POD OF JAKE
#109 - MATT KAEBERLEIN
AI-GENERATED TRANSCRIPT

Jake 02:18
Thank you, Matt, for coming on. And joining me on the show today, I appreciate you taking the time you are a professor at University of Washington School of Medicine, research focused on mechanisms of aging, with the goal being to come up with interventions that can actually increase health span and various animals and ultimately, hopefully humans. Then you're also co director of the dog aging project, which is a really interesting Longitudinal Study of 10s of 1000s of dogs. And you know, again, hoping to translate some of the learnings from that into humans at some point. So one of the sort of foremost individuals in the space I think of aging, and I've had some guests on from from the area before, but very excited for the conversation. For those who don't know, you will be great if we could just start by sort of hearing your story from as early as you're willing to start to where you are today and some of the decisions you made along the way.

Matt Kaeberlein 03:08
There. Thanks, Jake. It's a pleasure to speak with you today. All right, well, we'll we'll go back to the very beginning, I actually was born in Erie, Pennsylvania, but I grew up in Seattle, which is where I'm located now. And I would say, you know, I come from a family where I'm the first person to graduate from college and to get an advanced degree. So, you know, I was growing up, I would say I never really had a clear ambition to, to get a PhD and, and go on and, you know, do biomedical research at a at a top tier university. That really wasn't on my radar. So I, in fact, I would say I was sort of a late bloomer in many ways, from an academic perspective, I, you know, I was, let's just say fairly immature, in my, my teens, as many people are not very focused on school, didn't really, you know, put a lot of effort into into academics. And actually, after I graduated from high school, I didn't go directly to undergraduate college I spent about I guess, was probably three or four years working for United Parcel Service initially as an unloader. And then as a package sorter in the very early morning shift, loading the brown Big Brown trucks and and then also had a second job delivering auto glass for safe light. So you know, maybe not the typical academic track, although I think everybody has their own their own path for sure. And it was really, you know, after being after being working those two jobs for for a couple of

years that I decided I probably didn't want to do that for the rest of my life. started taking classes at a local junior college again, I hadn't really narrowed it down even to buy anything biological at that point, I was just kind of getting my feet back into the academic world and with the plan to get my associates, associate's degree, and then and then see where, where I ended up. And there were really a couple of things that happened at that point. And this was, you know, I was probably 2021 or 22. Around this time. One of them was I met the woman who would become my wife. And, and I think that helped me grow up and become motivated quite a bit. We're still married, by the way. And, and I had a really fantastic biology teacher at Highline Community College, near Seattle, who, you know, I think it was just the right time and right place. And I became very inspired by evolution and natural selection, and the beauty and complexity of biology, in large part because of this teacher that I had. And so once I completed my two year degree, went to State College, about 90 miles north of Seattle called Western Washington University, where I majored in biochemistry. And my wife majored in, in biology. And, you know, and at that point, I think, really started to take learning in academia very seriously and sort of immerse myself in, in biology and biochemistry. Such that when I graduated from Western, I ended up going from there to MIT, the biology program at MIT, where I got my PhD. And as you can maybe imagine, that was a bit of a culture shock, coming from, you know, a relatively small state school to MIT. But it was fantastic. And, and I actually started studying what I study now, which is the biology of aging. When I was at MIT, so during my first year at MIT, I heard a talk by one of the professors in the biology department there, Lenny garantie, where he talked about how his lab was using genetics and molecular biology and biochemistry to try to understand the the cellular and molecular mechanisms of biological aging. And, you know, I was, I had never thought about aging as something you could study, or would study. I was pretty young at the time, and it wasn't personal yet. But I still don't know exactly why I got turned on to that topic. But, but you know, Lenny's talk really resonated with me. And it was, it was absolutely a, you know, one of those moments in life where your trajectory shifts, and, and I became fascinated by the idea that we could, we could study something as complex as the biology of aging. And that's what I ended up doing my PhD thesis work on in Lenny's lab, studying the genetics and molecular

biology of aging in a single celled organism in budding yeast. And I've, you know, continued to work in this field since then. And so I feel, I feel very fortunate to, to have sort of had that opportunity and to have gotten turned on to this topic. When I did, because it's been a great ride. It's been a super exciting and fun path. And, and I think right now is a particularly exciting time in the field, because I feel like we're really on the cusp of this, this field and this science becoming mainstream and becoming appreciated by the general public. And, and I think we're also on the cusp of big discoveries that that can have an impact in the real world, on people's lives. So So again, I just feel extremely fortunate to have to found my way to where I met.

Jake 08:56
Wow, yeah, that's that's an amazing story and appreciate you sharing it. I knew about some of the more recent stuff coming in, but I did not know that you sort of took some time between high school and college and worked at the post office basically, it sounds

Matt Kaeberlein 09:11
awesome. Yeah. Funny story there. i My family is a has a long line of United postal service workers. So when I went to work at UPS, I was sort of the I was gonna say, the black sheep of the family, maybe the brown sheep of the family for a while there.

Jake 09:26
That's fine. Yeah. I mean, it's just, it's a pretty remarkable story. And then sort of finding in the midst of that, the motivation or drive or whatever it was, sounds like some of it had to do with with meeting your wife and maybe growing up a little bit, but realizing like I want to go and, and sort of do something bigger than this, and, you know, whatever that might be and just sort of taking one step at a time, going to community college, developing an interest in bio, then go into graduate school, finding aging. It's just a very cool, incremental story that I think hopefully is is encouraging for pupils, sort of, regardless of where they are now, if they're young, there's always or even if they're not so young, it's really time to, you know, take a different path. And I think you mentioned, sort of there's,

there's moments in life when your trajectory just sort of takes a turn. And that's, that's really cool.

Matt Kaeberlein 10:15
I think, can I just chime in on next I think that's super important. Super important point. And, you know, I've got two sons 20 and 16 years old. And, and, you know, I see kids these days, and kids have, you know, college undergraduates who work in my lab, and so many of them are so impressive. And I look at them, and they're so far ahead of where I was, you know, at that age, but I also think it's really important for people to appreciate, you don't have to have it all figured out. By the time you're 1819 2021, some people mature at different rates, some people have experiences in their lives early on that, you know, that influence where they're at, at a given age, you don't have to have the rest of your life figured out, you know, by the time you're 20, in order to have a fulfilling and successful future. And so I just want people to know, you know, if you're in that position, it's okay, you can, you can always change your trajectory, and, and just keep trying to find the path that's right for you the thing that you're passionate about, keep looking until you get there. Because, you know, it's not, it's not too late. And I think that's really important for people to appreciate.

Jake 11:31
Yeah, no, I totally agree. And I think, you know, it sort of reminds me of this interesting point that I consider sometimes being, you know, relatively young, in my later 20s. Myself, I think that, you know, if you ask, like, the average person, and I've seen, like polls about this, but you know, if you ask people, if there's a chance that like, people alive today, whether you know, middle aged, or on the younger side might live, you know, well past 100, or 110, or even 120, as people assign, like a pretty decent probability to that just your average person, you know, doesn't know anything about the field that you're in, and the work that you're doing, and your colleagues, but just sort of senses like, you know, humans seem to be living a bit longer, and we're figuring things out, and technology is getting better, etc, etc. But no one actually really no one that I know, at least like sort of plans on, you know, or probability weights that possibility until like, their life planning, and so we still sort of

think on like, the old template of you know, you go to college, at this age, you work for this many years, you retire at 60, you know, you get old and you die. Yeah, no one that's sort of Christ in the thing that they all sort of agree, at least has some decent probability of happening, which is that the whole lifespan actually is gonna get extended, and you can do useful things for a longer period of time. And I think that's even, you know, it just supports your point even further that like, you know, take your time figuring things out, no need to rush through things you might have given longer than other people in the past have had to do everything you want to do.

Matt Kaeberlein 13:05
Yeah, I think there's going to be all sorts of interesting and important social discussions that go along with that. I will say, though, you know, it's still a little bit of an open question, what the actual life expectancy, you know, is going to be and what that trajectory is going to be at sort of a population level, obviously, it's an open question, nobody can, can predict the future, I share your, your perception and your optimism that it's likely that we will see, you know, relatively significant technologies come online that can enhance human lifespan, certainly human health span, I think maybe that's even an even more important concept to consider the period of life that is spent, you know, high functioning, relatively good health, that that that will be expanded through the kinds of discoveries that have been made and continue to be made in the field that I work in, you know, how long it'll take to, to see those technologies become widely available, I think, is an open question. But you're absolutely right, that that many people are very likely to have, you know, 20 years of additional healthy life and thinking about what that means for that, you know, the sort of stereotypical path of you know, you get you get you start your career in your early 20s, you work for 40 years, and then you retire, you may have another 2030 years on top of that, that are you know, that are quality years of life, and many people do already right. And so, thinking about what that means, can you have two careers? Sure, you can have two careers, can you find something that you absolutely love and you're not going to want to retire? I'm sure you can do that. But definitely thinking about that. Now makes a lot of sense. And, you know, I think the I think that there are a lot More people thinking along these lines and

starting to think about what are the potential policy implications? What are the economic implications? You know, do we need to change the retirement age? Absolutely, we're going to if this if this continues, but on the other hand, and I don't want to be negative at all, but I do think we have to be realistic. You know, when you look at some of the the population level trends in terms of obesity, and sedentary lifestyles and things like that there are these sort of counteracting forces for health and life expectancy, that it's a little bit unclear to me, you know, where that's going to shake out and how long it's going to take, you know, before we we really do start to see the life expect in the United States, in particular, the life expectancy get to where we want it to be. And I don't know if you've seen the recent data, but you know, in the United States, there has been pretty dramatic flattening of the the average life expectancy trajectory over over time in the last four or five years. Some of that might be due to COVID. Certainly, but I think a lot of it has to do with the, again, the population level lifestyle factors that are depressing, healthspan and lifespan for many people right now.

Jake 16:21
Yeah. So when you talk about these counteracting forces, you know, it sounds like obesity generally, you know, with the driving factors behind that being, you know, how much food we eat, what kinds of food we eat, how much we exercise versus how much we're sedentary? Are there other forces do you think about that are counteracting the improving technology? And generally, I think improving knowledge around sort of what we need to do to be healthy, for example, you know, not smoking cigarettes and things like that.

Matt Kaeberlein 16:51
Yeah. And I mean, actually, the non smoking cigarettes is a really good example of a positive change. Right? Again, I remember when I was young, you saw people smoking in public all the time. And you don't see that so much, at least in the in the United States, or at least the parts of the United States that I live in. So that's been a very positive change. I think, you know, I think, certainly, there are a lot of a lot of factors that might contribute to depressing healthspan and lifespan, again, my personal view is that the two big ones are sedentary lifestyle, and being overweight and obese, combined with the

types of of food consumption that are driving that obesity epidemic, the, you know, the very high sugar loads that a lot of people are consuming that contribute to diabetes combined with obesity, well, you know, which is a huge problem. So. So I think those are probably the big two. And, you know, if I had to pick one, I would actually pick sedentary lifestyle as the single most effective thing that most people could do to to increase their likelihood of living a longer and healthier life potentially living long enough and healthy enough to benefit from the things that we're developing in the field right now would be just be more active, you know, even if you're not going to change your diet, exercise regularly. And you know, that's going to help almost everybody have a better odds of being healthier later in life. You know, I think the other the other macro things that are harder to quantify right now are, you know, things like, pollution, contamination, chronic stress, which I think a lot of people certainly are feeling right now, you know, we're just hopefully coming out of a global pandemic, the pandemic itself, obviously, you know, depressed, average life expectancy for a couple of years, the sort of longer term effects of just going through that are a little bit harder to quantify. I think a lot of people, though, are certainly suffering from chronic stress, which affects sleep quality, we know that sleep quality is really important for health. So, you know, I think figuring out strategies to manage those parts of your life are really important. That's a little bit outside my area of expertise, right, I focus more on the biological mechanisms, but you know, there are definitely lots of people who are working on the relationship between chronic stress and wellness and biological outcomes that influence health. I think that's, that's super important. sleep quality, in particular, I already mentioned is is you know, certainly one of the pillars along with diet and exercise for optimizing your your health going forward. But, you know, I again, my feeling is that, that we have a lot of control over those things. It's hard I get it, it's really hard for a lot of people to to manage the sort of pervasive, inexpensive, really good tasting food that's everywhere. But you do have control over that and you do have control over your activity levels, and you have some control over your stress levels. And there are strategies that you can take. And so I think if people take, if people try to achieve, you know, healthier lifestyle, that will, that will go a long ways towards, you know, maintaining health span as long

as possible and potentially benefiting then from more from the discoveries that are happening in the biology of aging.

Jake 20:27
Yeah, I think, you know, when you talk about these issues, I know, it's like, not directly in your wheelhouse, you're more focused on the biology, but I do think it's an interesting point to think of these like counter trends and with with sedentary lifestyle, at least, and obesity, I like to think about, like, you know, the most common excuse for, for these things, because, like you said, it is sort of, you know, it's in your control, for the most part, but the one thing that's sort of, at least reasonably sort of hard for some people to control is they just sort of simply don't have time or don't feel that they have time, among other priorities, like family and, you know, working a job or two, or whatever it is. So I think about, you know, what are the things that I can do, because I'm trying to, you know, make effective use my time just like anyone else, and I think like, what are the things I can do, that actually don't take time. And so you know, and might actually save time, so like, for example, you know, fasting and not eating, actually saves time, it doesn't take any time to not eat, obviously, and it takes time to eat, and then maybe I can allocate, like those 15 minutes that I would allocate to lunch to like going for a walk, and suddenly, you know, you're like, beaten down the sedentary issue in a couple of different ways. And obviously, there's a lot of ways to attack it. But I think, you know, it's a decision and people need to like sort of feel empowered, empowered, by realizing that like, there's, there are choices that they can make, if they really care about living a long and healthy life.

Matt Kaeberlein 21:52
Yeah, I think that's absolutely true. And the one thing I would add a couple things I would add, one is, I think, you know, a really important step is what you just said, Right? Recognizing that you are empowered to make some of those choices and thinking through, you know, just in your day to day life, what are some things that I can do, you know, that will kind of move the needle in the in the right direction, you mentioned, fasting, I think fasting can work really well for some people. The other point that I would make, though, is, I think that it's important to have some self exploration in what works

for you, fasting isn't going to work for everybody. And, and so I think that, you know, we should stay away from a one size fits all approach. And people should, should try to be empowered to figure out for themselves and try different things and see what works. I mean, I think, you know, again, some of this, you know, it sounds, you know, kind of sound simplistic, but I think there's a lot of value in it, right? Take the stairs instead of the elevator is a really simple one, right? That sounds obvious, but a lot of people don't do that. And so I think, you know, those are the kinds of things that are that, you know, anybody almost can can implement things like that into their daily life. And, you know, start small again, this is, you know, this is sort of, you know, an echo of what I said before about, you know, knowing what you're going to do when you're when you're 20, and, you know, being on that path, immediately. The same thing is true for health, I think in a lot of ways, you know, where you don't have to be on the health and, you know, optimal fitness path from the time you're 20, wherever you're at now, you can take steps to improve your health. And, and so again, I think it's really easy for people to, to feel beaten down, because they've, you know, gotten in this mode, where they're not healthy, and they're not necessarily particularly happy with, with where they're at. And I think that can keep people from taking steps to get out of that or to make changes in their lives. And so, yeah, I again, you know, this is not my area of expertise, but I but I do, I do hope that some people listening can get some value from it and, and maybe think about little ways that you can, you can tweak what you're doing to to, again, give yourself the best chance of living a long and healthy life. And the last point I'll say is a lot of these things do intersect with the biology of aging. And that's something that I think a lot of people don't recognize, you know, nutrition in particular, has been one of the most studied environmental factors that we know directly impacts the biology of aging. caloric restriction, for example, is is in many ways, still the gold standard for slowing aging, increasing lifespan extending healthspan in laboratory animals and and, you know, we've learned a lot about the biology that underlies that the molecular mechanisms that are driving that relationship, but there's no question that our dietary choices can impact biological aging in people. And so maybe that's another way for people to think about it is you know, The

choices you make about what you eat and how much you eat, could actually be affecting the rate at which your body is aging.

Jake 25:09
Yeah, and I think it's hard because like you said earlier, it's it's very personalized, it seems, at least from my sort of outside perspective, and there's sort of few general rules that seem just like automatically applicable, no matter who you are. And I think I mean, I'm excited over the next decade, or however long it is to see hopefully, some more products come out that can help people, whether it's a product or you know, an occasional visit to see a specialist or whatever it might be. But hopefully, it's something that's relatively accessible for people that can help them figure out, you know, with their, with their genetics, and, you know, with their habits and their lifestyle and various defaults, that they sort of half the deal around, like, what are the best, most impactful decisions that they can make? You know, that are personal to them. And I don't know if there's anything that's amazing, existing today. I know, I saw you went on the podcast with Gil blander, and I have his product inside tracker, and had him on the podcast, I think that's a really interesting product, you know, still very much developing but already probably very useful. And I've enjoyed it. There's, you know, continuous glucose monitoring levels is a sponsor of the podcast, and there's not to plug all the sponsors, but or also, you know, sponsors podcast, and they do a lot around sleep and an activity and things like that. And I'm hopeful that a lot of these products will just continue to get better and better. As we move forward. You know, you mentioned that this seems like we're sort of on feels like we're on the cusp of both thumb, you know, sort of the mainstream, recognizing the work that's going on and becoming more excited and more involved about it. And then secondarily, actual, you know, Pivotal discoveries being made. Maybe we can start by talking about like, if any of that is going on along, like the product side that's helping go mainstream, but then more generally, like zooming out, what do you think, makes you feel like we're on the cusp, because you've been in the space for her in the field for, you know, going on 20 years, I think or so. And I assume you haven't felt that same way for like, 20 years, it's more of a recent growing phenomenon. So I'd be very curious, like, what, what's driving that feeling for you?

Matt Kaeberlein 27:30
Sure. So so let's start with the first, the first question, which I think, you know, if you more broadly, classify the kinds of things that that are available now, like you talked about glucose monitoring, or rings, but then we can sort of put those under a general heading of biomarkers, or what what some people even would, you know, would call biological aging clocks. And there are a variety of these clocks that look at different parameters. And I think those are, it's still really early, but the concept is sound. But the idea here is that there are a variety of different tools that we can use to sort of query your personal physiology to get a feel for how what you're doing. And it could be, it's going to be a combination of genetics and environment. So your individual genotype, combined with the environment that you are in, and I would put diet under environment, that all goes under the environment, umbrella, as does activity. So when you combine that genetics by environment, to get a whole picture of what's influencing your individual biology, there are a subset of markers that we can use to understand what what is happening at the biological aging at the level of biological aging. And in principle should be able to predict if you tweak this aspect of your environment, we're not yet to the point where we can easily tweak our genomes. So you're sort of stuck, you know, with changing the environment, which by the way, would also include medicines that you take, can you tweak your environment? And when you do that, what is the impact on your biological aging rate or your your biological age, right, and use that to personalize approaches that people can take? That's the that's the goal, right? That's the Holy Grail? To some extent, we're not there yet. You will find people selling these biological age tests. And, you know, they may or may not they tell you something, they may or may not tell you something useful, I guess, I would say, but I think we're getting there. And I think absolutely, you know, things like continuous glucose monitoring, which to me are a little bit more direct measures of something that we're pretty sure it's physiologically important. If you have bad glucose homeostasis. You want to change that we're pretty sure that that's true. I think those kinds of things can absolutely tell you about about lifestyle modifications, but you know, I put it Over the next five years or so, we will see a pretty significant maturation in these biological aging tests or I don't really like the

word clocks, but that's what a lot of people call them, we'll see a pretty significant maturation there and some validation that will give us a lot more confidence that these things are really telling us, you know, something important and actionable. I think that's, I guess that's what I would say, most of these tests that we have today aren't truly actionable. And we don't really know whether they're, they're informing us about underlying biology of aging. And it's the biology of aging, that's going to drive your future health outcomes to a large extent, you know, ignoring stochastic things like if you get run over by a bus. So So I think that's kind of where we're at. I think we absolutely will continue to see improvements there. So so then the second question, which is, you know, why do I feel like we are sort of on the cusp of the field going mainstream, I think there are multiple things that contribute to that. Certainly, I see a lot more interest and popular interest in in the field, I think, you know, people like David Sinclair, and I don't agree with a lot of what David says, but I think he has had an impact at popularizing the field. And, you know, getting it recognized a little bit more in the in the public sphere, I think there has been a lot of resources coming into the field, you know, in terms of financial resources to support research in the field. And that's been both in the public sector and the private sector, which has been really interesting. And then I also feel like, you know, there is a start of growing recognition among physicians of the importance of, of actually modifying the biology of aging. Let me let me break that down. First thing, I would say, just the fact that some physicians now recognize that biological aging is a modifiable risk factor is a big change. That has never been the case previously, I think, as we educate more and more physicians that aging is actually a modifiable risk factor that will change the way that physicians practice medicine. So I kind of call this 21st century medicine, the idea that, you know, over the coming decades, physicians are going to stop, hopefully, mostly stop being reactive, certainly, we will continue to treat disease, don't get me wrong, but there's the shift will go away from the First Order approach being waiting until people are sick, and then trying to treat their disease to keeping people healthier, longer. And absolutely, the single best way to do that is to target the biology of aging, because the biology of aging is the single greatest risk factor for every major cause of death and disability in the United States and every other developed country in

the world. So it just makes a lot more sense to target health that way, as physicians are starting to recognize that, that that's possible that you can actually modify the biology of aging, I think we'll see this shift to 21st century medicine. And actually, I want to give a shout out to my friend, Peter Atea, who is a physician, and I think is really one of the great communicators in this space of that concept. So Peter calls it medicine 3.0. But it's the same idea, right? That there are strategies that we can take now, to actually have an impact on the biology of aging, to maximize health span and longevity, and we're starting to see more and more of that kind of communication. So I think it's all of those things. The last thing I would say, is also there in the last maybe three years has been a proliferation of biotechnology companies in this space. And, you know, it's been pretty dramatic and pretty rapid growth. And I think that's an indication that, you know, we're kind of making this transition from purely laboratory based, basic research, so preclinical research to actual clinical approaches now, that companies can take where they can start to develop things like these clocks, that they can market these assays that they can market, but also therapeutics that can go through the the regular FDA clinical trial process, you know, I think that's something that's pretty new that that, you know, that we're seeing dozens, maybe of companies trying to develop therapeutics that they can move into the clinic and get approval for from FDA. So that is really, I think, an indicator also that the field is on the cusp of of, you know, really going mainstream and really having an impact.

Jake 34:40
I think it's great, I mean, obviously attention and and money should help you know, all things equal and talent as well. Should all sort of everything else equal help to accelerate progress in the space. I think the more it becomes sort of mainstream, the better and and to your point also, you know, getting physicians on board and treating you know, the status quo. case of, you know, healthy person growing less healthy and aging over time, little bit differently than we have in the past. I think it's all really good stuff. And I mean, from my perspective, which is much less, you know, inside and much less lengthy than yours, but I sort of first became interested in this space generally, I think in like 2017 or so, stumbled upon, like some of Laura Demmings work and was able to go to a couple of meetings she

was having in San Francisco at the time, and I didn't really know or hear anything about it from anywhere at that time. And just over the last couple of years, I feel like, you know, like you said, David Sinclair, I think has been a big part of it, maybe and some other influential figures, but it just seems that it feels to me as well, like it's gaining momentum. But for you to say that it sort of feels like it's on the cusp obviously carries a lot more weight in my mind, that that's sort of an accurate feeling of the momentum that is increasing. I want to raise a tweet that, that I saw of yours that I think is sort of relevant to the point you were making about, you know, if you want to have the largest impact, you target aging directly. So I'm just gonna read the tweet, and then I appreciate if you'd like sort of just elaborated on, you know, what you meant by this and just sort of expand on it a little bit. So the tweet was a prediction, the first set of Morphix analytic to be widely used for that purpose parentheses rapamycin question mark, will be greater than tenfold more effective for healthy lifespan than the top five cancer therapies combined, achieved with geroscience research receiving less than 1% funding of cancer research.

Matt Kaeberlein 36:42
Alright, lots to unpack there. So I'll start with the very end of that, which is, you know, obviously, expressing a little bit of my frustration with how underfunded the field has been. And these are just simple numbers. And then I'll give you the rationale for why I said what I said, But, you know, prior to the last year or so, because I don't know exactly what the budget is now, the budget for NIH, so So NIH, NASA, the National Institutes of Health is the primary federal government funder of biomedical research, DOD funds, some as well, I don't have the statistics on DOD. So we'll just look at NIH, NIH funding for cancer, just at the National Cancer Institute, there's research on cancer outside of that. So the number, the real number is probably bigger, but just at NCI is about 6 billion with a B, dollars a year. Research for the biology of aging, which is what I study, again, it's a little bit hard to get the exact numbers, but it's probably around 300 to 350 million with an M dollars a year. So about 15 fold, or so a little bit more than a little bit more than that less for biology of aging than specifically for cancer. Okay, so that those are just the numbers. And that's been true, you know, that's been

skewed even more towards cancer, and other specific diseases in the past. And, again, you know, we've had a war on cancer for more than 50 years now. And, you know, when it started, cancer was the second leading cause of death behind heart disease today, maybe with the exception of COVID. Cancer is the second leading cause of death behind heart disease. Now, I don't say that to minimize all the people who've been cured of cancer, obviously, at an individual level, curing cancer is immensely important as curing individuals heart disease, or kidney disease or whatever. But at the population level, I think it's useful to ask, you know, have those resources really been put towards the most effective strategy for keeping the most people alive and healthy as long as possible. And I think if you really look at the data, it's immensely difficult to conclude that targeting individual diseases, with our resources is the most efficient or effective strategy. So there are a lot of ways you can look at that. But I think again, just to look at the statistics is helpful. If you just look at deaths due to X write different diseases, so the CDC is really good at keeping track of what people die from. So if you just look at deaths due to cancer, for example, you can pretty easily mathematically calculate what is the effect on life expectancy if we got rid of those. So if we had a pill that cured every single cause of cancer, and every single person that ever developed cancer, what would the impact be on life expectancy and it turns out for a typical 50 year old woman, it's about three years. So when I first saw that I was surprised because I kind of thought it would be bigger than that. It it's also about the same. By the way, if we cured all forms of heart disease, about three years if you cure both cancer and heart disease, you get about six or seven years of added life expectancy. So and that's you know, when you when You stepped back and think about it. The reason for that is pretty obvious. Because if you're only fixing cancer, you're not fixing dementia, or kidney disease, or liver disease or diabetes, right, all the other age related diseases are still there. And so one of those is going to get you not too long after when you normally, you know, would have died if you got cancer. So that's why the numbers are pretty small. So then you can ask the question, well, what would the impact be if we had an intervention that successfully targeted the biology of aging? And again, I think we have to be honest, we don't have that, at least that has been proven in people yet. So we don't know the actual numbers, right? We can't say with certainty what the

impact of an intervention that that that significantly, positively impacted aging biology and people, but we can look at the effects in laboratory animals and at least be guided by that to kind of put, you know, bounds on the potential effects and people. And we know of several different interventions that can increase lifespan in mice by, you know, between 15 on the low, well, 10 on the lower end, and all the way up to like 50% For something like caloric restriction. So I would put rapamycin, which is the best drug that we've got for slowing aging in there at about 25%, maybe as high as 30% increase in lifespan. So senolytics are a specific class of molecules that also impact the biology of aging. And we can talk a little bit about that, if you want to, I can get a little bit more into the weeds, but for now, they're just one class of drugs that we have that target part of the biology of aging, they seem to increase lifespan in mice by you know, maybe not a huge amount, but 10 15%, and maybe more significantly improve healthspan. And so if we had an effective analytic that worked in people, you could estimate what would the impact be on lifespan and healthspan for that same typical 50 year old woman, and it's much, much bigger than it is for curing cancer. So if we look at the imbalance between the resources that could have gone towards curing cancer versus targeting the biology of aging. And we compare that to the potential impact on life expectancy and health span, it seems out of balance, and that really was the point that I was trying to make in that in that tweet. And I, you know, it's still way out of balance. And that's historical, cultural. And also, I think, because, you know, you could have made a reasonable argument 20 years ago, 25 years ago, that we didn't know enough about the biology of aging, to throw a lot more money at it, you could have made that argument, I would have disagreed with you. But you could have reasonably made that argument, I don't think you can make that argument anymore today. And so So I do think that there needs to be a shift in prioritization to keeping people healthy longer, rather than waiting until people are sick and trying to cure their disease. Yeah,

Jake 42:55
I think that's a great overview. And you also could have made the argument back then that, like, you can now with, you know, with billions of dollars put towards biology of aging, it's sort of unknown what the progress could or would be, and at that time, it was sort of

unknown, what putting x number of dollars into curing cancer could yield in 20, or 30 years, or whatever it's been. And so now we sort of see, and so you can sort of like, change your probabilities a little bit and be like, okay, you know, what we can do in the field of aging with billions of dollars is much more of an unknown at this point, it would seem, then what we can do with that amount of money and cancers, sort of the progress is more measured at this point. And we can sort of, I feel like you sort of know what you're getting for the incremental dollar. And the unknown is very exciting. Because rather than, like you said, you know, you eliminate cancer, and someone lives two or three years longer, and then gets got by, you know, whatever. The next thing is heart disease, or whatever it might be, you're extending the full runway, because all these things have one thing in common, they're coming. I mean, there's forms of cancer, of course, that come early in life and various other things. But generally, aging is the common thread that makes you you know, vulnerable to all of these things. So if you extend the runway, you know, slow aging by 20% 30%, whatever it might be, it's just a huge impact. And so the possibility that the dollar, you know, may he value I think, is just huge. And I thought that was a great tweet and the the elaboration I didn't know exactly what you were gonna bring with the elaboration, but the elaboration is better than I could have expected.

Matt Kaeberlein 44:30
I think and one other thing I would, I would just tag on to the end of that is I think, we don't know again, how, how hard it's going to be to significantly modify the biology of aging in humans. I will say everything I've seen from from studies and other animals suggests that it's probably easier to successfully do that than it is to cure cancer because of because cancer is you know, such a, such a wide spectrum of actually different mechanisms that drive different types of cancers, the ability to cure cancer after somebody has got it, and particularly after it's metastasized, across the board is, I think, immensely more challenging than having an impact on the biology of aging before the system has, you know, become so perturbed that it's that is pathological. I could be wrong about that. But that's my intuition. And I think certainly, that seems to be the case in the preclinical studies in laboratory animals.

Jake 45:30
Right. So I want to move and talk a little bit about the dog aging project, which is a really interesting project. I mentioned at the top of the episode that you've been co directing for several years now. Can you introduce that project and sort of, you know, provide an update of sort of the history and where things are today?

Matt Kaeberlein 45:48
Sure. So so the dog aging project is kind of what the name says, it's a study of aging in dogs, and not just old dogs, we're broadly trying to understand what are the most important genetic and environmental factors that influence healthy aging, in companion dogs, so this is all in pet dogs, we're not doing any studies in dogs maintained in the laboratory, these are all dogs living with their owners. So there is there's two parts, I guess, to the dog aging project. One is what we call a longitudinal study of aging. And what that means is, we're just following dogs over time. In their natural environment, which it turns out is very similar to the natural environment of humans. And again, trying to understand what are the factors that cause some dogs to have shorter lifespans to develop diseases of aging, where other dogs, you know, live longer and live healthier. And it's purely observational, so we're not asking owners to do anything different than they normally would. And there are right now I think about 40,000 dogs in the Longitudinal Study of Aging. And I'll come back to how people can get involved, we're still recruiting dogs. And so I absolutely would, I would encourage anybody who's listening, if you have a dog, and you want to contribute to this science, go to the website, dog aging project.org and click the nominate your dog, but it's really easy. And again, we're not asking you to change anything about what you do with your dogs. So that's the biggest part of the dog aging project is that Longitudinal Study of Aging. There are some what we call sampled cohorts within the Longitudinal Study of Aging. So right now 10,000 Dogs get their genome sequenced, the owners get a report back on on what information comes from that 1000 Dogs are selected for what we call the precision group, those dogs annually in addition to getting their genome sequenced annually, the owners will take a kit to the veterinarian when they go in for their annual exam. And we will get blood chemistry, blood plasma actually metabolome blood epigenome and so we haven't gotten into the epigenetics and epigenetic clocks, but

one of the very popular aging clocks right now is what's called an epigenetic clock. And so we will be getting that annually on the dogs. And then we'll get fecal microbiome to understand how you know how the dog's microbiome is associated with the tail. So that'll happen every year. Related to the precision group, we have a healthy brain aging study, where we're specifically looking at brain aging and cognitive decline and dementia in dogs. So there are about 200 dogs that will be enrolled in that study. And then, and then the other part of the dog aging Project is an actual clinical trial. So you can think of the longitudinal study as trying to understand aging in dogs, the clinical trial is trying to do something about it. And that's really you know, where my passion lies. I'm a dog person, I've always had dogs. I have a German Shepherd now who's getting older who I love very much and and so I certainly recognize why it's important if we're able to increase the healthy longevity of our of our companion animals. And so, for the clinical trial, we're testing a drug called rapamycin, which I mentioned briefly previously, and it was in that tweet that you alluded to. So rapamycin right now is currently the best small molecule intervention we have for targeting the biology of aging, increasing multiple parameters of healthspan in laboratory mice, and extending lifespan, as I mentioned by about 25%. So the goal of the clinical trial is really to test does rapamycin have similar impacts on lifespan or other healthspan parameters in middle aged companion dogs, so we are enrolling 580 dogs into this clinical trial. At right now we have nine clinical sites that will be probably be up closer to 15 or 20. In the next six months where it's a double blind placebo controlled clinical trial, half the dogs get placebo, half the dogs get rapamycin. And and like I said, the goal is to test whether rapamycin can increase lifespan and improve healthspan in companion dogs. So those are really the two big parts of the dog aging project. At the moment we are, as I mentioned, continuing to enroll dogs in the longitudinal study. We're also continuing to enroll dogs into the rapamycin trial. It's called triad test of rapamycin and aging dogs. In order for dogs to be eligible for the rapamycin trial, they have to be at least seven years old, and between 40 and 110 pounds, and they can't have any significant pre existing health conditions. Because it's a study of normal aging. We can only enroll dogs that don't already have, you know, cancer or significant heart disease or kidney disease or something like that.

Jake 50:59
Right. Yeah, no, it's a super interesting project rapamycin, I know you're very excited about it, and testing it with the dogs. What's your perspective on, you know, when this might be, you know, a thing that's recommended for humans and you know, in what doses and what's the path from where we are now to like getting to that point?

Matt Kaeberlein 51:18
Yeah, so that's a really hard question to answer with any certainty in in part, because, you know, right now, I would say rapamycin, which which most physicians who are familiar with rapamycin, we'll know it under the name sirolimus. Because that's just what it's called. In the clinical world. It's the same molecule, same drug, or rapamune, which is the Pfizer branded version of rapamycin. So they'll know it in that context. And they'll know it because it's mostly been used in people to prevent organ transplant rejection. And and so in that context, the doses that are used are pretty high. It's given in the daily dosing regimen, and it's given with with strong immunosuppressants. And so in that context, in that patient population, rapamycin has some side effects. They're not terrible, but but I think that, you know, it's got sort of a bad reputation in the clinical community because of the way it's been used. So, in order for rapamycin to ever become widely prescribed, so it is a prescription drug, you need a you need a prescription to get it legally in the United States, in order for it to ever become widely prescribed. A couple of things have to happen. One is we have to have, you know, rock solid data from clinical trials, suggesting that it's actually beneficial for for the biology of aging and people. We have some hints, but I would say we're not to the point where there's a lot of certainty around that yet. And we have to get enough data on side effects and safety in, you know, healthier people who are not organ transplant patients to convince the clinical community to overcome that stigma that the drug has, because of the way it's been used. My personal intuition is that the first of those is going to be easier than the second but I don't know how long it'll take to get there. There are some clinical trials happening right now. And in the following months that I think will get us closer to understanding you know, how effective is rapamycin at targeting specific age related endpoints and they're really interesting because

in mice with rapamycin and seems to affect the the aging process in pretty much every tissue in Oregon, where we look, it's really remarkable in some cases, actually restoring function that has been lost. So in mice in the heart, in the oral cavity, in in the reproductive tissues, ovarian aging in particular. And in the immune system, you can actually see an aged organ. That is a lower function function better after the mice have the old mice of getting rapamycin for between six and 10 weeks. So we can start to look in people at multiple of these age related indications. And asked do we see similar slowing of the aging process or maybe more excitingly, improvements in function that has already been lost? And so some of the clinical trials that are starting up right now are for mild cognitive impairment, Periodontal disease. So colleague of mine, Jonathan on the University of Washington is running a clinical trial looking at whether rapamycin can reverse periodontal disease and people we publish that it could in mice, and ovarian premature ovarian failure. So Zed Williams, and you shouldn't Sue at Columbia are running a clinical trial in women to see whether rapamycin can have an impact on ovarian failure. So we're starting to get these clinical trials up and up and going. And I think in the next couple of years, we'll get more and more data to give an indication, you know, where does rapamycin seem to be working? Maybe where is it not working? Hopefully from our dog studies will will impair We'll be getting data there on whether rapamycin is having an impact on aging and dogs. And I think as all that stuff starts to coalesce and come together, then maybe we'll reach consensus How effective is rapamycin? But importantly, from these clinical trials, we'll get, I think, really good quality data on whether or not we see any evidence for side effects of the kind of dosing that people are thinking about with rapamycin for age related indications. And, and I will say, from everything I've seen, and I've seen more than almost anybody else out there, I don't see much evidence for significant side effects of the doses that that most people are using for, you know, putative healthspan, and lifespan promoting effects. So I think we'll find that it's, it's quite safe in that context. The question is how, in my mind, the question is, how much efficacy will we see? And we just got to do the trials? That's why we do clinical trials.

Jake 55:54

Yep. Makes sense. So I know, we're already over on time. And I want to wrap things up here respectful of your time, but closing out on on the dog dog aging project, you sort of introduced it and talked about some of the history. But where are you hopeful that things go from here? You know, several years in, I think you said 40,000 dogs or so seems to have sort of exceeded expectations, I think you've set out to get like 10,000 or so. Yeah. And it's just really popular. It's interesting, because it sort of weaves together these dynamics of, I think what you know, it's called Citizen Science, basically, just average people contributing to, you know, getting involved, and, you know, volunteering their dogs and things like this. And then there's also like a crowdfunding element to it. So it's like, it feels like a very sort of new breed of science, to me at least being not as familiar with the space. So I'm just curious sort of what your hopes are for, for the future. And, you know, where, where things might go from here?

Matt Kaeberlein 56:52
Yeah, so yeah, I mean, I think that the term that we have sort of gravitated towards is community science, but community science, citizen science, I think, absolutely. The the participatory aspect of this project is really unique and fun. And I absolutely believe that, you know, this is a good thing for science communication, in general, because it engages people who wouldn't otherwise probably participate in science in the scientific process. And because people love their dogs, I think we're able to engage a much broader community than a lot of other community science science projects, I think it's also been good for the geroscience field or the aging field. Because I think the dog aging project has played an important role in the concept of biological aging, reaching a broader community. And and this is actually something that I think is it's a really use dogs are a really, really useful example for what I mean by the biology of aging, right? We all we all sort of, except by the time were, you know, kids, that one human year is about seven dog years. That's, that's not perfect, right? That's not exact, but it's pretty close. And if you really think about what that means, all that means is the dog's age about seven times faster than people do. And so we people understand in that context, that, that there is a biology of aging, right, that there the genes and environment influence why some animals age faster

than other animals do. And dogs, I think, are a really perfect example. That's a little bit of a tangent. But I really, I like to emphasize that because I think once you can get people to recognize that there is a biology of aging, then it's not so far fetched to think that we can actually understand that biology and when we understand it, you know, at least partially, we can actually do something about it. And that's really what we're trying to do in this field. So, okay, so where do I hope the dog aging project goes again, you know, I mentioned that we are still actively recruiting dogs, even though we have more dogs than we initially, you know, conservatively set out to enroll in the longitudinal study. We are We are definitely underrepresented for some, you know, demographics among the canine population. So particularly puppies, I think part of that is the name people see the name dog aging project, and they think we only want to, we only want you to sign up if you have an old dog. That's not true. If you have a puppy, please sign your puppy up. And also, you know, people from diverse backgrounds, I think, you know, because we one of the goals is really to understand the effect of a very broad environmental diversity on aging in companion animals. And so so we definitely want more people to sign up for both the longitudinal study and the the clinical trial, you know, where I, there's a lot of things I hope to see again, for me, you know, my real passion here is to actually have an impact on lifespan and healthspan in companion dogs. So I hope that and I don't know whether this will happen in the dog aging project or are, I think it'll probably happen more broadly in the field in general, but I hope over the next, you know, three, four years, now that we've created the template for how you would do this kind of a clinical trial, that we will see more people approaching therapeutics to have an impact on healthspan, and lifespan and companion animals, and really, you know, aside from the, you know, the fact that it would be amazing if we could, you know, slow aging in our dogs by 20%. From a, from the perspective of just a pragmatic perspective, you can actually get the answer, much, much faster in dogs than you can in people. So, I think we're just starting to see companies think about, you know, okay, we could go down the path of a clinical trial for, you know, an age related indication in people, but in parallel, maybe we can go down the path of a clinical trial for having an impact on aging in companion animals. And so the first company, I think, to really, you know, be public about this sort of an

approach, which I love, I'm a big fan is a company called loyal, where they are actually, on the for profit side, you know, developing therapeutics, and in a, in a very strategic way, testing those for effects on the aging process in dogs. So I would really like to see multiple clinical trials, multiple interventions being taken forward in the veterinary world, at the same time, that we're seeing this proliferation of clinical trials, you know, for age related indications in humans. And so I think I think that'll happen. And I hope that, you know, I can't see any reason why five years from now, we can't have clinically proven therapeutics to slow aging in dogs like this biology will work, we just need to have enough shots on goal to figure out which interventions work and how, how, how effective they are. So so that's really where I hope we are five, five years or so from now.

Jake 1:02:06
Awesome. Well, I know we're over on time, like I said, but very exciting future, I think ahead for the dog aging project. And for the field at large. It does feel, you know, just talking to you, it feels like we're on the cusp of something and I certainly hope that's the case and that there's a lot of great breakthroughs and increased attention and funding and talent and everything like that in the years to come. So appreciate you again for taking the time that and just wrapping things up. Where can people go to follow along, you know, you and various things you're working on, you know, moving into the future.

Matt Kaeberlein 1:02:39
Yeah, so I mentioned the dog aging project, website, dog aging project.org. My laboratory website is Caber line.org. So just my last name and then I'm, I'm not great on social media, but I'm, you know, somewhat active on Twitter. So if you're interested in following me on Twitter, it's at M Caber. Line, my first initial and my last name