Bill Andrewsu2019 Background and Telomere Origins

For many of you interested in telomere biology, doctor Bill Andrews needs no introduction. His vast knowledge of telomere biology requires that I interview him in two parts.

He is the founder and CEO of Sierra Sciences, a company focused on finding ways to extend human lifespan and healthspan through telomere maintenance. As a scientist, athlete and executive, Bill continually pushes the envelope and challenges convention.

He has been featured in Popular Science, The Today Show, and numerous documentaries on the topic of life extension, including most recently, the movie The Immortal Lists.

Bill has been a medical researcher in biotech since 1981, focusing on cancer, heart disease, and inflammation research. Though his passion has always been aging, in the early to mid 1990s, while at Daron Corporation, Bill led the research to discover both the RNA and protein components of the human enzyme called telomerase.

Bill earned his PhD in molecular and Population Genetics at the University of Georgia in 1981. He then served as Senior Scientist at Almost Corporation and Codon Corporation, Director of Molecular Biology at Burlesque Sciences and at Geron Corporation, and Director of Technology Development at EOS Biosciences before starting Sierra Sciences in 1999, where he now serves as president and CEO as well as Chief Scientific Officer.

Bill is also a named inventor on over 50 U. S. issued patents on telomerase, and author of numerous scientific research studies published in peer reviewed scientific journals.

Bill is also an avid ultramarathon runner. He regularly competes in 50 and 100 plus mile races, often finishing at the top of his age group. He considers endurance exercise, when done properly, to be a way to significantly slow down the aging process.

Bill's obsession is to cure aging, and that includes his own aging. His regimen to slow down his own aging and declining health is unique and based on years of his own research.

Well, Bill, it is fantastic to have you on the Telomere Summit. I've been waiting to interview you because, of course, talking about telomere biology without talking to Bill Andrews is, you know, there's just that's not something you can do.

So you've been in the field for decades, and I'd love to have you start by just giving the audience a little bit of perspective about that. You know, you kind of uniquely have on where, you know, why you got interested in your biology, what you've been doing with it, and where a little bit you think things are going in the future.

Well, I got I mean, I've been in telomere biology for 40 years, I guess I started in 1992. So yeah, for almost 40 years, in 39 years, 40, and mostly I got into telomere biology because of previous, thoughts on on what aging is and stuff like that.

And I kind of I kind of like, always thought aging had to do something to do with the Hayflick Limit. Leonard Hayflick has shown that, our cells can only divide a certain number of times, and then they stop.

And before I knew about the Hayflick limit. Used to always bother me that, you know, we're made up of cells. And, when cells get old and unhealthy, why isn't that?

Other cells don't divide and replace those cells. Just like bacteria in a petri dish. If if some bacteria get sick or unhealthy or something like that, they just disappear because the healthy bacteria, alcohol.

Oh, that might happen to us in our younger years, but why doesn't that happen to us when we get older? And so that was always a bother. Me. I mean, I'm not talking about right now, but the cells that don't divide like our nerve cells, but those are also like they have cells that take care of them.

I call them caregiver cells. Like, like, glial cells and Schwann cells that take care of the neurons. Those do divide. Okay. So so the division is still involved even in the non mitotic cells.

But why why is it that we don't we, we know that our cells are dividing. Why is it that they get old. There had to be something going on because a bacterial culture doesn't get old.

Why do human cells. So then. Then I learned about the Hayflick limit. And, I learned, I guess he, Leonard Hayflick learned about it in 1961, but I didn't hear about it until I would say, early mid 1970s.

And at that point, and actually, actually so it was early 1970s, because I know that when I started applying to graduate schools and stuff, I started saying that I want to go someplace that's looking at what's causing the Hayflick Limit.

So, because I kind of felt that had something to do with aging. And so what would cause something so specific to happen? There had to be something like almost a program in our cells that told ourselves to stop dividing.

I, I kept coming up with the analogy. It was like ride tickets at an amusement park. Okay. Every time our cells divide, you know, you lose a ticket and you only have a certain number of tickets.

So I'm. I'm just struggling with this. Year after year, I'm talking to people like doctor Mike Rose, and, so the so the our vote for Harvey Arbor, about starting companies and stuff like that back in the late 80s, early 90s about focusing on trying to find out what's causing this, Hayflick limit.

And then just one day, I'm sitting in a conference in Lake Tahoe, and I. And, guy named Calvin Harley is getting up on stage to talk about telomeres, and I had no idea I knew what telomeres were because of my background in biology, so like that.

But I had no idea that he was going to say what he did. And that's what he said, that telomeres shorten as you get older and that you can actually measure the length of a telomere and you can tell how old a person is.

And more importantly, you can guess how long it be before they die of old age. I'm I'm jumping up and down in my seat because I thought I got these. These could be those right tickets right.

The only thing that ever came that I ever heard of that could be they tried to fix everything else. Every theory about aging did not have the two and 2 or 2 is all adding up to something that made sense about aging.

So it's telomere stuff. So fantastic. And as soon as Kelvin got done, I was at the bottom of the podium as he was coming down the stairs before he even got off the stage.

Just saying, I want to work with you. You know, I want to get involved in this. And I, I literally jumped ship. I was working with a company called Birla Sciences and I used to call myself a lifer.

I was never going to leave that company. I loved it so much. But all of a sudden here I am getting ready to go work with Calvin Harley. And so it was literally three months later that I was actually working with Calvin at Geron Corporation as the director of molecular biology.

That was I think 1992 might have been 1993, but, that's when my career in fuel and biology occurred, and I just became obsessed with it because suddenly I found these ride tickets.

And so I wanted. And the way to show that the right tickets were causing the aging was to figure out a way to to add more ride tickets back and see if they they gave you more rides or more celebrations.

So I became just obsessed with that. I literally, Geron Corporation had to build a separate bringing a trailer with beds, so that I could sleep there because I was working there around the clock. Wow.

But, you know, and there were other people working on trying to discover the enzyme telomerase at the time. And, you know, suddenly I found myself working with them, collaborating with them and stuff, but I felt like everybody was making too many assumptions and going the wrong way.

So I, I started a whole program at Geron Corporation. Geron. But three quarters of the employees all working for me. So we started a program to, to start working on some other approaches that I thought made more sense.

And lo and behold, three months later, we were able to discover the RNA component of, of human telomerase, which didn't have any similarity at all to the previous one that had been discovered in or hymen.

And that was one of the mistakes that other people were making is they were expecting it to be similar. And so they thought they could identify the human one by sequence identity to the.

Yeah, but it wasn't so. So we ended up discovering it through, probably one of the toughest research projects I've ever been involved in, of brute force.

But we ended up stirring it, and then people still wouldn't believe we discovered it. And to prove that we had discovered it, we mutated the sequence in the RNA component so that instead of encoding the normal tags to get together these, we had it.

We mutated it so it now could produce t gtgt or DTG again. And so we made these things and put them in, put these RNA components in the cells. And then isolate the telomeres and sequence them.

And lo and behold they were the sequence we wanted them to be. So that proved that we had discovered the RNA component of telomerase. And then that shortly thereafter led us to the discovery of the protein component of telomerase.

And very first thing we did was, okay, let's see if this abolishes the Hayflick limit. And lo and behold, it did. Now, at the same time, we we did an experiment where we took the antisense of telomerase and put it into cancer cells, and we showed that it killed our cancer cell.

Discovering Telomerase and the Cancer vs. Aging Split

So it was almost in the exact same week that we'd come up with a potential cure for cancer and potential cure for aging. At the same time. Wow. That was that was exciting, but heady times.

The frustrate, the frustrating part of it was that all biotech companies are business first, science second. Right. And so there was a big meeting I had at all.

The investors came to a big meeting. We had a big board meeting for two and investors, I, I gave a presentation. I've discussed those things and I'll never forget the, the head of the scientific, head of the board of directors and chairman of the board, said, well, we can't do both.

We've got a cure for a cure for cancer. We can't do both. We have to pick one. Which one gives the quickest return on investment? Obviously. Well, even though Geron was short for gerontology aging, they chose to go for the cancer.

Now, I had previously had many discussions with Calvin, Harley and others saying because because of my background in cancer was, you know, I'd already been awarded the second place for National Inventor of the year for my cancer research.

I had been involved in a lot of cancer research prior to going to Geron Corporation, so I knew a lot about cancer,

and I was saying that inhibiting telomerase, an antisense, isn't going to cure cancer.

It's going to make it go away that it's going to cause telomeres to get shorter. And we already knew that mutation rates skyrocket and tumors get shorter, and that inhibiting telomerase was just going to make tumors get really shorter.

Mutations rates were going to skyrocket. Some of these mutations were going to convert those, cells into ways to survive, any cancer treatments or in fact, start producing their own plants.

And, so I was pretty upset when they decided to focus on that. I am the real inventor of a multistate. I'm not even certain to pronounce it correctly, which is the antisense that's in clinical studies now for Geron Corporation.

That they use to inhibit tumors. And I would always say that that's, that's going to the cancers are is going to come back and then they're going to be resistant to the not just that and resistant to whatever you treat them.

But if it gives six months, it'll get approved. Yeah. Well, I mean, it is it is anything that helps. I, I strongly agree that they should continue pushing it because it does very effectively makes the cancer go away.

But people always have to be aware of the fact that it's going to come back. So people do live longer because of it. But it's like it's not really the cure for cancer.

And we do have a cancer program here at Sera Sciences, but we're, we're trying to focus on not inhibiting telomerase. We're trying to poison cells that produce llamas.

So so instead that keeps the telomeres long. In fact, it's a two hit kind of thing where we first, even if it's a cancer cell, we induce a long range to lengthen telomeres.

And then then then take the telomerase inducer away so that all the other cells in your body shut this whole machine down. And then, at a, a poison net. We have two different types of poison.

One is a nucleotide analog that, incorporates into the telomere that will actually kill the cell that other polymerases won't recognize. And the other one is the, using the same approach that we used to prove that we have telomerase.

That was to make a mutation to the RNA and infect cells with a, gene therapy that delivers this, mutated RNA to actually, produce a mutant telomere that would kill cancer cells.

And we've even though the ones we originally used, the ones that converted tag to gtg or rt, gtg, we've done a lot of work on, like all the different 5000 plus different combinations of tumor and found some that are very, very lethal to cells.

The problem is delivering the gene therapy to all the cells is the issue. But the nucleotide analog, which we don't have yet, we, we we're still searching for things.

So what do you write in Jerry Shea or with Jerry Shea? Because what he wrote passed away. Jerry Shea published a paper recently out of MIT the tide analog.

But it's not it's not sufficient. It nucleotide analog that actually poisons cells, but it's still incorporated. It gets incorporated by the polymerases.

So we're looking for something like that that would that would be totally ignored by like RNA polymerases and DNA polymerase is besides telomerase. So so we do have a cancer program, but the idea is to keep tumors long.

Not until they're short. So I so getting back to the subject, as soon as they decided that cancer had a quicker return on investment, despite everything I had said, I resigned.

In fact, I stayed there a little while, and I, I, I, you know, led the first studies that showed that we could overcome the Hayflick, and, when I presented the data, strategy meeting, I was reminded that I wasn't supposed to be working on that.

I was still working on cancer. And, at that point, I kind of, like, walked in my office and called a venture capital firm that I'm friends with and said, you know.

Yeah, think I'm looking for something else to do. I want to start my own company now. Is there something I can help you guys with to, earn some money?

Well, I'm trying to start my new company, and they just had me, consult a lot for, you know, go to other companies to salvage their science and things like that.

And so that was a win win situation for me. And, and it allowed me to get time to write a business plan and get investors and start Sera Sciences. So Sera Sciences has been focused on trying to find a way to produce telomerase inside of our cells, despite the fact that some people believe that that's going to cause cancer.

I can't really say if it is or isn't. I mean, there's no data okay at all of it. Everything is hearsay. So far. There's not like I go to conferences and there's people, scientists and doctors that believe that there's actually been studies showing that when you put the telomerase gene into the cell, it becomes a cancer cell.

But there is no data at all saying that at all. And there's data that shows that when you turn on telomerase in a model that that it doesn't necessarily get cancer.

Yeah, actually cancer gets decreased. There's several studies now showing that surprisingly, in fact, Doctor Rhonda Pennell married he was a cancer. He still is. He's a cancer researcher.

He when he did his mouse studies, he wasn't trying to show that the mice were going to have a remarkable reversal of the aging process. But what he called it, he was actually trying to show that they were going to get cancer, because he was going to try to use it as proof of how important it was to find a way to inhibit.

So you should probably just explain a little bit about that, that experiment that was so, serendipitously good for, for the aging, for aging research and for telomeres, as, as as anti-aging.

Just what he did, because I don't think we've talked about that at length. You have a perfect person to talk about it. Yeah. Well, what what Rhonda done, he got he got the genes from Geron when I was there.

Ron, Ron and I actually collaborated a lot on, trying to figure out whether or not, like Maria Blasko original data, where she originally announced that telomerase and telomerase have nothing to do with aging because when she put, performance into, mouse, or when she knocked out that flourishing mice, they still died at normal age.

But you know, Stone age by telomere shortening, the age by other mechanisms. And their telomeres were so long that it had to go, you know, Ron, depend on I work together to show that, it was actually predicted that it would take six generations of mice before the tumors got shorter enough that they would start showing signs of aging like humans.

And lo and behold, that turned out to be the case. So Ron, Ron, and I had a good working relationship. Geron Corporation provided him with the tools, but he, you know, he wanted to show that the the tolerance causes cancer, and I was all for it.

I mean, like, let's let's get this done and I'll see it. And so what he did is he first engineered mice that were knocked out for the telomerase for the most telomerase gene, and he, and incorporated a new telomerase gene that was under the control of the, tamoxifen, what it was I was going to say, and or the estrogen receptor.

Okay. So yeah, for, for hydroxy tamoxifen, but I hydroxy too much. I can't remember what it was, but so he put it so

the mice had telomerase turned off in the absence of the tamoxifen drug.

And then when they got old and the Taylors got really short and they got old, so he let him go. The six generations to get short telomeres. Then, then when those six generation mice started to show signs of human aging, he then fed them before a drugs tamoxifen.

And they got younger by every measurement he could do. Okay. Brain size just got bigger. Memory came back. Spleen size came back. I can't remember this in ten years, but all this, he had the pictures of the gray coat went, nice and glossy brown.

And, you know, they had good subcutaneous fat. They just looked like younger mice. And on the inside, there were younger mice, too. But it was also refresh my memory.

Was it a 50% knockout so that they only had 50% of telomerase? And then again, it was a full, full knockout. Yes. Knockout. Okay. Knockout. So they so they they had regular telomere shortening, but the, when he got interviewed by Barbara Walters on that, he called it a remarkable reversal of the aging process.

And I was then thinking, you know, that just destroyed his whole theory. You know, I mean, what's he going to do now? Well, he he he, he had a very successful career.

And as a result, he became the head of MD Anderson in Texas. So, he's still focused on cancer. And probably there's still probably benefits in, in cancer cells inhibiting cancer and inhibiting telomerase to kill the cancer.

Just got to do it in a way that doesn't increase the mutation rate at the same time. So, I'm hoping that some of our research here will contribute towards Rhonda Pennells.

So I think that's a that's what a lot of people, doctors and other health care practitioners, to think about doing something to a therapy that will increase telomerase activity.

They say, well, gee, I mean, what I know about telomeres and telomerase is that, you know, all cancer cells, 90, 95% of them have turned on telomerase.

And that's what helps them do the job. So what if we turn on telomerase. Are we going to cause a problem with our cancer cells. And you know it's it's on the surface reasonable to think that way.

But the details which are you're just about to explain, are that it's more complicated than that. Well, yeah. The one is one of the main causes reasons we get cancer is a weakened immune system.

And keeping the telomeres long in our immune cells is going to help our body fight the cancer. But also, one of the main causes of cancers is the short telomeres.

One of the reasons why cancers, evolved so late in life is because of the tumors get shorter and the mutation rates go higher to increase the chances.

I mean, people used to talk about accumulation of mutations with age, and you just build up more and more and more mutations. But a lot of studies have come out so lately, less like 5 or 10 years, showing that these accumulations don't occur gradually.

They cure occur all of a sudden in the older cells. And so it's probably being induced by the short telomeres. I mean I'm not saying short telomeres is the only causes rotations.

Other things can cause to. But usually when you get a mutation it causes the cell to be unhealthy, some somewhere recognizable by the immune system. So either other dividing cells replace it, or the immune system will knock it out until the immune system gets weak because of short telomeres.

And then you get immune senescence. That's this is still theory, because the only way we're going to ever know is to, is to find a way to actually lengthen telomeres.

And I'm not talking about just some of the tumors, like some some great products on the market right now will lengthen telomeres, but they'll lengthen the shortest telomeres, the length and maybe the average telomeres and some of the cells.

But what we need to do is we need to make it so that all the cells in the body have the telomeres lengthen so that they have a young phenotype, and also that they're not causing high mutation rates.

To actually see if telomerase is going to cause cancer or prevent cancer. And when when I take all the pros and cons and read all the papers and do my critical meta analysis of the scientific peer reviewed studies and try to weigh different things, I come up always with the idea that if I had to bet money on it, I'm going to say that inducing telomerase is going to decrease cancer incidences more than it's going to increase.

It can do both. It's just that in the in the long end, what's, what what caused more cancer, lack of telomerase or present sex hormones. And I think it's the lack of Thomas is going to cause more cancer than presents, Thomas.

But we won't know until we can actually test it, and we can't test it until we have a drug or a gene therapy that does lengthen the tumors and all cells.

And that's what I'm trying to do. I'm trying to come up with something to do something like that doesn't exist in my opinion, even though there are some papers that, are, I wish I would see reproduced.

Let's see if they actually can be reproduced. Right? Yeah. I mean, I think, you know, you're talking about more like a 30% increase in telomere length.

That would have those kind of super rejuvenating effects. And, and in every cell, you know, there's been some signals in papers with increase in telomere length.

But, not like the Stanford paper where they did it with, I think it was, an RNA or an AI or like a messenger RNA where they lengthened in vitro telomere length by 30%.

Then, you know, something like that might be, have these incredible effects. What was the lengthening of the Pinto's telomere length? 30%. What percent?

If you had 30% increase in tumor, like 30%? I thought that was why you just picked 30%. You know, I thought it was the Stanford study as well. I think that had somewhere around that length, in vitro in petri dishes.

I mean, we we I guess I'm saying. Yeah. Yeah. And we've been able to do that for 40 years that, we did RNA back when I was still at Geron, but we took telomerase mRNA and put it into cells like that work.

But the big problem with the mRNA is to deliver it, delivering it to all the cells is this really big problem. But, it's, so it's really there's there's all kinds of publications coming out where people are saying they've got big new breakthroughs on how to do it.

But the bottom line is I just really want to see it get done. I mean, it's like I'm not trying to get publications myself. I'm not trying to make a lot of money myself.

I just want to cure aging. And right now, I think the best way to cure is to length and telomeres. And I don't want to waste my time on things that that really are just going to give me a paper published.

Because I really think we got to find a, a drug. I, you know, we do have a gene therapy that, I'm hoping will be effective, but I don't believe that's the end all either, because it's it's still doesn't get delivered to all the cells.

I think the the best way to actually learn from tumors, to find a small molecule drug, which for some reason has a lot of bad neck. That feedback on too, is people are saying small molecule drugs don't work, but that's because there's not a lot of poorly designed small molecule drugs.

There's a lot of small molecule drugs that work really well. I believe that designing a small molecule drug that induces that small machine is a much better way to get delivery of the telomerase to every cell in the body.

And so that's that's my thoughts. Do we know, I mean, we've talked about this before, but, telomerase is repressed, suppressed, in, in most cells in adulthood, even after birth.

That do we know? Because what's the mechanism? I mean, the mechanism some of the small molecules is to repress the repressor. But I know you've said that.

Well, I don't know that anybody's ever really shown that. I mean, the reason I'm asking is, is that could if we know what the mechanism is or have an idea, then it could well be that a small molecule will work quite well.

Is that an active area of research for people or are they just looking to do gene therapy? Yeah, we know we we we spent over ten years just trying to figure out how is the telomerase gene repressed or is it is it repressed?

Or maybe it's just, so coiled up in the chromosome that it needs some strong activators?

Telomerase, Cancer Risk, and Rejuvenation Experiments

And we, we, we came up with a lot of candidates. We found a lot of things that work, in ectopic expression of telomerase or, and, and in, in a test tube.

But we could not get any of these things to work in detail. Okay. And my when I say in view, I'm talking about even human cells in a petri dish, I like to call that in people.

In the past, people call that individuals. But the so we finally after ten years and we've done just about everything we can, we never published any of our work because our focus wasn't publishing.

But a lot of people in the last 20 years, ten, ten, 15 years have published papers reproducing our results. But we know our my team knows. Yeah, that's not going to get anywhere because it's not going to actually work in a normal human cell.

In a body. We finally just decided, okay, so we've done everything. We can't imagine anything else to try. No, we haven't figured out what other telomerase promoters regulated.

Nobody else has. And I came up with the thought that for maybe, maybe there's multiple repressors. And when there's multiple repressors, you can't use the standard technologies to do repress to see that the gene turns on.

Because you have to you have to do you repress several at the same time. And how do you find, several. To find one of them, you have to do repress all of them.

So so we we decided we decided to to do it the hard way. Okay. And that's where we're we're obsessed with this goal. So we have to do it our way. Let's go for it.

So we developed an assay that everybody else had said was impossible. And that was a high throughput screening assay that used, real time PCR, to detect, telomerase amyloid, and even though mRNA is so low and even cancer cells at the level, the mRNA for two hours is so low is something like one minute for cell, so low that, PCR was thought not to be practical.

But I had some pretty good people here, and we developed a really good, powerful, real time PCR assay that we can do in high throughput. It's still a trade secret.

We didn't publish your paper. Nobody else has figured it out. Nobody else. If they have, they sure aren't using it. But we we were able to screen, like, 500,000 different chemicals, including a lot of natural products, in this assay, without knowing what the repressors, without knowing how the genes regulated.

But we ended up finding 900 different chemicals that actually did turn on the Chalmers gene. Not not to the level that we see in cancer cells. And we we picked Hela cells as a standard to go with because Hela, the ones from Henrietta Lack, those were the cells that we had determined when I was still at Geron Corporation.

Produced the lowest amount of Mr. Thomas mRNA. Oh, we're still immortal. So we decided. Okay, that must be, the amount that we need to get to to make a normal human a non-cancer cell.

Immortal. So the highest we've gotten is 16% of that. Okay, so we have we have gotten, chemicals that, induce telomerase to that level. We still don't know how they work. Okay.

So we know that they, we've done a lot of studies on on toxicity and things like that, and they're not causing any side effects for some are. But but the ones that we're pursuing aren't the don't call them side effects, what, 16%.

You know, you hear about the trap as a, as what you use to sort of figure out whether something's turning on telomerase or not. And, you know, you talk about one fold, two fold, three fold increase, a lack of cell will be how many fold we can cause it's like dividing by zero.

Okay. So when you get really good at measuring telomerase activity, you find out that there really isn't any mRNA or any telomerase activity. And like, endothelial cells or, fibroblast cells at all.

And so, so when we do our PCR tests and stuff like that, we have to go through many, many seats and, you know, some measure and PCR, before we actually see anything from, normal human cell and we just figure that's, that's zero.

That's I mean, there's zero mRNA, so we can't really say a fold increase, but we can say how much fold are we away from getting to what Hela is? Right.

So 60% is about, what, 1618? Right. So if we can increase, if we can find some way to increase it eightfold more, we could know. Okay, let's go back to this idea that there's multiple repressors.

Okay. Well we're we're planning to now try to do a synergy study okay. To try let's say maybe some of the repressors that we found, attack one of the repressors, some attack another repressor, and some attack a third repressor.

And maybe we might find that mixing them. We'll attack all three repressors, and we'll get to 100% or even higher. That that experiment hasn't been done mostly because of the lack of funding.

You know, it's, but we're we're we're geared up to do that. We just it's just a very expensive experiment to do. And, it's, I mean, literally when we were doing identifying the first 900 chemicals before we did to even get a chance to start talking about in synergy, we were spending $1 million a month on the screening.

And, then the lots of things happened. The global financial crisis, Tokyo earthquake, the pandemic, Covid and all these things started interfering with our ability to be able to do this research.

But that's still what I'm trying to do, and I'm trying to I'm trying to find some way of bringing in funding to do that without losing control of the science.

Okay. One of the big from one thing I learned when I did have investors, and I used to only own 70% of the company, I found that I had very little control of the science.

Not some of the some investors were outstanding. Many of them would completely take over our strategy meetings

and get our scientists geared towards other things.

And then there was even talk when I used to complain about it, that they were going to fire me and replace me with somebody else. And it's like, my upset that would be that would in my life, because I'm so obsessed with this.

And so finally I was able to, buy out all investors I own 100% and at the company now, but I, I don't want to bring in more investors that are going to have control.

So I'm, I'm trying to find funding without losing control. But I got some great opportunities for investors to make a ton of money off of marketing discoveries.

They just let me focus on the science. So that's I'm hoping something will turn up soon. And and we can get back onto this. But I think when we do get the funding that we need, we will be able to, make some, get some a lot of these questions answered.

Does telomerase cure aging? Does telomerase cause cancer, all these things? Well, we'll be able to answer very straightforward. Right now they're just all hearsay people are looking at, I mean, obviously you hear the, the sort of the, the thought from the gerontology community that it's perfectly valid that trying to cure individual diseases will only add about 7%, seven years to the, to the average lifespan.

But if you cure aging, obviously you're gonna add, you know, decades to it. But there is work going on looking at, well, there's lots and lots of observational studies looking at the role of telomeres or any, any other association of telomere length with cardiovascular disease, dementia, osteoporosis, of course, cancer in the opposite direction, short telomeres increase.

And some of that's probably through affecting the aging process. But some of it's maybe more direct, to the pathology for those particular diseases. There's some research and a lot of research on cardiovascular disease.

What's your thoughts about sort of that, that area and clinicians trying to keep telomeres longer in their patients, to stave off some of these chronic diseases?

And, you know, particularly Alzheimer's and cardiovascular disease. I get misunderstood a lot. I think it's because I'm not a semantics expert. But when I say curing aging, I'm talking about curing Alzheimer's, curing cardiovascular disease, curing osteoporosis, curing, multiple sclerosis and all the demyelinating disorders and things like that, because I believe that telomere shortening plays a critical role in almost every disease we've ever heard.

In fact, I don't I, I am totally unaware of any disease that's ever been discovered that there hasn't been. Now a scientific peer reviewed publication showing that telomeres played a role in inducing that disease.

So I believe that lengthening telomeres is going to correct many, many diseases and especially target Alzheimer's and cardiovascular disease. We have a as I mentioned before, we do have a telomerase gene therapy that we're trying to get clinical studies underway with.

I think it's going to have a delivery problem. We're not going to be able to get all the cells, but it still might help. But the big problem with it is it cost like $1 million to treat one patient once.

And even though it's great proof of concept, it's not going to be something that is going to be readily available to everybody. And so it's not my priority.

But I do I, I do have clinical studies, designed protocols designed, and you're involved in actually, the, to, treat Alzheimer's. That's our main one to treat, cardiomyopathy, critical limb ischemia.

Do my leading disorders, idiopathic pulmonary fibrosis, which is actually something new promoted that we, focus on. And many other, diseases. I mean, it's the list is mind boggling, but, you know, I, I these things are super expensive.

And, it's it's like I am in contact with the FDA and stuff. Forgetting the guy's name. But there's a guy at the FDA I want to say. Don't think that. I don't think it's him.

That, he's very on board. But the big problem with aging, and I agree with the FDA totally on this, is that you can't measure it. Okay? And even though people are constantly saying they have markers of aging, they really aren't markers of aging.

They're just markers of the markers. Well, yeah, I mean, there's a there's the team trial that you're looking at right now and that's sort of not aging per se.

It's multiple multimorbidity markers, clusters of diseases. And when they and when they have onset. But, you know, I guess, the DNA methylation clocks, are kind of interesting as markers.

And, you know, there's a lot of buzz about them. It is an area I actually did want to talk to you about, which is, you know, for a long time, measuring telomeres is sort of a biomarker that you looked at.

And I've been measuring telomeres in my practice for 15 years now. They are square with aging. The chronological age isn't that great. But then along came these these clocks that were the R squared with chronological age is like.95.98.

Then there was the Trim trial that was published, you know, with where they looked at growth hormone DHEA and metformin, very small. But because Steve Horvath clock was used and he saw like a two year reversal of aging, would you expect someone who was treated with, let's say, Ron De Pinto's mice?

I mean, it would have been interesting if they use Horvath clock on dependent mice. And I wish somebody would do that experiment wouldn't be that expensive to do.

Where that would validate that as a, as a marker. If you saw a, you know, a real significant reversal of DNA methylation, it's because you see that when you do the Yamanaka factors, the epigenetic clocks get get reversed as well.

Would you say that that's, oh, you know, of course, being a clinician, I'd be like, yeah, the lungs got to work better, the muscles got to work better.

The brain's got to work better, too. But as a short term marker, would you would you accept that? Yeah. No, I actually I openly say that I think DNA methylation or DNA is, is a better marker of aging than telomere length measurements.

Yeah. But not only because telomere length measurements are very difficult to do. Okay. I believe that telomeres, tumor lengths are probably controlling the methylation.

Okay. So and one of the studies that I would love to do, and some people have already done some studies that really suggest this is true. That's in at least in vitro human cells and features that children are shortening and re lengthening but have shortened re length and see if that corresponds with the length of changing back and forth of the methylation pattern.

Well, yeah. Might even be better than DNA methylation is the glycosylation. The Gordan now stuff, I guess. Yeah. The what did you call it? Oh, you talked about glycosylation.

You mean the, you talked about I think the, the home, the, or are you talking about, hemoglobin A1, c glycosylation? I'm forgetting the name of the guy Gordon Loper now.

Yeah. Wouldn't that stuff. Yeah, yeah. So I think I think he's brilliant. I think he's what he's gotten on do is, is amazing. And I think again though I think that that's probably controlled by telomerase.

And oh that's interesting. If you talk to Gordon about that. Oh, yeah. Yeah. Gordon, I have become good friends ever since I first heard him talk and was just impressed because, you know, what I look at is, is how good are people at doing critical meta analysis of scientific, peer reviewed studies and building theories out of that?

And Gordon is just amazing at that. And so are a lot of other people. And, and I kind of like, like to work with them. That's one of the reason I like to work with you. Too.

And it's like, and so, so getting all this stuff put together is, is, I think, putting a model together, a lot of these people agree with the idea that telomeres are probably controlling the methylation and the glycosylation and things.

Biomarkers of Aging and Telomere Measurement

But the markers for aging, like, like oscillation, like oscillation might be a better marker for aging them. Methylation. I can't really say yet. But I know that telomere length measurement is so difficult to do.

And so many people do it incorrectly. There is, you know, at least one company that I recommend people go to. I don't know if they're the company. Okay, a life length. Yeah, definitely.

If you're going to get your teeth and their length measured, I think life length is really the only place you should be going and not repeat diagnostics.

Peter, length or company, not six would be okay, except that they don't really measure the percent of telomeres that are short. Okay, so that's what I know.

Yeah. I mean that is a differentiation between the companies. But my question about the percent short telomeres is when we first did that study, with, you know, the precursor to life length, and Maria Blanco's lab, and we measured the percent.

It was the bottom three, 3% or something like that. It was or three kilo bases and below. They're reporting out 20% percentile. And when we did, remember, we did the, the telomere, workshop at 4 a.m.

and we had that cohort of people, the 20th percentile had almost like a R-squared of 70 0.7 correlation with the median. So there wasn't I wasn't getting the same.

If it wasn't extreme, I don't know why. I don't know why they switched to the 20% or just doing like I thought it was two and a half kilo base pairs that they were doing, but they're maybe it's because it was it was much shorter than in, you know, 20 percentile just it's doesn't add that much information.

That's that's my concern about it. I know that the theory and you've talked about it before is that it's the critically short telomere that that causes the problem.

But, you know, we're not I don't know that we're getting that measurement. That's that's my only the issue, I think I think measuring the critically short telomere gives a better, correlation with aging and disease than average.

But I think it's only because the average is so hard to measure. Okay. Yeah. And but it's so, so the percent of critically short telomeres correlates with the average.

But it's easier to measure the percentage for telomeres. Now I'm not exactly certain why repeat diagnostics doesn't measure doesn't report the percent of tumors that are short, but they're actually looking at host cells okay.

So they're looking at the average telomere length. Purcell as the cell goes through their full cytometer, whereas Lifelink has the ability to look at each telomere individually and measure it.

But I've noticed lately they're actually look they're reporting actually average cells too. So I think technologies need to be improved even more. We actually have two protocols here that we're trying to develop right now that look at,

not just percent of short telomeres, but look at each individual telomeres and also identify which chromosome it's on.

And we also, you know, essentially doing high throughput sequencing of telomeres, long range, long range sequencing of tumors, and because nobody's really looked at this, but actually one paper and how it's come out on this, we don't know that telomeres are all saggy all the way through.

There are probably regions that might be different and they might be correlated with disease. Okay. So it'd be good to start finding out. So so I think I think the ultimate would be when we can actually get, technique.

And we're, we're working on this right now, even though it's going to be unaffordable as a, personal personalized medicine kind of thing. It be great for research.

We're working on trying to make it so that we can sequence every tumor, and, know which what the whole sequence is, what chromosome it came from, what its length is, and then be able to correlate it with all kinds of diseases.

And, and, you know, very computer intensive. You know, algorithms that like that. I think that's going to give us a lot of information. Again, funding is the issue.

We've been trying to raise funding to do this, for quite some time. And even the, long range sequencers are, are more expensive than people want to invest in.

It's so it's I do believe that tumor length measurement can be the best thing in the future, but right now, I, I I'm, I'm I'm thinking, DNA methylation and, like, isolation are probably the best place to go.

And and believe me, repeat diagnostics is a very, very good company. I definitely believe in their company. I just, I just don't I wish they would, provide the percent of sure tumors.

I think that information would be very valuable if it's presented correctly. And that's that's why I, I just I'm not certain that, I it might be a cost thing.

It might be in order to make it, affordable, life length has to go with different methods, to, you know, otherwise they won't get any clients to get their children.

I think the main, the main, the main reason probably is with them is that they're more focused on the telomeres, biology disorders and, bone marrow transplant stuff where they're looking just really short telomeres, people with telomeres in the bottom one percentile, you know, under five, under four KB.

So the percent shortage doesn't really make a difference. Do you have a tumor biology disorder or not. And and the mean telomere length that they report out is is pretty good for that.

They have a good, good percentiles on that. They're, they're you know, I send lots of samples to them. Other doctors do. But I think their focus is on, on that.

I mean, I was think about asking Geraldine Oberg to come on and talk about it, but, you know, I don't I'm not sure they're much or they're that interested in.

That's that's my thinking about it. So I wanted to shift gears just a little bit. We were talking about telomere length and telomerase, but there are other these other sort of.

And I want to get your take on it, these non-canonical, activities of telomerase in the mitochondria. You talk about it shuttling into the mitochondria, and the beneficial effects that it has.

What's, what's your take on the importance of that role of telomerase? And, you know, I personally I haven't seen

any studies that really convince me that that's for real.

It's something that I want to take on and we get more funding is I want to look at that more critically, but it's almost like, irrelevant. Okay. As long as for as long as our cells aren't producing any telomerase to begin with.

Well, I mean, that's that's a very good point there. So, but so, I mean, just thinking back to the study, out of the Pinto's lab, I think, Sahin did, where he showed that there was increased, you know, mitochondria biogenesis through, you know, the PG one, alpha and beta, and that's, is that through telomerase tracking?

You know, no, that that was probably due to, to changes in gene expression on the, main chromosomes that were because, remember, most of the proteins in the mitochondria are encoded by the chromosomes rather than a hundredth. Right.

And so that was probably an effect of gene expression on the main chromosomes, which was causing the, energy levels. But I, I can't remember the name of the genes for how to, to, the I remember they had a letter E and I the, the details of those, but those.

Yeah. But I think that telomere length does have a big effect on their conjugate health. The data that I'm not convinced about is that telomerase if it does get inside me a conjugate, is it actually doing something there.

Is it just completely irrelevant. What what would it be doing? I be I mean, no, there's no end. Yeah. A contra DNA circular, but but it's the question is does telomerase have other activities besides lengthening telomeres.

Right. And that that I haven't seen any convincing data of. And from an evolutionary perspective, there's a lot of reasons to suspect there's a lot of things that happen in the cell just because.

Why not? You know, it doesn't do anything. There's no there's nothing to cause it to be there and nothing there cause it not to be there. It just is there.

And it's completely irrelevant. And so, so a lot of these things haven't been addressed, really, as far as the why, what is it look like telomerase actually gets inside of mitochondria?

And I would think there'd be a lot more studies out now if that was actually reproducible by a lot of labs. But I can't say that data that is published right now is wrong until I I'd like to get my hands on that myself and look at that.

And the mechanism through which telomere shortening changes gene expression is that through that, what's the term that they use? Telomere, gene expression change at a distance.

It's called I'm blanking on it right now. That's what differences are. No. It's it has to do with the way when the when the tip gets smaller, it changes the way in which it touches the DNA.

Like ten megabase is proximal to the telomere. And so just even a small amount of shortening can change gene expression. And that's why it's, I mean, I, I've always thought that the theory of it's not only important not to have critically short telomeres, but to have exactly the right telomeres that, you know, that are, that you start out with, if, if it's if it's if that mechanism is affecting gene expression, even with a small change in telomere length, then is that is important to maintain your telomeres at a certain level?

Not so much as like like you can let them go down. So as long as I don't get below a certain length, but, you know, the aging process starts, you know, and, you know, you start seeing aspects of it in the mid 20s, late 20s.

So is it is it that kind of you talked about gene expression, DNA methylation, you know, sort of picking up the changes in aging and that's somehow controlled by telomere length.

Is it through that way in which the slight change in to on length changes gene expression? Well, a lot of what you just said sounded like the theories I've proposed.

Okay. Which haven't been generally accepted by a lot of people. And that's I, I've read some papers. I can't cite them right now, but I have read some papers where they do talk about that and showed some data, like what do you write?

And Jerry Schade did published some papers showing that they could affect gene expression, and they shortened and lengthened the telomere. That gene went up and down.

And there was a position effect. Yeah. I don't remember this particular PPA. If you did. Yeah I definitely believe in TPI to telomere position effect.

But I think of the telomere as like a magic wand. Okay. And like I remember when I was in the early 70s, studying molecular biology for the first time in, textbooks written by Bruce Alberts, where he talked about he gave a really good explanation with a lot of papers.

Explain why genes can be regulated by other elements that are a long ways away. Okay. These enhancer sequences that can be 100,000 bases away but still affect the gene expression of that gene is 100,000 bases upstream.

And it was just the DNA folds over and transcription factors bind to the enhancer and bind to the promoter. And then these things come together and turn the genome okay.

So I think of the telomere. The tumor actually does have a lot of similarities to transcription factor sites okay. And TRF one and two of two which bind telomeres do have a lot of similarity to transcription factors.

No really I think the telomeres are actually working like an enhancer sequences and that they fold over and essentially touch genes, turning them on and turning it off just like a magic wand.

Okay. But the shorter the tumor gets, the less likely it is to reach the genes that are further away. So it might change gene expression in some other genes that you don't necessarily is not in the salubrious direction, but indirectly.

Telomeres, Gene Expression, and Mitochondria

Yeah. Those genes. There's like one thing that I noticed is that a lot of like zinc finger transcription factors, their genes are located near the tumors.

So the tumors are folding over touching these genes, turning them on and off. These are going over touching other activating or repressing other genes.

Okay. So so there is this theory that, you know, I proposed a lot. I've got some hypotheses to do testing and things like that. But again it's, it's, you know, when can we do it?

How do we do it? Things like this, funding and priorities are a big issue. But I do believe that the length of the telomere is affecting gene expression.

And, it really only favors so far as what do you write in Dr. Shay's paper, which is really good, showing that they could lengthen this telomere position effect.

The gene was dux. The, I think the duct gene, where they show that they could control this expression, but just by changing the length of the tumor as far as position, relative concealment, and I believe a lot of genes are regulated, like that.

We just don't know yet. But, you know, people seem to forget about Bruce Alberts textbooks back then, which show that this, this phenomenon already exists.

There's a precedence for it. Why wouldn't you be doing this? Okay. People want to envision some type of chromosomes. Are chromatin molecules, histones moving along the chromosomes, regulating things.

And there's no precedence for that, really for, doing that. There is precedent for, histones moving along chromosomes, but not long distances, that are needed to actually contribute a, effect on gene expression.

So who knows? But it's all it's all still research. We just got it. But there's what I really like about tumor biology is there's there's so many good theories that explain everything about everything.

Okay. And and I say this the only theory of aging that can do that, okay. Everything else is nothing that you can't say that some of the other things like methylation is affecting tumor.

Right. But you can't say tumor necrosis factor methylation okay. It's it's and so telomeres. So you know, I, I compare this to the searching for the source of the Nile or what I call searching for the source of what is the ultimate source of is like methylation a symptom of aging or is it a causation?

Well, I think I call it both. Okay. I calls it I call it something calls. But I think telomeres could be the cause of aging and other things are symptoms and then indirect causes.

So it's the most upstream you believe of them. But I mean actually just getting back to the methylation potentially methylation around the telomerase gene could I mean, affect effect telomere length.

So it could work both ways potentially. Joint cancers. Yes. Right. Yeah. Yeah. So I mean, I think that's the the whole idea behind a sea change in approach to Alzheimer's disease is in focusing on the glial cells and their caretaker role and their role, in, keeping the neurons healthy so that they don't start producing a lot of beta amyloid, rather than focusing on removing beta amyloid.

And when you talk about curing aging, I mean, I think there's a difference between curing aging. When I think about it, which is someone's old, like an older, dependable mouse, and then fixing them as opposed to preventing aging where you keep them in the healthy state.

And the aging process just doesn't happen. For me, it's seems like it would be easier to do that with Alzheimer's than prevent it, than to cure it. Particularly if you're able to keep those cells doing their job indefinitely, then.

So and I think that's, that's, I guess, why we should start looking earlier on, but to get a clinical study to use telomerase to prevent Alzheimer's is going to be next to impossible relative to doing a clinical study to actually treat Alzheimer's well.

So that's where, you know, the the biomarkers, the models, the, you know, the fMRI and some of the the new techniques that they have, I was talking to Tom Dowd about looking at the retinal epithelial cells and how they can be a signal for, early changes that could precede Alzheimer's disease and getting validated biomarkers that.

Yeah, in order to fully validated and you'd have to follow those biomarkers for a long time. But, you know, it's probably worth taking a flier on it for, for, you know, potentially.

And then, you know, it may work in slowing down Alzheimer's in early Alzheimer's as well, potentially. So you might be able to do it that way. And that's where the team trial is probably important because it's going to start to focus on looking at the aging process.

And hopefully, you know, when it finally gets underway, Covid, but you put the kibosh on that, too. They'll, they'll, they'll then start to think about things differently.

I mean, it's all about the biomarkers. I mean, that's what I've always been involved in because, you know, no one's going to make a career waiting for 25 years to see if you prevent a disease.

And that's one of the reasons why I want to focus on reversing the disease now, because I can see a reversal of the disease a lot, a lot faster than you can see the, prevention of the disease.

Absolutely true. But, it's like when I was talking about getting it's hard to get a clinical study for those. I'm talking about getting approval from the FDA to treat somebody with somebody, something like a telomerase inducer, because of fears of it causing cancer and stuff like that.

Now, some of the other things, like the team study and things like that, with metformin and things, those are different. But those, those things have already shown there that people aren't really saying these are going to cause potential health problems.

Okay. So so getting a study right there, I think is a good idea. And I strongly support them and encourage. And I, I take my metformin every day and I've been taking it for ten years, you know, because I believe that, you know, it's, it's something.

But I don't believe it's the end all. I think the end is going to be lengthened. Yeah. So, I mean, look, it's been fantastic talking to you. I mean, is there any kind of parting thought you'd like to to leave?

I mean, I think about the future of telomere biology and and aging, or just yourself. I mean, I'm I can't think of anything. There's so much that I could talk about, I, I, you know, I we had another hour I'd love to talk about, like, what is aging?

What causes aging? Why do we age? My background and evolution gives me a unique perspective on that. But it's it's it's a long there's YouTube videos where I spend a lot of time talking about those kind of things, but, it's it's really it really doesn't help us come up with the cure for aging by looking at those things.

And so my focus is on trying to just come up with something that's going to kind of cure aging. And again, semantics. My definition of curation means preventing Alzheimer's.

You know, things like that. It's it's so it's just cure. Aging is just become a coin phrase for my company. And in fact, my father, those are the words my father said to me when I was ten years old, when he said, why don't you grow up and become a doctor and find a cure for aging?

So I read that on Wikipedia and I was like, did that really happen? Or is that, just to worry about? I'll never forget, I, I remember where I was, what I was doing, I was, I was like, I was, obsessed with science and medicine, and I wanted a telescope for Christmas.

And my parents got me a really crappy telescope, and I cried about it. They went on, bought me a nice eight inch reflector telescope, from a garage sale.

And that night, I was out on the front lawn of our house, finding craters of the moon, wounds of Saturn, rings of Saturn, moons of Jupiter, things like that.

And my father just came out and said, hey, Bill, since you're so interested in science and medicine when you grew up, you should become a doctor and find a cure for aging.

And he was serious about this. And then he said, I don't know why nobody's done this yet. My father wasn't a scientist. He just didn't not like the whole idea that he was aging.

He wanted, he thought maybe his son, because his son was so obsessed with science and medicine that his son would be the person that's going to come up with a solution.

Future Therapies, Reprogramming, and Closing Thoughts

So I got I got hooked on it. I mean, all through schools, I mean, I used to even in, elementary school, junior high

school, everything like that. People would get sick of me talking about curing age.

And high school. College. I did experiments with fruit flies in the early 1970s, to try to cure aging. I wish I knew my, Mike Rose at the time because, And we should have mentioned Mike fossil.

I just thought because we were talking about Alzheimer's. Mike Fossil and his company has got a program underway to try to use telomerase induction to, treat Alzheimer's, and I, I just want to, you know, mention it just to help them get support, to get this thing underway.

But but Mike Rose, I end up meeting Mike Rose in, early 1960s. In fact, Mike Rose and I started a company together called, Methuselah Research and masks.

And, it was like the next day I learned about filters. And so I walked away from the company and brought my father in and my father took over as the president.

Okay? My my father and I were like, best friends because we were both so obsessed with aging my entire life. This is what we talked about all the time.

So when I, when, when he, when I, when we my girls and I and for this board started this company called masks, and I suddenly wanted to go work on tumors.

Instead, I, I brought my father, and he became the president. Work with Mike Rose and or Lisa more. And, made some significant progress. But again, funding was always the issue.

And, but I, you know, Mike's what the plan was to apply everything because Mike was leading and still is the leading expert in the world on extending lifespan and fruit flies, even though I'd worked on it before, I did nothing like I.

In fact, he probably worked on it before I did. I just didn't know he was doing that. But the work I did was nothing compared to the work that Mike Rose did.

And when I met and talk with Mike Rose and perfect, we talked about let's let's apply everything. Mike Rosen learned in Fruit Flies. Let's apply that to Mike's service aboard who was who was working on wild cards.

And that was the whole focus of masks. Oh. You were going to do that? Just breed, older, older mice, and see if you could have the same longevity effect. Yeah. It's very significant.

The fact that there's a lot of work was a lot of work, but it was a lot more work than fruit flies. But all it needed was a bunch of money in a big warehouse where you could have lots of mice and breeding and stuff like that.

And then when you when you got longer in mice and find out what changed, what genetic, what genes were selected for, that was the whole plan. And, you know, I'm surprised I'm somebody should still do that.

Right. Exactly. But the funding sounds well, I mean, the obstacle I think there's been a sea change just in the last couple of years in, in interest in, in funding aging.

And then just recently with Bezos, $270 million, you know, creation of the company, paying the scientists $1 million or so, I think. Right. I think what happened for all over the news raving about the great salaries they have now.

Well, that's not the issue. There's curing. Aging is supposed to be the important things. Now, I'm I'm concerned about the Yamanaka factor. We've we've been working a lot with the Yamanaka factors and I work collaborate a lot with, like a West like, you know, and, he, he and I, we've done a lot of work together on the Yamanaka factors published and things like that.

The only knock factors are really a differentiating. Yep. Technique, not a rejuvenation. Right. And I compare it to,

like, the turning a butterfly and back into a caterpillar.

Make it younger. Or just turning a tadpole back into a frog. Back into the tadpole. Does that make it younger? Just differentiated. It didn't make it younger.

And I'm afraid that that's what's going to happen with the Yamanaka factors. And I'm concerned that these billionaires might have been. This led into thinking that this is going to actually be a cure for aging.

And maybe it will be okay. I mean, it's like, let's let's get it tested. But I'm just I'm just I'm just feeling that I'm I hope the investors know that this is really a, discovery research, not an actual application to try to get it done.

But again, I can't even say that because it might just work. What happens to telomere length is it get reset with a young man when the Yamanaka factors get induced, when you do you with four Yamanaka factors, telomerase gets turned on.

And so telomeres get longer. We've done a lot of research here. And we've presented posters and stuff like that trying different combinations like one Yamanaka factor, two, all different combinations of what is it, four different factorial, different ways of treating and trying to find some combination that turned on telomerase without you differentiating.

Right. That would be and it never happened. It was quite only thing. The only time we could get to Lorentz induced was when all four Yamanaka factors were added.

And and it's like this, this partial reprogram, this whole idea of partial reprograming. I don't know if that's going to really do anything because it's still going to cost differentiating.

It's going to cost. Telomerase again, doesn't make tumors get longer, but it's it's we got to figure out a way to turn on telomerase without to differentiate themselves.

Except we want to differentiate senescent cells in the nonsense in cells. And that's, that's the only thing we want to do. And that's, that's been successfully done by juries.

Again, I mentioned their names like Jerry, Jerry Shea and Woody. Right. They've they've done experiments, work in vitro. They've been able to turn senescent cells into nonsense cells just by looking the tumors.

But, it's again, we could talk for hours if you wanted to. Well, we we we may may have you back for a redux, if possible. I think, I think, you know, we could talk about aging processes.

I think you do have to really understand why aging occurs. To buy into why it would make things a lot better if you can, you know, stop aging. You know, some people are like, well, that's not really going to do it.

And that doesn't make that much sense. And so if you really understand the biology behind, you know, why aging comes, and, you know, it's pretty good, I think consensus on that, in the, in gerontology communities, then I think it makes looking at diseases of aging differently, you know, so nobody nobody knows nobody knows what causes age and nobody knows why we age.

They're all theories. Okay. Right. Well, yeah, but I mean, there's there's some consensus on, you know, the the idea that it comes in through the back door.

I mean, there are some people who still think that might be actually programed. I don't forget which camp you're in. But, you know, many people think that, that, you know, it's, it's a trade off of resources versus the environment and, you know, so why are there species with negligible senescence?

Because they don't have a lot of predators. You know, the field mouse is going to get eaten, so there's no reason to invest in keeping his body in good shape.

That kind of stuff is pretty well agreed upon. I think that the molecular mechanisms of it are less so. Everything you're saying is making me hope that you invited me back so we can have a discussion.

All right. Good. We'll have that discussion. Yeah, I'll be back. Very good. Well, it's been a pleasure, Bill. And and we'll we'll talk soon.