Reversing Aging: The Path To Longevity Escape Velocity Transcript

(Transcripts are generated by AI and may contain errors)

Introduction to the Longevity Summit

Welcome, everyone, to this first edition of the Longevity Summit. It's an exponential longevity summit, by the way, and we're here to learn about how to leverage AI to outlive disease and to live young for a lifetime.

And to kick this off, I have a guest that is probably known to most of you. Aubrey de gray. Doctor. Aubrey. Dr.. Gray. And he's been kind enough to join us in this conversation.

I think you're going to find it really fascinating. Aubrey, welcome to, the Exponential Longevity Summit. Well, good morning, Jeff. Thank you very much for having me.

Yeah. So maybe you can, rather me read your bio. Why don't you, maybe rattle off a few things that you'd like the audience to understand about where you're coming from?

Yeah, sure. So, yeah. Well, as you just said, my name is Doctor Aubrey to Gray. My current affiliation is. I'm the president and chief science officer of a nonprofit based in California named Elevate Foundation.

Elevate stands for Longevity Escape Velocity, and we might talk about that later on. It's the third of the nonprofits that I've led over the past 20 years.

And, during that time, and indeed for the previous, I got to ten years before that, I guess. I, I've been working on identity. I've been interested in trying to bring the rather ghastly process of aging under comprehensive medical control.

Aubrey de Greyu2019s Background and Mission

I got into the field, in my early 30s, basically, as a result of discovering that hardly anybody else was trying to do this, which I find extraordinary.

I was previously a computer scientist. And, you know, during that time of a homemade, I guess, a few contributions to science and, come up with new ways to think about how we might bring aging and to comprehensive medical control.

And I've also spent a lot of my time and effort, essentially building this community, growing the number of people who, involved in this, which has certainly also had, quite a significant impact.

But of course, there's still a very long way to go. So I'm definitely not resting on my laurels anytime soon. Sure. No. That's great. No, you've done tremendous things for the field.

And to your point, the the community is growing rapidly, quite honestly. And, a lot of people jumping in, which is great, but honestly, to so, you know, I want to one of the things that I've discovered in, you know, the pursuit of longevity here at Gladden, longevity is that you can do a lot of things to try to optimize health.

You can do a lot of things to try to intersect the hallmarks of aging. So we say, but at the end of the day, I don't think any of us get to be, 100 and have a body of a 30 year old.

If there isn't rejuvenation going on, and I don't know, would you like to speak a little bit about your insights into rejuvenation? Oh, absolutely. So, first of all, the word.

So, so I think 17 years, I had a journal, an academic journal and rejuvenation research. And, I had to work quite hard to get the publishers to accept that name.

The word rejuvenation back in the mid 2000, was very much associated with, you know, cosmetics basically. You know, with what we're talking about. And I thought that that was a shame.

And we need to reclaim that word because, if there's one single most important contribution that I've made to the science of longevity, it is to realize and to promote the idea that repairing the body, in other words, restoring its molecular and cellular structure and composition to something like how it was as a early adulthood, is actually better than slowing down the rate at which the body deteriorates.

Very counterintuitive. A massive paradigm shift relative to the way that academics were thinking 20 years ago. It's. It's interesting you say it's easier than, I mean, that's, that's that's kind of a stunning statement.

So, so the audience understands that, right? Because a lot of, practices, are focused on slowing down the aging process. And yet you're talking about rejuvenation being actually easier.

And in one sense, we've kind of come across that in our own process here. So tell us about the ease of rejuvenation. Okay. So let me first of all, clarify that when I say it's easier than slowing aging down, the comparison I'm making is with slowing aging down a lot, like, you know, birth rate, whatever.

Right.

Why Rejuvenation Beats Slowing Aging

Clearly, we already have ways to, slow down aging a little bit, and get people to live a few years longer in a healthy state. Maybe, if we're lucky. Which is definitely a lot better than nothing, but it's not what I'm talking about.

Of course. That much, then rejuvenation is demonstrated by the fact that we can do it already. But the thing about rejuvenation is you, effectively sidestepping, ignorance of how the body works.

Idea is you look at what the body's made of, you know, the structure and composition of the fat at the molecular level. And you say that it's different in an older person that is in a younger person.

And when especially focused on what happens before people get sick. So let's say comparing a six year old to a 20 year old, not comparing an eight year old to a six year old.

And here, the the difference is, you know, pretty established, you know, things that, you know, types of, molecular waste product that accumulate, for example, or mutations that accumulate or stem cells that are depleted, things like that.

And so the thing is the ways in which those changes happen, still very poorly understood. And that sounds like a big showstopper, and it's a big show stopper to stopping those changes from happening.

But what it is not is a showstopper to to simply restore reversing that by, restoring function. So for example with stem cell therapy, restoring the number of stem cells.

One of the, one of my innovations was to bring in, enzymes from bacteria that could break down waste products that the body doesn't know how to break down on its own.

But here we are, you know, completely we don't have to alter or slow down the rate at which these changes are being, brought about at all that can, we can just leave that process alone.

We kind of just, run that process by doing the opposite, but I, I don't that's why it's easier. Yeah. That's fascinating. You know, I think a lot of people, when they start to think about when it, I think when they sort of reached this point where they feel their own mortality.

Right? In a way, they they don't look like they want to don't feel like they want to can't do what they want to. It's a

fork in the road for them. And then they decide either I'm going to acquiesce to aging or I'm going to adopt a get healthy strategy.

And I think to get healthy strategy to your point, pays dividends, right? They are healthier. They can do more. They can play golf longer or whatever they want to do five, ten years, but it doesn't really solve the problem.

Everybody that adopts a get healthy strategy is still aging, and they're still getting older, and they still basically go over the Niagara Falls. Right.

So and it's worse than that drive because the difficulty is that when you're doing all those things, you have a tension, a trade off between quality and quantity.

A lot of the things that are bad for us are things that we enjoy doing right. I mean, I first, there's a good example of that. If she died a month or two ago, at the age of 79 from lung cancer, she had, quote, a pack of unfiltered camels every day of her life.

And since she was 14 years old. Pretty impressive that she didn't get lung cancer until 79. But the point is she's a biologist. She's actually the reason why I got into this field. But, so she knew perfectly well what she was doing to herself.

But she enjoyed smoking and she knew that the, benefits of not smoking would only give her a few more years of life, but it just wasn't worth it. Similarly, you know, if you don't actually enjoy jogging or whatever, you know you're not going to do that.

Whereas in the case of proper, you know, medical control of aging by rejuvenation, there is no trade off between quality and quantity, well worth quantity.

You get lifespan, you get life extension as a side effect of health extension. Yeah. No I think that's a really interesting point. You know we think about longevity in one sense as being a, you know that it's kind of a byproduct of being healthy.

But what you're saying is that being healthy is a byproduct of longevity. So you're kind of flipping the equation, right? Well, no, I say that on purpose to have a side effect of being healthy.

It's just a question of how you get healthy and how healthy stay healthy. Yeah. Very interesting. So let's talk a little bit about, escape velocity. You mentioned that earlier on in your, in your introduction.

And, you know, this is a term that's been kicked around now for some time. I think Ray Kurzweil may have been the one that initially maybe you were the one that initially introduced it, but I don't know, I heard it, I've heard it, for about a decade now.

Longevity Escape Velocity Explained

I would say maybe a little more. Talk to us about that. Yeah, it was me. In 23, if I remember. Rightly, it was you. Okay. Right around the same time, started to, promote the same concept.

His original phrase was live long enough to live forever. Yeah. No, I think my phrase, which I'm quite happy about. Okay. Anyway, yeah. So it had become a bit of a meme now, and it's a very simple idea, and it arises from the fact that the way we're going to get this control over aging is by rejuvenation.

So, you may have noticed that your audience may have noticed that I have been using the word comprehensive to describe the, amount of control over aging that medicine needs to achieve.

I didn't like it. And the reason there's a difference there is because if we get fairly close to complete, if we can think of like two thirds of aging.

Right. We buy ourselves time if you consider someone who's, let's say 60 years, an average 60 year old, a biological 69. We are fairly good at rejuvenating.

Not 100%. We might be able to take them back to biologically let's say 40. Okay. Now the thing is they're still going to be aging. They're still going to be have these processes that lay down this damage I was talking about earlier.

Right. Eventually they're going to be biologically 60 again, but not until they're 80. Right. That's handy because it means that we can, try and, re rejuvenate them when they're 80, but which is not, you know, if we think about what incomplete rejuvenation means, what we mean is we're essentially talking about two types of damage.

The easy damage and the difficult damage they would define as the damage that we know how to repair, the damage we don't know how to repair it. Right.

So then we can apply these interventions the damage repair interventions as often as we like. So for practical purposes we're going to assume that our eight year old who is biologically 60 for the second time, is actually completely full of difficult damage because the easy damage being repaired all the time. Right.

That's really a shame really, because it means that, the when we apply these therapies again they're just not going to work. The person is going to carry on getting biologically little bit because we've had those 20 years.

That's not going to be the case. It's going to be a long time in biomedical research. And that time we're going to have shifted some of the damage from the difficult category into the easy category.

In other words, we're going to be able to fix them and that that we will be able to re rejuvenate the same people, 80 so they won't be biologically fixed for the third time until they're hundred.

And so so this is what I've called escape velocity. It's the minimum rate at which researchers will need to improve the comprehensiveness of the damage repair therapies.

You know that that people who are always going for the, treatments will stay one step ahead of the problem and never have enough damage to make them sick.

Right. Yeah, exactly. Now it's interesting, I think if you're listening to this, I think the idea is still and, you may disagree with this, but I'll run this by you is to stay as healthy as you can right now, because there are therapies coming that will take you back in time.

And I think what I've experienced is that the deeper somebody is in the hole of aging, the harder it is to pull them out, at least at this point in time. Right?

So good. Right? So, so staying young. And I also wonder if the 60 year old, they got rejuvenated back to 40 since there was still some unrepaired damage.

And we know aging is an exponential process. If that wouldn't accelerate so that he's 60 again, maybe in ten years instead of 20 years if you don't. So yeah, no, I mean, the point the feedback that you just spoke about this like accelerate exponential acceleration.

But mostly, I mean way of stating it is the rate at which damage accumulates is proportional to the amount of damage you've already got. Right. Which means that actually know what's going to happen.

And if you take someone back from biologically 50 to biologically 40, they will get back to biologically fix the at the same rate they used to. It'll be an exponentially increasing rate, but the the initial rate at age six.

Interesting. Interesting. So certainly we cut back to a couple of other things you just said. Staying healthy. Absolutely. As long as you can is completely right.

So I mentioned how, you know, at the moment we can slow down the process of aging. We can't reverse them at all. Really? But we can extend them down a little bit.

I want it to be understood that I'm not in any way disparaging that there are two reasons why that's a good thing. First of all, in its own right, it's a good thing because any extension of healthy lifespan is better than nothing, but also for exactly the reason you said that it improves one's probability of making the cut.

And because and then when the the real, McCoy comes along. Exactly. So speaking of the real McCoy, how far away do you think we are from that? When do you think we might reach escape velocity?

Yeah.

AI, Drug Discovery, and Biomedical Acceleration

So, of course, this is pioneering technology, which means that any prediction of how soon it's going to come to fruition is very, very speculative. But I believe, you know, I unlike most of my colleagues, I will have to say, I, I believe that the this experts in this field have a duty to give some kind of prediction.

So the only thing I always do is I make sure that the probabilistic one. So I said that at the moment I think we have a 5050 chance of getting to learn gravity escape velocity, essentially getting those first 20 years of postponement of the pathology to make life, within the next 12 to 15 years from now.

Interesting. I do definitely think that at least a 5 to 10% chance that we won't get there for 100 years because we hit all manner of unforeseen obstacles.

But, you know, that's fine. A 50% chance is quite enough to be worth fighting for. And so it means that most people alive today are in a position to benefit if that prediction is correct.

You know when I, when I look at the AI world. Right. And I look at the the acceleration in AI, and I look at what's happening in the quantum computer space, and the fact that quantum computers may be closer than we, than we ever thought.

And then you've got, general intelligence AI and you get you get this acceleration. It's almost more than exponential. It's almost like a double exponential of, basically computing power and the ability to solve problems.

It makes me wonder if we may not reach escape velocity even sooner, quite honestly, because it's hard to underestimate or overestimate what? It's hard to overestimate the impact that might have.

Yeah. Yeah. Okay, so quantum computers probably won't make much of a difference. Firstly, because big ones won't be around for a while. I think the first problem, the first, change that's going to happen in society when we get going, who copied it is that everyone's bank accounts are going to be, emptied because, you know.

Right. Sure. That's, the, but with regard to AGI on classical computers or indeed narrow AI, but still very smart AI. We're already seeing that, no question.

Right. The most conspicuous examples of how we're seeing is are ones that do not relate to longevity per se, but to biomedical research in general. So the single best example of that had undoubtedly AlphaFold, the right.

That, that, that determines the three dimensional structure of a protein from its amino acid sequence, which was a classical problem with AI for decades.

And it's not been completely cracked, pretty much. Right. But there are many other examples like that in drug discovery. Essentially what machine learning as of today can do is take very large datasets, including very heterogeneous datasets acquired in different ways by different groups, and discern patterns in them that, you know, you never be able to do manually.

And that rather powerful and high quality predictions of what kinds of drug we're going to have, what kinds of benefits. And this is certainly being used in longevity.

One of my oldest friends in the field, Alex Veronica, runs a company named in Silicon Medicine, which is almost a unicorn now purely as a result of having, leverage that concept.

You know, other, other variations on that same are happening all the time. There are going to be many, many ways in which I will accelerate medicine for sure.

Yeah. Yeah, I agree with that. I think we may be surprised, quite honestly. I'll just leave it at that. And I think we may be surprised. So, let me ask you this.

What what areas of research, is your, not for profit kind of addressing now that you think are maybe the most neglected or the most in need of attention?

Yeah. Well, you've definitely hit on the right word, the neglected. So that's always been what I've chosen to do to focus my time and my efforts on is to identify the areas whose importance is not reflected by how much effort money is going into them.

In general of that, because the near term benefits of doing work in those areas, not appreciated. So first of all, explains why I have continued to work in the nonprofit sector rather than start a company like almost everybody else.

Neglected Research and Mouse Rejuvenation Studies

And, companies, a place definitely, because investors tend to write bigger checks than the others do and get done. But there is an inherent short termism in what you're allowed to do.

Basically pretty much always. Right. Time in academia, of course, for a different reason. You have short termism because people need to get their next grant application funded.

So they need to get a paper out in nature or science or salary and that that determines what they can do. So I work on neglected things. My previous organizations, Methuselah Foundation and Science Research Foundation, I was focusing on individual components of damage repair.

And then, by definition, divide and conquer approach. It means basically you have to identify all the various ways in which the molecular and cellular structure of the body changes with age.

And then you have to develop ways to repair that damage and of course, different types of change. Require different treatments, though some of them are much less developed than others.

Some of them I never even worked on at all, because they were already being worked on by other people, because they were doing progress. Was was nice and rapid.

But some were much harder. And that's gone. Well, you know, a number of the things that I pioneered back then have now been spun out of startup companies that, proceeding quite happily.

But any divide and conquer strategy for anything necessarily has a second stage, which is having got your components working reasonably well individually, you have to stick them together.

And that's what the whole bunch of other stuff, all the unintended and unanticipated interactions that might happen is, right. So that's what we're focused on anyway.

Foundation, big flagship research program takes multiple different interventions linked up with, interventions in general and, fix them together all together in the same month.

Of course, we start with mice that are already in middle age, because that point and the idea is to say how much longer we can get them to live. Of course, as with humans, how long they live is a side effect of how long they stay healthy.

But we do measure health as well in a lot of different ways. Right. And anyway, so the first experiment in that program began early last year, 18 months ago.

And it's, some of my mice are still alive, which is nice because the mice that 18 month old and the other mice that normally live only to, two and a half years, they had one year to go and to live.

Six months later than that. We very much hope that some of them will live longer than that, because going. All right, it's, you know, we've learned a bunch from this experiment, but even even, without just without taking what we've learned from this experiment, there are still lots of other interventions that, individual promise, and that we absolutely want to combine in a follow up study and then another follow up study until we get to what I've called robust mouse rejuvenation, adding an entire year to the lifespan of of these mice, starting in 18 months.

The, best that anyone could do at the moment with basically calorie restriction, which works far, far better in mice. It does in humans, is about 3 or 4 months.

So we want to treble that, actually. And, we might be able to beat that with the first experiment, but we won't treble it. So we've definitely got more to do, right?

Because the difficulty inevitably, is that these experiments are expensive. They, do need to be, mostly front loaded because. But what are you going to buy the mice then?

You're also going to do these because they're rejuvenation treatments. You apply them once at the beginning of the experiment, and then basically you just keep the mice alive and wait and watch them. Interesting.

That's interesting. So basically, the bottom line is that I need $3.5 million. I can kick off in this next experiment. And it's very frustrating because we've had the next experiment design.

It's up on our website anyway after orgasm or two. It's been up there since December. And, you know, of course, we're using that time that we're waiting to try to build a build the war chest.

We're using it. Well, you know, refining the study, incorporating, knowledge not only from our ongoing study, but from the literature and from other groups.

And so, you know, that's not wasted, but it's definitely a delay, which is obviously going to cost lives in the long run. So the sooner I get that, we'll test will be saved.

Got it. Okay. Well that's interesting. You know, when we think about, longevity over here, we've been thinking about this symphonic approach to it where there's a timing, a sequence of frequency, intensity and duration with which you apply different technologies as you go through this.

It's not it's not like you just, do one thing one time. In humans, per se, we, we see it as an ongoing process, concert with symphonic process. It's interesting. You're doing kind of an initial, intervention and then seeing how it lasts.

Have you thought about, sort of us more symphonic approach to it, or is that down the road or what are you thinking about there? I mean. It's there's a logic to that.

But my belief is that the general way of thinking about intervening and aging applies much more to the current interventions that we can do, the ones that slow down this or that thing.

So damage repair, which repair I mentioned earlier is it sidesteps, ignorance of how damage is laid down in the first place. But another way of saying the same thing is that we don't actually manipulate metabolism at all, because I

tell the body how to be out, how to operate more.

Cleanly so to speak. And really the symphonic approach is all about that in the same way that, you know, for a simple manmade machine, whether it's a car or an airplane or whatever, you know, there are ways to, make it work better that involve damage repair, like, you know, getting rid of rust.

But there are also ways to slow down the rusting in the first place. And the other types. That's right. And then the more I, I do like your word symphonic.

The human body, of course, that's true to a much greater degree.

Epigenetic Reprogramming and Yamanaka Factors

Right? Let me just let me just roll this out in front of you, too. You know, Sinclair has done some DNA methylation rejuvenation, right? Turning back, the methylation clock with the Yamanaka factors and then with chemicals.

And I think he's doing it and has done it in cell cultures, I don't know. Is that any thing part of what you're thinking about, too, is this sort of, epigenetic.

Reprograming. Is that a piece early? Yeah, absolutely. So, yeah, as soon as the, Yamanaka factors were discovered back in the mid 2000, people, you know, we're very excited about the potential rejuvenation effects in vivo, but people knew from the get go, that they actually wouldn't work per se, because it would basically turn the body into an embryo again.

Oh, I mean, no, that's. Yeah, but each cell would become embryonic and that would be bad. But then people said, well, look, I think, I think we just recognize that this is a process that takes a period of time in cell culture.

And therefore, if we apply the process only briefly in vivo, maybe we'll get away with it. But, the first question was, can you play anybody that at all?

And a great friend of mine, Manuel Serrano, who now works at Altos Labs, try this. He just, they're expressing these genes in life and sure enough, that it work.

The effect was, deleterious to their health, as expected. They got two cancers, a special type called a teratoma, right? When you look at it. But they showed the principle work.

So actually, Serrano decided to do other stuff at the time thereafter for a while anyway. But, a colleague of his, in Belmonte in California ran with the obvious next step, which was to do the thing only briefly or episodically.

And sure enough, in mice you can get nice rejuvenation benefits without at least without and immediately seeing any anti-cancer effects. And this is what I, I just to write a check for $3 billion and, and about the same kind of thing and certainly, you know, we're excited by this to, indeed.

One way or another, expressing the Yamanaka factors, probably without, one of them, say, make. That's also an innovation that David Sinclair, anyway, doing that can be it definitely on our list is one of the interventions for our Amato for our next, nice, nice.

So just so the audience understands, there's four Yamanaka factors, and now they're to avoid the cancer risk. They're just activating three of them and still getting rejuvenation.

Yeah, actually, it's it's more than that. It's not just that this is another gene, and therefore it's probably a bad idea to express it. It's also that if you only have a F and K and not an, then you get left, differentiation and function.

It seems that you don't push cells back into into complete pluripotency, only to a kind of, more regenerative state. And that's rather important, not just because it means you don't get to every time.

There's one thing that has been somewhat swept under the carpet, I have to say, and I think it's very important not to, is that in vivo? We've already got a whole bunch of cells that are already pre-cancerous through mutations that have accumulated over the years.

And those cells are unpredictable in terms of how they will react when you hit. They're you know, they're they're sort of static. With a sledgehammer, which is basically what they are.

They're not effective. They're right. We have to hit it with a very gentle sledgehammer, in order not to create a bunch of cancers from pre-cancer or something like that in cell culture in the first place.

Yeah. You got to rejuvenate the immune system faster than you do the cancer cells. Right. So they could and is plenty of progress there as well. And please. Yeah.

Yeah. There has well, great. Well this has been a lovely conversation. Let me just finish by asking you, you know, for the audience, are there, any takeaways that they could that they can have from this conversation?

Any advice that you might give them? Well, first of all, the same advice that you give them, namely, you know, live long enough to live forever, if you want to be done, but also, of course, bring, that long enough closer, you know, do whatever you can to hasten the arrival of these therapies.

Audience Takeaways and Supporting the Field

Of course, some of your audience may be able to help financially. Some of them may be able to help in the same way that you are helping right now by interviewing me, for example.

And in other work, you know, because there's a lot more going on right now in the policy world in terms, improving access to unapproved therapies, for example, this is something that is really overdue.

And that's something, again, some of your audience maybe in a position to influence. But at the end of the day, when we come back to the financing again, it's very easy to look at the landscape right now, and form the conclusion that financing is no longer an issue, that there's lots and lots and lots of money in this field and therefore, you know, no more money is needed.

Ghastly, inaccurate, simply because that money is so drastically, unevenly distributed. Getting the plenty of money that the money is no longer a rate limiter, but the other equally vital area of money is very much a rate limited still.

Yeah. So if you're interested in supporting, Aubrey's work, I'm sure you can go to his website. What's, what is that website. Leviathan. Org longevity escape velocity Foundation.

Okay. There is, You know, one thing I found encouraging is that the Bahamas have now declared aging a disease. And so that's pretty exciting. It's to your point about regulation, regulatory and all that sort of thing here in the state of Texas.

We have, right to try law. So we're able to do some things here that, other places can't necessarily. So just let me actually let me actually talk about that for a moment, because this is a very, very important area that you may be able to help with.

Yeah. So the right to try law, of course there is a federal right to try law. Right. But you have to be terminally ill to get a hold of anything unapproved, right?

I don't know exactly what the law is in Texas, but what I do know is in Montana last year, there was a new, bill passed, a legislation passed which extends right to try to anybody just on at the thing you want to try have gone through phase one.

Okay. If Texas could pass a law like that, that would be an enormous step forward. So if you want, if you fail, you

might be able to contribute to an effort to make that happen.

Then I can absolutely put you in touch with the people in Montana who spearheaded the success. That'd be. Great. Again, I'd love, love to chat with them.

Love to chat with them. That'd be great to collaborate. So a wonderful chat with you. So appreciate your time and all your wisdom. Absolutely. And thank you for having me.

So you're going to. See you again.