biogenesis and, and efficiency.

I, you do have you have you have any thoughts about that? Well, I think the, the autophagy, component, is, I think central, to, to helping us, stave off some of the age related diseases and anything that will boost, autophagy, I think is, is good for us in general.

The the sake of synthetic activity of retinol. We have psyllium, I think is central to the, to the eye, age related eye disease and, yeah. So to speak, with at least some sense of, authority on that.

I'll kind of stick with that, I guess. Okay. Yeah. Well, I mean, and then just as an ophthalmologist and, you know, for our listeners guiding their, their, their patients, what are sort of the top five things you do you recommend to your patients to maintain good eye health?

You know, you hear all sorts of things about you should do this, you should do that. You shouldn't do this. You shouldn't do that. Sunglasses. No sunglasses kind of thing.

You know, you know, it was, quite a few decades ago that the ultraviolet spectrum of light, was recognized to, over over periods of long period of time caused damage to the retinas.

So, so every bit of eyewear today, would have the, UV protection in your eye, in your eyeglasses. I don't think you can buy a pair of glasses that doesn't have you be protection.

And for individuals like myself who's had cataract surgery, all the implants I know, the cataract comes out and the new lens goes in. All the implants have a UVA filter as well.

That's interesting. Yeah, yeah. So, so that's, you know, UV protection. I see, some of the sports now, in the Olympics. And, occasionally I see somebody who probably should be wearing eye protection in their sport and isn't, it, disturbs me just a little.

The volleyball's too big for their car, so I'm not worried about the volleyball. But, you know, the, Mediterranean diet, the mind diet, all these things are good for, system wide, for sure.

The, You know, there a lot of people, you know, I think that there's this or that reason for, inducing cataract, cataracts, age related problem and, certainly there's some light, Capacity to make that progress a bit.

But on the other hand, if you're going to get a cataract, you're going to get cataract. And, and, and that's it. So, so, is as far as the, the other thing some people would say, why shouldn't grandma shouldn't read so much. She's got the eye disease.

She's got these aging changes. She shouldn't read so much. That's a falsehood, of course. And, there's no amount of using your eyes that's going to make the eyes worse.

So, I think even the macular degeneration patients, I encourage them, even if they need magnification to read, I always go, yeah, good. Yeah. So that's that's that's definitely, good advice.

You, also have interested in infectious diseases. And what do you tell me a little bit about, about that. And, yeah. So. Yeah. So, so I had a patient some years ago again, as an ophthalmologist, you see quite a range of things.

And this person had an inflammatory process in her eye. And that's quite characteristic of sarcoidosis. So that's the new great masquerade or sarcoidosis.

And, and so I sent her out for a chest X-ray and told her that don't get too excited if they get excited about your chest x ray. And sure enough, she had a mask and, and she had a, biopsy of the mass.

And so from my microbiology days, I recall that there were two diseases associated with a certain bacterium, a cousin of tuberculosis, Mycobacterium avium subspecies, para tuberculosis or a map.

And so I got Ahold of some of the tissue, and I sent it to a lab that specializes in a map. And sure enough, she had a positive, biopsy and that kind of and that was in 2001 and that kind of set my, motors running, right.

The National Institute came out with, PubMed, and the internet was, available. You could, you know, search the internet, PubMed and learn a lot. And so, as it turned out, I found that there are a number of, genetic susceptibilities for certain diseases.

But that same genetic susceptibility was shared for risk of mycobacterial disease. And so that put me on, to a number of, diseases that might be triggered by this disease, by this bacterium map.

And so if there is a granuloma as part of the disease. So that would be Crohn's sarcoid this unusual disease called Blau syndrome. Then I would think that this bugs in the granuloma and sure enough, both my sarcoid and my, blouse syndrome tissues that I use the internet to request tissues from, articles where there was tissue was part of the pathologic diagnosis.

I said, well, based on these genetic reasons, I think that this bug is in that tissue. And so I got tissues from around the world, and, and blood syndromes, rare, sometimes called juvenile sarcoidosis.

And it shares a genetic risk factor with Crohn's disease. So I said, well, Crohn's sarcoid I had to think that this bug syndrome. And so, so we had, tissues, granulomas from liver, kidney, these, show up in children, the, arthritis, you get uveitis inflammatory problem in the eye as well.

And so we had, we had these granulomas.

Mycobacterium avium paratuberculosis and Inflammatory Disease

We had skin and we had, articular, biopsies. And every tissue was positive for the DNA of this bug. And so, so that really let my fear. And I've been kind of following along, this, ever since, this bug, when it's, sits within us, it makes a protective protein.

Those heat check proteins, 65, and it makes it in abundance. And, as it turns out, that that heat check protein looks like some of our own proteins. And, the most interesting one is glutamic acid.

Carboxylic acid. So if you have a, child with type one diabetes and now you have a second child, you'd go to the doctor and you say, well, is this child going to get type one diabetes too?

And the doctor will do some blood test and he serially will be looking for antibodies against glutamic acid. The carboxyl is the pancreatic enzyme. So the thought was that we had a saw this molecular mimicry.

So this bugs in protein 65 and our own glutamic acid the carboxylate the the insulin producing cells of the pancreas become, collateral damage to the inflammation that comes from this.

And so, we we wrote an article. Could this be the trigger of type one diabetes? And now there's been 21 articles following up showing that this is involved with type one diabetes.

So not type two type one. So you're now. Yeah. That is just another one of those fascinating stories where it's an infectious agent that's triggering a disease like H.

Pylori and and gastric gall. That's, that's the classic. Right. Classic. Yeah. I think my is taking a little swig of his, of, of his H. Pylori. So, what, I know, I know you also have an interest in, in Alzheimer's disease.

And, I mean, you were talking about, a mycobacterium, but also you've looked at this, BCG vaccination against tuberculosis. That is. Yeah. So this. Yeah, this is my current, clinical trial.

And this stemmed from actually my circle of, mycobacterial friends. And so, I have, mycobacterial professor in Israel who, when, when he and colleagues were kind of wondering, well, why does it seem that, diabetes.

I'm sorry that Alzheimer's is so much more common in the Western world compared to the non-Western world. Even when we adjust for confounding things, longevity, wealth and this sort of thing.

And so they they did a deep dive into populations and basically found an inverse relation between the population getting the vaccine for tuberculosis, BCG and incidence of Alzheimer's disease.

And then they said, well, we have a natural group that we can test that in and that, that, revolves around the standard of care for bladder cancer of all things.

Now we're really broadening our, our clinical work. But anyhow, the if a person has a bladder cancer and the bladder cancer doesn't, go through into the muscle of the bladder wall, the standard of care is to exercise the cancer and infuse the bladder with this BCG vaccine for tuberculosis.

But why would you do that? The risk of recurrence drops significantly. So this is now the standard of care. So they said well let's look at people who had and they have good medical records in Israel.

Let's look at people who had bladder cancer, got BCG bladder cancer, didn't get BCG. And the average age that they got the BCG was 68. And 15 years later fourfold less risk of Alzheimer's disease.

And the people who got BCG. And again when when the when the world health are BCG is you know than 4 billion doses given 140 million doses every year to infants.

We never gave it in America when the World Health Organization said, yes, the world should do this. America, Italy and the Netherlands didn't adopt. Over the last few decades, most of the Western Europe has has discontinued okay, using BCG.

And so, you know, India, China, South America, that's routine. This is what you have, you know, so there was a discontinuation, was it just anti-vax type stuff or, or, yeah.

The in America, we didn't think at that at that point that, that, that it was as big an issue as it was around the world. We thought we could, contact, trace, isolate and had the sanatoriums and that sort of thing.

So, that's why they didn't give the BCG. So anyhow, there is this thought that, maybe the BCG induces these nonspecific effects and, and this would what the, the simplest way to say there's, there's an immune reset when you get this BCG in somehow maybe that throws up things that, needed revving up and maybe the, autophagy, declines.

That's part and parcel of Alzheimer's disease. Maybe the, the immune boost would improve that too. And so that's a clinical trial we're doing right now.

There's a new, blood based, biomarker for Alzheimer's, a, plasma amyloid test. And, this plasma amyloid test correlates very strongly with a Pet scan for amyloid.

And when we started the trial a year ago, it, it was a investigational tool, this blood test. Now, the government has basically approved it. CMS hasn't approved it.

So, you can get the test, but your insurance won't pay for it yet. At any rate, this this test is, pretty, pretty good indicator of either if you have a high, a risk probability score with this test, that the chances are then that you would have a positive Pet scan or that you will develop one within four years.

Okay. So it's a really a powerful tool. So I'm quite interested in, giving a try to, to 65 and with this blood test as a, as a marker and, just in a local publication by an Alzheimer's group, I put out a call for people who are ApoE4.

Positive. And that would be one of the genetic risk factors for late onset Alzheimer's. If you have one of the AP fours, your Alzheimer's risk is increased 2 to 3 times.

If you're carrying both of them, which is only 1% of the population over ten times the risk.

BCG, Alzheimer's, and New Biomarker-Based Trials

And so so those people we would understand would come understanding that they have some risk because a number of people get the 23 to me and they do the medical module and they find out, well, yeah, you have this increased risk of Alzheimer's.

And so those are the people I'd love to, do the trial on, with a 260. I to try going to 23 and me and see if, they would, potentially advertise that. I mean, they sort of they do things like that for genealogy and other things that and so, so I'm kind of a semi-retired old guy here in northern Wisconsin.

And so, I, I have to realize anything I do is going to be considered a pilot study, and I'm very happy with that, because I'd like to move on to the next pilot study.

And, so, what just other community, ask I think I can get, you know, a, an appropriate number of people. And of course, if I could collaborate with an individual like yourself, Who knows?

Well, we'll get to all the patients, you know? I mean, I would love to. I was looking at my database, and I have a fair number of, epilepsy for, And I know I've done more tests, so I just have to locate those individuals.

I'm going to look at those. But, you know, it strikes me that you're really this kind of a Renaissance ophthalmologist that goes all over the place and follows, follows these.

I mean, if the if the, the National Institute picks up this 65, telomerase activation in macular degeneration, it turns out to be a big thing. You know, you and I should mention Carl Harley, who is one of the fathers of tumor biology in this country, with your coauthor on that paper, may have, you know, done something incredible to to help, you know, preserve the eyes of our aging or our aging population and then also in Alzheimer's, potentially, you know,

another sort of, I consider a very, expert, person in, in telling me biology.

Michael Fossil has, you know, Michael, he's he's, he's basically created a company called Telos AI to look at this hypothesis that telomerase, decrease in telomerase, an increase in senescent cells.

The, you know, the glial cells that support the neurons is the problem. And, you know, Alzheimer's is not actually in the neurons themselves. And and, you know, that goes along with the whole autophagy, concept and, and how this is this may well be the way to approach it in a totally different way from going directly that bad.

And it's still a good marker that it's going on, good biomarker that's going on. But but not the top level, you know, passive physiology. So what what just for the listeners, what's a what's the name of the blood test that, that you get the it's the the commercialized blood test?

No, it's called passivity. De de procedure de civet y ad passivity ad. The company is C to M. That's the letter C, number two, letter M diagnostics. It's in.

It grew out of Washu and Saint Louis. And they look at the the blood test that they also then have an algorithm that has other clinical, things that sort of give a rest.

They look at the plasma amyloid, they, they, they can do, protein nomics on the blood test, too, so they can get your AP status and they look at the age and the, the by far the greatest way that thing of those three is the plasma amyloid.

But they way also the AP for status and then your age and then they come up with this amyloid probability score. And that's the passivity. And that's amyloid prevalent in the brain.

But not call sign messages as a clinical diagnosis. And knowing well that therein lies the rub. And that is if you wait until you got MCI or or Alzheimer's, it's too late to try these things.

And I think the the goal is to identify people at risk 20 years prior, to them having some cognitive issues. And. Yeah, well, it's like coronary calcium score in, in for cancer if you've got a lot of calcium, you know, or if you once you have a positive stress test, the horse is out of the bar and then you're going to get a stent bypass 20 years earlier.

You're accumulating calcium just as I suppose you're accumulating Drew's in, or you're accumulating amyloid in the brain, and you want to pick up those signals and start to treat, before you have to, to, you know, a full blown disease.

So, yeah, I mean, that's that is really fascinating work you're doing. You're you're going from one pilot to the next. I like that. Just got the idea.

And then, you know that the other people take take it away with it. Really? I didn't know you had this many interests when, when they they built the building for me.

Is that, you, as a cardiac surgeon, just have this wonderful experience working with one person at a time, you know? And it's just the best. But I got to say that the, these broad, diseases, macular degeneration, Alzheimer's and the thought of doing something with a broad sweep is just intoxicating.

And it, it drives me every day. Yes, absolutely. So, is there anything that you would like to say in closing? It's been a fascinating conversation with you.

About, your next project or, Well, yeah. It's I don't think we have enough time for that, but, I, I did see the, to 65 and, an immune profile, study that you were one of the authors, and, I think this all, immuno senescence, the inflammation thing, these, these terms.

Now, there are, you know, our age related inflammation and aging relating, running out of gas, if you will, of our immune system. I think they play an enormous part in, age related disease.

Closing Thoughts on Immunosenescence and Telomerase

And, and to to see that, telomerase activation, can, can help reset some of that, I think just, really is exciting work and, applaud you for that. Yeah. I think that's a great closing thought.

And I would I would add that, you know, the the beauty of that as, as Michael Fossil would say, that sort of upstream cause is that you could be looking to treat Alzheimer's, or you could be looking to treat, you know, macular degeneration with the but it's still going to turn on telomerase in other tissues.

There's a trial going on right now looking at, immuno senescence, and its role in secondary misses, and seeing if we can reduce the senescent T cells.

And people have had an MRI within six months of starting to 65. And see if, we reduce the immune senescence, which we did show in the trial already. But if that has an effect potentially also on, repeat events, and which, you know, that's a going to be collateral, not damage, but collateral benefit, you know, everywhere in the body.

And that's what the killer biology and, it's been great to hear about your work in the. I had this other stuff, the the mycobacterium, the BCG, keep that brain cranking and turning out these good ideas.

I really appreciate you talking to us. Yeah. Thanks so much. No, I appreciate.