Alexander "Zan" Fleming (00:00:50):

Yeah. Well good evening. I apologize for the delay, but welcome to our global audience to a very special session of our 2025 session of targeting healthy longevity. I'm here with my colleague Thomas, sir.

Thomas Seoh (00:01:12):

Good day. Good evening, good morning, wherever you are.

Alexander "Zan" Fleming (00:01:16):

We've had a few technical issues. We're broadcasting live from across the street from the Metropolitan Museum in New York City and we have a stellar local audience, so you can hear that chatter going on. But we're going to bring a few people up before we start the formal program and we'll try to do that at 30 minutes after the hour. But that remains to be seen in a fluid situation as say Thomas,

Thomas Seoh (00:01:59):

This is improvising. You only live once.

Alexander "Zan" Fleming (00:02:02):

Yeah,

Thomas Seoh (00:02:02):

Welcome. Shall I go get our first?

Alexander "Zan" Fleming (00:02:04):

Yeah, we're going to bring up a few people and quickly give you a flavor, this soiree we're holding and just to say

(00:02:22):

We are running a little late. It's probably going to be just past, sorry, 6:30 eastern time, but I see Dave Fox, my partner in crime, Dave, I jokingly say Dave was charged with FDA with keeping me out of jail when I was a worker in the division of metabolic and drug products. Dave is now a senior partner at Hogan Lovells, but also the author of the Thrive Act. And Dave, great to have you in New York, although you've got a PA Deter here and you were, I think for some family fun, but great to have you.

David Fox (00:03:16):

Well, thank you ZI think I was marginally successful in keeping you free roaming around so much so that you were able to form one of the most successful regulatory consulting firms. Oh my gosh. Wow. In terms of the Thrive Act, I think I'm a more appropriately described as the scribe. So I listened to your Brilliance Thomas's collection of examples and goals and all of the amazing people you've woven into the process. And I'll just do my best to put into clean language.

Alexander "Zan" Fleming (00:03:53):

Well, Dave, seriously, you really have conceived the concept of an alternate set of pathway or alternate tiers, or we call them tiers one through three. And we won't get into the details of that right now. But the fact is this is very audacious, it's comprehensive. A lot of thought has gone into it. You started years ago with the concept and we've just kind of echoed back and forth about it

David Fox (00:04:32):

Once you educated me about the problem and the challenge of trying to translate all the new science, neuroscience and aging biology into regulated products. So first translation from the bench to the clinic, but then from the clinic into products. I mean, once I understood the problem, some of the frustration, I think the solution emerged quite elegantly that the existing pathways that we have for therapeutic products would almost always inevitably stand in the way of the types of products that you long to develop. Because the system is really built around weighing risk against benefit, where the benefit is acute specific, very highly characterized around a specific target, a specific disease. And then the FDA is phenomenal at trying to assess whether the benefit derived the drug for the therapeutic intervention is worth the costs. But where the benefit is more amorphous as in aging biology where it's not as targeted around specific disease specific symptoms, specific outcomes, then that whole risk benefit proposition becomes a whole lot more difficult to manage. And so we need a different pathway and that's what we've done, we've worked on together. So I'm privileged to have been this, well,

Alexander "Zan" Fleming (00:06:27):

The privilege is mine, Dave, and really it's just remarkable how it has come along from where we started really going back even before we started calling it the Thrive Act, we had the Health Span Act back before 2020. So this has been a long work in progress and it's basically been driven by your regulatory mind with a little bit of clinical insight thrown in. But we'll talk more about the Thrive Act and future meetings. We've already covered it to some extent and we'll look forward to having you back to further unravel what we're trying to do.

David Fox (00:07:21):

Thank you, sir. Dave, thank you. Great evening. Thank you.

Alexander "Zan" Fleming (00:07:23):

Great. Thanks for being here.

David Fox (00:07:26):

Yes.

Alexander "Zan" Fleming (00:07:26):

And now I want to bring on another ex FDA person. Dr. Janice Soreth, thank you very much for coming

Janice Soreth (00:07:42):

Be here.

Alexander "Zan" Fleming (00:07:43):

Well, Jan, I say that you had the best job ever at FDA. You were responsible, you represented the agency.

Janice Soreth (00:07:52):

Yes.

Alexander "Zan" Fleming (00:07:53):

The FDA, and this is on top of what you had done as division director of the anti-infective,

Janice Soreth (00:07:59):

Which was the other best job.

Alexander "Zan" Fleming (00:08:01):

Well, yeah. So you went to an even greater job. But the point is, for many years you were the representative to the European Medicines Agency when it was in London and not just covering drug issues, but the range of FDA issues as pertains to DNA

Janice Soreth (00:08:23):

Say

Alexander "Zan" Fleming (00:08:23):

About that.

Janice Soreth (00:08:25):

It was really a privilege, and I think you probably know the background of I think why Congress gave an appropriation to FDA to open overseas offices. And it was three things that happened between probably 2006 and 2008 involving lead painted toys, substance like for MICA and baby formula that in China. In China. And then last but not least, what did affect the us, the adulterated heparin pharmaco terrorist event I call it, which we never really found out who was behind that, but so clever that you could change the chemistry of the drug to read out with a higher degree of protein, not recognizing it was going to be fatal for patients on heparin like kidney dialysis. So with those congressional hearings, it prompted converse to say, well, you can't just lock arms and forbid everything to come into the United States from elsewhere, including from China. So having shoes on the ground gave people in the India and China office is the ability to inspect with maybe a few hours notice.

Alexander "Zan" Fleming (00:09:44):

Yeah. Well, I mean it's remarkable, but this came about and what a great experience you had. But you also are in part here tonight because you have an interest in this topic of healthy longevity and targeting. You might say a few words about that.

Janice Soreth (00:10:02):

Sure. Well, when I thought about it, I realized that even though I had no idea of the concept of longevity or even lifespan as a child, I grew up in a family and an environment where food and its preparation was very important, particularly the aspect of sharing it with family and friends. Physical activity was not something we thought about. We just did it. And last but not least, I think we definitely had a spirituality in our extended family, and it could be something traditional like organized religion, but there's just this sense of there's something greater than oneself. And as I grew up, I realized that, well, I traveled to Europe as a junior in college, studied in Germany for a summer and had a year rail pass, a student rail pass that brought me to some vineyards in France and in Italy and opera. And all of that made me realize there are some folks that are living much longer into their nineties and hundreds and so forth. And it

piqued my interest further around 2018, I heard about the drive by Peter Atia and all of that kind of coalesced to make me start reading about it and thinking about it.

(00:11:36):

And here we are. Well, and

Alexander "Zan" Fleming (00:11:38):

Here we are. And so glad that you are here. We want to get your greater involvement in this movement we call the geoscience world. It's been a kind of world unto itself, but we really, the kind of expertise and experience that you bring to bear, and it comes from a deep love of serving humanity. You really set out as a global health doctor.

Janice Soreth (00:12:11):

You

Alexander "Zan" Fleming (00:12:11):

Had amazing experiences there. So you bring to bear so many things that are relevant to what we're done.

Janice Soreth (00:12:20):

I've been blessed and lucky in many ways.

Alexander "Zan" Fleming (00:12:24):

Well, we can't thank you enough for being here tonight and look forward to having you on another session with more time to drill down to a few things.

Janice Soreth (00:12:35):

Terrific. Bill, really happy to be here. Thank you so much.

Alexander "Zan" Fleming (00:12:38):

Great, well thank you Jan. And we'll see you in just a few minutes once we get the purpose going.

Janice Soreth (00:12:46):

Sounds good. Okay. Thank you

Alexander "Zan" Fleming (00:12:47):

Z. Thank you, Sir. Mark. Sir Mark, it's just we're delighted to have you

Sir Marc (00:13:07):

In town. So it's nice to be invited. Well,

Alexander "Zan" Fleming (00:13:09):

I mean, it's our luck that you're in town, sir Mark, you are a prime mover in the field of anti PNF factor therapeutics. Until recently, the largest pharmaceutical market in the world maybe knocked down to second by the GLP one. Crazy.

Sir Marc (00:13:36):

Yeah, it's knocked down to second by anti PD one.

Alexander "Zan" Fleming (00:13:43):

Oh, yeah. Well that's

Sir Marc (00:13:44):

81 is now the first the glp, an agonist will soon take over.

Alexander "Zan" Fleming (00:13:51):

Well, I stand corrected, but yeah, that has been another big advance in immunology and directed against cancer.

Sir Marc (00:14:01):

But the thing that is important that's not well addressed is that there are many paths to increasing longevity. So TNF blockade is one of them. And of course it is not at all consumed. There's quite an increasing number of papers. And of course you can say, well, is longer life the goal? But it's what's very interesting and it's the end of, I did something very unusual for me now, which is yesterday I went to Yale. I hadn't done a scientific trip for something that one did routinely for years, but with COVID it got interrupted. But the end of my seminar is really to highlight what we have learned from studying anti TNF using operations. So the reduction in Alzheimer's is monumental rheumatoid patients, ankylosing spondylitis, patients, IBD, all of the stark life with 50 to 250%. The incidence of average in all of these long-term anti CNF reduces this to below average. And so one of the things that should be considered is how can we leverage data that already exists in a way to submit the benefits to be scalable When the drugs were new, when they were patented, it was not a thing that could be considered. But the world now has tons of anti TNF, there's probably 20 generic forms of adalimumab Humira. And so this is no longer a hypothesis. I think it's something that should be considered.

Alexander "Zan" Fleming (00:16:40):

Yeah. Well I think you make a great point. We actually have now biosimilars that are much more affordable in general that could be directed towards actually preventing multiple chronic disease, not just treating them.

Sir Marc (00:17:00):

I mean the same studies show reduction, heart attacks, reduction in strokes, reduction in heart failure. So the long-term benefits of less inflammation in our own. Very interesting.

Alexander "Zan" Fleming (00:17:17):

Well, I think we are just about ready. And so Mark, we can't thank you enough for coming tonight. It was great luck that you were in town.

Sir Marc (00:17:28):

It's a pleasure to be here. So

Alexander "Zan" Fleming (00:17:30):

I hope to get you back for a longer session so we can get into a bit more detail about

Sir Marc (00:17:36):

Well, I think yes, I think there is a need to try and leverage data that exists in populations to treat populations. These are not clinical trial studies. These are records based on records of millions of people.

Alexander "Zan" Fleming (00:17:59):

Yeah, well, couldn't agree more. Great to see you and keep going. You haven't slowed down to

Sir Marc (00:18:07):

I did until I had a bad couple of years where I was getting all my joints replaced. I got two new hips and new knee, a back fusion. But at the moment, all good. Well, you're violent

Alexander "Zan" Fleming (00:18:24):

Man. Well everybody, we're going to try to bring the group. Yeah. Come in. David, David. David, have a quick seat. We delighted you could come. We had such a great meeting with you last.

David Duncan (00:18:47):

That was fun. That was a fun dinner. Yeah. Yeah.

Alexander "Zan" Fleming (00:18:52):

In a few words, tell the audience what you're doing that relates to healthy longevity.

David Duncan (00:19:00):

So I've actually as a journalist, been covering longevity since the late nineties and back when some of the first genetic work was being done on being able to extend the lifespan of sea elgan a tiny little worm by up to 10 times by just over expressing a particular gene. So I've been following this for a very long time. I wrote a book on it. I also once gave a talk, a TEDx talk in Brussels called When I'm 164, about what happens if we actually succeed at extending lifespan. So I've been following this for years. I just did a big investigative story on the human immuno and I'm becoming convinced as a lot of people are that the immuno keeping your immuno healthy is how you live longer and live a healthy life longer. And if you weaken your immune system or something happens, that's not going to serve you very well down the line. And we have some exciting new therapies. People have heard of CAR T cells to treat cancer, but there's a whole nother generation of manipulating bioengineering your own immune cells to not only deal with diseases but to boost your immune system.

Alexander "Zan" Fleming (00:20:23):

Well, amazing stuff. And what it means is we need to have you as lead a session. We'll try to schedule in the next, well, as soon as you can do today. Probably few months maybe.

David Duncan (00:20:35):

Yeah. Well I would love to do something with you guys. I'd love what you do.

Alexander "Zan" Fleming (00:20:39):

I can't thank you enough for your hospitality last night and for being here tonight. You're welcome.

David Duncan (00:20:44):

Thank you. Alright. I'm looking forward to this. It was fun to, I haven't seen Bill in a while

Alexander "Zan" Fleming (00:20:48):

In the kitchen one. Here we go. I think we're going to get started. Alright, well we're going to bring our special guest forward and get our farside chat going between Larry and Bill Stars of our show

Thomas Seoh (00:20:49):

Alexander "Zan" Fleming (00:21:31):

We are starting to herd cats here. Professor Larry Steinman. Hello. Hello. Just terrific to have you and to be in Bill's home. This is not the first time you've been actually featured here. I've been fortunate. It's

Larry Steinman (00:21:54):

A very interesting lio to be able to talk casually in front of a live audience about important subjects.

Alexander "Zan" Fleming (00:22:02):

Yeah. Well it's quite remarkable that we have a really stellar group gathered here in upper Manhattan. You just heard Bill quite a few notes to get us going and we'll need to adjust the camera a little bit to get us all on camera. But Larry, you of course are in Palo Alto. You have kids here in Manhattan. That's right. Which is good. Some close Bill

Janice Soreth (00:22:02):

Alexander "Zan" Fleming (00:23:09):

Thomas, will you get the audience in their seats

Janice Soreth (00:23:17):

Fireside.

Alexander "Zan" Fleming (00:23:25):

Well ladies and gentlemen, welcome tonight. We are so excited that you are here and that we are in this iconic location. It's unique and we're so grateful to Maria Eugenia and Bill Heseltine for having us in their home. I wish our audience who is on the web could see this beautiful place, but we're privileged to be here with two icons in the field of biomedical research. And I'm not going to spend a lot of time

introducing you because your fame is well known. But I do want to say that this is an opportunity to bring your life history together, to have been friends for a long time and to give us insight into how you got here and what you continue to work on. So we'll be of course turning the floor over to you in a moment. I did want to say just a few words about the Catis Institute, which you've probably not heard of unless you have watched one of over, maybe now 200 different sessions that started back in 2017.

(00:24:54):

Larry Steinman actually was a co-founder of the conference series and we have had just an amazing set of people come forward and participate. Bill in particular has put on quite amazing sessions including one I remember with the Prime Minister of New Zealand, former New Yorker and FDA commissioner, Peggy Hamburg and other life people. And that was right in the middle of the pandemic and we had a lot to chew on there, but what a amazing kind of coming together we've had in this conference. Larry, I remember you got off the plane at Heathrow and made it just in time to the podium back in that October weekend where we started out. But let's not dwell too much on cata other than to mention that besides conferences that we do put on, probably the most important thing we're trying to do is to develop something called the Thrive Act.

(00:26:14):

I won't go into the details of that, but it is meant to solve some of the obstacles that stand in the way to advancing the very approaches that you're going to be speaking about tonight. Just because the regulatory framework is not suitable, it will take too long, too much money to get these products that prevent disease as opposed to treat disease to who would benefit from it. So the Thrive Act is audacious, it's comprehensive, it's intended to help not just drugs and biologics but medical devices and even dietary supplements. And the author David Fox is an old trend and colleague FDA, but now a senior partner at Hogan Levels is here tonight with us. We're honored to have him. And so this is just another thing that the CATA Institute does. Well enough said about that. And let's just get into the show and I thought it'd be great if Bill, you would start off talking about why you decided to go into research as opposed to say clinical medicine where you would of course been brilliant as well,

Bill Haseltine (00:27:36):

Kind of you to say. I think my wife can answer that question pretty well because her daughter is now in medical school and I refuse to look at the pictures of operations in progress, which your daughter beams to her. It turns out I'm very queasy that the things you can do as a doctor, you can be a radiologist for that and you never have to see the actual patient. You just see some images of it. So there are some very few things you can do. You can be a psychiatrist doctor, look inside somebody's body, you can look inside their head. But when I was making that decision, I had the great good fortune to talk to two men who became Nobel Prize winners Par, who many, many of, and the other was Huble, his partner. And I'd been accepted to medical school. I had turned it down.

(00:28:33):

I was going back in the story getting along, but I'll tell you what. And they were doing these experiments for which I got to Nobel Prize and they were really excited and Jule took me aside, he said, you're going to get back in, but let me ask you a question. Do you really want to be a doctor? He said, let me tell you my story. I'm a doctor, I'm a father, I'm a scientist. That's one too many things. He said, the second thing I want to ask you is are you compelled to put your hands on a sick person? And I thought, no. And the result was a happy one. I'm a scientist. I've been very, very happy. The only time I would have some doubts about that when I'd be in the elevator at Dana-Farber Cancer Institute with some very sick

patients. And that is very sobering experience. Something many of us had with very sick people. And all I can say is I'm glad that my science has helped some of them.

Alexander "Zan" Fleming (00:29:32):

And just to say, Larry also made a kind of pivotal decision. You were going into physics and you would've done a great theoretical physicist I'm sure, but you decided to go to medicine but also research,

Larry Steinman (00:29:50):

Right? I'm not so sure that I would've made any contribution in physics, but I have an interesting story to tell about the same gentleman and weisel. So I went to medical school in 1968 at Harvard and I wanted to do something having to do with neuroscience and maybe immunology because my sister had polio a couple of years before the Salk vaccine. So I went to work as a student for a year, took a year off of medical school and I was assigned by David Hubel and Torsten Vil to identify the cells in the visual cortex of the brain that are tuned to appreciating something like a Mondrian painting lines at certain lengths angles. And we were supposed to, I should say I was supposed to record from those cells and then inject them with a fluorescent tie and actually identify what they were assigned at.

(00:30:52):

The next bench was another young man in his early twenties, also a Harvard medical student named Jim Hudspeth. And Jim just passed away. There's a beautiful editorial about him obituary in the New York Times, but Jim had immense talents in both intellectually and with its hands. My hands were not as good as Jim, but it was as if I could play the cello. But this guy named Yo-Yo is much better. I shouldn't go into even try to become a professional cellist. So I pivoted slightly into immunology because you don't need a lot of manual dexterity to pipette things. It's really true. Anyway, Jim turned out to be the giant of the auditory system Swedish and as Bill said, shared the Nobel Prize with David Huble, nominated him three times for the Nobel unsuccessfully even as a Swede, but he won all the other prizes, the cobbley prize. So that's how I ended up in immunology by default because I could not compete with the great Jim Husbeth, but it all worked out.

Bill Haseltine (00:32:09):

One thing, I didn't know that story about Hug Louisa, but it shows you what a great scientist can do to help other generations. It is something that is really passed down from generation to generation and I think it's been both of our great privilege to be educators. Some of my postdocs and graduate students are here in the room and they've made their own contributions. It's one of the really great things about being a scientist. The other thing that's interesting is the experiments I saw Al and Measel do were the same ones a couple of years later that he just described to you. They had a monkey skin probes in his head and he said, Hey Bill, bill, look at this. If I put the bar this way, it goes click, click, click, click. This way it doesn't. That means there's something pre-programmed in that animal brain that sees among your online that's that way. And that's exactly what you then were following up and figuring out what cell they stuff that prob into. Right,

Larry Steinman (00:33:15):

Exactly.

Bill Haseltine (00:33:16):

So, but lemme say one other thing. I am happy to be sitting next to this man. I have a son with Ms and he's had it since his early twenties and for the last 30 years he's been stabilized thanks to the drug that this man discovered. And it is, I'm really privileged to be with Larry and many other people around the world have been benefited by that very same job. Awesome.

Alexander "Zan" Fleming (00:33:42):

Bravo. And of course Larry, you and Smar Feldman who is here tonight have been close collaborators and is field of immunology and developing monoclonal antibodies.

Bill Haseltine (00:33:56):

But then we have to start talking about longevity pretty soon.

Alexander "Zan" Fleming (00:34:02):

We indeed. We'll start right now, bill, because this is actually the subject of a book you wrote pretty recently. The thing is though you're so prolific, you've since written two books and so it's now kind of becoming

Bill Haseltine (00:34:22):

A little boring.

Alexander "Zan" Fleming (00:34:24):

But no, it is a great book. I've actually learned a lot from it even though Thank you. I would like to

Bill Haseltine (00:34:29):

And make sure on your way out you pick up a copy.

Alexander "Zan" Fleming (00:34:32):

So we're making a gift to that book and Bill has kindly signed 'em. It's a memento for tonight and we look forward to your taking it home and continuing to benefit from bill's writing. But Bill, take it away.

Bill Haseltine (00:34:45):

Well, the first thing that is to say about longevity is we all are harboring what I call the immortal molecule. Immortal in the sense that it has been going on for 4 billion years and that is the DNA in your cells. It has been replicated, essentially copying itself. It makes a few mistakes. If it's a good mistake, it will make more of that and eventually it ended up with us. But we are a carrier of imal molecule. And so the essence of life is actually immortal. That is I think a major insight that has helped us understand what longevity is and it isn't. And then we look around the world and we see, well, there's some things that live 10,000 years. I have a book, it says the world's living things. As a kid, I actually stamped on some of them trying to hunt lizards unknowingly, okay, there was three assault oceans out in the desert, but there's other things.

(00:35:47):

We were in Namibia, we saw this thing that looked like a wielded cactus. It was 15,000 years old, a single entity. This is a same, this is one single entity. And of course there are mammals that can live 400, 500 and maybe longer. So why is it that we have this timescale and what can we do about it? And I'm

happy to say that although I can't give you a pill, I can't give you a shot. I can't send you a doctor and say we're going to pick you up. We are really probing deeply into the nature of why we age and we're making a whole lot of progress. It's really interesting. And what the book does is for one of the first, I think the first book, one of the book is in three parts. It really goes into what we are learning and we're learning a lot.

(00:36:46):

And as we learn it, we're beginning to experiment. And by now we're beginning very good at extending the lives of worms and even some mice and hopefully some monkeys. Now we're not so good at extending our own mind at this point. What we can do and what the doctors and scientists like Larry are doing is making sure we get to the age where we can live longer. That is a very important thing. You've got to get to the age first of all. And I myself and probably many people in this room are sitting here because of medical advances and we wouldn't be here if it weren't for modern medicine. And modern medicine is getting more and more modern and there many more things we can do. I'm happy to say that I can foresee seeing what's now in the works a day when there'll be very few people dying of cancer, at least people with access to medicine.

(00:37:47):

I'm not talking about the social aspect of medicine, we're talking about the cutting edge of medicine. So we are extending the possibility of getting to the point where we can now extend life and we are getting to the point where we can manipulate many of the things that we found and extend the life of simpler creatures a problem. The big problem and is something that's been recognized a long time with aging medicine is it takes a long time to figure out if it works. If it's really working, it's going to take you 10 or 20 years to know the answer and who's got the money to invest for 10 to 20 years. That is a big problem. So everybody's looking for biomarkers, what can I take out of you? What can I examine? Is going to tell me that this is going to improve your longevity?

(00:38:40):

And that's kind of a mismatch. We're looking at the short term for something that's going to work for the long term. Will that work? Well, the book also describes five or six different ways and some of them are pretty new and now they're calling it multi omic. That means we're going to look at every single part of you. We're looking at your chemistry, your DNA, your RNA, your proteins, maybe other parts we have yet to find. And believe me, there's still a lot of parts defined we haven't found yet. And so that's really what the book is. It takes you on the journey. But the final chapter is one I'd like to focus on just briefly, and that is what can you do right now? Yeah, you can go to the doctor when you're feeling bad. That's the first thing you do, I would say.

(00:39:24):

So you get to be older. But the second thing is something that has been recognized forever by the ancient Greeks, by the Pharaohs, and probably even longer means, and that is exercise. So I hope everybody's exercising as much as you can. Diet. That means don't get overweight and eat properly. Sleep is a lot more important than most people thought it was. That sleep is one of the biggest things you can do both for your brain health and for your body's health. And then gatherings like this, stay with your friends, stay with your family. All of those things are really fundamental, but those are all things we can do and they're not that hard to do, especially if you take a little bit of a time. About two years ago I started exercising after a long, long time. As long as I've been around, I haven't been exercising. And it turns out if you don't exercise, it's not so good for you. But by slowly doing a little bit, a little bit more, I'm getting there. So I'm a lot more exercise than I was for. And I think those are the things that you can

do yourself and just keeping yourself in good health, keeping yourself as happy as you can be. And so I'd like to turn it over to Larry who will have his own views.

Alexander "Zan" Fleming (00:40:55):

And Larry and Lucy are very good about exercising. They've been doing that well for a long time,

Larry Steinman (00:41:02):

Right? Well, we're fortunate. We live in some hills and at our advanced age we get to walk up the hill and we don't even, we're just fighting gravity, which is a good thing. But let's say that some scientists through serendipity and brilliance, figures out a way that we all routinely live to be 110 that could happen. Bill said that we may not see cancer, so that will help. So what will societies be like if everyone is living that long? We assume that we can do at 110 what we can do at 75 and 50. If that's the case, where are all the people going to be? Will people want to stop working and enter into what's hopefully a purposeful life in retirement? What is that going to do to the younger people in society who are trying to get jobs in finance in academia, if they're blocked by us elderly people who aren't going away, who's going to set the rules in Europe, as Mark knows, you reach a certain age in most of those countries and it's a relatively young age.

(00:42:29):

It's in the sixties and you must retire at Stanford where I've been for 53 years. You don't have to retire. But by occupying a position, there's only a certain number of professors. They can hire only a certain number of labs. So by occupying those spaces without any social engineering or dicta from the administration, we're wrecking the lives of young people in the old days. I mean, just to see how advantages in medicine transformed science. In the old days, I think men and women made a lot of babies because so many of the babies died from infectious diseases. Assuming we get back to sanity in our country, will continue to develop vaccines and we won't see childhood diseases like measles, but that created a real social pressure. People have much smaller families, in fact, they're so small in some countries that there's going to be a decline in population. So there would be a tremendous impact. Should we be fortunate enough to get that elixir of life, biotech medicine that works splendidly, then we have additional problems that we'll have to deal with. It's better if we deal with them before they occur. But along with success in medicine, we're going to have to rethink a lot of the social aspects of the implications of a success.

Alexander "Zan" Fleming (00:44:15):

Well, a good problem to solve and let's hope that we will have it to work on. Coming back to your specialty in immunology, Larry, you've had quite a career in attacking a range of autoimmune diseases as well as other conditions that really go all over the map. And talk a bit about the role of immunology or what is now being called the immuno in understanding aging biology.

Larry Steinman (00:44:58):

Well, there's a great intersection for the past few decades at least. The quintessential malady of aging Alzheimer's disease has been considered by some a neuroinflammatory disease. And the culprit are these sticky molecules called the amyloid molecules, amyloid beta tau. These molecules have a propensity to bind to each other, and you get these sheets of proteins that have certain patterns. So the question is, Alzheimer's does not look like the stereotype. Neuroinflammatory diseases a disease like Bill mentioned, multiple sclerosis where there's inflammation all over the brain. In fact, if you look at an

Alzheimer's brain, there's very little classical inflammation at all. When Stan Ner discovered prion diseases, he wrote in his autobiography that when you looked at the spinal fluid, there was no hallmark, no trace of an inflammatory response. And the prion proteins are quintessentially amyloid in their nature. They form these sticky sheets that just get bigger and bigger.

(00:46:33):

So immunology has impacted the study of Alzheimer's disease, but in a very peculiar way. My colleagues who focus on Alzheimer's talk about inflammaging and inflammation in the brain in Alzheimer's. But if you look under a microscope, it doesn't look in any way, shape or form like a true inflammatory disease of the brain. Bill and I had a chance to write about that a few blocks away at the Rockefeller famous animal model of multiple sclerosis was first studied in the 1930s by a man named Thomas Rivers. And that model has been extremely productive in developing new medicines for multiple sclerosis. But that model, it has an abbreviation, EAE, it was 90 years old. Bill wrote an and I wrote anniversary paper with another colleague, Roberto Patar. And again, whatever my colleagues are talking about in the realm of Alzheimer's, it doesn't look inflammatory to me. So you asked about immunology and Alzheimer's.

(00:48:04):

Now the immuno is a collection of molecules. Bill referred to multis and for instance, one of the molecules that we associate with the immune system is compliment. I'm giving you a compliment, but it's a series of proteins that actually bore holes into microbes, into bacteria. But these same compliment molecules, if they're overproduced lead to psychiatric diseases like schizophrenia and the trouble with molecules. They don't know what department they're supposed to belong to. They're just molecules. And it turns out that had complement first been discovered by psychiatrists, they would've said, what are these immunologists doing with our molecule? So we become more humans and we make these silly mistakes. Anyway, I don't want to go on too much about the immuno Once upon a time, I was on Science Friday talking about amyloid molecules that are good for you. And people were so flustered by that that they said while driving their car and listening to science Friday, they got into fender benders. I don't believe them, but that's how well that work didn't go over.

Alexander "Zan" Fleming (00:49:31):

You've always had a little bit of iconoclast in you. I bet. And there's benefit of that. Likewise, bill, you have been such a great teacher and you use your writing to help bring home very complicated points to the lay public and even to people who think they know something. Your books are very elucidating and you and your book break down some of the major categories of therapeutic interventions and maybe you could talk a little bit about that.

Bill Haseltine (00:50:08):

Well, thank you for talking about my books. My latest one is currently out for review with various publishing houses and we'll see how it does. It's called the Biology of Desire.

(00:50:22):

But the title hides a few things. One is he, we humans have many desires. It's not just the obvious desire. We have desire for sleep, we have desire for food, we have desire for adulation, we have all sorts of desires. What's really interesting though about modern science is we can peer into the brain actually located and say right here is where when you see some good looking person across the room, your brain lights up. And by the way, this is exactly what's lighting up and this is the chemistry that's going on. And whether you like it or not, you're stuck. So the image on the top of cover of the book is the brain is the unknowing public master. It's below consciousness. You don't know all the things your brain is doing,

but your brain is doing a lot of things. And so I have to say one of the great pleasures, and thanks for mentioning it, is continual learning.

(00:51:20):

And by the way, that is one of the other tricks of aging. Keep your mind as active as you can. It's not just through friendships, it's keeping your mind actively engaged. And you can show direct correlation between that and the lower incidences of serious neurological neuropsychiatric issues. But on the topic of what the substance is, one of the things that Larry was just talking about is inflammation. And there are not a lot of connections in different parts of the body where the immunologists are getting into aging. And if you look at what's happening throughout your body, your immune system is going awry as you get older. Part of it is manifest in the brain, but it's manifest in many other parts of your body. And so a new aspect of immunology isn't only fighting infectious disease, not only fighting cancer, but trying to figure out how to get your body to get rid of the dead cells or to do other things peacefully without causing more inflammation, other problems. And that's, I'd say, a very promising one. One of the things that you'll have read about are your ome, the ends of your chromosomes.

(00:52:46):

The way DNA replicate is either a circle or it's got to have an end, but it has to have a starting point. And for humans, you have your end of your chromosome. We're just hanging out there and they have a certain length. And by the way, you're born with different lengths. And as you get older, they get shorter and shorter and shorter. And at some point they get shorter to the point where your genes begin to unravel and your cells begin to die. So part of aging is almost inevitable shortening of something that's meant to keep yourselves alive. We had a speaker here, Jack Tack too long ago. Some of you were here for that. Jack did a friend a favor, discovered something important, got a Nobel Prize for helping Fred understands human birth. Now that we understand them, we understand that like many things in U, they have a giant that is on the one hand, yes, they'll keep cells alive longer.

(00:53:47):

On the other hand, they'll keep cancer cells better and they'll have cells that aren't cancer become cancer. Because one thing cancer is, is it solve that problem. If you look at the telomeres of a cancer cell gets longer and longer. And although I give that example, lemme just give an example of something recent. People are trying to find drugs to knock out what they call senescent cells. Your cells go on perfectly well. They divide, they divide, divide. And even in a Petri dish, they reach what's called the hay limit from a scientist who first observed it. They stop growing, but they don't die. They sit there, but they don't sit there harmlessly. They sit there pumping out substances that aren't good for you. Some of these very same inflammatory molecules they talk about. So certain people come up with the idea, Hey, wouldn't it be great if we had a drug that knocked out those sleeping cells that are poisoning us?

(00:54:45):

And the answer is yes. But by the way, there are a lot of other cells in your body that may not be dividing. For example, your brain. Okay? And you really want to knock off those cells too. And that is a kind of conundrum that we face when we look at many of these aging advances. And it's true that you can. And the book goes through five, six other ones. Another great book I'll recommend if you want to pick it up, it's called Why We Die, Nobel Prize winner, Vicky Raman. And he wrote a very good book, which basically takes all of these ideas and spikes them, okay? But he said it, I said, really gentlemanly way. I asked him in a conference, why were you so nice to X, Y, or Z? He said, bill, I'm working in Great Britain now and the libel laws are different.

(00:55:42):

Two lawyers have gone through my book with a five tooth code. But if you really wanted to understand what the forefront is and what the pros and cons and limitations of those for fronts are, that's a very good book to read. It's also a good book for young people getting enough science to read because it's a lot about science. You try to go to the edge where it's not known and you dig there. I give you a feeling for what it's like. And Larry probably has these same sentiments. When you're a scientist and you come up with a new idea, you're looking for something, you think there's going to be a really interesting answer. It's like being in the bottom of a deep coal mine side at it where you're right at the face. It's a mind China, you're banging away with your act. You think there's something in there but you don't know.

(00:56:39):

The thing about the unknown is that you don't know. I don't think most people understand how unknown unknown is, but when you're at that rock face and bagging away, you don't know if there's anything back there. You don't know what you're going to find. And very often what you find is trivial is sometimes it's deep and you can't tell that in advance. You can't know what you're going to find. That's how it feels like. But that is also exciting if that's the kind of thing you want to be excited about. I think Larry and I are both grateful for people who've trained us for the work that we're able to do. I'd say one final thing that one of the things I write about is the sadness of our current times. Everything that Larry and I have just talked about has been made possible because there's been a wind in our back ever since budgeting.

(00:57:37):

It's been a fantastic win, right? Left center, everybody's supporting us. They've opened door after door after door, not just for me, for all people my age and for our students. Those doors are closing, they're slamming shut. And I can't tell you how many young people we talk to who are saying, bill, where should I go? Should I go to France? Should I go to Japan? Where should I go? I don't see a future for me here. These are the people that we've nurtured that are the people who brought us our parent health and who. But it's not just our health, it's our wealth. You look at our wealth today, it comes from these self saving people and the self saving long-term support. And it is so dismal to think if you're Larry or me and looking at what made our lives possible, that the lives of our grandchildren are not going to be paved the way our lives work. And that's something we can all try to do something about. So we're fortunate. We've, I think, made some contributions, but we've only been able to do that. The system has worked for us there.

Larry Steinman (00:58:52):

There's a couple of tales I want to talk to. Somehow we scientists failed to convey to the general public, not to the people obviously here this evening about the thrill of doing science. So I'm looking at Mark Feldman in the front row. He developed the most successful drug, the first monoclonal anti-tumor necrosis factor for treating rheumatoid arthritis and inflammatory bowel disease. They showed pictures at a company where I was on the board that had sponsored some of the work about the outcome and it seemed like science fiction to me. These were people who said the pain went away and they're doing things that they haven't been able to do for decades. Of course, the experiment was repeated and extended, and as we say, the rest is history. The drug was approved and it's enormously successful.

Bill Haseltine (00:59:48):

You can't get that off your TV screen.

Larry Steinman (00:59:51):

Yeah, it's a high class problem, especially for the people benefiting. But just to go back to that, one of Bill was talking about being in a mine and with your pick an ax and you don't know whether you're going to hit gold or hit nothing or get black lung disease in the process. But once you do get an exciting finding and it is reproduced in your own lab and by others, there's very few experiences in life that are more thrilling. You've actually discovered something. And that goes a long way. And it, it's changed life here in the United States, and yet there's vast segments of the population who have no appreciation whatsoever. So after, and one of the enemies is US scientists not doing a good job, but it's also what we refer to as Hollywood. So I'll tell you a story. Paul Berg, who won the Nobel Prize for genetic engineering, called up Steven Spielberg after the first Jurassic Park and said, sir, I'm Paul Berg.

(01:01:07):

And I don't think Steven Spielberg had any idea of the kind man who was talking to him who was one of the great scientists of our time. And he said, would your next version of Jurassic Park perhaps portray scientists in a more positive way? And essentially Spielberg put the phone down and said, I don't care. So this really remained with me. I'd like to have Steve Spielberg sit down and hear about that tale from Paul Berg, but we have to make people appreciate science. Now, bill brought up Sputnik. So we have a lot in common because we're the same age. We talked about Hubel and Weasel. So Sputnik, when I was in high school, we could go outside at an appointed time and we could see Sputnik traveling over the United States. So Congress really freaked out and they set up the National Education Defense Act. And for a couple of summers I was to campuses to study Boolean algebra and computer science.

(01:02:26):

And they really wanted to make sure that we had an opportunity to do science. And the first job I got was at this new institute in La Jolla called the Salk Institute. I met Salk, but there was a young postdoc there named David Baltimore who discovered reverse transcriptase. But I was paid by the National Defense Education Act as a young college student at the Salk Institute, $100 a week to live in La Jolla. And I thought not only was I getting a great experience, but I was getting to be a very wealthy guy a hundred dollars a week. But how times have changed, all of those opportunities for young people are drying up and we'll have a real problem in this country if we don't remain the epitome of science and technology, the Chinese will certainly be well ahead of us. Western Europe will. It won't reflect well on our progress and our economics and our military prowess. I just don't understand how this can happen. I mean, it's a really disastrous self-inflicted wound and be tough to overcome.

Alexander "Zan" Fleming (01:03:55):

Well, it's sobering, but let's not end it there.

Bill Haseltine (01:03:59):

Yes, something when you watch it in the news, I have to turn it off after a while because I have to sleep. It's about me. Well age me more than anything else. Watching evening news. Now, go ahead.

Alexander "Zan" Fleming (01:04:16):

Why don't we bring the evening to a close here? Of course, we're going to continue

Bill Haseltine (01:04:23):

And have some questions

Alexander "Zan" Fleming (01:04:25):

With some questions, but from each of you look ahead over the next five years, what do you see as encouraging? What is potentially achievable? What do you think is likely to happen if you want to make a prediction, but let's get a forward looking statement from you both.

Bill Haseltine (01:04:49):

I would say the first thing is AI is making a difference. Now, it will make a bigger difference in five years to your medical diagnosis and your medical treatment. People haven't worked it all out yet, but I'm reading a lot, talking a lot of people, and it's really making a big difference. And I think the biggest difference we will feel is that your grandchild lost his job. But the second one is that when you go see your doctor, they're going to have behind them a voice or input exactly what's wrong with you, and they're going to get more and more and more precise. That's the first thing that's going to happen. Second thing is we're really going to make a lot more progress in cancer. Just in the last five years, there's really big kinds of cancer. Nobody could really care before that they're not getting cured.

(01:05:39):

Yes, we've built on a long trajectory of that, but we're getting better and better all the time. And I foresee maybe not in five years, but in 20 years where there'll be very little cancer. And that's the other biggest thing that's happening right now is being able to change genetic destiny. Even kind enough to refer to my books. I wrote a book called Destiny's Child No Longer. The argument is that I make in the book is there's a lot of things we can do now to change genes to you're born with to your benefit, whether you're old or young, but especially if you're just been born or just before you were born, that you can really change genetic destiny now. And I'm happy to say just today I'm writing an article, article on the New Law of all Things Florida. Would you imagine that Florida just passed something called the Sunshine Act?

(01:06:34):

What that means is they're now doing an experiment that says we should test a hundred thousand, do total genome sequence in a hundred thousand babies and intervene with drugs or genes as appropriate in Florida. They're already doing it in very few other factories, but you can make a real difference that is going to make the difference. And it's not just what you inherit. All of us, as we go through life, our DNA gets banged up just by breathing, for example. That's going to burn up a little bit of your DNA. And there are now ways to change it. If we find out what it is, we forget really good at a hundred dollars a complete genome sequence, we can figure out what's there. And we are beginning to get ways to change that, change that G to an A and BGA or substitute this whole piece for that piece that's happening now. It's happening in real time and all these things are going to accelerate over the next five years. So we're at the cusp of really amazing medical advances. Larry?

Larry Steinman (01:07:45):

Well, I think along with the medical advances, I think that sometimes when positive, Larry positive, it's always darkest before sunrise. And I think that it will be a natural response of our society to say We need to be number one and to hear those U-S-A-U-S-A cheer that you hear at sports events apply to other domains like scientific discoveries and successes on those. So it won't take, I think, a great transformation. And there's a lot of good people in sales and publicity who can be enlisted by the scientific community so that we're much better salesmen, but there's nothing like adversity to make the best in people to come out sometime. And I think that will happen.

Bill Haseltine (01:08:43):

I'd like to call out a few people who are in the audience on this behalf. One of the things we need to do is communicate science and Tracy, are you here? Tracy Day is the organizer. What the organizing brain behind the World Science Festival that we all enjoy here in New York? So Tracy, New York is hard. It is Tracy. It is now, what, 15 years?

Tracy (01:09:13):

2008 we launched.

Bill Haseltine (01:09:14):

So a good long time and now expanding in other sessions. She was just telling me they're now including offers like Ian mc Human as part of their program as well. I think Bob Millard is, we had a conversation this morning about his science education efforts. He's been the chair of MIT, but very interested in the MIT museum, which has a different mission, which is to communicate with not only the people of Boston beyond that. And so there is a concerted effort on our part. There's a real interest in putting science not into something. We all know that our kids before the age of hormones love science, but somehow get switched off along with a hormone flood. But to try to educate people who are 10 to 15 years old and their parents and older people. And so we're very happy you're here. Part of this is, believe it or not, educational mission. So you're participating.

Alexander "Zan" Fleming (01:10:19):

Well, we do have a very distinguished audience here, and why don't we take a few questions. We've got a few minutes and maybe you can, Thomas, if there's the questions.

Speaker 10 (01:10:32):

Okay, bill. Oh, thank you. I kind of speak loudly.

Bill Haseltine (01:10:39):

She's already done pretty well. If I, no,

Speaker 10 (01:10:41):

I have to say

Bill Haseltine (01:10:42):

In her nineties.

Speaker 10 (01:10:43):

No, what? I am the oldest person in this room for sure. I am 96. I am 96. And so I have to tell you what I have to add to your last chapter is schedule. You can't wake up in the morning and say, should I go to my exercise or shouldn't I? If it's in your schedule to get to your exercise at 9:00 AM you get there. You don't want to, but

Bill Haseltine (01:11:21):

You do something. I have just read an article on schedule.

Speaker 10 (01:11:25):

Now the second thing is

Bill Haseltine (01:11:28):

I left it out.

Speaker 10 (01:11:29):

The second thing is you said to keep engaged is to want to learn. I have to tell you, I'm still hitting the ball on the tennis court

(01:11:44):

And I'm not playing playing. That's another story. But my tennis pro said she knows who I am for a long time, but the fact that I keep wanting to learn is the amazing part. I still do pottery twice a week and the fact that I still want to learn new ways to see the glazes or to do the things, but that's the important part is to want to learn. Some people learn bridge or golf or other thing, but that's good. I knit and I knit very complicated patterns. I like it. And that's good for my brain.

(01:12:40):

And

(01:12:41):

One of just one quick thing. I did want my brain to be studied when I die, but I want to know what you learned.

Speaker 11 (01:13:14):

So Bill, they say that in biotech that mice lie and monkeys exaggerate. What are the monkeys telling us about how long a human being could live?

Bill Haseltine (01:13:30):

First of all, Mr. It was a friend of mine who said that it was about vaccines. Maurice Hillman, if she knew Maurice, she was quite a character and he brought us many of the vaccines that you've got. He said, my sly and monkeys don't necessarily tell the truth. We can't extend the life of monkeys yet, as far as I know, Larry, I

Larry Steinman (01:13:54):

Understand. I'm unaware.

Bill Haseltine (01:13:56):

Yeah, if we can, we don't know how to do it. There are some chimps that live happily and captivity into their thirties and even forties so they can, in fact, there's just a new study published. It says that female chimps live long past their reproductive age. It's a new discovery like us. So that is something. Can we replace young blood with old blood? With young blood? It makes a big difference. It may make a short-term difference. Nobody's proved it makes a long-term difference. And I would say, direct answer your question, these are Larry, or I know of anybody who's been able to keep a monkey alive much longer than their international lifespan. And it's a little hard to do because when it takes care of a monkey in a laboratory setting, he is likely to live longer than he would've if the monkeys in the wild.

(01:14:59):

So it's hard to tell. And if it weren't hard to tell, it takes a long time and it costs a heck a lot. So all of those things argue against that and people are working very hard to try to make what they called organized a whole new field of science is to take little bits of you and try to reproduce it in a test tube so that you can substitute it for the person. And that's had some success. You'd be able to take a little bit of lung and substitute it for this virus or this and that virus or anything. It's a whole new field and it is pretty interesting. So organoids and it's a very interesting field moving fast and needing more support.

Alexander "Zan" Fleming (01:15:45):

I saw a question. Here we go.

Speaker 12 (01:15:55):

So we heard, I think from the person in the audience of the most advanced age, I think I'm probably the least advanced aged in the audience right now. No, that's nothing clap for. That's clap for. I'm just, so what I do in my day job, and I think X obviously knows this, is I run a lobbying organization for next generation biotech solutions, longevity specifically. And I work a lot with people in my cohort and a lot of them are researchers. What advice do you have to them? What can I tell them to give them solace in these difficult times? Obviously it's hard to get an NIH grant. Biotech companies aren't really hiring as vigorously as they were in the past. So what advice do you have for people that I talk to about how they can get their start in science?

Bill Haseltine (01:16:42):

Let's just take that. That's a very hard question.

Larry Steinman (01:16:47):

Well, we're spending a lot of time agonizing about it, and I think that when we're in a situation like this, small steps are good. So offer opportunities one might, some will be unpaid opportunities, some will turn into real jobs. But for the young people, I think the drought will end at some point and then there will be a huge flood of jobs and opportunities for these people. But it's hard to, I mean, societies have been in worse straits. I mean, our country has been at war, we have oceans around us. We've never been bombed, but we have to think of this as a crisis time and rally. And I think by rallying and being with other people in the same boat, there will be added strength. But these are some of what I'm saying is a cliche and a football coach pep talk, but there's some truth in it

Bill Haseltine (01:17:58):

That's optimistic. I would say that you mentioned a couple of things. One is the opportunities in academia for somebody in the biotech area of growing up. The venture capitalists are out of money that may be changing, may not be changing, but the fact is they've not been liquid for a long time. But most companies and many of us who've been in the field have seen bankruptcies. We've never really experienced the same rate at all. And so if you're Chinese, go back to China, that would be one piece of advice, which isn't exactly the right advice right here, but I'm reading what they're doing. And it depends how you look at the world. If you take a stance, I say I'm a humanist, not an American, only American, an American and a humanist, what's good for humanity. But from my point of view, science has never been healthier, just not here.

(01:19:03):

If I look at India, I look at Barcelona, I look at Australia, I look at Japan and Korea. They're doing amazing work. And China is breathtaking. They are now certainly in most fields equal to us and in some cases ahead of us. And I see that gap only getting old. Is that bad for America? Yes. Is it bad for humanity? Not necessarily. Because those advances, there are companies now that specialized in buying Chinese inventions. I was just reading this week about a big fund that was just several hundred million dollars just to pick up hot opportunities from Japan. That's good for us. And a lot of the books you take were invented in say, Japan. That's also good for us. So if you take that humanity view, we're in great shape. If you take an American point of view, maybe that's a great shape for the moment.

(01:20:07):

And as Larry said, let's talk about changes because we do have the potential for change. The other thing that's very important, most people don't realize it about science is it is really one of the last vestiges where it's passed down from generation to generation. I am the grandchildren of people who were kicked out, child scientific grandchild of people who are kicked out of Europe. My mentors, mentors were all the great scientists that fled the horrors of the thirties and the forties in Europe. And they trained my mentors, they trained me. I've trained and because generation after generation, and it's really interesting because science is a process of what's called abductive reasoning. It means you can't get that necessarily by deduction or induction. You have to make a guess and then you've got to pursue that guess. But in order to have a confidence to do that, you need to be trained by somebody who's done it and won the lottery. I was trained by four Nobel Prize winners.

(01:21:13):

Those guys won the lottery. They made those guesses and they were right and they were rewarded. And there's nothing that can help you better than to be in the presence of those people who have the confidence to do it again. And I think that is one of the things when you start doing what we're doing, it's cutting off some of that seed part, cutting off those connections that wonderful past that we've had. It can be devastating. And that's why we're so concerned about the young people because those are the people who are afraid the next young people. And I think that isn't a direct answer to the question, but it's sort of putting it in context that you're working in really important areas. So keep it up. If we can help you, let us know. How

Alexander "Zan" Fleming (01:21:57):

About one last question here.

Speaker 13 (01:22:00):

Was that me? Yeah. Was there someone else? No. So I'm curious, are there any theories about why women do live beyond fertility age? I have my own theories, but I

Bill Haseltine (01:22:12):

Have a theory.

Speaker 13 (01:22:13):

Please do tell.

Bill Haseltine (01:22:15):

I'll start with your theory grandparents. Exactly. But very specific. There are two species in which it's been longevity of the grandchild and the thriving of the grandchild has been attributed to grandparents, the human being or however, I have to say with some humility, it ain't the grandfather, it's the grandmother. The link is between a living grandmother and the thriving of the grandchild. So that's one really good theory. I know you're a grandmother and I know my wife is a grandmother and I can attest great

Speaker 13 (01:23:00):

Grandmother.

Bill Haseltine (01:23:01):

You're a great and probably a great grandmother too, Joe, true sensitively. But it is very important. The grandmothers, I can say by watching my own contributions to my grandchildren and watching my wife's contributions to the grandchildren, I would endorse the theory.

Larry Steinman (01:23:22):

I think one of the things that may really help science in the United States are women in science, because I know many of them are mothers raising children and going off to work in the morning. How they do it, I have no idea. Men are a certain amount of help, but we have our limitations having our genetic background. So I think that maybe we need to have a larger role for the women in science to kick the backsides of people in the government to get with the program. It's a hope. But maybe the women can lead us forward, maybe someday we'll even have a female person in the White House, not in that.

Bill Haseltine (01:24:12):

There is one story that is recently been produced that is there is of course a big difference between men and women in our chromosomal composition. My sister once wrote a book called Dr. Xx. She's a doctor that refers to the two female chromosomes. And the idea is women live longer, which they do in many societies. In fact, almost all because they have an extra chromosome and that produces backups if the other one fails. So that is a physiological explanation that's come up. Whether it's the actual answer, I don't know, but at least it's an answer. It's a little bit more than grandmother's.

Alexander "Zan" Fleming (01:25:00):

One last question.

Speaker 14 (01:25:04):

If it's all right, I'd like to ask another question for you. I think that the question I would've asked for you, he's a lobbyist for all his students, and we're so lucky to have the two of you talking about longevity. It'd be really great to hear you say, if you have, with these students working in longevity, here's some ideas of where I would work. We see all these things going around, but we don't really have any sense how to put a stake in it and what I do. Cool.

Bill Haseltine (01:25:30):

Did you ask a question? Yeah. The question was, could you give him

Speaker 14 (01:25:33):

Students of where you think now the key areas in longevity research that it's more than Alzheimer's, right? The two of you are uniquely qualified to be able to give them some advice. Most

Bill Haseltine (01:25:47):

Of you have first answer

Speaker 14 (01:25:48):

Thanks.

Bill Haseltine (01:25:50):

One thing I'm reasonably sure about is that that fundamental aspects of aging is driven by not inflammation. Not inflammation, but inflammation. The very fact that you breathe is burning up your DNA. Just that simple fact. If you make a correlation between the longevity of a species and their ability to repair DNA and other oxidative damage to their cells and their DNA, it's almost a linear correlation. So anything that we can do to reduce that. Now, there's very little things that I can see right now that you as an adult can do, but at some point we may be able to engineer babies so that they fix up their DNA super well, and those babies would live a very, very long time. So my guess would be look at gene therapies that can be delivered in your neuro or to newborns. And at the very beginning, don't change your life, but make sure their life is a long life. Now that has some ethical consequences and complications. Okay. But I don't think we can do it once the adult is reached. I think we can do it at a much younger age by changing the fundamentals of DNA damage and repair.

Speaker 14 (01:27:26):

That's

(01:27:26):

A great answer.

(01:27:28):

And didn't love the answer. I don't love

Bill Haseltine (01:27:30):

That. No, nobody loves the answer because you're alive. Okay. But it is an answer. If there's a place to do it, idea that's way to do

Speaker 14 (01:27:40):

It. That's great. Does your partner have an equally insightful idea?

Larry Steinman (01:27:44):

Yeah. The so-called killer experiment I would do is to study people who have been successful at living a long time and look for those individuals who have all of the bad risk factors for having become demented. And they're not a POE four, for instance, aprotinin E four variant. And let's see what other changes in their genome. Proteome have guarded against the inevitable lapse into dementia. So I think there's a great virtue of studying extreme outliers where everything's stacked against them and yet they're doing fine. Their brains may be full of amyloid plaques. It's another favorite one. What else is

going on that left them free of the disease of aging, the quintessential one. So I would get a group together, a hundred of them and study the heck out of them.

Alexander "Zan" Fleming (01:28:53):

Are you signing up? Well, this has been a great discussion and we're not done yet. We'll have a little more informal back and forth in just a few minutes for those who are gathered here. But we're going to say goodnight to our web audience and appreciate they're hanging on late and some people's evening. And again, Bill and Larry, we cannot thank you enough. And Maria Eugenia, thank you for having us into your home.