Primary Care Cures

Episode 55: Dr. David Sinclair

Ron Barshop: Most problems in healthcare are fixed already. Primary care is already cured on the fringes, reversing burnout, physician shortages, bad business models, forced buy outs, factory medicine, high deductible insurance that squeezes the docs and is totally inaccessible to most of the employees. The big squeeze is always on for docs. It's the acceleration of costs and the deceleration of reimbursements. I want you to meet those on this show that are making a difference with us, Ron Barhop CEO of Beacon Clinics, that's me.

Ron Barshop: Fruit flies share 60% of our genetic makeup and nematodes, which are a roundworm, have 75% of the similar DNA as in humans. When you get up to mice, you're jumping to 92% and chimpanzees are 98% biosimilar. This biosimilar menagerie all progressively makes better research subjects as you move up the ladder. Because, say you have a crazy theory that aging is not a thing, but it's a reversible disease. You might try different experiments on easy to find creatures like these, and you might try something like red wine because Resveratrol is an active ingredient that actually can reverse aging as we found. And then, you may remember a few years ago that it came out that red wine is good for you, so [inaudible 00:01:34] sales doubled overnight. That was as a result of the research of our guest today. So today's guests created that demand. Now there's similar news that'll be coming out about NAD NMN, which is Nancy, Mary, Nancy, and DHEA, and even Metformin, which is a pathway opener for acceptance of insulin in diabetics.

Ron Barshop: And while these are all promising age reversal strategies, the problem is it's hard to get these because you don't know how to buy them in a pure form. They're not a pharma grade form out today, if you were to go on Amazon. And there's another called Rapamycin, and again, you can go spend a bundle on Rapamycin and know what quality you're getting, or you can go lick the ground on Rama New, better known as Easter Island, but that's a pretty risky strategy. So there's a big problem to reversing aging is number one, it's not a cure yet, it's under study, but it's extremely promising. And today, I'm proud to announce to you a bestselling author of Lifespan, a book that was introduced to me as the most important in the last decade by Peter Indiaman, who was the co founder with Ray Kuril's of Singularity University.

Ron Barshop: Dr. David Sinclair is an entrepreneur, and a true world-class leader in Asian research. He's a tenured professor of genetics at Harvard, co-director of the Paul F. Glenn Center for Biology of Aging research at Harvard, and he's best known for his work on genes and small molecules that delay aging, including sirloin genes, resveratrol we talked about earlier, and then AD precursors. Dr. Sinclair's published over 170 scientific papers. He's named in over 50 different patents, and he's co-founded 40 biotech companies, mostly centering around the era of aging vaccines, diabetes, fertility, cancer, and bio defense. And he works with leveling national defense agencies and NASA, but he's received 35 honors including Time magazine's list of the 100 most influential people in the world a few years ago and the top 50 in healthcare last year. David Sinclair, welcome to our show.

David Sinclair: Hey, thanks Ron. Appreciate it.

Ron Barshop: The premise of getting you on the show is that we want to see clinically inactive all of what you're researching once we know that the medical research is behind it, that we have proper studies, evidence-based studies, and where are you now in terms of getting your ideas out into the marketplace with what you've discovered?

David Sinclair: Well, there are a dozen or more companies working on various aspects of age delaying medicines. Typically, we go for diseases of aging or even rare diseases. The reason being that, as you mentioned, aging is not a treatable condition yet, at least it's not considered one. Personally, I'm involved in a couple of companies that are working on medicines that may delay and in one case, reverse aging, if it works, quite dramatically. How far are we away? Well, you could argue that there are already medicines. You've mentioned Rapamycin. There's Metformin, which is the diabetes drug. These are drugs that show a lot of promise in animal studies and even looking at hundreds of thousands of patients in the case of Metformin, a lot of promising associations with protection from diseases, such as cancer and heart disease and Alzheimer's and even frailty. You could argue that we may already be here.

David Sinclair: There are things we can do. There are certainly things we can do in our daily lives besides take those medicines that would close to undoubtedly slow down aging. The drugs that are in development, some are in phase two, which means there's still about three to four years away. Some are just entering human trials. So yeah, there's a pipeline and they're coming online. Some fail of course. Biotech is never a sure thing going from mouse to human. But we're in a world where it's not just a theory anymore. It's actually here.

Ron Barshop: Well, so you picked up a 50 plus year old theory that aging is not a state of life. It's actually a reversible disease, and I've never really recommended a book to our listeners before, but I'm going to recommend your book, Lifespan, and to get it in an audio form because to hear you, David, tell about your discoveries, it's almost like you are reliving them again. When the mouse, I'm going to call it super mouse or mighty mouse, not only ran further than any mouse had run before, but it broke the machine. It literally broke the wheel because it went past, like, three kilometers. Can you tell that story? Because it was so fun to hear you tell it on the audio book.

David Sinclair: Yeah, it was great to live through that. And actually one of the great things about the book, as you were saying, is as I was writing it, we were fortunate to make these amazing discoveries. So I wrote them down on the page. And so it's rare that the public gets to see what it's like to be a scientist.

David Sinclair: So this particular experiment was taking old mice, which were two years old, and they don't run very well on little treadmills that we have in the lab. And we gave them NMN in their water supply for those four weeks. Then we put them on a treadmill side by side, and a typical mouse would run about one, if they're lucky, two kilometers before they get really tired and full of lactic acid and that their muscles are burning. They want to stop. We had mice that, old mice, that were running two and a half. And one mouse, it passed the three kilometer mark. And the software had not been written for a mouse that would ever run that far cause that was considered impossible. And here it happened. And actually the scientist, young scientist who was doing the experiment, called me up screaming saying, "I can't believe the mouse had broken the treadmill." And we hadn't realized it was a software issue. But nevertheless, it just shows you that old age is in many ways reversible.

Ron Barshop: So you said in the book, and you said in speeches, I heard you at the Exponential Medicine conference in San Diego, that not only is aging reversible, but you said there's going to come a time, perhaps in the next 10 or 15 years, when a cream or a pill or a vaccine or some other substance is going to allow you to actually reverse ages up to 22 years. Can you explain that?

David Sinclair: Yes, sure. We in my lab have a theory called the information theory of aging, which says that our bodies are losing information over time and not so much genetic information in our DNA, but the next level of code, the software of our bodies, which we call the epigene. And we can now take blood samples of mice and even in people, and tell them how old they are actually biologically, not how many birthdays they've had, which is a rough guide. And also quite accurately predict when somebody's going to

die, assuming that they cross the street carefully. And that actually is a huge breakthrough in itself to be able to say, objectively, this is how old a tissue is or a blood sample is. Now that epigene, which are the structures that tell a cell its identity.

David Sinclair: Brain cells have to stay brain cells for a hundred years in some cases. How does that happen? That's the epigene. Because remember, every cell in the body has this, essentially, the same genome. So this epigene information is lost over time. So why is that relevant age reversal? Well, we've made a discovery, that we hope to publish in the next few months, that shows that a particular gene combination in a gene therapy is able to reverse that information loss. Somehow, there's a backup copy of that AP genetic information, and essentially when we give that gene therapy, say to a mouse who is blind from old age, if we deliver those into the eye, we can reverse the age of the retina and the nerves come back to life. And they aren't just acting young, they are literally now young again, and the mouse gets its eyesight back completely in almost all cases.

David Sinclair: It works for glaucoma. It works for a damaged optic nerves. Now that's a proof of principle. It could be applied, not just to the eye, but of course to to every possible tissue in the body of a mouse and eventually a human. And that's why I think it could be many years. It could be decades. It doesn't matter so much, except the fact that we've proven the principle that there is a backup copy of youth in animal cells and almost certainly in our own.

Ron Barshop: So theoretically a 50 year old woman, according to this theory, might be able to reverse her age to 30. Now it's not an overnight, you look in the mirror and you suddenly look 20 years younger. This is a gradual thing. But she would have the darker hair. She would have the younger skin. Her neuro-plasticity in her brain would be back to where it was when she was 30. And her organs would basically generate back to their healthier state. Her eyesight would revert back to its healthier state. Is that all possible in the future, you think?

David Sinclair: Well, we will see. There have been reports of things that we regard as irreversible, such as gray hair becoming brown or black again, so there's the capability. The body actually can heal itself and recover far better than we think it can in my view. Now, I don't think it's going to be overnight that we'll have these, drugs or even that they will work overnight. We typically see results of vision reset, takes about two to three weeks. So that's pretty interesting, right? That it's only a few weeks of treatment. And when we do a clinical trial, we're expecting to see improvement in vision just in a matter of weeks. But I couldn't promise that somebody's going to suddenly, in a few weeks, go back 20 years. But what I can is that just two, three years ago before we'd made these discoveries, that was

considered ridiculous. Impossible. How could you even say such a thing? And now at least we have some evidence that it's theoretically possible.

Ron Barshop: You stated in your book that you have the heart of a 20 year old, and you're not 20 years old, are you David?

David Sinclair: No. I turned 50. I'm getting as old as everyone else on the planet. But yeah, I've had myself tested over the years. I'm curious. I'm a scientist. I measure with biometrics. I do blood tests. Look at my blood sugar. My heart, it was 3D rendered by a friend here at Harvard. And yeah, I mean, it's so far so good. Things seem to be on track. My father, who's 80, is stronger and fitter than me. So it is possible to be younger than your actual birthday candles would suggest, but that's not clinical proof of course. These are anecdotes and I'm trying to learn things ahead of clinical trials, which take a long time and costs many millions of dollars. So I'm not going rogue, in case any of my colleagues are listening, but I'm trying to learn things that would be useful to guide medical research and test hypotheses rigorously.

Ron Barshop: It is a little unusual to come out with a book about Lifespan. Its really got a giant movement behind it and a lot of people going online using your face to sell their products, even though they're not doing it without your permission. I know you've got a healthy budget for legal to stop people from using your name, but there are people that are following you and believing that they can reverse age with the really huckstering of products on Amazon. You're pretty involved with putting a stop to that, aren't you? That's a big problem?

David Sinclair: Yeah. Thanks for mentioning that because it's very easy for someone to get the impression that I'm trying to make money off this science. I'm not. I'm trying to make medicines. And I don't sell any products. Period. I don't make any money off products. Period. So yeah, you go in line and there are a lot of people using my quotes, my name. There's even companies using my name [inaudible 00:00:14:11], Sinclair Labs for example. But yeah, so I'm sending out cease and desist letters pretty consistently. Sometimes I get a reply that, I had one actually a few days ago that said, "Oh, I didn't know David Sinclair, his name, was trademarked, nor his image." Well, I will fight that one, but that's the attitude of people out there. All of my hard work and reputation is apparently fair game for some people.

Ron Barshop: When you started this movement, and I don't know if it's age reversal or age extension that you call it, but how many labs now are following you around the world that are what you would consider world-class labs and world class researchers that are now studying this? Whether it's with mice or chimpanzees or whether it's with nematodes. I think yeast, you do some

research in that. What type of community do you have now taking a hard look into this research?

David Sinclair: When I started in the early 1990s, there were just maybe five labs around the world that were world-class doing this kind of research, the genetics of aging. And we've discovered a fair number of longevity genes. The sirloin's are a major class of those. There are others, one called [inaudible 00:15:33], another one called AMPK. So I don't want to start out by saying everyone's following me. I'm part of a rebellious group from 30 years ago. Over those 30 years, the number of labs have grown, oh, probably, to 5,000 now from just a handful. And working on various problems, whether it's human clinical trials, genetics of humans, all the way back to still studying yeast cells and plants But it's all coming together actually. What I'm finding, which is really quite rewarding, is people studying the plant world are discovering that the molecules that plants make, such as resveratrol, are healthy for us for reasons that they're activating these longevity pathways.

David Sinclair: We also have people studying, well, olive oil and other molecules that come from plants that activate these sirtuins. We have genetic variants in our bodies, so the sirloin genes are different between you and me, and well presumably between you and me. And that gives us seemingly different rates of aging as well. So yeah, it's a super exciting time. In terms of looking back at history, it would be the equivalent of, so the Wright brothers have built a plane, They're flying around and now there's a lot of people building different planes and figuring out how to build a jumbo jet.

Ron Barshop: I'm sure you're aware of the Blue Zones theory, that there's five or six zones in the world where people live to 120 regularly and in large numbers, and it has to do with lifestyle and family connection and food and hydration and sleep. But do you subscribe to the theory that our soils are being depleted so people aren't getting the proper mineral content they need in their foods?

David Sinclair: No, I wouldn't say I'm an expert, so I can't judge it. I do think that probably the biggest thing that people do in Blue Zones is they eat less often. Then the second most important one in my view, is the type of foods they eat. And these molecules I just mentioned, we call them xenohormetic molecules, the ones that activate our body's defenses. As for minerals, no, I think it's probably better left to the experts in that to be able to say for sure.

Ron Barshop: Okay, but you are a fan of intermittent fasting and whatever that entails?

David Sinclair: Oh, yeah. Well, there's no question that we eat too often and obviously too much. Nutritionists have said, probably for the last 30 years, that we don't

want to stress the body, so we constantly are eating small meals throughout the day. The science says that that's not helpful. Now, there might be medical conditions where it is. But for an average person who's middle-aged, even older, being constantly fed and never feeling hungry really just makes sure that our longevity genes don't fight against aging and our bodies are complacent. The field has studied this for the last 50 years. So it's really not really a question anymore. And I'm actually encouraged that the general population is getting this information. And I also try to skip meals every day. I don't eat breakfast, and I try to skip lunch if I can.

Ron Barshop: Okay. So I told my son, who's a first year gastroenterologists in his fellowship at Harvard, he's at Beth Israel next to you there, that I was taking NAD and NMN and resveratrol and DHEA. And he looked at me like I was crazy. He said, "Dad, don't take that stuff." He goes, "It's not proven yet. It's not been tested." He said, "When you're doing that, you're turning yourself into a lab rat, and you're not good at being experiment subjects." He said, "Quit doing that." I probably should listen to my son, but I'm taking it every day because I was excited by your book and excited by the opportunity. But I also recognize it's not pharma grade.

David Sinclair: Right. Well there were two attitudes or two ways to go about this. I mean, of course you want high grade material. Anything that you put in your body, you want to be able to trust, and that's often difficult. I fully appreciate that there's different grades of material that you have access to. The other thing, you can take the attitude that let's wait until something's proven. But in the case of aging, it's similar to if you have cancer. I truly believe that aging is a medical condition. It's just something that's very common, but still something we should address. It's not just because it's natural, we should leave it alone. We used to think that about cancer. But yeah, getting to the point, the idea that we should wait until this is all proven. That's probably 30 years away and, I don't know how old you'll be, Ron, in 30 years, but it's going to be too late for me.

David Sinclair: So if we're going to be able to benefit from the science that's come out of the last 20 years, we have to take some risks, and it's not for everybody. I certainly don't want anybody to live any longer than they want to. But bear in mind, look at my father who's 80. He hasn't got 30 years to wait. No way. So that's why I think that it's certainly personal choice, but it doesn't make sense if somebody wants to take, what I think is a relatively low risk, and try and avoid what is the inevitable. Because we know all know what's going to happen if we don't do anything different.

Ron Barshop: I spoke with a nutritionist about what I'm taking and she warned me that DHEA has some estrogen like qualities. If it's going down the wrong pathways in a man and it's not something that I need more of as I age

cause I got that growing as I get older. Are there some definitely don't takes with things like DHEA, and maybe consider taking [inaudible 00:21:39] and NMN and the reservatrol?

David Sinclair: So remember I'm a mouse geneticists. I have to give you that disclaimer. I don't recommend anything. But I can say from my personal experience is it's very important to monitor yourself. So I think if anybody's got to take something like a NMN or a reservatrol, it's good to have a blood test beforehand and then follow up. Whether it's a month or a few months later just to make sure that their individual metabolism and genetic makeup isn't a problem. Remember it. It is an experiment, personal experiment, and liver could be an issue, but it's extremely rare. Actually, I haven't had any reports or clinical evidence that resveratrol or NMN are dangerous. Now, there was one study with resveratrol where a company gave, I think it was 10 grams of resveratrol a day, which is at least 10 times higher than the dose that I'm taking. And those patients, a few of them had kidney failure. Now these were end stage cancer patients that were very sick.

David Sinclair: But in terms of the regular doses, anything less than a gram, I've never heard of a problem. And there've been, oh probably a dozen studies now in humans with resveratrol with no negative side effects. And in fact in mice, resveratrol is quite effective at preventing and slowing cancer. So with all that said, I'm not saying anything's risk-free, but in terms of compared to some of these drugs like rapamycin are relatively low danger.

Ron Barshop: Well the rapamycin is the only thing that is like $300 a gram on the internet. And again, you don't know if you're getting sand or flour or sugar or rapamycin itself when you order some of these products. But tell us about the rapamycin. That seems to be sort of a newer chemical that you're experimenting with. What results are you getting with your mice in with rapamycin?

David Sinclair: There were three main longevity regulatory we call networks or genes. We talked about the sirtuins, which are responsible for the defenses that go up when you raise in [inaudible 00:23:58]. Okay. So just to recap, the mice that had that NMN [inaudible 00:24:04] and the sirtuins were protected in that system. The two others are, one is AMP kinase, which is acted upon by the drug Metformin, which I mentioned earlier. And then the third one, which we're going to talk about now, is called TOR, or in our bodies it's mTOR mammalian TOR, and it exists to sense how much protein is available. And when protein levels are low in the body, the body hunkers down and tries to survive. Similar to when it has low NAD or low energy. And so in many animal studies, mostly done outside my lab, so I'm now just talking about other other labs research.

David Sinclair: But rapamycin has been the most effective drug to slow down aging and extend it. Not just mean or average, but maximum lifespan in everything from yeast cells through to mice and there's even evidence in dogs that it's effective for protecting the heart. But it's a drug that also inhibits the immune system. It's given to transplant patients, and it does have some kidney toxicity at higher doses. And so for that reason, it's a very potent drug that reason most people don't take rapamycin in an abundance of caution that it might do some damage as well.

Ron Barshop: So in the Torah, it says if may you live to be 120 that's one of the nicest compliments you can get from somebody. Do you think it's possible that your and my children might see 120 as a reasonable lifespan to live? And what are the implications for that about retirement, and work life and work span?

David Sinclair: Right. Well already, children born today are expected to live on average, so half of them will make it to 104 in Japan to 107. So our children are already going to likely make it there, especially if they look after themselves and just do the right things. They exercise, they don't eat too much, they don't smoke, they get good sleep. The usual good things that we all know. They eat the right foods. But by the time they're old, let's say 40 50 years in the future, the technologies will be incredible. I think about how little we knew going back 50 years from today. So yeah, it's hard to predict the future, but we always underestimate how quickly things change and that the longer we live, the more medical treatments we can have. Already if we live for an extra year, we get another three months of life.

David Sinclair: And so yeah, you just want to live longer and longer. Can we make it to 120? I don't see any reason why we cannot. There's no law that says we have to die. It's just that we haven't all been optimizing our bodies. But with the combination of monitoring devices that we can wear on our wrists, the lifestyles that we now genuinely believe will extend lifespan and the medicines and supplements that we're learning are useful. I think that we could break the barrier. Now 120 is our maximum known lifespan, but those people that made it 120, they didn't look after themselves. They didn't do all the right things. So I think it's quite possible. Now, can we all live that long? I don't know. I think our children have a great chance. For us, I think we have some work to do.

Ron Barshop: Has huge implications for the government. Writing checks to social security retirees for 40 to 45 50 years. It has implications for your working career. It's no longer 40 years and you're no longer useful at 65, but you're going to be useful until you're 85 95 perhaps. So they're not going to be drummed out of the company because of age because you've got a lot of good years left and all that experience. So it really has huge implications for workforce, and for our economy and our federal budget.

David Sinclair: Well, we already quote unquote waste a lot of money taking care of people who shouldn't be sick. There are ways to live healthy for longer. And that money already takes up 17% of our GDP. Now what we need to do is to keep people healthier for longer. And what you get with that is a boost in GDP. We've run the numbers. It goes up quite dramatically, and the savings are in the trillions of dollars every year, actually, across the globe. And that's money that can be put to other things, education and even better healthcare. So I'm bullish on this. I think that in the future when people look back at today, when people expect to be healthy in their eighties and nineties and hundreds they'll wonder why we took so long to get onto this problem.

Ron Barshop: Very interesting. Well, David, if people want to find you, how do they reach you to learn more?

David Sinclair: Oh, well I'm on social media. So Twitter is David A Sinclair. Instagram is David Sinclair PhD. And I also have a newsletter, so I update my book because of course things are going on. People can reach me at lifespanbook.com and that's where my monthly newsletter is that I will keep everybody updated.

Ron Barshop: Thank you for your time. Last question. If you could fly a banner over America to give a message to Americans, what would that message be?

David Sinclair: Oh, well I would say that that their health, their future health, is in their hands and that 20% is genetic and the other 80% is up to how they live their lives. And if there's one recommendation I could give that would undoubtedly give people extra five or 10 years for the life, it is to eat less often.

Ron Barshop: Wonderful. Thank you for your time David. Really appreciate it.

David Sinclair: Thanks Ron. I appreciate it. Thanks for having me on.

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