POD OF JAKE
#44 – JACK HARLEY
AI-GENERATED TRANSCRIPT

Jake 00:10
Thank you so much jack for taking the time to be with me on the podcast today. Appreciate you coming on the show first discovered you from you wrote a piece called the anti aging state of the art on less wrong.com popular website for people interested in like being rational and tends to be kind of an optimistic technology leaning, effective altruism type of readership. Would love to start, you know, obviously, I want to dig into aging itself. And you know, maybe cover some of your background how you got into it as well. But we'd love to start by just getting kind of an overview, kind of Allah, your article on your thoughts on aging, which a lot of people you know, maybe are not paying attention to or just haven't really had the appropriate hook to get them intrigued about and would love to, you know, your article super interesting and how to point people there, certainly after the episode, but a voiceover I think could be super helpful as well. So would love to kind of start there.

Jack Harley 01:16
Right, well, thanks for having me, Jake. So I'll just summarize what I talked about in this article, which, as you said, is anti aging state of the art, you can look it up. So basically, aging is one of the biggest problems on earth in the sense that nine out of 10 people in developed countries, seven out of 10 people in the world die of aging. So it's it's the elephant in the room. It's been described by some neuroscientists who are aging researchers, as the climate change of healthcare, you know, it's this enormous problem that unfortunately hasn't quite yet captured the public's imagination. And as a result, if you ask people on the street, should we cure aging? Can we cure aging? Most people will be well, first of all, they'll reject the scientific feasibility of being able to cure aging and think that that's science fiction. But many people also don't even think we should cure aging. They say that, you know, it'll lead to overpopulation, it'll lead to a mortal dictators, it'll lead to distributional justice issues. And so there are all these kind of responses that we have. And these fears we have about actually slowing down or even completely eradicating the aging process. So with that in mind, I'll just talk a bit about Okay, what is aging, how can we solve it is a anti aging a real scientific field. So, aging kills 100,000 people per day, and the way they die can vary, some of them will die of cancer, some of them will die of heart disease, diabetes, Alzheimer's disease. But all of these, these diseases of aging, which are responsible for these age related deaths are all driven by the same underlying biological processes, which we call the hallmarks of aging. So these are basically you can think of them as forms of damage. A good analogy that Aubrey de Grey, who I knew previously had on the podcast gave for this idea of damage accumulation is that of a

car. If you don't service a car, it accumulates damage over time. And eventually that damage becomes so pervasive that the car will break down. Well, the human body, although it's many orders of magnitude more complicated, is analogous to a car in many respects, in the sense that we're made up of trillions of cells. And just by virtue of being alive, in the normal wear and wear and tear of normal life, we accumulate damage, and that damage ultimately does kill us, this process is the process we call aging. Now, many people don't think of aging in those kind of hardcore biological terms. But if we're thinking about biological aging, which is distinct from chronological aging, that's essentially what we're talking about. We're talking about this process by which you take a healthy 20 year old, and you just let them live for 60 years, and they become an 80 year old who typically has multiple comorbidities, which means they have multiple age related forms of decline. So that decline doesn't happen for no reason, it happens due to these forms of damage. So if someone has wrinkles, or gray hair, or they have diabetes, as a result of their their aging, you know, most of these age related phenotypic or in other words, changes or bodily physiological changes are the byproduct of cellular forms of damage that accumulate and without getting too much into the weeds, these include things like changes to your metabolism. So in particular, deregulated nutrient sensing, telomere attrition, so most of the listeners may be aware that you know, your telomeres contract or the you know, the telomeres the caps, sorry that telomeres which are the capsular chromosomes, they contract with age, which is telomere attrition, but also you have, you have things like mitochondrial dysfunction, so, the past Houses of the cell they decline. You have more zombie cells in your body. This is cellular senescence, which we'll talk a bit about later. So essentially, these forms of damage drive the diseases of aging. So, in my neuroscience background, we looked at diseases such as Alzheimer's disease, Parkinson's disease, and a key factor in these diseases are the hallmarks of aging things like cellular senescence, this accumulation of zombie cells that occurs just by being alive, it results in inflammation that harms the nervous system, to put it simply, and this results in the kind of neurodegeneration associated with with aging with with normal aging. Now, all of this, what I'm describing, which we call biological aging, is distinct from chronological aging, which is the process of simply being alive. And I think in people's minds, a lot of people. They think that chronological aging and biological aging are the same thing. But actually, they're distinct, they're independent. And one way of thinking about this is to people who are biologically sorry, to people who are chronologically 50 years old, could have different biological ages, someone who exercises eats well, sleeps well, etc, even if they're chronologically 50 years old, may have a biological age of 40 years old, because they they're young for their age, and they might

even look young for their age. Another person who maybe smokes, eats a lot of fast food, doesn't exercise doesn't sleep very well may have a biological age of, say 60 years, which means their aging is accelerated. So chronological aging and biological aging are not the same thing. And what we're ultimately trying to do with anti aging is not stop people from existing chronologically, but stop them from accumulating biological damage. In other words, to retard the aging process, the biological aging process. Now, to give you the white mirror perspective of what this looks like, it means that with anti aging technologies in the future, we want to have a world in which every single human being on Earth, they develop until the age of say, 20 or 30 years old, and then they stop aging. Another way to phrase that is they don't accumulate damage over time. So even if they're chronologically 80 years old, they would still look like a 20 year old. And that may seem very science fiction. But actually, we've already shown in mouse models that we can do this to a small extent, we can take a mouse that is equivalent in human years of say 70 years old. And if we give them drugs to kill this, in essence, cells, which are called synthetic drugs, we can make those mice look like an act like and, and perform physically as though they're a say 40 year old or 50 year old, in, you know, in human terms. So we know that this process of aging is malleable. In other words, the damage that accumulates over time it can be modified. And so really, the goal of anti aging is to find therapies that can keep us young, keep us youthful, and keep us healthy. I think a lot of us when we think about health, we neglect the fact that aging is such a crucial part of health. If you're a health quote unquote, healthy 80 year old, you're never going to be as healthy as a healthy 20 year old. Why is this is because your body has accumulated damage over time. And so even if you're in the top 99th percentile for an eight year old in terms of your health, you're still much less healthy than, you know, the 50th percentile 20 year old. And that's because you've accumulated a lot of damage. And unless we use anti aging therapies to repair that damage, then even though you're healthy for your age group, you're not as healthy objectively unless we repair that, you know, you're not going to achieve your maximum state of physical health and fitness. So just to touch on one other point, I think a lot of people think that the fact that we're trying to cure cancer and that we're trying to cure Alzheimer's and so on, means that eventually aging will just solve itself. But that's not quite true. Because trying to cure cancer is like white to use the car analogy is like waiting until a car completely breaks down. You never maintain the car, you just wait till it completely breaks down. And then you try and repair the car versus anti aging which is basically maintaining the cost systematically, you know, every few months so that the car is always or always in near perfect condition and is always functioning effectively with the human body. We are

an unlucky species as homosapiens in that we don't exhibit Negligible Senescence. Negligible Senescence is a phenomena that some species such as tortoises, hydrous and these, you know, some species exhibit and the naked mole rat which is a mammal like us, whereby they don't age, which means their biological risk of disease does not change over time. As humans, we have an exponentially increasing mortality curve. This is called Gompertz law, you can look this up on Wikipedia. And basically it means that every after the age of about 30, every eight years, your chance of dying doubles, why does it double? It doubles because the damage that you're accumulating associated with aging predisposes you to the diseases of aging. Now, if you're 90 years old, you're probably going to die Pretty soon, you may die of diabetes, you may die of heart disease, you may die of cancer. But the common, the lowest common denominator is that you have aged, which means you've accumulated senescence cells, you've, you're telling me as a short, you know, all these underlying biological hallmarks have predisposed you to die. Now, what actually is the straw that broke the camel's back, and that ends up killing you, that can change. And that's why if you look at statistical data, you may get the wrong idea. You may think, oh, cancer kills this many people. But you may not see that, even if and this is a really crucial point that I want your listeners to take to understand is that even if we cured every single form of cancer on Earth, with a with, you know, with a click tomorrow, that would only stand healthy human lifespan by two years on average. And that's because cancer is an age related disease, such that if you don't die of cancer, you die of another age related disease, so that people who would have died of cancer due to aging probably will now die of something else, such as heart disease, such as diabetes, and so on. So really, the purpose of anti aging is to is to solve the root cause of all of these diseases. Not only is this a more feasible strategy for radical life extension to live past, you know, 100 150 200 years old, but it's also probably one of the best strategies we have for preventing cancer, for preventing all these age related diseases. Because the truth is, if you look at the data, you know, the rate of cancer and Alzheimer's and diabetes, and heart disease is very low, up until the age of about 40. And then after 40, it just starts to ramp up ramp up such that the right at 80 years old for these age related diseases, or use diabetes, as an example, is 1000 times higher, at 85 years old compared to 35 years, it goes up 1000 fold. And that's not a coincidence, it's because the body has accumulated this damage, which is the hallmarks of aging, those nine forms of cellular rust, if to take the take the car analogy that ultimately predispose us to these conditions. So, so really, with anti aging, we're keeping the car functioning, we're keeping it well maintained, so that we don't get cancer so that we don't get heart disease, or at least we get these diseases with the same frequency as we would someone who's 20 years old, or 20. Think about the

last time you heard of a 20 year old who had Alzheimer's disease, extremely rare. In fact, they're, you know, I don't even know if I've heard of a case such as that. And that's because it takes time for the damage to accumulate for the neurological damage associated with Alzheimer's to accumulate, you know, it takes time and it takes these, you know, this inflammation, all of these hallmarks to to for that damage really to progress to such a level that you start seeing symptoms. Now, the other thing I'll note is that, you know, all of these are long term processes, you may think someone just gets cancer, and you know, it's a tragedy. It is a tragedy, but it's not an immediate phenomenon. It's the product of a long time period of accumulating this damage. And there's some great papers published in the world's leading scientific journal, which is called nature, where they explain the changes associated with these hallmarks of aging that I've been referring to, that show how the the macro environment within the body, you know, changes such that it's favorable for tumourigenesis, which is the formation of a cancerous tumor. So we can see if we look at neurodegeneration, if we look at cancer, if we look at any of these individuals diseases, we can see that there is a very clear link between these underlying biological phenomena which we call the hallmarks of aging. And that's also a really great scientific paper. That's the most highly cited scientific paper in the aging field. I think it has 7000 or more citations. You can Google it, the hallmarks of aging. There's a clear link between these hallmarks and all of the diseases of aging, which are the things that kill most people on earth today. So that's the basic kind of premise. The premise of anti aging is that we accumulate this damage in our body and we're using an engineering approach to kind of repair That damage. And the way that this differs from current medicine is current medicine actually allows all that damage to accumulate to such a degree that people start having severe symptoms, you know, whether they have clinical symptoms of Alzheimer's or they, you know, they have cancer or so on. And then we try and intervene. That's called geriatric medicine, or, you know, we're trying to treat the diseases of aging. But that's, that's pretty obviously not the best approach if we think about things from the car analogy. And if we just think about that old adage, which is, you know, nip it in the bud, or prevention is better than a cure, you know, we should try and target things. The root cause the root cause of cancer, and neurodegeneration and heart disease is basically aging. Now, there are other factors that can play a role. For example, if you have a lot of head trauma, so for me, I'm very interested in mixed martial arts probably not the best, if I were to, you know, take it to a higher level and compete, probably not the best thing for Alzheimer's disease, because if you take a lot of blows to the head, if you do boxing, or other combat sports or other context sports, you know, you're accumulating damage at a faster rate. That's another way of

saying you're aging faster. And in fact, you know, many behaviors that we undertake, such as smoking, or eating a poor diet, and so on. One way to formulate those in your mind and understand those is that you're accelerating the aging process, you're increasing the rate at which damage is accumulating in your body, and therefore smokers have higher rates of cancer, etc. But the point is that actually, young smokers don't have a particularly high rate of cancer. So the rate of non smokers in the 80s is like hundreds of times higher than the rate of cancer in smokers who are in their 20s. And again, this is because it takes time for all that damage to accumulate to such a level, whereby people start getting cancers and these diseases of aging. So really aging is the is really the root cause of so many of the public health challenges we have today. It's not only responsible for the leading the most deaths worldwide, but it's also responsible for immense suffering. If you think about the fact that most people alive today, and definitely in the Western world, but even in places like Africa, where the two leading cause of death, a stroke, and I believe cardiovascular disease, both of which are age related diseases, you know, most people are dying of old age, which involves 10 to 15 years, typically, of this slow, painful decline. You know, if you die of, say, a natural disaster or something, it's a tragedy, but it's quick, but with aging, it's a slow, painful death. And yet, that's the default, that 70% of deaths worldwide is this slow, painful decline, you know, you lose your faculties, you lose your, you know, your ability to be pain free, you know, you're in pain, and so on. And, and this is just the default. And so anti aging, even if you don't think that we should solve death, I think it's pretty easy to make a case that solving aging is good, just from a suffering and kind of like a utilitarian hedonic utilitarian perspective, given how much suffering worldwide In fact, it's actually 30% of all disability adjusted life years lost, if we want to quantify it, which is the single largest source of delis worldwide is attributable to aging. So then the next question is, well, what evidence do we have that this Damage Repair approach is actually feasible? If someone had told me like, 10 years ago, that we're trying to solve aging, most people and even scientists in the field would probably have laughed at them. And, you know, I probably would have not taken them seriously either. But the good news is that in the last five or 10 years, a lot of compelling evidence has come out that indeed, aging is malleable. In other words, it's plastic. It's flexible, it's modifiable. And this old kind of dogma that I think many people hold in their hearts, that aging is just this inevitable process. This this, you know, this fatalistic view that we have, which we can touch on later, which is the pro aging trance, you know, it's not true. And then we can do things to modify aging on a simple level, we can exercise and eat well and sleep well. But on a more advanced level, we can actually start making use of therapies. So analytics,

mTOR inhibitors, you know, in the future, you know, parabiosis, or blood plasma kind of transfer or basically filtering certain factors in our blood that are associated with accelerated aging, and also things like cellular reprogramming, which is what David Sinclair, the Harvard scientist who wrote a great book, which is called lifespan why we age and why we don't have to in 2019. What he talks about, it's this idea of reprogramming your epigenome reprogramming cells by using these Yamanaka factors to basically turn back the clock. Excuse me. Dr clock and to revert cells to a more youthful state where they can differentiate into tissues in a younger form and basically regenerate your organs. So there's a lot to look forward to in the anti aging space. I think the key things for listeners, and for anyone who's interested in aging and anti aging to understand is number one, aging is potentially one of the biggest problems in the world. I mean, tell me something else that's killing 70% of people worldwide. That's a solvable problem. Number two, we have a decent enough understanding of aging, where therapies and therapeutic approaches are beginning to work. And we're seeing that in many mouse models, we can extend I think Laura Deming, who I know you're familiar with Jake, has a page on her website actually wishes compiled all of the scientific literature regarding different methods of extending mice lifespan, and there's well over I believe, 150, or, or so. So, we know that there's many different ways to extend lifespan in model organisms. But we also have data in humans now as of say 2019. whereby we can actually reverse the epigenetic age of individuals using different therapies, for example, using an injection into the thymus, what's called thymic rejuvenation, where you provide growth hormone, and Metformin, and thta, this kind of cocktail of drugs to rejuvenate the thymus. And in this paper by Greg Fay, they actually reversed epigenetic age by 2.5 years after one year of treatment. So although you know, epigenetic age is just one biomarker of aging, and it doesn't tell the full story, that's a very promising sign that as a proof of principle, that aging in humans, not just in mice bottles, but also in humans is malleable. And although we may not be able to extend the lifespan in humans by 1,000%, as we can do with the worm see elegance by modifying a few genes. It's promising that between all the new approaches that are emerging, as I mentioned, cellular reprogramming, power viruses, cell analytics, and torian, ambition, and many other approaches thymic rejuvenation, it's very feasible that within the lifetimes of most people alive today, we will definitely start seeing the beginnings of the longevity revolution and the emergence of the anti aging industry, not the anti aging industry that exists today, which is this basically a sham industry $60 billion industry based on cosmetic program, cosmetic products that don't actually modify the underlying hallmarks of aging, but a true anti aging industry with therapies that can be taken to kind of supplement the diet and supplement the existing strategies

that people are undertaking, such as exercise and sleeping well, and so on to extend lifespan beyond the, the limits set by nature. You know, if we really think about it, who wants to die of aging, aging sucks, we don't want to die of aging. But unfortunately, without anti aging technology, we don't have a choice. And we certainly don't have a choice to remain youthful and physically capable of running, you know, marathons into our hundreds, right? Like that's not possible unless we have technologies that can keep us youthful and keep us young. And so as a high level overview, that is essentially the problem. And just a brief introduction to anti aging.

Jake 23:40
Thank you, jack. That's a excellent intro and an overview. And I appreciate you, you starting us off there. And now we can hopefully dig into some questions on some of these concepts that you've introduced, and maybe something that you haven't yet kind of addressed as well. One thing that I think may be an interesting place to start is I had Balaji Srinivasan on the podcast previously, and he raised this concept that a lot of his listeners were interested in, which was that it's actually originally a Larry Page concept, which is that 10 acts can sometimes be preferable to 10% and actually easier than 10%. And I think the strategy and engineering approach of attacking aging directly and the damage that accumulates over a person's lifetime, versus the kind of existing approaches of gerontology and geriatrics is kind of representative of that. Let's go for 10 x versus 10%. You mentioned how if we were to solve cancer, for example, we might save two years on global average lifespan we might increase global average life expectancy by just a couple of years. Because they would die of heart disease or Alzheimer's or another aging related disease. Whereas if we can, you know, even just by 10%, figure out a way to slow aging, that might be eight years. And if we can do it by 20%, maybe that's 16 years. And this is rough math, obviously. But if we can have small success on a 10 x type of goal, then you start to see how not only can we start to extend the healthy human healthspan, and lifespan, but we can also potentially buy ourselves time to figure out additional technologies to extend the lifespan and health span further, and that kind of gets to what Aubrey de Grey talked about with you know, longevity, reaching longevity escape velocity, which we can talk about as well. But just to start, can you talk about the difference between this engineering on you know, damage focused approach versus existing fields of gerontology and geriatrics?

Jack Harley 26:00
Yeah, great. And, you know, I love that concept of targeting the low hanging fruit, the big wins the 10 X, because ultimately, you know, aging is the

elephant in the room, the diseases of aging are the symptoms of aging. What that means is that, you know, aging is like, is producing Hydras heads if you have cancer, diabetes, heart disease, Alzheimer's, the Hydras heads, you know, this this mythical tale of Hydra, you chop off one of the heads and other one grows back. That's how it is with age related diseases, even if we cure all cancers. Well, guess what, we may have reduced the the global number of cancer deaths. But guess what the number of deaths due to what's called Talbots paradox doesn't actually change that much, it doesn't change at all, because those deaths are redistributed amongst the remaining causes. So you cure cancer worldwide. Well, what happens outside is right increases heart disease, right increases, and, you know, people they live one or two years longer, but ultimately, because of this underlying process of aging, they're still dying, and there's not a huge amount of benefit. So I absolutely agree that we need to target the big wins. And in this case, it's the damage that's leading to all of these diseases, like we now have evidence that cellular senescence is implicated in like, literally probably 20 to 30 different age related conditions, everything from diabetes, near generation osteoporosis arthritis, we see that the the negative impact of having these senescence cells, these zombie cells, which are basically these death resistant cells that through a power grind fashion, infect other cells nearby and turn them into zombie cells, in the same way that you know, a zombie will eat another human and turn them into a zombie. And they release all these pro inflammatory cytokines, interleukins, and so on, so forth. And so you know, it creates this inflammation, this chronic low grade inflammation that we know is associated with a whole host of age related conditions. So you're absolutely right in thinking that current medicine, geriatric medicine, for example, is kind of the wrong way to do things. And not only is it the wrong way, in terms of conceptually, but it's also harder, right? Like, if you never maintain your car, and you just wait like 50 years, it's, uh, you know, it's going to be very badly broken, like, you're gonna have problems across all the different systems, and possibly, you know, dysfunction in one system will affect the other system and so on. I'm really not a mechanic. So forgive me for my description of the analogy. But the point is that, you know, nipping things in the bud. In other words, preventing the causes of the problem is going to be a lot easier than allowing the problem to manifest for in the case of human biology 80 years, and then trying to reverse all that damage. Because if someone has cancer, of course, you want to kill the cancer, but you also need to, you know, fix the damage that's basically caused that cancer, like if you don't fix the underlying damage associated, the hallmarks of aging, that person will, will soon die. And, you know, obviously, there are exceptions, if we think about cancers in younger people, which, by the way, extremely, extremely rare, like 1000s of times less common

than in the elderly. But in the vast majority of cases, like 99.9% of cases, you know, aging is the key factor in cancer. And so, this is why we actually see that cancer survivors, interestingly enough, they have accelerated aging, because ultimately, you know, cancer actually contributes to that damage accumulation. So it's pretty unfortunate, you know, you take a cancer therapy, you know, you survived cancer, let's say in your 40s, but you've accumulated more damage based on the you know, the effects of the tumor and cancer. And ultimately, this means you're more predisposed to those other age related conditions. So if we think about if we take a step back and think about, okay, what's the goal of medicine? What's the goal of biomedicine? I mean, you've got to think you've got to think that extending healthy human lifespan, and notice it's healthy human lifespan, we're not keeping 90 year olds alive for longer, we're keeping people alive in the state of good health for longer, you've got to think that that has to play a central role, like, what is the point of curing cancer, if you're only allowing someone to live a couple of years longer only to dive another age related disease. And yet, although this is so rational, to think that we should be targeting the root cause, this is not how society operates. If you look at the funding that the National Cancer Institute receives, if we take the US, for example, and we compare that to the amount of funding that geroscience receives, I noticed that I didn't say the NIH, the National Institute of aging, because only a small portion of the funding of the NIH budget actually goes towards targeting aging, the rest goes towards, you know, managing aging or dealing with the consequences of aging, and the psychology of aging, rather than actually trying to fix the thing. You know, we can see that society has a huge bias towards solving cancer, curing cancer, you know, curing Alzheimer's. And you know, I don't have any any bias against these conditions. In fact, my mother died of cancer four years ago. So I'm very familiar with with cancer and the devastation that earaches. But my main focus is, let's focus on the root cause, because curing cancer doesn't actually help society as much as most people think it does. And if we think about the billion actually trillions of dollars worldwide, the figure is $1 trillion worldwide for dementia, the trillions invested, and trillions of dollars of expenditure on the age related conditions that are not actually treating the root cause. It's quite astounding, because you would think that if you have this one thing, or in this case, these nine things that the nine hallmarks of aging, if you have these nine hallmarks of aging, that are contributing to not only cancer, but heart disease, but Alzheimer's by diabetes, osteoporosis, arthritis and any other age related disease, you can think of surely targeting that root cause is a more rational strategy than just allowing all these hydrous heads to develop and then playing a game of whack a mole, you know, you hit one mole, and another one comes up, you know,

you solve the diabetes, well, guess what, you know, the heart, the heart issues, and the cardiovascular issues have emerged. So So really, current medicine has a big problem, which is that it's not preventative, it allows the problem to manifest over many decades. And then we try desperately to solve the problem. But if you've got a 90 year old, you know, who has cancer, who has multimorbidity, maybe they have atherosclerotic plaques building up, they have cardiovascular issues, you know, the early signs of subclinical neurodegenerative symptoms, like, you know, early memory loss, and so on. By the way, this description is basically my grandfather, who's 99 years old, he turns 100, this year, born in 1921, you know, if you have this elderly person who has this multimorbidity, you can't just like solve the individual conditions and expect the person to live longer. And we have good data to suggest that, right? So you know, if someone has all this underlying damage that's driving with this multi morbidity, you can't just like, you know, pick off the individual diseases and expect to have this radical change if you're not targeting the source of that damage, essentially.

Jake 33:45
Yeah, I think that's a really interesting perspective on that. And you point out how, you know, like, chopping off the different heads of the beast, I forgot the hydrous. Maybe you called it. I'm not familiar with the fable myself, but it's relatively a futile effort, versus attacking aging itself. And I think it's kind of interesting. You also mentioned how, you know, there's this tremendous amount of funding that goes to this collection of some of the most prevalent aging related diseases, but very little funding that goes to aging. And I'm hopeful personally, that over the course of my lifetime, I will see aging recognized as kind of the root of all of it. And hopefully, you know, some of some of it will be funded, hopefully, by new people coming in and funding the research, but it may, it may be that we need to reallocate some of the funding that's going towards some of these different causes to aging itself. And I think, you know, while that might be somewhat controversial, like at face value, if you can get these, you know, get certain people to buy into the premise and believe the concept that aging will Not only help solve the issue that they care most about, but also this laundry list of other issues that people like them care with a similar amount of passionate about that that might actually be the best path forward at the end of the day. Currently, of course, we don't have that situation, we have a very small amount of funding going into aging, which you pointed out, even the money that is going to like the NIH, for example, isn't actually targeting the types of research and technology that we're talking about today. And a lot of this has to do with the pro aging trance which you brought up. In the beginning, can we dig in a bit more to describing what

exactly the pro aging trance is, I believe Aubry coined the term in or before his book, perhaps ending aging. And, you know, not only describing the term, but maybe addressing a couple of the the key kind of supports that people draw in that trance, which is, you know, one people say, Well, if everyone lives forever, we're gonna have these vast population issues, which then lead to climate issues. And maybe there's just not even enough room on earth for all of us, aside from the energy issues, you know, that that'll result in climate crisis and everything like that. And people just kind of come up with all of that, you know, category of, of responses. And then separately, there's also this concept that death gives meaning to life. And I would love to hear, you know, I've personally kind of worked my way around that. But I'd love to hear your perspective on why both of those are more so myths than kind of facts that we need to be you know, that not to prevent us from seeking to slow and reverse aging.

Jack Harley 36:43
Yeah, so there's a lot there. And I'm just feeling listeners benefit to give more kind of quantitative, quantitative kind of account of the funding situation. So the NIH, which is the National Institutes of Health in the US, they have a budget of approximately 45 billion. The NCI, which is the National Cancer Institute, their budget is 6 billion, the NIH, which is the National Institute on ageing, their budget is about 3.5 billion, but of the NIS budget, about 100 million goes to actually try to look at aging, from a basic biology perspective and treat aging. So that kind of I think, if you do the maths, it's about point 2%, if I'm not mistaken, of the total NIH budget, and if you think about it, it's quite disproportionately small, given that this is the thing that kills 70% of people. In the US, it's more because the developed nations more like 80 or 90% of people, the thing that kills 80, or 90% of people only only attracts point 2% of the National Institutes of Health budget, in terms of actually treating the root cause of the problem. So that's just something for you to think about. But also on the on the economic side, think about it from a broader system, like a broader scale. You know, I was looking up yesterday, the military budget of the US, and I think the military budget is close to 700 billion. Okay. So think about this, we spent 700. Well, if you live in the US, your government spent $700 billion protecting, you know, the country from threats and so on. But it spends 100 million, which is like 1000s of times less on, on actually trading the thing that's killing most people. And you could make the argument that well, you know, if we didn't have the military expenditure, then you know, a lot of more people may die of wars and so on. But you've got to think about the marginal utility, like if, if a one year the US military budget was to decrease by 1 billion, and that 1 billion was put to aging, that would be a

tenfold increase in the geroscience budget. And and given the budget is so so small, in comparative terms that are the 100 million, it seems quite rational that, you know, if there's one thing killing 80% of people, you should probably put a lot more resources to fix that thing. But yeah,

Jake 39:06
let me brought in on the on the budgeting piece, because I actually have another tangential example that I think might be relevant, and you might like to expand upon a little bit as well is that and then we'll get to the pro aging trance. But COVID you wrote in your article is really you can think about it as an aging related disease and an aging related and promoted pandemic, basically, because you have this situation where it's mostly people with, you know, either in old age or with comorbidities that are kind of, you know, exhibits of the type of damage that we're talking about. And those are the people that are dying at very high percentages, whereas the young and healthy have done relatively well. It certainly wouldn't be the pandemic that it is if it if it treated or if it impacted old people and you know, people with those comorbidities like it does youthful and you know, in shape, healthy types of people, and you see how much money that we're spending on the pandemic, it's, you know, it's in the trillions, we're printing trillions of dollars, at the very least. And, you know, taking these vast actions to counter it, one could argue that, you know, if anything, we should learn from this and spend a great deal on aging, so that the next time something like this might come around, you know, we have a lot healthier of a population that's equipped to fight diseases such as this, along with the laundry list of, you know, things like cancer and Alzheimer's, that people would be, you know, theoretically less subject to if they weren't aging, quite as, you know, quite as we do now.

Jack Harley 40:41
Absolutely. COVID-19, for the most part is the straw that broke the camel's back. And I'll explain what I mean by that. Two facts need to be true for someone to die of COVID-19 COVID-19, they need to have the virus, obviously, but they also need to be sufficiently immunocompromised, and just compromised in terms of their their physiology and the immunology, the immune response, and so on, to the point where they can effectively fight and kill off the virus and remove the virus. So, so the media, and most people who think about COVID-19, focus on that first fact. Okay, who's getting the virus? Right? How do we stop the prevent? How do we stop the spread of the virus? How do we lock down countries, you know, and implement social distancing policies and so on, to prevent people getting the virus, but this is only half the equation. The other half of the equation is how good a shape of people's

immune systems because if we go back to this white mirror scenario that we we kind of elucidate earlier in the conversation, whereby everyone is biologically 20, or 30. So imagine right now, every human being, so a billion people on earth are all biologically 20 or 30 years old, so they look like a 20 or 30 year old. And whether they're 50, or 80, or 150 years old, chronologically, they have the same body basically as a 20 or 30 year old because the damage that would normally occur has been ameliorated. So, in this hypothetical world, this ageless population COVID-19 isn't a global pandemic, why is it not a global pandemic, it still spreads. And, you know, there's some I was looking into this the other day, you know, there's some dispute over what constitutes a pandemic, but usually, according to the who, the severity of the the consequences, and the repercussions and the symptoms and so on, are a factor. Now, if you have an ageless society, whereby everyone in the population is 20 to 30 years old. COVID-19 isn't a global pandemic, because the death rate is so exceedingly low. And in fact, really, the only people who who would be dying would be those who have very severe, you know, immuno compromised, compromised immune systems, right. So they maybe they have some from birth, some issue with with their immune response, or, or they are like morbidly obese, and they have some sort of problems there. But even so, you know, if you're, if you if you're, if you are morbidly obese, one way to think of that is your aging is accelerated. So even in that case, you know, with fat extirpation, and with, you know, other anti aging therapies, even that could be addressed with anti aging. But the bottom line is that the reason people die of covered is not only due to COVID, it's due to the fact that their body can't fight it. And, you know, for me, I had covered living in the UK, it's pretty unsurprising given given the, you know, how many cases we had. But because I'm fairly young, you know, I can fight it off, and it wasn't pleasant, but I also didn't die from it. And if you look at the mortality curve from COVID-19, across age brackets, the interesting thing is the doubling time of COVID-19 mortality across age, there's been research on this, it actually matches the all cause mortality curve. And it's actually at the same level as something like pneumonia. Now, the death rate is higher than from the normal influenza, but the doubling rate is basically follows the same trajectory, which means that it's COVID-19 has been described as an emergent disease of aging. Yes, it's a communicable disease, in the sense that, you know, unlike something like diabetes, which is a non communicable disease, or Alzheimer's or whatever, you know, it's actually transferred from one person to another. But if we're thinking about mortality, it's an age related disease. And it's a very, it's a very clear trend that you see across the age demographics that the older people are the ones who are dying, and I think they're in many countries. There's a very interesting statistic that the average age of death from COVID-19 is actually

higher than the average age of death nationally, which means that basically, if you think about things from an overall person It goes back to Talbots paradox. It's like if you have a vaccine, that, that and you vaccinate everyone, sure you reduce the number of covered deaths. But guess what you increase the number of cancer deaths and heart disease deaths and Alzheimer's deaths because the people who would have been knocked off by COVID, this is why it's the straw that broke the camel's back. And now dying of something else, because the same aging process that results in immunosenescence and compromises their immune system, you know, these hallmarks of aging, this damage accumulation that we've talked about, is now resulting in them dying of cancer or dying of another age related disease. And the I'm not even suggesting that vaccination is is ineffective. I'm just saying that if our ultimate goal is to extend healthy human lifespan, we we can't neglect the other half of the equation, which is how do we boost people's immune systems? not only how do we fight the virus, but how do we actually keep people younger, so that not only can they fight the virus, but they also don't get cancer at near the same rate that they otherwise would. And it's very interesting, because in the last year, there's been interesting clinical trials of analytic drugs, these drugs that kill those zombie cells, there's senescence cells for COVID-19. And there's some good data coming out suggesting that, yes, if you kill senescence cells, which is basically an anti aging approach that in mice extends lifespan, up to 30, and 40%. Anything and there's about five to 10 companies, by two companies in the US that are trialing this in humans, various phases, phase one, phase two, phase three, there's evidence suggesting that these analytic drugs actually can help to revive the immune system. Now, that may seem kind of strange, but the idea is that if you kill these pro inflammatory cells, this senescent cells that are releasing all this, these inflammatory factors, you can basically restore the immune function because chronic low grade inflammation is actually bad for the immune system, to put it in simple terms. So there's very clear kind of mechanistic connections between things like analytics, or sorry, between senescence cells, these zombie cells and a weakening immune system. Now, we don't fully understand it's worth pointing out, we don't fully understand how aging actually weakens the immune system. There are a few different kind of theories that are being explored and a few different experimental designs that are being pursued. But we know that aging is the thing that is the by far the biggest factor. So it's only a matter of time before we figure out, Okay, why exactly is aging, resulting in this COVID sort of mortality. In fact, that's actually a project I'm considering doing a bit of research on this year, a bit later in this year, when I head back to Australia. So ultimately, said analytics could be beneficial not only to prevent cancer and prevent your generation, but also COVID-19. Because you

kill the senescence cells, you're kind of cleansing, or you know, you're, you're washing away all of these harmful zombie cells. As kind of pseudoscience as that sounds, it's real science, you can look it up. And then basically, you know, you're the idea is that you're just able to extend healthy lifespan. And part of that means you're maintaining a solid and a robust immune function for a longer period of time. There are also other anti anti aging approaches being pursued for COVID-19, such as Metformin, which is a type two diabetes drug that's been used since the 1950s, which is an inhibitor of the mTOR pathway. So the idea there, without going into too much technical detail is you know, you're slowing down sort of your your kind of metabolic processes, in a way and the mechanism of action of Metformin is not fully elucidated. But you're basically attenuating, this this key mammalian aging pathway, and in so in so doing, you're allowing the immune system to kind of prosper and better five COVID. And there's some good data that's come out recently about the use of Metformin, which is this cheap, off potent drug for diabetes, for COVID-19. So, ultimately, I think when we think about COVID-19, I really want people to think of it as an age related disease or an emergent disease of aging. You can phrase it in different ways, but basically to recognize the extremely strong, exponentially increasing rates of COVID-19 mortality with your age with your your age, your age bracket. Now, you might also say well, okay, some young people die of covered but are they going to have long term symptoms? And, you know, being at Oxford here and having some friends in immunology, you know, I have I have taken a look at some of the data and discussed with some of the experts here. And, you know, we don't really know much about long COVID. But it could possibly be that a lot of the kind of symptomatology associated with long COVID is somewhat psychosomatic not to say it's all in the person's head. But similar to something like irritable bowel syndrome or fibromyalgia, which are real, which produce real symptoms, though, like an observable, an identifiable biological cause, or kind of disease origin, it could be that long COVID is based on this bio psychosocial effect that we've seen, as a result of all the doom and gloom in 2020 people being isolated, you know, all these headlines about people dying, and this extremely negative environment and this isolation, and the button, you know, this bio psychosocial effect that this has, whereby social effects can influence your psychology, which can in turn influence your your biology, to produce this kind of symptomatology associated with long COVID. Now, I should qualify this by saying, you know, more research is needed. And it's quite possible that COVID-19 actually accelerates aging, in the sense that it does have some long term consequences. But even then, we still need anti aging therapies. Because if it's true that COVID-19 say damages your lungs, or has some other effects on your immune system, then we still need anti aging to repair that damage. So the bottom line is that whether we're looking

at non communicable non communicable diseases of aging, such as diabetes, Alzheimer's, and so on, or a communicable disease, which is also an emergent disease of aging, such as COVID-19. The bottom line is we have to start looking at repairing the damage that occurs over time, these hallmarks of aging, to keep people in a healthy, like a truly healthy state, not healthy for an eight year old, but healthy for a 20 year old state, so that they can fight off these viruses. And unless we want to have another pandemic, with covered, you know, 2021, COVID, 2022, etc, we really need to bolster people's immune function so that we can fight off these diseases successfully.

Jake 52:13
Glad that we went down that that tangent a little bit, I think it's very relevant. And people today, you know, can really relate to the immediacy of the issue. When you relate the issues of aging, to COVID. You know, I did bring up the question of like, the pro aging trance earlier, I think we've made or you've made really a quite a compelling case, on why aging deserves a lot more funding and attention. And ideally, with those two things, we have a lot more acceleration of progress. Can we discuss the pro aging trance and why that hasn't happened to date? and address some of those, you know, primary concerns I brought up earlier, like the overpopulation, death brings meaning to life, those types of things.

Jack Harley 53:00
Sure. So to go back to the question that you raised earlier, we can talk about this phenomenon which Aubrey de Grey has pointed out as you, as you yourself mentioned, which is the pro aging trance, this phenomenon by which people kind of delude themselves into thinking that aging is natural, will or natural, normal, even good, it is natural. And you could say it's normal. But it's not. It's not it's definitely not a good thing. Yet most of us from birth were conditioned to think of life as this kind of evolving process where you know, you're born, you go to school, you get a job, you retire, and then you live happily ever after. But guess what that happily ever after looks like, it looks like Alzheimer's disease, it looks like cancer, it looks like these age related diseases that most people get in the world today. Even in Africa, the two leading causes of death are age related conditions. That's what the happy ever after scenario looks like if we if we strip away all of the kind of Disney fairy tale perceptions, and we look at things objectively. So So the question is, you know, how do we, as human beings respond to that cycle psychologically, and there's some really interesting literature about learned helplessness, and about terror management theory that is very relevant here. Okay, terror management theory, this idea that, you know, when we're faced with the the terror of our own mortality, we know that we're

going to die of aging, if we don't have anti aging technologies, which most most people probably aren't aware of that thing's feasible. So how do we respond to that? How do we respond to the fact that our biology You know, this organism upon which our conscious, you know, our sentience, our consciousness is operating, you know, kind of functionally computationally and so on, that this consciousness exists in this biological animal? Basically, this this evolved ape that's going to die? How do we how do we come come to terms with that. And the thing is? And the answer is, well, it's difficult and we just ignore it. So I think the thing is that in different cultures, the way people think about aging and death, it does differ in a lot of religious contexts. I think people, they deal with this by, you know, by describing what may happen after you die. And I'm not one to question people's beliefs, or whether it's true or not. But I think it is fair to say that it is a psychological way of dealing with the trauma of mortality and the horror of mortality. But in the West, you know, we also just largely ignore it, like, people don't really like to think about aging and death, because it reminds them of their own imminent aging and death. You know, you might think that, well, 80 or 90 years, which is, you know, 70 8090 years, the average lifespan is quite a long time. But just talk to people in the 60s and 70s, a lot of them, you know, from the inside, it doesn't feel that different from when you're 20, you're just you've just been alive longer, and you're a bit weaker, you know, and you might have some health problems, you've gone through more, but you're the same person. And this is why I think when people are young, they think that something's going to happen in their life, after which they're happy with dying. And even people in middle age, you know, people hold on to these. And this also describes my own psychology to an extent, you know, people think that if they get something, right, if they, if they accomplish something, or if something happens, they'll be happy to die, right. But this, this isn't a reality. I mean, just spend some time on a cancer ward. And it's really interesting, you know, when people get these terminal die, diagnoses, suddenly, it's like, they wake up from the trance, it's like, holy crap, this whole time, I've just been going about life, you know, as Oh, I kind of live forever, and not really facing my own mortality. And then suddenly, they're snapped into seeing the truth, and it's put right in front of their face, like you are going to die very soon. And the thing is that that actually applies to all of us. It's just the timescale is a bit longer. But it's still very, very, very soon in any kind of, you know, cosmological terms or, you know, any kind of kind of timescale, you want to look at things. You know, from, from the perspective of the universe, or, you know, even in the perspective of other animals, I mean, went on even the longest living animal by a longshot. So the longest living animals include things like the greenshot, which can live 400 450 years, we believe.

So compare our 70 or 80 year lifespan to a 450 year lifespan. I mean, we think we're kind of like the, you know, the apex predator of earth or whatever. But we actually have quite short lifespans, even tortoises live 234 times longer than we do. So the thing is that we've got to really humble ourselves and see things objectively and realize that we actually have pretty short lifespans. we undergo senescence, and we declined fairly rapidly after the age of, you know, 60 7080. And we should try and do something about that, because aging sucks. And although we can kind of delude ourselves, which is this pro aging trance into thinking that aging is just something natural, it's kind of evolutionarily developed or it's normal, or it's just an important part of growing up or something like that. We can we've got to really check ourselves and, you know, check out priors and really question that that premise, because although existing chronologically, again, coming back to the distinction between chronological aging and biological aging, although existing chronologically is great, you know, you get to live more you get to self actualize, you can spend more time with your friends, your loved ones, your family, etc. That's great, but biological aging, the physical decline that occurs, basically, you know, after the age of 20, till the time you die, this this process of accumulating damage that will eventually kill you. That sucks. And I think society as a society, we need to really wake up and think and be honest with ourselves and realize, okay, chronological aging, that's great, biological aging, that sucks. Let's try and deal with that, rather than just conflating those two concepts of chronological and biological aging, and pretending like they're the same thing. And then just saying, having this fatalistic attitude of well, you know, this is just this thing that happens, we can't really do much about it. So let's just distract ourselves with our menial jobs, or, you know, power sports or whatever it is. And by the way, I have nothing against people's jobs and sports. I'm just saying that ultimately, in the face of your own mortality and the permanent erasure of your consciousness if you take, you know, materialism and computational functionalism seriously, I think a much more important priority at this stage is to secure a much longer lifespan. And this is what ties into this concept that you raised Jacob back longevity escape velocity, this idea that at some point, most likely, and probably in the next 100 or so years, we're going to reach a point where everyone alive will basically be functionally immortal, not because we currently have the technology to bring us to that point, but that we will, we will have therapies that will keep us alive long enough, say, say an extra 10 years, by which point better therapies will keep keep us alive for, say, 50 years, and so on. And so this is called longevity escape velocity, this idea that society reaches a point in which anti aging technologies are good enough to keep us alive for a set amount of time, after which advances in the anti

aging research field allow us to live even longer to the point where you can essentially survive indefinitely. Now, by the way, I was reading something really interesting, which was an analysis by some insurance companies, actually, that suggested that if we didn't have aging, the average lifespan would be somewhere between two and a half, 1008 1000 years. So I thought that was quite an interesting kind of thing to think about, you know, how old would we actually live to if there was no aging? Now, obviously, without aging, you can still die of other causes, you can dive in natural disaster, you can die because you're murdered or you're in a in a conflict or something, or even infectious disease, although it's much less likely, or even cancer and so on. But again, you know, because of the extremely strong role of aging, it's much less likely. So, but this is a longevity escape velocity. And it's this idea that we live long enough to kind of, you know, benefit from these cures, to aging, that even though they don't come within our natural life's time, we can still reach that point based on therapies that do come within our lifetime. So yeah, so basically, I think a really key concept for society to understand is this concept of longevity escape velocity, because when you frame your life, in terms of, okay, there's actually a decent chance that I could live to 1000 years old. So rather than spending my life trying to optimize for 80 years old, and just trying to, you know, have a family or like, you know, play sports or entertain myself, whatever, for eight years, why not try and do everything possible that I can to actually unlock that extra, you know, 920 years of life, right? So this is kind of like a psychology that may be useful to some listeners, you've got to prioritize, what would you do, if you had 1000 years, instead of having 80 years in your life, you had 1000 years, anything that you want to do that gives you value in life, you can do that. But you can do it better, you can do it for longer? And you might say, Oh, it's gradients, you ballistic? But really, I mean, the same argument would apply in the past 200 years, when we extended our lifespan from 40 years in the 1800s, average lifespan to 80 years today, you know, is it hubristic that we did that? Are we greedy for now living 80 years? Or is it just like way better that we get to live longer? And the same argument applies from 80 years to say, 1000 years? You know, is it greedy? Or do we just like being alive. And this kind of nicely segues into a point that you raised, which is this notion that people raise which is death, or aging, you know, brings meaning or happiness to life, death brings meaning to life. And, you know, when you when you talk about anti aging, a lot of people have this intuition that death is somehow good for us. Like it gives our life a sense of purpose. Without death, life becomes meaningless. Who would want to live in a world without death? Now, this is actually quite absurd. When you really think about, you know, if you're dead, how can you? How can that be meaningful? It's like life gives

meaning to life. Right? Like, like, Why? Why do you have to die in order to give someone meaning in life? To take it take an example, right? Let's say, you know, let's say you capture someone, you kidnap someone, and you say to them, okay, I want to make your life better and more meaningful. So I'm going to kill you in two years time. You know, that's, that's essentially what people who make this argument are saying, they're saying that like, Okay, if I give you a sense of finality, your life will be better. But the thing is, I think, ironically enough, the reason why, if that were to be true, it would be true is because it would force them to wake up from the pro aging trance, which they can do without having to die anyway. Right? Like, if people break free from this idea that you know, aging and death is a good thing. That naturally is going to allow them to, you know, kind of, you know, focus on the things that really matter. And that's why you see things like you know, when people have a cancer diagnosis. Suddenly, a lot of the trivialities in life and frivolous concerns kind of evaporate because they realize oh, shit, you know, I'm alive. Now, that's not going to be something that exists forever. But the key point is that that realization can take place without having the cancer diagnosis or without having death, like you can, you can just kind of wake up. And so how do you wake up? Well, maybe you, you, you know, you reflect you meditate, you think thoughtfully about things you understand, you know, your place in the universe. And you know, you do a bit of philosophizing, and so on, and you kind of see what's valuable in life. But to say that you need to enter into someone's conscious existence, in order to bring meaning to their life is absurd. life brings meaning to life, death does not bring meaning to life.

Jake 1:05:53
And other right away, it might just be to listen to this podcast, I think it's been for people who, who come into it open minded, has shed a lot of light, and hopefully, brought some hope to people who just thought that there was no possible way of living meaningfully longer to realize that actually, if we attack aging, and give it the proper funding and attention, and you know, global effort, it's actually a reasonable, you know, idea that we could live to 150 years old, 200 years old, 500,000 years old, whatever it might be. Briefly, I want to touch on the overpopulation thing as well. We don't need to go too deep into it. But I heard something kind of interesting. Today, I was listening to a conversation with Jeff Bezos, he's obviously got Blue Origin going into space. And he talks about how, you know, part of that is because he wants to, you know, bring industry off of Earth and into space, as kind of like a climate type of effort to you know, preserve earth. And he talks about how humans, biologically, we use, like, metabolically, I suppose we use about 100 watts of energy per day. But in the developed world, now,

the average person uses about 11,000 watts of energy per day. And that amount has basically been compounding for over 100 years, and figures to continue doing so. And so my counter to the overpopulation argument, just thinking about that thing that I heard earlier today is basically. And so he Well, he basically said, you know, if we wanted to have enough energy for everyone, and 100 or 200 years, if we continue to compound at that low single digit rate from like, 11,000 watts per person that we are at today, if you wanted to provide enough energy for those people, you couldn't do so by covering the entire earth surface with, you know, solar panels. And so my counter to the overpopulation piece is like, first of all, we're working on things like space, we're working on counters to the climate crisis. And, you know, solving aging alone, sure that that probably isn't a perfect solution. But there's no reason not to pursue it while we work on these other dimensions at the same time, because we're gonna need to solve the climate crisis separately, whether we, you know, you know, reverse or slow aging or not, we have a population that's increasing energy meet needs that are increasing. And so the overpopulation concern strikes me as somewhat arbitrary. I'm second to that. I want to, you know, touch back on the point that you made about, like, kind of going back to the budgeting thing, I suppose. And I think, from my perspective, and let me know if you have kind of any points to add here. But obviously, I would if my goal was to extend the human health span, which is just, you know, I think a term which combines increasing lifespan, but also not the concept of like, being at forever in terms of like, what the biological age that we associate with the chronological age of ad, but being like 20 or 30, biologically for an extended number of years. So I would focus a number of, you know, the vast majority of our budget on solving aging, but then secondarily, you know, I would put a lot more money into like, autonomous vehicles, which, you know, cars and road traffic accidents are the leading cause of death for people who essentially don't have leading causes of death, which are related to aging. So like 20 year olds, 30 year olds, 40 year olds, other ones, like you mentioned, you know, how long could people live if they didn't have aging, and what would kill them maybe like homicides and things like that. So mental health may be a good area to kind of allocate some funding there for for not only homicides, and suicides, which are also, you know, near the top of the list of leading causes of death outside of aging for people in young age. And then lastly, you talked about how we've transitioned from, you know, being like the the average lifespan was like 40 to 80. And the same logic For why that was good should apply beyond a large piece of how we're able to get there with by reducing child morbidity. And that'd be like a fourth bucket where I would allocate some funding is this kind of a better structure? You know, that's

just my perspective. But is this a better structure structure from your perspective to kind of extending the human lifespan?

Jack Harley 1:10:20
Yeah, so a lot of really great points there. And I want to start by completely agreeing with your rebuttal to overpopulation. Like you said, the problem we have is not like we do have a problem with overconsumption. But the goal is not to like, kill people, right? Imagine if people looked at COVID-19 and said, okay, we were actually gonna let COVID-19 kill as many people as possible, so that we can reduce our carbon footprint, like imagine how absurd that would be, because that's basically the argument that people are using when they're saying, Oh, we should allow aging so that we kill enough people so that our, you know, our emissions are low, or our food production doesn't become too too vast. And if you think about it, you know, it's an absurd argument. Right. So as you said, the actual solution is to use technology to help us sustain a larger population size. And by the way, that's what's already been happening happening since Thomas Malthus initially came up with this whole premise of overpopulation, these Neo Malthusian concerns in this idea of like Neo Malthusian collapse, this idea that the population grows exponentially to the point where there's not enough resources to provide for everyone. And that's been debunked. And the way that we've seen that being kind of invalidated over the past couple of 100 years is because technology improves to help us sustain a larger population. An interesting fact is that we would actually be overpopulated. Today, if we were on a hunter gatherer technology, but because we have better technology, we have agriculture, and so on, we can sustain a much larger population. But there's a few other points I'll touch on. Regarding overpopulation, the first thing is that population is actually a lot of people think that population is just exponentially increasing. And if you look at the historical graph graph of population size, you might infer that looking at the graph, but actually, because of the demographic transition model, it's actually the case that the population according to you know, who and so on, you know, the population size is predicted to peak at somewhere between 10 to 11 billion people, somewhere between 2015 and 2100. Under the status Corps, and actually a much bigger problem that we have today. And countries like Japan, Italy are already experiencing this is this idea of dependency ratios being unfavorable, which means it's, it's not so much how many people you have, it's the ratio of, you know, the elderly people, to the younger people. Now, the crucial point is that when we talk about the elderly, I'm talking about, you know, biologically older people, because if you're in your 70s 80s 90s, and you're not able to support yourself, you're not able to work etc, because you know, you don't have that cognitive capacity, or the energy and so on

just because of your aging, then having a population where most people are in that state is, is quite, it's quite challenging. And that's what a lot of Asian countries, certainly Japan and China in the near future as well, are really likely to suffer from even in the West, because of the baby boomer generation, you know, as the baby boomers get older, suddenly you have a huge bulk of the population who are undergoing biological aging, you know, they're having to retire, they're having to kind of, you know, be supported by the healthcare system as they develop multiple morbidities associated with with the aging process. And so, you know, the dependency ratio is a really critical factor. Now, the good news is that solving aging or not even solving aging, but just retarding the aging process, and extending healthy lifespan, helps with this issue, I mean, helps to deal with this issue. Because if you have people in their 60s who are as healthy as people today who are in their 30s or 40s, suddenly they're not a burden on the healthcare system. suddenly they're capable of, you know, working as much as they used to, because they feel like they did when they're 30, not only from the inside, but but you know, like physically they're able to, to, to work. Yeah. And and, you know, today, with the current, you know, economy, you see a lot of people transitioning multiple times in their career into, you know, different career paths and different jobs and even into their older age. No, you know, people have some interest in doing that. But because of biological aging, it becomes harder and harder. Like if you're in your 80s today, you know, it's going to be hard for you to start a biotech company, right or a technology startup. Why is that? Well, you know, you've you've stuff in your generation to some extent, which is just part of normal aging, or even what we'd call how Healthy Aging. I mean, it's inevitable. If you saw my friends here, you know, they're they, they look at the brains of people who have Alzheimer's disease and the brains who have people, sorry, the brains of people who have been quote unquote, healthy, they both have signs of, you know, amyloid plaques, and so on. So, you know, there's no way of escaping your degeneration, even with the best dietary protocols and so on, again, which is why we need the anti aging therapies. But basically, going back to my original point, you know, we need to enable people to remain healthy for longer, right, in order to escape these issues of dependency ratios. So yeah, so that's a couple of ways to look at overpopulation, the population is actually predicted to peak at about 10 to 11 billion and then decline. And this is because the areas of high growth at the moment are Southeast Asia and Africa, both of which are areas that as they develop in terms of their economic development, you know, according to the the the demographic transition model, you know, we see that as countries develop birth rates decline. So although birth rates are fairly high now, and their population growth is quite, quite high. That is, if you look at the trends across all the countries in the world, that kind of tapers

off, as the country develops, birth rates fall, and then, you know, the population size stabilizes. So although it looks like population of the world is just exponentially increasing, it's actually on track to kind of plateau at around 2050, to 2100, at around 10 to 11 billion and then decline. Now, with anti aging technology, it does change things and to the extent that we can extend healthy lifespan, you know, the population size will, will grow at a faster rate. Or, or in other words, after 2100, it'll decline at a slower rate than it would otherwise have. And it's interesting to note that, you know, Elon Musk actually mentioned in his interview at the axel Springer awards recently, that under population is actually likely to be a bigger problem than overpopulation in the near future. He also gave a shout out to solving aging in that interview, which you can look up. But anyway, I digress. So the point is that, if we are able to slow aging, a lot of the resource issues, as you correctly pointed out, we're going to have to solve anyway, because of the unsustainable levels of consumption. So we don't have to kill people, right. But by not solving their aging and allowing them to die of cancer, heart disease, diabetes, in order to solve that problem, in the same way that we wouldn't allow people to die of COVID-19. In order to reduce the carbon footprint of a country like that would be an absurd policy. So Neo Malthusian collapse is basically a myth. And another fun fact about sort of overpopulation is in 2012, there was this team from the per square mile project led by Tim de shot, and they produce this infographic to show sort of like how many people could fit into regions of the earth. And if populated as densely as New York, the entire world's population could fit into an area the size of Texas, right? Think about that, if populated as densely as New York, the entire world's population could fit into an area the size of Texas, right? So actually, you know, it's not like we're going to run out of space, right. And then we're also going into space with, you know, with Elon Musk's company, and SpaceX, and with Blue Origin and so on, Basil says company, so we also have potentially colonies on Mars in the future, and so on. So really, you know, it's just a red herring, this idea that the world is going to get overpopulated. And that we're all going to be, you know, dying of starvation. You know, it's just not the case, we have the resources, it's just about efficiently allocating them, and, you know, developing technologies to better allow them to be efficiently allocated. And, you know, we could talk about food production, we could talk about co2 emissions, I mean, if we look at the co2 emissions of the US versus Portugal, to develop countries that have equivalent kinds of living standards and quality of life, but Portugal emits less than, I believe, one third the co2 per capita than the US, right, because they have more renewables, it's, you know, it's just more efficient and so on. So, you know, we don't have to have high levels of co2 emissions, we just need to, you know, organize things in a way and you

know, align the incentives and so on to to incentivize renewables and to use technology, geoengineering, and so forth to solve some of these issues, as he said. And then finally, something interesting, you mentioned was about sort of mental health because, let's say in the future, we've kind of we've solved aging, and we have solved car crashes, maybe with autonomous vehicles and so on. And then what are people dying of, let's say the dying of murders and let's say I can't confidently talk about the influence of mental health, on murder. But I think the influence of mental health on suicides definitely could be a large factor. But here's a fun fact for you. Guess which age bracket has the highest rate of depression and suicides. It's the elderly, you can look this up. Actually, a lot of people think that, you know, depression and, you know, these sorts of conditions occur in like younger people, but actually the highest rates of depression. And this is something that I learned in my neuroscience course at Oxford, right? We had we had lectures about, you know, geriatric psychiatry, you know that the highest rates of depression are in the elderly, and the highest rates of suicide are in the elderly, especially men. But the point is that society actually sweep this under the carpet. And unfortunately, a lot of those suicides in the elderly are misclassified as euthanasia, even though they don't meet the criteria for euthanasia. So I think it's fair to say that if you're undergoing neurodegeneration, if you're losing your memories, if you're forgetting who you are, and you're not able to function, that that is correlated with depression. And we you know, there's there's very strong indications in the data for that. And it makes sense, right, if you're losing your mind, because of aging, and again, this happens in healthy aging. Again, my friend here, Oxford, who works in Alzheimer's lab, she's literally looked at the brains of deceased people who are quote, unquote, healthy and have Alzheimer's. And they both have signs of amyloid plaques, right, they both have these hallmarks of Alzheimer's, because it's just part of aging, like you can't age and have, you can't live to 90 years old and have no signs of new generation, it's not possible, because those underlying hallmarks of aging, are causing this accumulation of damage that's ultimately driving these pathologies in the brain. So the point is that if we want to improve mental health, I genuinely think that getting rid of aging is a good step. It's not It's not the only thing. I think we also need, you know, other strategies. And I think I'm quite confident that things like VR, could play a big role. There's some interesting work being done with VR for you know, overcoming trauma and social anxiety and that sort of thing. So I'm quite optimistic about that sort of approach. But, but also things like psychedelics for depression. You know, there's a lot of new companies and exciting work in that in that space. And even, you know, unknown unknowns, I believe that there's going to be soccer pharmaceuticals, as well, as you

know, possibly even more speculatively, you know, brain computer interfaces, such as neural link and open water, that will allow us to basically, with the press of a button, maybe this is 30 4050 years off with a press of a button, basically, turn off anxiety or turn off depression, as in, we have a program that's basically like an eg, but much more powerful, and, you know, has hundreds of 1000s, if not millions of nodes, that can basically identify the patterns of brain activity associated with anxiety or depression, and then basically produce electric electrical signals, in such a way that it can actually kind of untrain us out of those thought patterns. I know that sounds quite speculative. But I do think something like that will happen. Or we will have better psycho pharmaceuticals, that are like psychedelics, but with, you know, less side effects and even more potent. And that can target the sort of pathways associated with anxiety and depression. And interestingly, it's, this is actually why I switched out of neuroscience, and I'm more interested in the aging because the bottom line is your mental health doesn't matter if you're dead. Right. Now, currently, the thing that's killing most people is aging. So I'm focused on that. But guess what, when we solve aging, and the number one cause of death is suicides, then hell yeah, I'll go back into neuroscience and try and stop people from committing suicide. Because ultimately, I think, you know, however, we can, you know, get rid of death and just keep people alive, able to live their life without having to worry about death. I think it's, I think it's one of the most important priorities for humanity.

Jake 1:24:10
So let's talk a little bit about more about the brain machine. Yeah, brain machine interface concept. You know, we talked about longevity escape velocity as being a path towards where we could have theoretically, theoretically, we could have immortality. cryonics is another avenue that people, you know, they may not think that in their lifetime, we can kind of have longevity escape velocity, so they may pursue cryonics as a way to be able to kind of be revived and alive when we get to the point where we can kind of achieve significantly longer health spans at the very least. How do all of these other you know there's also like the mind uploading concept? How do those you know cryonics mind uploading brain machine interface, those different kind of categories tie in to this more, you know, scientific focused, aging conversation from your perspective?

Jack Harley 1:25:11
Yeah, that's a good question. Because I guess one potential rebuttal to what I'm suggesting about curing aging is well, and maybe some readers may find this quite a strange concept. But why do we need to solve aging if we could

just upload people's brains or, or something like that. Now, just to give a bit of background, this idea of brain or mind uploading, it seems quite speculative. But if you take computational functionalism, and materialism seriously, which are these philosophical ideas in, you know, the philosophical inquiry, area of inquiry of philosophy of mind, which are these ideas that basically, the brain is made up of physical stuff, atoms, you know, neurons, etc. And the computational processes that occur within the brain, basically, create this simulation that we live in, you know, this consciousness, right, allow us to experience something. So we exist within this kind of consciousness that's running on the operating system of our brains. And the idea is that we can kind of recapitulate that same program, that software that our consciousness exists on on a computer. And, you know, there's a lot of philosophy of mind associated with well, would that really be your, you know, like, if I scan your brain now and put you in a computer, but you're still alive now, with the one in the computer, the version of Jake on the computer still be you? So? And that's kind of an open question in philosophy. And there's actually quite a lot of disagreement amongst academic philosophers about this kind of old transhumanist question of, will you still be you if you get your mind uploaded? So for me personally, the reason I'm very interested in aging is because I think it's such a low hanging fruit. Like, I think, in terms of mind uploading, we need to do a bit more research and to understand consciousness better, and to, you know, progress, those sorts of fields forward. Before, I think we can just confidently say that, yep, we can just upload a billion people's minds and we can live forever. I think that there are a lot of steps that need to happen before that situation. And I think the lowest hanging fruit, even if we want that situation to come eventually, is just to stop people dying of aging. I mean, we have 100,000 people dying per day of aging. And obviously, those people, especially if they're, you know, they're not being cryo cryogenically preserved, and even more so if they have neurodegeneration, it's very unlikely that we're going to be able to bring them back. Right. So the question is, well, how do we get as many people who are alive today to make it to longevity escape velocity, or even to make it to a point where, you know, we can achieve some some kind of immortality, hopefully, or at least some way to live a much longer life. So we can, we don't have to be restricted by the kind of biological limitations that we are currently bound by. So I think something like cryonics now, I actually saw I interviewed Aubrey de Grey, like you did recently for the Oxford aging society. And, you know, I asked him about cryonics because that was a question that came up. And Aubrey de Grey. He's a big proponent of cryonics. But he actually because he's quite bullish, and quite optimistic about longevity escape velocity timelines, in the sense that he thinks we will probably reach longevity

escape velocity by around 2036, which means people who are alive in 2036 will be alive to benefit from therapies that will then allow them to live long enough to benefit from even better therapies to, you know, ad infinitum to exist basically forever until they die of something else. So but even despite his quite optimistic projections of longevity escape velocity with that 2036 estimation, which he estimates with 50% probability, he actually still thinks cryonics is important, especially for people who are old now, right? Because if we take seriously Well, if we look at the data, and we see that 37 million people die per year, I mean, if we're talking about 2036, that's, that's almost if my math is correct. half a billion people. Yeah, that's, that would be potentially more than half a billion people would, would die, even in those 16 years, between, well, 15 years now between 2021 and 2036. So for those half a billion people, you know, that's kind of, you know, we we want to save as many of those people as possible. And the way we do that is by accelerating anti aging so that we can get these therapies into the world sooner. So that we can save those people because if we can push longevity escape velocity as early as possible, in other words, if we can do that velop therapies to keep us alive long enough to essentially live forever, your will to be functionally immortal. If we can push that date earlier and earlier and earlier, it means that a lot of these people who otherwise would have been dead forever, okay, you know, dead gone, will now make that cut. Because think about this, right? Who wants to be in the last generation to die? I imagine you're 90 years old, right? You're 90 years old, and you have a terminal cancer diagnosis. And you watch the news. And you see that scientists are saying that in two years time, we're going to have successful anti aging therapies, but it's too late for you. Right? How depressing would that be to be in the last generation to die to know that after you, like, you know, other people are going to live forever, but you're going to die? And that's going to be it? Right? That's extremely depressing. And we really don't want that situation. So how do we avoid that? The way we avoid it is we invest heavily now, we get anti aging therapies, we get as many people to make the cut as possible. I mean, ultimately, it's like a, it's like a game theoretic situation. If we all prioritize our own lives, and no one really contributes to anti aging, then we're all gonna die, like all of the a billion people on earth will die. But if we all kind of like band together, and we take anti aging seriously, and we really try and accelerate this research, knowing that it's in our best interest, because we're all screwed, if we don't do it, then we can actually get these therapies. Like if you really look at the science, and you look at how much progress we've made, even with the small amount of funding that we have had in this field, it's quite remarkable. And if you scale that up a few orders of magnitude. And then you think about, you know, what we could achieve in terms of being able

to retard the aging process, basically repair the hallmarks of aging, and so on. You know, there's pretty good reason to think, optimistically, you know, to be optimistic and think that we could get this technology fairly soon. Right? How soon? We're not sure. But surely, we should try and get it as soon as possible given that 100,000 people per day are dying, and every day sooner we get this technology represents 100,000 lives saved. So ultimately, I think cryonics is definitely possibly useful for people who, who are older now, especially because if you're in your 70s, or 80s, now, you may not live long enough to reach a time in history, it will in the future, in which we have anti aging therapies. So cryonics this idea of kind of freezing your body and with the hope to be revived in the future is probably a safe bet. Now, for those who don't know much about cryonics. I recommend the white but why.com overview of cryonics, it explains it very well. But basically, the premise of cryonics is that when we classify someone is legally dead today. That doesn't mean that in the future, that point of degradation will represent biological death, in the same way that if we go back 100 years, if someone has a heart attack, and then we can sit it dead in that time period to in today's time period, they're no longer considered dead because we have defibrillators, we have CPR, etc, we can revive them. And the idea is that in the future, even if we have things like cancer, because I think cancer is actually a harder problem in many ways than slowing aging. In the future, when we can actually kind of very easily remove all cancers, then someone who maybe died of cancer, you could unfreeze their body and repair their body, bring them back to life. Now that is more speculative. And I don't place a lot of confidence in cryonics working, a lot of estimates from experts have are in the range of, you know, well, they they have like a middle kind of normalized distribution with a median value of around five to 10% probability that cryonics works. And personally, I don't want to really risk my life and the life of all my loved ones and everyone on Earth. I don't want to, I don't want to put a 5% probability of success on that, you know, and that's what cryonics is. So that's why I think anti aging is a much better strategy, because it's 100%. Like, you know, if your anti aging is working, there's no uncertainty about it. You don't have to, you know, be asleep in cryostasis for 100 years, and then hope to wake up, you know, you're just awake the whole time. So, so yeah, so I think ultimately, in the long term future, maybe 1000 years or whatever it is, something like neural link that can safely upload our minds in a way that can be realized we can reliably Be sure is still us and preserves our identity. I think, yeah, that would be great. That would be cool. But I think the the much more pressing problem, as far as I can tell, is the fact that we have 37 million people which is the size of Canada, dying every year of aging, and it's such a low, low hanging fruit. For even if we don't fully self solve aging, we at least get therapies to get

most of those people who would otherwise have died of aging, to live long enough to benefit from these possible futures in which we have, you know, mind uploading or, or some other kind of brain preservation and so on.

Jake 1:35:18
Right, so you talked about Aubrey his estimate of 15 years, maybe reaching longevity escape velocity, I like you, it sounds like, like to take kind of a conservative approach to these issues. Because if you start getting into kind of these out there seeming issues, and you don't take a conservative approach on the, on the one hand, you lose a lot of people. And on the other hand, it's probably just like, not, I don't know, it's just not my personal approach to things. So I'll take Audrey's 15 year estimate. And, you know, I think what he's doing is awesome. You know, don't want to take anything away from that. But I'll just take a more conservative view and say, Okay, well, what if it takes twice as long as he thinks, and so, you know, 30 years from today, instead of 15. And at that point, I'm like, you know, well, I'm closer to, like, in my middle age will say that. And then, you know, if it takes another if it takes three times what Aubrey says 45 years, then I'm like seven years old. And at that point, it may be like, almost too late to apply some of these technologies, or whatever it is. So if I want to do kind of the best thing that I can best things that I can do to be alive and relatively healthy and somewhat eligible for the various therapies and treatments at the point at which we may or may not reach longevity escape velocity, if that's in 15 years, or 30 years, or 45 years, whatever it might be. I know, there's certain things that I think about his like, my personal health and longevity strategies. And they're not like super out there, like, you know, exercises is maybe first and foremost. But we'd love to hear kind of your perspective on what some of your personal strategies are on being kind of alive and well at the point where we may reach some of these therapies and be able to, you know, bring reinforcements on living longer and healthier lives. And then, you know, after that we can wrap up, wrap up the conversation with talking a little bit about what got you into all this in the first place.

Jack Harley 1:37:19
Yeah, cool. So just to clarify all breeds prediction. So he gave 50% probability estimation of reaching longevity escape velocity by 2036. But he also assigned a 10% probability that we won't have reached by 2100. So I think, you know, as you've suggested, there is a conservative view that we won't have these technologies for a while. And I think, if we live in that sort of world, I think the most likely reason for that are things like the pro aging trance, and people's unwillingness to actually accept that aging is a bad thing, and a bad thing that we can solve. And that's why you know, the

work that you're doing, and many people who are, who are trying to promote the science and and people in the field who are doing the science are doing is so important, because we need to accelerate the timelines as much as possible. Because if we don't, everyone alive today, the 8 billion people live today will all die, and there'll be permanently gone like the 100 billion humans who existed before us. So moving on to kind of personal longevity strategies. Now, there's kind of two schools of thought. So one school of thought is what Aubrey de Grey kind of proposes, which is basically, there's not a lot you can do now, besides what your mother would have told you. And that the best thing you can do is just try and promote the field. So Audrey's answer would probably be instead of buying a lot of supplements, instead of, you know, trying to pursue the best and most expensive anti aging technology that we have today, you would be better off probably, you know, just telling your friends and family to donate to sens Research Foundation, which which is a charitable organization in the US that kind of finances some of these research projects and this this field of neuroscience in order to basically get better therapies that will completely overshadow anything that we have today. So I mean, today we think things like exercise and good diet are fairly important, and they are for today's standards. But if we go in 100 years time, and we have some nanotechnologies that can instantly remove all our atherosclerotic plaques, which is something that people are working on at the moment. Then, and we have all these other technologies that can, you know, repair can repair all the damage of the hallmarks of aging, then in that kind of situation. Exercise doesn't really matter. Like you won't have to exercise because all of the benefit of exercise you can basically artificially accomplish So that's one school of thought. Right? So one school. So Aubrey de Grey school of thought is basically, you don't need to worry too much and get obsessive about anti aging strategies or taking all kinds of supplements, because in the long run, what's going to make a much bigger difference is whether we actually progress the field. So I think there's some merit to that. And I think most people, if they, if they are serious about living a very long life, I think at least being aware of the field, and maybe telling a few of their friends and family, colleagues and so on, is probably a good thing to do. Because I think it's sort of like, once we have a critical mass of society who cares about this problem, then you have funding, you know, the government has to take it more seriously. And you know, the NIH budget and the geroscience, budget kind of increases, and suddenly you start seeing more rapid development. And when you see like kind of more consumer interest, you know, that the market is going to drive a lot more kind of developments on the biotech side. But anyway, so that's one apart. Now the other approach, which is the approach of someone like my friend, Sebastian, brew Meyer, who's the longevity biotech

VC, who's co founded to longevity biotech companies, his approach is to basically try and do both, like you want to try and progress the field, but you also want to focus on personal longevity strategies. Now, he knows the science a lot better than I do. And I've just got a document in front of me that has some of his protocol. So why don't I go through some of the things on his protocol, because I would defer my sensemaking on personal longevity strategies to Sebastian because he's a lot more, you know, a lot more knowledgeable in this area. But I'll just go through a few of the things here. I mean, daily multivitamin, omega three tumeric, resveratrol, Metformin, quesiton nr, which is nicotine amide, rubber nucleus, sorry, nicotinamide, riboside, vitamin D, vitamin C, B, 12. And in terms of lifestyle, you know, intermittent fasting carbohydrate reduction, low stress, exercise, walking, biking, swimming, you know, a bit of strength training, or maybe a six reduction, animal product reduction, eight to nine hours of sleep, stress reduction, sunlight exposure. And yeah, and that's sort of the some of the main things that he does. And because he's much more deeply familiar with some of the research and has been involved in the field for much longer than I have, I would just defer My my, my recommendations to him. But by the way, this is obviously not a, you know, medical, you know, it doesn't sort of cheap medical advice. But those are just some things you can start looking into. So if you want to just go back in the recording, just have a look at some of those compounds that I mentioned, start googling them learning about them. I think, also David Sinclair's book lifespan has some really good suggestions for basic strategies that you can employ today to extend your healthy lifespan. And I also think they're fairly robust as well. And they largely overlap with what Sebastian has suggested here. So to summarize, you know, there's the Aubrey de Grey approach, which is, you know, do whatever you want, because it's not going to matter at hand. Aubrey has publicly stated that, you know, he doesn't really sleep that much. But he he actually is lucky that he has quite a low biological age for his chronological age, which he's had measured. But I think someone like David Sinclair, or Sebastian would probably promote a more proactive approach to anti aging, which involves, you know, exercising meditation, stress reduction, sleeping, dieting, and taking certain supplements. David Sinclair is a big proponent of Metformin, and resveratrol, and an ad precursor molecules such as an Amen. So, yeah, so I think those are some of the main things to think about, I think, to learn more about this field because it's such a new field. And a lot of people won't have learned about it I think reading David Sinclair's book called lifespan, why are we aging? Why we don't have to, is probably the best kind of manual like introductory manual to anti aging. And then from there, you can start looking into resveratrol. But for

men, you know, there's a lot of companies now like do not age that produce these sorts of compounds that you can you can purchase.

Jake 1:44:26
Right? Yeah, I think that's a helpful overview. And obviously, people can do their own due diligence and, you know, maybe read David's book or explore some of the the alternatives that you pointed out. I want to close out our conversation. I mean, it's been a fascinating talk about aging and, and how we can all live healthier and longer. I think this is hopefully going to be a great conversation and interview for a lot of people to listen to and if you come in with an open mind, I think it might change a lot of people's minds. But I want to end on how you came to be interested in aging. In the first place, and in talking before this conversation, you told me something pretty interesting. I mean, on the one hand, you, you talked about how you see life as an optimization problem with two variables, one being subject to subjective well being, and the other being longevity. And obviously, now we're talking about mostly the ladder. But I understand you have a lot of experience to say the least with meditation. And I don't know if you're comfortable sharing kind of the practice and, and actually how long you've, you've meditated in terms of like time in the day, but we'd love to hear about how kind of all of that led you to where you are today working on aging. And then if you if you don't mind expanding on the meditation practice a bit, because I know when when you told me about it, it was something that stood out as highly unusual. And I think, on this podcast, at least, I like to talk to people about their most unusual habits, because I think they're oftentimes some of the most interesting. So I would love if you could kind of touch on all that.

Jack Harley 1:46:02
Yeah, sure. So the first thing I say is, I definitely wouldn't say I'm an expert at meditation. Although I have thought a lot about the role of meditation, and other sort of, you know, Buddhist practices, but also other psychological practices that you'd find in trauma therapy. I mean, here at Oxford, we have some of the best trauma researchers in the world, and other CBT techniques, and basically, you know, optimizing your psychology using a lot of these practices, if we really simplify life. Now, this is a gross simplification, but I think some of the most important things are, you know, how good do you feel this is kind of hedonistic utilitarianism, like how much psychological wellbeing do you have? And then how long do you have that for? That is broadly what most of us on some level, are seeking. Now that can manifest in all kinds of ways people are interested in sports, or in relaxing on the beach, or being with family or being productive, and so on, but some

kind of psychological well being. And, and then I think another factor that is important is longevity, because you can have a great life. But if you die when you're 10 years old, that somehow not is not as good or not as meaningful as if you at least for that person, as if they were to have lived to say 70 or 80, because they have more time to self actualize. Maybe they learn more about themselves in their 20s. And so even if they die when they're 10 years old, they haven't actually experienced life as fully as I could otherwise have. So then, in my case, you know, I just spent a lot of time thinking about, okay, I exist within the simulation created by my brain, which is basically this emergent phenomena that's, that comes out of the computational processes in my brain. And, okay, what am I trying to achieve? Well, you know, in the past, I ran a business. And, you know, there's different games that we play, right? Like in academia, people are playing a game where they want to get as many publications as possible and citations and be respected in their field. In business, people are playing a game where they're trying to, you know, raise as much revenue as they can for their, for their companies, and so on. So there's all these different games in life, but I tried to think about, you know, What game do I want to play? And why do I want to play it? You know, because I was in business before, and I've spent a little bit of time in academia. But ultimately, I think, you know, these games just service a deeper underlying kind of goal that we have on some level, which is to feel good, we just want to feel good. And when I thought about this problem it and and when I, when I started thinking about all of these neuropsychiatric conditions that I studied in my Masters depression, anxiety, bipolar, as well as neuro degeneration, and so on. I think what I concluded is that, you know, overcoming all trauma, and trying to work through, you know, you know, your deepest kind of like, basically, I don't say floors, but aspects of your psychology that are limiting you from optimizing your well being, which is not a single thing, but requires, in my opinion, different angles. So I do think there is a role in even from religious teachings, not even if you don't think their religion is correct. I do think there's a role for using religious teachings to kind of optimize your cycle, your psychological well being across different conscious states. And this isn't something I've written a lot about. So I can't really give a very robust explanation of this. But I think certain practices, spiritual practices, you know, they can provide certain levels of existential, you know, calm and so on. And, you know, ironically, it's kind of part of the pro aging trends. So I don't endorse it at the expense of rationality. But in terms of improving psychological well being, I think it can be quite useful. And personally, I found that especially a lot of practices from Buddhism, you know, basically realizing that most suffering comes from attachment, like you know why you're unhappy. Now, because you're a little bit hungry. You've got

an attachment to that. Because you, you would like a slightly higher paid job, or because you're unhappy with this friendship or this weekly, you know, there's all these attachments we have, we want the world to be in a way, that's different from it currently from how it currently is. And that's basically what the Buddha 2000 years ago said, he said, if you're attached, you will suffer. If you let go of all your attachments, you won't suffer as much, and you'll feel better. And in my case, when I, you know, I had known about Buddhism for a while. But when I started actually practicing it, and actually kind of following some of the steps that the Buddha recommended to actually let go of some of these attachments, I noticed that the marginal utility of my psychological well being improved much faster using this approach than any other approach. For example, if I earned like, 10%, more revenue with my business, back in 2018 2019, you know, that didn't really affect my well being that much. But if I meditated 10%, more, that had like a, like a proportionate increase in my psychological well being, this was the observation that I noted. So to me, it just seemed like, well, really, all you need to be extremely happy is these practices. Now, I'm talking about the Buddhist practices, but also is also very valuable aspects of trauma therapy, you know, books like body keeps the score, and things like that. Even some of the work by Anki, eulas. at Oxford, she's one of the most, this has also been quite a big influence, and having lectures from her and talking to her, in my course, has been quite a big influence. But basically, I think, you know, understanding your psychology, and adopting certain practices, such as Buddhist practices, and meditation, I do think, is one of the most robust ways of improving psychological well being. That said, I understand why a lot of people wouldn't want to do that, because it involves doing things that are challenging and that people don't like doing, you know, letting go of things that you've held on to your whole whole life, is actually quite an emotional, challenging thing to do, which is why a lot of people don't like doing it. And it does actually involve somewhat letting go of parts of your identity, it doesn't feel good when you're when you're introspecting. And you're seeing all these attachments you've held on to your whole life, to certain ideas about yourself and how you'd like the world to be, you know, I've always viewed myself as this, I've always wanted this. And then you see that that thought actually creates suffering. And the only way to kind of resolve that is not to get the thing, which will temporarily provide a fix for you only to later attached to something else. But to actually systematically uproot and remove all those attachments. I think that approach is not appealing to us in the West, because of our culture has evolved. You know, your materialistic pursuits, and so on. But I think objectively, if we, if we if we, if we track our subjective well being, and we kind of correlate the extent to which we follow and adopt these sort of practices with how good we feel, in my

opinion, it seems to work. And it seems to work with a pretty strong correlation that leads me to think that it's causative, but other people can try it for themselves. And interestingly enough, this is what the Buddha actually said himself. 2000 years ago, the Buddha actually said, you know, try these practices, if they work great, if they don't work, then you don't have to use them. And so you know, and that's kind of what what I like about Buddhism is that it is a lot of the teachings, the core psychological teachings are completely compatible with a secular worldview, you don't have to necessarily adopt any, any sort of belief, or dogma, to improve your psychological well being. And you might say that, well, it's not it's not technically Buddhism, if you're if you're not adopting certain beliefs about the afterlife, and so on. But in my case, I'm not necessarily practicing these Buddhist practices to be a good Buddhist, I'm doing it to improve my psychology, and I find that it works. So to me, you know, being you know, following Buddhism the right way, or however you want to phrase it is not necessarily what I consider most important, I consider what's most important to be, how does it influence my psychological well being. So that's a little about what I think about, you know, the ways in which we can improve psychological well being now, after I went through this process, it led me to another question. Okay, well, I've got a pretty good strategy for improving my psychological well being, I don't need tons of money. I don't need tons of friends. I don't need, you know, fancy car, fancy house. I don't even need productive work, or I don't even need anything really. All I need is just to meditate and to follow these Buddhist practices to feel really, really good. So after I'd kind of solved that problem, then my next one Question was Alright, so this is great, I'm feeling good. But there's a problem, which is that I'm going to die. And what I actually I had COVID-19, which was the catalyst for some of these thoughts, because I never really considered my own mortality, as most young people probably, unless they've had the death of a loved one or a close friend, they may not have really considered what it means, for their consciousness, the same consciousness that is listening to these words right now, for that consciousness to be permanently erased. And for that experience, which is we can assume similar to that of a general anaesthetic to remain indefinitely. It's kind of horrifying. And when I kind of had COVID nose, as because obviously, I'm young and tying back to what we talked about before with immuno senescence, and having a robust immune system as a young person, I didn't expect to die. But let's just say death was on my mind, just because, you know, when you have this sort of thing, and again, it ties back to the biopsychosocial model, that it describes the interaction between what you see and the social environment. And you know, in this case, the media frenzy of people dying, and how that affects you psychologically, and biologically. You know, I was I was thinking somewhat about about death.

And when I started thinking about death, it made me think about my mother, who died of cancer at the age of 55, in 2016. And that was, that was an experience that I never really understood. I didn't understand, like, Why did she die? Why did she die at this age. And another event that kind of catalyzed my interest in this aging field was my grandfather, who I mentioned, he turns 100, this year, he was born in 1921. The reason why a lot of these realizations came from thinking about my grandfather was because he's like, my best friend. And he and I, even though we are, you know, decades and decades apart, in terms of when we were born, we're very similar. And when I talk to him, it's like talking to myself in the future. With that similar, he was a scientist as well. He's got a he's got a very curious mind. And we make jokes. And he's like, it's like talking to your best friend growing up, except that he's, he was born in the 1920s. Right, which is quite a long time ago, and he's turning 100. And so when I talk to him, it's so It's so inspiring, yet also so tragic, that this friend of mine is in a body that is decaying, right? Like my best friend is in his body that has early signs of cancer, you know, has early signs of neuro degeneration has early signs of cardiovascular disease and some heart problems. And there's nothing I can do about it. And this is like my best friend. So So this person who I talked to who I see so much of myself in her who's just like, you know, not only family, but like one of my best friends, especially since my mom passed away. This This person is is dying before my eyes, he can barely walk. And he's slowly losing his memory. And, and and that's healthy aging and a good life. And and here's the crucial point is that, number one, there's nothing that the doctors can do for him. He's He's turning 100 years old, what can they do for him. And it's remarkable, because he actually smoked for 75 years of his life. And we can talk about certain factors involved in healthy longevity, but just very briefly to touch on this point, and and I'm kind of dipping in and out. But some of the longest lived people like there was a Japanese woman who recently turned 118, just a couple of weeks ago, I think she's the third, she's only the third person to reach that age. And she drinks coke. I'm sure there's a photo of her on the internet drinking Coke. So there is a genetic component to aging as well. And especially in Super centenarians, in the general public, a lot of the a lot of the longevity that people have if and their life expectancy is based on their lifestyle factors. It's about 8020 20%, genetics, 80% lifestyle, but in the case of these super centenarians, there can be a strong genetic component. And there's also quite a strong, you know, social component and quite a strong interaction of like their community and their family. And that's why we see the certain families and certain regions of the world called Blue Zones where people live much longer. And then well, they have higher numbers of centenarians, and actually last year in 2020, actually visited two of the Blue Zones, which are

Sardinia, so this island in Italy, where they have these small mountainous villages where they have the highest recorded number of Oh, the highest density, I suppose, of centenarians in the world, and he Korea in Greece, so during the pandemic, I wanted to kind of escape the mayhem in the UK, so hopped over to these islands in in Europe where they have these long live populations. And that's another that's a whole nother story that we could go into about, you know, what did I learn talking to these 100 year olds, there's actually a documentary on I think amazon prime on Netflix, with With Zac Efron, and he actually talks to the same people that I talked to in this village called solar, which is in Sardinia, in Italy. And, you know, it's very fascinating to talk to these centenarians. Because this village, which apparently has a population of about 2000 people, has something like 20 people in the last decade who lived over 100. So they have remarkable longevity, which is, you know, 10 or hundreds of times higher than the typical rate of centenarians. And we can go into that as well as another angle, or maybe another time about, you know, what are the longevity strategies have these people in these Blue Zones who live remarkably long, but ultimately, I'm not as interested in the Blue Zone kind of stuff, simply because I think whatever they have done with famines that kind of resemble intermittent fasting and with strong social ties, all of that will be superseded by technology Anyway, when we get better anti aging drugs. So I'm less interested in that anyway, to go back to my grandfather. So my grandfather, number one is that medicine can't do much for him because he's old. And that really saddened me, you know, I want my grandfather to keep living because he's my best friend, he doesn't necessarily want to die. And I think and number two, is that having a long happy life, doesn't mean you want to die. If anything, it would mean you, you would want to keep living. So if you look at my grandfather, he's got, he's got children. He's got five children. He's got many grandchildren, and he's got great grandchildren. He has lived with his wife, my grand mother, who passed away a few years ago, for 75 years, they were married 75 years. And he owned his own house, he lived the first 40 years of his life in India, before moving to Australia, where I live the next well, 60 years as of this year. And you know, he had a good job that he enjoyed as a scientist, as a chemist. And, you know, if you look at his life, it's the quintessential long, happy life, he also smoked for 70 years, a pack of cigarettes a day, and he he drank port, this fortified wine. So he lived a long happy life. But that doesn't change the fact that right now, he is a conscious entity like me, like you like everyone listening, who is trapped within a body that is decaying, that is the horror of aging, it doesn't matter if you've lived literally 100 years of a happy life, you're going to be trapped in a body that is decaying from the inside out. And that's going to kill you. Unless we solve aging, and like these sort

of realizations, what what really prompted me to realize, okay, I might feel good with my meditation, and you know, these Buddhist practices, and so on. But I'm also aging, and that doesn't seem good. So now that I've kind of sorted out the psychological well being side, let's take a look at aging. And let's take a look at keeping the psychology, the psychological well being let's take a look at how we can keep that going for as long as possible. So this is quite a brief description. But this this kind of introduces how I got involved in the field. And the initial kind of thoughts that I had that led me to think that aging was a big problem. Now, when actually woke up from the pro aging trance, it was very horrifying. Because after I had these sort of realizations that I just described, I was very shocked. I was like, Oh, my God, I'm actually dying right now, like, in the sense that my disease risk and the changes in my body that are occurring right now are actually going to kill me. And this was also compounded by the fact that during my neuroscience master's degree, I learned about how the onset of Alzheimer's disease or any neurodegenerative disease is preceded by, say 10 2030 years of kind of changes, right? So Alzheimer's doesn't come out of nowhere, right? There's a long, protracted period of subclinical progression whereby your your brain is actually deteriorating, but you don't, it hasn't deteriorated, deteriorated to a sufficient amount where you can actually notice the memory problems, right. So, you know, these psychiatric conditions are diagnosed primarily by symptomatology. But that doesn't necessarily reflect the underlying biology, in the sense that you could have a very long period where it goes on diagnosed, which is normally the case for 1020 years before someone gets Alzheimer's disease, where you're actually accumulating more and more damage in your brain. We don't really have the technology today to measure that. Although that's kind of getting better with imaging and you know, neuro imaging and so on, but you're actually getting closer to Alzheimer's for a long time before you get Alzheimer's. And when I learned about these sort of facts that made me really think that oh my god, even though I'm quite young now, I'm Actually, I'm actually dying. Like that was such a paradigm shift for me. And I talked to a philosopher philosopher here at Oxford, who told me I should write a book called when living became dying, because that kind of summarizes this paradigmatic shift I had in my psychology when it was like, Oh, shit, you know, I thought I was healthy. And even though I am young and healthy, I'm also dying every second because every single second, I'm accumulating more and more damage in my body, that's eventually going to kill me. And unless I can repair that damage, I'm screwed, as is everyone I love as everyone in the entire world. So then, that actually was quite horrifying, and temporarily took me out of my you know, meditative state of well being, ironically enough. And so I started looking at, okay, how can we solve aging? So I did a lot of googling, I basically spent three months on my computer,

watching talks by David Sinclair, Aubrey de Grey, reading their books, reading, you know, 1000 or so scientific papers about the hallmarks of aging, about different therapeutic approaches, you know, research from here at Oxford with Lynn Cox's lab, David Sinclair at Harvard, professors who are Pedro at University of Liverpool, Eric Verdun at the buck Institute, and Judith campisi, at the buck Institute, people like Brian Kennedy from us, and I started watching all these talks, and, you know, going to some of the conferences like the Cold Spring Harbor laboratories, mechanisms of aging conference, the, the IR, dd conference, and so on, that are their own co hosts. And I started really learning and immersing myself amongst all these aging researchers, because basically, I was pretty deeply concerned about the fact that I was dying every second and I wanted to know, okay, is there a way that I can slow this process? Is it even possible? And what I learned through going to these conferences and talking to these people? Is that, yeah, it's actually very feasible that we can slow the aging process. And we have a lot of evidence to suggest that healthspan and lifespan are malleable. And as soon as I I, I kind of appraised the field of neuroscience and the anti aging and longevity biotech well enough to kind of reach this conclusion, suddenly, that became my life focus. Because if you don't have life, you don't have anything else. And right now, the two biggest threats to our life are aging, and probably, you know, Ai, if we're being honest, so, Ai, I don't feel particularly qualified to kind of help with that problem with AI safety. So I'll leave that to the experts. But with aging, I think that, you know, there's such an opportunity for any young biologists or people in the medical space involved in, you know, medicine is doctors, or even people in biotech, even the general public to really take an interest in their own aging and their own anti aging. And the way they can do that is by learning about the field by reading David Sinclair, Aubrey de Grey, by maybe attending some of these talks or conferences, and just trying to become educated, because what really astounded me as well. And this is also ties into why I was invited to give a lecture at Oxford University and Monash University in Australia, on this topic of aging in your generation, was that we go through entire medical courses without learning about aging. Now, I didn't study medicine, I studied preclinical medicine, which is called biomedical science in Australia. But I went through four years of biomedical science without a single lecture explaining what are the hallmarks of aging? Now think about how absurd that is, you've got a full year course with hundreds of hours of content from some of the best lecturers, and you're not teaching people about the thing that kills 90% of people in Australia. Like, that seems pretty, pretty absurd when you think about it. So so what I did was I created a lecture, and I pitched it to my unit coordinators, when I was studying. And they said, yeah, this is actually a pretty important topic. Why don't you go ahead and give some

lectures. But the thing is, I'm not the most qualified person to do this. But I think that someone needs to do it. And I think that, you know, if there are people within the field, or even doctors who are interested in this field, you know, you guys can can start learning about this field can start reading up on this field, can start attending these conferences and educating others. You know, I'm just, you know, I'm just a humble scientist, but I'm by no means an expert in this field. But I just think it's genuinely important. And I think that the more people who can start looking at the science, start understanding what aging is, and why it's such a big problem in public health, and the different ways that we can start intervening, the better because at the end of the day, all of us if we don't die of something else, all of us are going to die of aging. That's That's a fact. Under the status quo, and that is something that although a lot of people don't realize that it is something that can be changed. And I think that there's a very strong rationale, both from a personal perspective and from an altruistic perspective, to want to contribute to this fight against aging.

Jake 2:10:14
Well, I think that's a great place to wrap things up. I know we've, this is actually going to be the longest podcast that I've done today. But I think it's appropriate, because we're talking about what it sounds like we both somewhat agree on is, you know, probably the biggest problem that we have to solve as humanity, which is aging, so we can all live longer, healthier lives, and then, you know, to your point, we can, we can worry about the happiness in parallel. But, you know, being healthy and living a long time, sounds great to me. And despite some of the protests of overpopulation, or death gives meaning to life, you know, I'll take my chances with with feeling like I'm 20, or 30, when I'm 150 years old, or something like that. So and I think that also, you know, you mentioned how you've only somewhat recently become interested in the space and you know, a lot of doctors and scientists and young individuals can kind of do the same. But I think very quickly, you've kind of developed yourself into one of, if not the best communicator, in the world of this science and of this progress. And, you know, I love listening to people like Aubrey de Grey, and David Sinclair as well. But as someone who just kind of picked up the science and started, you know, dove into a number of books, and 1000, you know, scientific papers and kind of familiarize yourself with the science and the background and science communication, I think, hopefully, this conversation has served as an excellent introduction for a lot of people. And that's really all you need to kind of open your eyes to the possibilities of some of this. And I think it's a very hopeful and optimistic and feasible future that we've been talking about. So I want to thank you, jack, for for coming on and spending the time

today. Lastly, where can people go to follow some of what you're doing and some of this work or, you know, maybe find places to learn and contribute in whatever ways they can?

Jack Harley 2:12:17
Well, first of all, thanks a lot, Jake. I really appreciate this opportunity. Because I think the more if I can convince one person to become interested in this field, that I think it will be an absolute success. And so, you know, I think doing this podcast and inspiring others is the way that we can get more people interested more people excited. So if people are interested in this topic, have a read of my post on the website, less wrong.com le ws wrong.com. Just type in anti aging, and it should come up and just keep posted on less wrong because I plan to write some other articles covering some of the topics that I touched on today very shortly.