Gene Therapy To Treat Biological Aging Transcript

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Introduction and Guest Background

– Welcome to another episode of the reversing inflammation, summit body and mind longevity medicine and I'm your host, dr robert Lufkin today. We get to explore gene therapy and the possibilities for longevity with someone who is not only an expert in the field but who has actually tested the longevity gene therapy on herself.

Elizabeth Parrish is an entrepreneur and founder and CEO of bio viva sciences. And now please enjoy this conversation with Elizabeth Parrish. Hey Liz, welcome to the program. – It is wonderful to be here with you.

– Yes, I'm so looking forward to talking about your work on gene therapy and the exciting things you're doing. But maybe before we do that, could you take a moment and just tell tell the audience all of us a little bit about your background and how you came to be interested in this fascinating area.

– Sure, well, um I have an M. B. A. But I think that's the least important part of my my background. I'm definitely humanitarian. I've been in the patient advocacy state um for let's see, I would say over 10 years a state of being.

And um I my my work is all based in sort of the humanitarian effort for health. In 2013 my son was diagnosed with type one diabetes after working two years in the stem cell advocacy space.

And uh I was just really shocked to find out how much of the technology that I had learned about didn't translate to humans. And um I really wanted to be part of that translation.

I wanted to figure out what were the problems, you know, why is today's medicine, you know, 15, 20 and sometimes 30 years old that we use and yet the nascent technology that actually has a lot of evidence behind it at this point, uh, isn't used in humans. And so that became a big charge of my life.

And two years later I ended up starting my company bio viva as a call out to the world that we were moving way too slow. – Before we jump into the work you're doing in the genetic space. I always like to ask our experts to give us their overall view on aging and longevity, sort of, what is it why do we age?

And it's interesting because everyone sort of comes at it from a little bit, a little bit different angle. – Yeah, I think because of the space that we're in, we look at the hallmarks of aging.

We look at what's happening at the cellular level as to why we age. So yeah, try not to get into what we do yet. Um we would be looking at treating aging at the cellular level, making cells behave youthfully.

So we look at things like telomere attrition, mitochondrial dysfunction, stem cell depletion, nutrient sensing loss. Um, all of these entrant extra cellular communication issues along with genomic instability, which is the number one driver of cancer. So we're looking at what's happening at the cell inside the cell at the surface of the cell and in the nucleus of the cell.

Aging, Longevity, and Other Promising Fields

– And are you in the camp where aging and longevity is a sort of a wear and tear phenomenon that we eventually just wear out. Or or do you think it's programmed?

like the salmon, you know, after they spawn they die immediately, that kind of thing. What do you have? A? – Well, I think that aging is a disease. I think it's a perfect pathology. I think it's actually follows a pathology even closer than than some things that we call a specific disease.

And yet, a category of people may have completely different symptoms within that title. We know what aging is by

what it looks like on the outside, but it also is doing a bunch of things inside predictably to humans as well.

And so, I mean it is definitely wear and tear, but it but it also seems to be a genetic program that's running right. You know, we're very viable. Um Well, we're we're we're actually having cellular degeneration. So I think it's cellular degeneration over time, but we're having cellular degeneration long before we have Children.

But then, you know, after that point there's there seems to be a degradation and and a and a lack of repair repair actually goes way down. Um So I guess again, I'll probably stick with just the hallmarks of aging.

But I think that it's all of those things. And so you can look at it in a different way, you could say, well it's just you know, entropy. But actually biology has an incredible ability to renew itself and we see that in different species.

So it's it's not just that and then you know on the programming side we can reprogram a cell to behave youthfully. So that does give us evidence that that's happening as well. So it's all right.

Some of it might not be um uh siloed to be correct all by itself. But I agree with all of it. – And uh well let's say given for this conversation that gene therapy is going to be the most exciting aspect areas of longevity work right now. Aside from gene therapy, what what are one or two other areas do you think are the most exciting in the longevity space right now that you're paying attention to Besides gene therapy?

– Well, that's a good question. Well I got my start in the stem cell space and I think that it's still really exciting whether you're talking about ex zones, you know, byproducts of stem cells or you're talking about the stem cells themselves, the ability to build organs and things like that.

You know the promise of that technology, some of its come to fruition through Wake forest and some of it is still building. Um So I think that that space is has been exciting and I think it will continue to be exciting, especially if we see more loosening of regulations around live stem cells and things like that and by products.

Um the other area is probably kind of unexpected because it's downstream of gene therapy, but it's exactly what we want to fix upstream is some of the blood work.

So you know, I'm really excited about some of these plasma freezes, uh you know, cleaning the blood, removing the antibodies and the potential benefits there that also has application in the gene therapy space.

So that's really promising as are the parabiosis studies that were originally done that I think now we're being all so much that they may not be as necessary and maybe a low hanging fruit for people who are very diseased, very old, having the introduction of diluted or cleaned blood so that the two processes together.

So those are, those are really exciting because obviously with genetics, those things also that we'd want to affect upstream. So um there there are areas to to look at and areas that are moving just a wee bit faster than our space. – Great, well now, now gene therapy, this is this is so exciting. The I I think our audience knows about about D. N. A. and genes at a general level.

What is the approach with gene therapy, how what do you, what are you planning to do or how do you affect longevity with gene therapy?

How Gene Therapy Could Target Aging

What's the 50,000 ft view? – Well, when we look at gene therapy and the applications that it's already been used for. Its vastly been used for congenital disorders. And there are now about seven approved gene therapies uh two that are newer to come through for beta thalassemia.

And there's one coming through for sickle cell anemia, that's more of an editing technology. But gene therapy is editing the insertion or deletion of a therapeutic gene and so that all falls under the same umbrella. But there are five curative gene therapies out there for severe combined immune deficiency and lipo lipo protein like paste

deficiency.

These are like all really big words. But the thing is, is that the proof of concept of gene therapy is, has been done. And the new emerging space that we're working in is not congenital disease, it's not in the rare disease area is for aging associated noncommunicable diseases.

So essentially those are the diseases that you most people watching this will actually die of without intervention. So it's the biggest medical unmet need. And so what we're looking at is taking this very powerful technology that's already been through proof of concept and gotten to drug status and starting to use it to see if we can actually etch away at what is driving aging at the cellular level. And so we look at several genes since we look at the hallmarks of aging is being where disease starts from.

Um these degradation things that are happening at the cellular level, we know that we will eventually have to have a therapy that treats all 10 of those.

But right now, you know, we're working on hallmark's sort of like three and five at a time. So, for you, what that means is that um gene therapy would be a type of technology that you would have injected in your body.

It might last for a lifetime or need to be redone every five years. There are different ways to intervene in disease. So, right now, what we do is we have a healthy body, we have a disease body, and then we start intervening with things to keep you from having the symptoms of a disease.

Um maybe Alzheimer's or heart disease. Um we would go upstream back over here and we would genetically modify yourselves to not behave old uh and accumulate the damage that would then cause the end state, which would be the diseases of aging.

– And so let me see if I understand this, right? So, with with the approach you all are taking is to take extra copies of good genes and adding them to the person. I think I've heard you use this analogy before about P 53 gene in elephants and that that's maybe a useful example too.

– Yeah. So, like what we actually do. So, gene therapy kind of as a whole concept is is probably one of the simple simplest medicines to kind of get your head around. It's the addition of therapeutic genes.

um That will then make yourself healthier. But then what are those therapeutic genes? Yeah so we we work with several candidates and there's four that were we would call live that we're acting on now that we're working with in research and development.

And those would be things like P. G. C one alpha which is a gene that you up regulate when you are working out. Uh So you know having a little extra dose of that uh when you're maybe sometimes sedentary in your life wouldn't be of harm.

We work with a gene called telomerase reverse transcriptase. It's a long name. But what it does is it lengthens the caps at the ends of the chromosomes that shorten as we age.

So that's important for lifespan. That would be a lifespan uh related gene. We work with full Stanton that increases muscle mass because as we age we get frail we lose muscle.

And then the last one we work with his clothes which is a general protector. And so kind of the names may be unfamiliar with you but these are all genes that make cells behave more healthy. And in animal models they extend lifespan and health span most importantly.

– And and these genes then the extra copies are are added on and we can talk about delivering a little bit but they're they're delivered to the patient somehow. And this is different than things like CRISPR that we hear about where there's gene editing going on, right. Um these are the actual genes from the patient, their own copies that you put put extra copies back in.

Is that how it works? – Well with with CRISPR. So that is also gene therapy but like you said, that's editing that's modifying the chromosome in the gene therapy that we work on.

We're not modifying the chromosome. We're putting genes in the nucleus of the cell. But without modifying your naturally occurring genes, we use human genes.

So these are gene bank genes that are familiar to all humans. And so they are human genes. Now there have been trials not from our company but in the eyes of blind people in which they used the genes of light sensing algae.

And you're going to hear more and more about this sort of xenotransplantation transplantation of genes from different species. We don't do that. We work solely with human associated longevity genes.

– Now you mentioned putting the these extra genes right into the nucleus into the chromosome. That sounds like a very tricky work.

Delivery Methods and CMV Vector Innovation

But actually the delivery systems, you've come up with some innovative ways that are relatively noninvasive for for delivering these. That would you could really see this scale very, very well for human use maybe you could talk about that a little bit.

– Sure. So we use vectors and these vectors are really adapt to docking with the cell and getting genetic material into the cell of a human. We're working on two forms of delivery.

One would be intravenous and another would be just an intra nasal spray. So you might just uh spray your gene therapy once every six months or once every year or uh less or more. That that would have to be tested and get the benefit of a gene therapy. The thing with the internet, it would be less gene therapy. Whereas if we did an intravenous, you know, you might be good for you know five or six years or more.

– I see, I see and the and the gene and the inter nasal spray. You're using a new model with cytomegalovirus, right, instead of the adenovirus that's much more effective or or it has a larger capacity I think, is that right?

– Yeah, absolutely. So um we're using the cytomegalovirus and so a lot of people hear the word virus and they kind of go, oh no, because especially, you know, we've learned a lot about viruses lately, but viruses, um what is done in gene therapy is they're not able to get you sick, we take out their ability to copy or replicate in your cells, we take out the genes that would cause a disease and we use them to deliver therapeutic genes. So we're kind of like outsmarting the virus and with our gene therapy delivery method. What we're trying to do is get a bigger payload into cells and therefore we can create what's called precision medicine.

So if you were born with one of those congenital diseases that I mentioned at the beginning of the talk but you also wanted to get a set of longevity associated therapeutics.

You could potentially depending on the size of the gene get those all delivered at one time and you know we all know that preventative medicine would be the best for society rather than uh you know acting later in disease. So I imagine these would be given at quite young ages. – Yeah it's really some exciting work you're doing. Maybe you could speak a little bit to your paper that came out recently in the archive with George Church as a co author and folks from Harvard, folks from Howard folks from a number of universities and and I believe that was some experimental results both in mice and humans. Maybe you could talk about that a little bit for our audience.

– So in the P. N. A. S. Paper where were vastly just focused on the mice in that paper. And it's it's pretty exciting because by using this C. M. V. Vector we're able to not only attain um the delivery of the gene therapy which was really the goal of the paper but we were able to create a significant lifespan through just giving these genes and we were able to re dose which is something that Historically with the most traditional delivery method for gene therapy. We're not really able to do without other interventions around that. So we got 41% lifespan um with mice in the the C. M. V. Uh And that was fantastic because what that did is that showed us that we could in that aging itself is

malleable.

And that we could increase the lifespan of these mice. The healthy lifespan of these mice. And um they were healthier by all accounts that we checked. Their blood glucose was lower even when injected with high amounts of glucose Sugars. And um they reacted much more quickly about three times faster or more than the untreated mice. Uh they just they looked better.

Um the lab technicians who took care of them thought that they were eight months old mice when they were 24 months old. And then um as the untreated mice all started to die are are mice carried on to be healthy. And so like what does this mean for humans?

Because like you know the mouse thing all becomes really boring especially to laypeople. Um so these mice were treated at the equivalent age of about 56 of human years.

Mouse Study Results and Healthspan Gains

And uh that that might be a point in time in which people decide to intervene with genetic technologies until you know we all know that they're safe enough to use within childbearing years. Um if you are only going to live to be 78 or or between 78 and 83 which is an average lifespan for American right now uh with these therapies, you would go on to live for about 100 and 10 years and you would have at least um you know, 15 to 20 years of health span along with that. So that that just means more of doing the things that you love to do. I mean if you look at the health span curve, um I know Dr. Lufkin, I we're all trying to square the curve so The curve kind of goes like this um you know, we, we start seeing population drops in the 30s and and then they go down quite steeply um and then, you know, the longest lived humans are about 120 years we think um and very, very few of them make it there.

But when you look at that curve, there's something that you're, you're, you may not be paying attention to that your, your your best years are actually all shifted towards your young years, your young years, when you're educating, going to college, um Goofing around um your actual years in which you are in retirement are not just in the years where your colleagues are, are passing away, they are not in optimal health years.

Um they are in the years of diminishing returns of what you can actually physically do. So, you know, the benefit of what we're all trying to do here um at this conference is, is really squaring the curve or or extending it. Um And you know, with genetics, we hope to be able to break that bottleneck eventual For people so that they get even more great years. But right now we're just working on that health span. So so the the translation of the paper to the average person is you know, 15, what could you do with 15 or 20 more years of active, healthy viable living, you know, in which you're not debilitated or diagnosed with any um critical diseases?

– Yeah, that health span concept is so important. I just want to geek out a little bit on the on the paper with the mice usually die normally. They high percentage of die of cancer as when they age out.

I'm curious the mice who had the gene therapy and the 40% longer lifespan and health Spahn did they, did it just push back the disease that ultimately killed them the cancer or did they get it earlier in a milder form that didn't quite kill them?

Do you know what I'm saying? Did it uh did they still get the same diseases even. – So we said that we saw no increased risk of cancer. We actually didn't see cancer and are treated uh they did seem to still die of aging associated disorders associated with the system wearing down.

And so um this is why it's critical. So you know when we look at something like lengthening telomeres and these were the mice that lived the longest. And and they were the healthiest by all accounts as far as like metabolic activity and everything else. The telomerase mice were the best.

Um the reason that we're looking at combinatorial gene therapies and and that's the focus of the company is because one gene therapy targeting one hallmark of aging and telomere. Attrition is a hallmark of aging isn't going to do exactly what we're we want to do. It would probably help enough people today live long enough to see the

next next technology who are under a certain age.

And so it's really important to get that out to people. But this is a very, very, very powerful gene. It's one of the most powerful genes in all of the regenerative medicine realm, but it on its own cannot cure all of aging.

And so um I think that that is one of the strongest points there, but it on its own uh probably could protect a lot of our pop population against something called genomic instability, which is another one of the hallmarks of aging because these mice were not getting cancer. And that, as you know, with a lab mouse is often what they die of.

– Yeah, it's interesting um unlike um like cardiovascular research or cancer research, the interesting thing about people that are researching longevity is they all have skin in the game because they're all gonna die of aging eventually. And so there's a real excitement or enthusiasm among all of us. We all want to be healthy and live as long as possible. But uh you are you are unusual in that as an investigator you have actually um taken had the gene therapy performed on yourself. It was a while ago but maybe you could talk about that particular, which genes did you get and you know how what was the experience like for you and what were the effects of it? – Yeah. Absolute.

Self-Experimentation and Human Data

So in 2015 upon starting the company we thought that the biggest impact that we could make is actually get human data as to if these therapies would work or not.

And we were we already knew that probably treating aging would be a combinatorial um type of therapeutic. So I took we planned and I was the first person in the world to take telomerase reverse transcriptase.

The one that lengthens the caps at the ends of the chromosomes that shorten as we age. That therapy. And then I also took a therapy called fullest statin. Uh it blocks something called myostatin that limits our muscle growth as we age. And so I took those together now since then in 2020 I took telomerase reverse transcriptase again and some full a statin.

But I also took P. G. C one alpha and clothes. So um to to new gene candidates to us to to actually look at treating aging and you know I think that this was it was an important part of of calling out and saying, look, we are moving too slow.

41 million people will die this year of aging associated diseases. And we don't have the legal authority to help these people get access to new medicine.

Most biotech companies are dying in the desert of drug development between a drug candidate and actually getting that drug candidate to humans. And um, this medicine is more succinct and powerful than any medicine we ever had before.

So what the regulatory system is set up for our, you know, drugs with potential side effects in a myriad of ways. So let's say we take a pill, you know, it could damage our organs, our digestive organs or stomach or liver, our kidneys.

Gene therapy is just up regulating the protein at the cell, the unknown protein with the benefit. Now, that's not to say that there couldn't be bad outcomes. It's just it's it's more sustained.

There isn't a lot of there's, well, there there's really no side effect except for the the up regulation of the protein that you're trying to up regulate and the therapeutic benefits of that protein. And that's why you're seeing one gene therapy after another be approved through the regulatory system for congenital disease.

So, um, so that was kind of our call out that uh we're moving too slow and that people need access to these technologies and trying to start generating the human data, which is the most important to human outcome. Not mouse data.

We are not mice. It doesn't work the same full of statin, doesn't work the same in mice as it does in humans and give them a little bit of full of statin these girls get so big, you cannot believe their muscle mass, it does it doesn't work that way in humans and and we need to know how these drugs work in humans. So um yeah, that was that was the beginning of the company and just as a, you know, like an insight to that um I really wasn't a traditional longevity person. I was looking for cures for kids.

And so um the risk that I took initially with that therapy wasn't based in me trying to live forever now. I I'm much more excited about the future. I mean, you know, people, you know, they're going to die of something eventually, but I think that by intervening, I'm a lot more optimistic of how long I think that humans probably could live now if we were not so risk averse.

– Well, before we talk about the future, one thing I wanted to mention is bio viva is us company and it it works in the US but you have collaborated with international companies that are testing gene therapy and some of your gene therapy on patients.

So there are opportunities actually, if people are willing to do that. Um could you speak to that a little bit? – Yeah. You know I so in my NBA my thesis was all around a new regulatory route for drug development humane route rather than you know, the route that we have today.

And and I'm not criticizing the regulatory system. I understand why it's so risk averse. Um but people who are terminally ill need new access and I really got a huge education in this working with medical tourism companies, companies who can legally use consensual experimental medicine by consent in humans.

And I just feel like um in the US right now we're really missing the boat on this. And because this gave us the first ability to look at data um how drugs perform these drugs, these gene therapies perform in humans. Of course if anyone wants to use a construct based around any of the work that buy Aviva's done.

We asked for extensive preliminary data. Um so there's pre and post data and we asked that the companies follow these people for years.

Regulation, Access, and the Future of Longevity Medicine

So traditionally in medical tourism people might you know, travel outside the us participate in something and there's really no real follow up. And so what we demanded is that we would like to be part of understanding this data looking at this data and that there had to be um 100% accountability and um and it's a difficult task. It's difficult because you know, people run off, they feel great and or you know whatever and they don't want to follow up with testing and so it's a it's a tall order for us but we think that it's vastly important but we think that it's even more important that regulatory zones like the U.

S. The U. K. And industrialized countries step up to the best choice medicine plan and allow people to get access to these technologies right in their countries uh you know more safely without having to travel. And and that we start helping more terminally ill patients now with more advanced medicine. – Well looking towards the future in this space.

What are you what are you excited about? What's happening next? What are the challenges you're facing? What can we look forward to? – Well, I mean, you know, one of the big challenges is always funding around research and development because it's it's it's a very slow process to product ties.

And you know as the economy is failing, we're we're hoping that people will you know invest in in the future of this technology, things that get me really excited about today outside of the couple of things we talked about in the beginning is the work that you're doing.

Not only are you bringing people here who are professionals in a space that are trying to bring together a plethora of new tools for doctors like you.

I mean the whole goal of our technology is that when people come to you in the future you have some really powerful tools to add to your arsenal, but your education and your, like, I was complimenting on you that, uh, for you on this earlier, about your posts, you know about diet and exercise and things that people can do now and you know, how we've been really tricked into a incredibly unhealthy diet.

I mean, if you want to live to see the technology of the near future, you you need to step up and do simple things now in which to help that, and you've just, you've just kept up on, on everything.

You know, you offer the latest of what can be offered uh, to patients. I mean, it's it's absolutely critical because it really starts with your doctor today. Very few people are going to go and look up.

You know, what we do in in genetics. I mean, they'd have to be very future forward people. I mean, you're you're the first stop to for an average person to go and find out how to intervene in their life and and the better steps they can make right now and get them interested?

Hopefully in the next steps. – Well, that may be the answer to the next question I was going to ask you, which was what's the what's the single most effective action we can all take to improve our longevity and stave off aging.

If there was one thing you had to pick other than genetics. – All of the things that you talk about. I mean like nobody, I don't even need to answer that question. They're already here because they're watching you not that well. – How can people reach you, Liz? Well put well put in the in the notes, how to connect with you, but maybe you could just tell us you're the best way to reach you on social media and your website as well. – Yeah. So you can look at bio viva B I O V I V A. Um It's bioviva-Science.com is our website. We have a plethora of different social media sites in which I probably off the top of my head don't have the links for um We we have a social media guru who runs all of that.

Make sure that all of our information is coming out regularly. If you want to reach out to the company. It's just info at bio viva dash science dot com.

And Katarina, my most amazing and tolerant P. A. Will be on the other side of it to answer your questions or or to streamline you through to the routes in which you might be enquiring about. – Great. Well thank thank you so much Liz for being a part of this program and spending time with us today and thank you also for all the great work you're doing. – Oh thank you, thank you for having me.

– I just had a great interview exploring gene therapy and the possibilities for longevity with someone who's not only an expert in the field but who has also tested the longevity gene therapy on herself. Liz Parrish is an entrepreneur and founder and CEO of bio viva sciences. It was a great time, wasn't it, Liz. – oh my gosh, it was so awesome. You!

I want people to come and watch it. Great questions and great conversation.