

How & Why You Age, And What It Takes To Be 'Young Forever' – Mark Hyman, M.D. – #1044

Dave Asprey:

You are listening to The Human Upgrade with Dave Asprey. In the studio today here in Austin, Texas, I have a 15 times New York Times bestselling author who has just written a book about aging, and, of course, a medical doctor as well. Also, a good friend. Dr. Mark Hyman, welcome back to the show you.

Mark Hyman, M.D.:

Thanks, Dave. Thanks, Dave. It's been a bit, but I'm happy to be back.

Dave:

You're looking young. What are you doing that's different?

Mark:

What am I not doing? Dave, I turned 63 last year. When I turned 60, I was like, "Okay, wait a minute. I think there's a bunch of stuff that I need to really understand about why we're seeing such a terrible epidemic of chronic disease and rapid aging in this country." I don't want to be subjected to that. I've been practicing functional medicine for 30 years almost, and using the principles to help upgrade my health, but I wanted to double down on looking at what's really the latest science of how do I optimize my biological age? How do I actually not just live longer but feel better, and how do I optimize my function, and not go down the trajectory of what I see as abnormal aging in America?

What we typically see is people getting older and getting decrepit and frail and disabled and dysfunctional, not able to do what they want to do, but I don't want that for myself or anybody else. I realize that we have within us this incredible healing system that we can activate through the understanding of this emerging science of longevity. So, when you're talking about 20 years ago looking at longevity, we didn't know as much, because it was sort of a step kid to science. People didn't study it. People didn't fund the research in longevity.

But now, there's a tremendous amount of research, and we've learned so much about what actually causes rapid biological aging, and we know what to do to reverse it. I'm biologically 63. I mean, sorry, I'm chronologically 63, but I'm biologically 43, because I've applied a lot of these principles to myself.

Dave:

So, you actually have a 20-year gap now?

Mark:

Yeah, 20 years.

Dave:

That's, what, DNA age. Which test is that?

Mark:

DNA methylation. I also did telomeres a couple years ago, and I was also about a 20-year difference.

Dave:

Nice. 20-year difference is at the upper end of what I've seen, and the DNA methylation clocks that we can use, if you're new to the science of this and listening, there's different ways of deciding what your biological age is. I've done a bunch of them. I'm only nine years younger, or no, 11 years younger, I think. I'm 11 years younger.

Mark:

Well, you know how it is. The more overweight you are, the more weight you can lose. The older you are, the more age you can lose, I think, something like that.

Dave:

There might be some truth to that. All I know is that-

Mark:

You're going to be 12. You can't go back to zero, right?

Dave:

I think I would've been 70 when I was 20, because I mean, I was really unhealthy too, but it's interesting. I know many people who are at least five years younger biologically. Then you and I both have known people who are way older than their age. How much do you trust those measurements?

Then you and I both have known people who are way older than their age. How much do you trust those measurements?

Mark:

I think there's a lot of companies that are coming out with DNA methylation, epigenetic clock testing, which is the way we look at your biological age. There are other metrics like telomere length and things, but I think there is some variability. But I think if you look at the companies that are doing the best job, I think TruDiagnostic is one of the best. I don't have any affiliation with them, but they're pretty good with reproducible results. Then you can track what you're doing over time.

So, the beautiful thing is that we have a program that we can change in our biology by understanding how to affect these underlying factors we call the hallmarks of aging that accelerate aging. So, we can literally reprogram our biology and our genes and our epigenome to a younger self at any time if we know actually what to do. That's really what led me to write Young Forever. What was the central thesis is that we have now finally unlocked the causes of aging, of abnormal aging, let's say, not chronological aging. That's just time. I can't do anything about that, but we've unlocked the causes of rapid biological aging, which is abnormal, and it's treatable.

So, all of a sudden, we're reframing aging as a disease, as a treatable disease. That's a very big frame shift for many people.

Dave:

It's something that was very hotly debated. Even going back as far as the '90s and the early aughts, when you would say aging was a disease, you would get a really reactive response especially from Western medical doctors. They get angry. Why does it make people angry when you say this is-

Mark:

Well, because I think there's a sense that there's inevitability to the process of decline and dysfunction.

Dave:

People just don't like that inevitability, so they get mad.

Mark:

No, because they think that it's actually a disservice to science to talk about something that's impossible, which is-

Dave:

Like flying or nuclear power, all those pesky things that actually changed the world. We shouldn't talk about those.

Mark:

Exactly. No, I would get to the moon. We just don't think it's possible. So, we have a paradigm shift that's happening. The paradigm was this is what happens as you get older. I mean, even when I was in medical school, and still today, we talk about chronic disease management, which drives me freaking crazy, because I don't want to manage someone's chronic disease. I want to get rid of it. I share a story in the book of a woman named Janice, who had such an accelerated path of HH. She was 66. Her body mass index was 43, which is huge. It was huge, obese, type two diabetic for 10 years, heart failure, multiple stents, hypertension, high cholesterol, kidneys were failing, liver was fatty, just a mess on 20,000 of copay a year.

She was on her way to a heart transplant and a kidney transplant. Three days, I'm changing her diet. She was off insulin. Three months, she was off all medications. Her heart failure reversed, which is something we don't see in medicine unless she get a heart transplant.

Dave:

What was causing this in her diet?

Mark:

What do you think? Ultra-processed food, which is what she lived on. I honestly was so shocked because... Let me finish this story, and then I'll tell you why I was so shocked.

Dave:

Sure.

Mark:

She had heart failure normalized, which does not happen. You can manage heart failure. Her diabetes was completely gone. Her A1C went from 11, which is way the-

Dave:

Bad.

Mark:

It's like someone almost should be hospitalized with a blood sugar that level to five and a half, which is normal. Her blood pressure normalized. Her kidneys normalized. Her fatty liver went away. In three months, she lost 43 pounds. In a year, she lost 116 pounds, and became a different human being. So, I don't want to manage her heart failure, her diabetes or kidney failure or fatty liver. I want to get rid of them. That's really what now we know how to do by activating these ancient longevity switches in the body.

As I began to dig deep into the research, I'm like, "Wait a minute. The body has all these switches, these levers that we can pull and work on, these pathways, and built in healing, innate regenerative repair, renewal, and healing systems that we can activate if we understand how." So, the book is about what are those systems, and how do we activate them, and what exactly do we do?

Dave:

We talked about ancient systems. I agree with you there. When I did my anti-aging book, which was Super Human probably four or five years ago now, I had-

Mark:

A great book.

Dave:

Thank you. I had seven pillars of aging. Now, when I go through Young Forever, you've, well, I don't want to say added three because they don't all line up. They're very similar thinking, but you have 10.

Mark:

There's 10, and now, there's a couple more that have been added. So now, there's 13. The scientists keep parsing it, but essentially, these systems that actually we start to understand are all interconnected and can drive aging.

Dave:

They do. You have a history of 30 years of practicing functional medicine. So, you've got great pattern recognition that I think only starts to happen after maybe 20 years. If you put on your 10 years from now hat, how many causes of aging are we going to have?

Mark:

Oh, I don't know. I mean, I think, look, I think the body has these certain biological networks that are becoming clear that we now can understand are underlying all disease. So, the hallmarks of aging are one attempt to map those out. Functional medicine has really created seven physiological systems, and the hallmarks fit in that. They do. I think it doesn't really matter, honestly. It's just it's not really separate. They're not like, "Oh, it's 10 different things or 13 different things." It's really one system that's like a web all interconnected, and we're just parsing it to be able to describe it, and be able to work on it, but all these things relate to everything else.

So, any one of those hallmarks interacts with all the other hallmarks, right?

Dave:

Exactly.

Mark:

So, it's not like you can say, "Oh, this is the thing, or this is the thing." It's very different. I feel like if you understand how to do the right thing in terms of your lifestyle and certain behaviors, certain supplements, certain medications, certain lifestyle practices or biohacking techniques, then you can actually change those hallmarks, and reverse the downslide toward rapid aging, disease and death.

Dave:

You definitely can reverse that. For some people, we don't know how for whatever's going on with them yet. For many people, it's easy. For a lot of people, you don't even have to know what's wrong. You just have to say, "Okay." I like to look at this as herding sheep, and maybe because I've raised sheep on my regenerative farm, but the people are, "Well, what's the one thing that's most important? How many things do you need to know to herd sheep?" I don't know. There's a dog, and it moves around, and when one sheep is out, it gets pushed back in, but we know you have to give them water. They have to have enough food and sunlight, because it doesn't work if you don't do those.

It feels like our systems are not that different.

Mark:

Not that different. No.

Dave:

We can come up with... I love your list of 10, by the way, and I'm going to go through some of these with you. We can come up with those, but there's probably five more. If you handle all of these, maybe you don't have to even know the other five.

Mark:

Well, I think what you just said is so profound, because as a functional medicine doctor, I don't treat disease. I don't try to cure disease. I try to create health, and then disease goes away as a side effects. So, the hallmarks of aging are, in a sense, a map of how we deviate from health, and so really, it's about restoration of function. That's what functional medicine is. It's restoration and optimization of our function, and that function of all these systems. How do our cells regulate themselves with proper mitochondrial function and immune regulation and the microbiome, and how do proteins function? How do our nutrients get regulated? How can we properly divide ourselves so we don't get damaged?

So, there's all these systems that are part of the hallmarks of aging, but we can actually, like you said, with the very few basic principles, fix all these things. Pierre Laplace said, "We can explain a large number of complex phenomena by a small set of general laws." Think about physics. There's just a few laws of physics. Think of everything you can do with physics. You can build a bridge. You can send a man to the moon. You can create our cell phones and whatever. I don't even understand what... I mean, I took physics in high school. That was about it, so maybe... I had to take physics in college, because I had to go to medical school, so I took Physics.

But I mean, it's just mind-blowing when you think of how many things can be manifested from a few set of small laws. So, I would say what we're now discovering, Dave, is the underlying fundamental laws of the universe, the nature of nature, the laws of biology, because we've never had those. Biology is so complex.

Dave:

That's so minimal.

Mark:

It's been so reactive. You have a headache. You go to the head doctor. You have a stomachache. You go to the stomach doctor. You go to the joint doctor if you have a joint pain. That's not how the body's organized. Because if you go have a joint pain, it might be from your microbiome. Your rheumatologist doesn't say, "Can I please see your poop?" They should, and I do, but that's not generally what happens. When you practice medicine that way, you see extraordinary things. You don't have to treat all the diseases separately. The hallmarks of aging, the theory around this, is that these are things that go wrong that can explain all the disease of aging.

So, what we're seeing are leaves on the trees like diabetes, heart disease, cancer, dementia, all these things, high blood pressure. These are just downstream of things, effects of these problems that could occur in the hallmarks. Then that's something you can actually treat. Now, for me, as I begin to think about this, I was like, "Wait a minute, the hallmarks are great, and they provide a target for treatment and thinking, but they're also reductionists too." The real answer to solving aging is figuring out why the hallmarks become dysfunctional in the first place. So, why do we see these problems?

Now, what's the cause of the hallmarks? So, the hallmarks are the cause of all these diseases. What is the cause of the hallmarks? That's what I really think is different about Young Forever is that it's through a functional medicine lens, which allows you to treat the root causes of everything, so not treating the hallmarks with a drug. Oh, inflammation is part of the hallmark expansion. Let me give you an anti-inflammatory drug, right?

Dave:

Right.

Mark:

It doesn't make sense.

Dave:

It doesn't make sense.

Mark:

Metformin, I think this is really good.

Dave:

Well, let's talk about metformin. This is interesting.

Mark:

Well, so one of the hallmarks of aging that I think is, if we can dive into it, super important, and I think it's a meta hallmark. It's above all the hallmarks, because it influences all of them.

Dave:

The God of all hallmarks.

Mark:

The God of all hallmarks. Exactly. They call it deregulated nutrient sensing blah, blah, blah, whatever.

Dave:

Yes.

Mark:

It means basically that your body's regulation of the food you're eating is screwed up, and when that's screwed up, it turns on all these pathways that accelerate aging. So, there are really four of these pathways that are key, or I call them longevity switches. Two of them sense too much of stuff that we're eating, and two of them sense a lack of scarcity of nutrients. So, insulin signaling is probably one of the major drivers of aging. Too much insulin is the worst thing you could possibly think of for aging. So if you want to measure a biomarker, that's 10 bucks, that any lab can do, that your doctor is not doing, that probably the most important metric in terms of determining your progression to aging is your fasting insulin level.

The insulin signaling is such a big factor. We eat too much sugar, too much starch, and that pushes this pathway to go, go, go, go. That creates everything we see is aging, heart disease, cancer, and diabetes, dementia. The high levels of sugar and starch we consume, the mountains of pharmacologic doses about almost a pound a day per person of flour and sugar just drive this pathway into the ground, and cause obesity, cause heart disease, cancer, diabetes, dementia. It's the worst. Then it also drives inflammation. It drives mitochondrial dysfunction. It drives damage to protein that drives zombie cells production. It drives epigenetic changes. It drives-

Dave:

All of the 10 get driven by insulin, right?

Mark:

That's right. It screws up your microbiome when you eat too much sugar and starch. So literally, everything that happens is that. The second... The key to that is eat very low glycemic diet. Low starch or sugar diet is so important.

Dave:

Low or zero?

Mark:

I wouldn't say zero.

Eat very low glycemic diet. Low starch or sugar diet is so important.

Dave:

Low or zero?

Mark:

I wouldn't say zero. We don't have to have zero. I mean, I think zero is we... You can be a carnivore, and have a zero carbohydrate diet. There's no biological requirement for carbohydrates, but I don't think...

We're very metabolically flexible when we're healthy, so we can manage different kinds of carbohydrates from whole foods and from whole grains. I mean, even if... [inaudible 00:17:14], for example, a marathon runner, or you're really active, you can consume a lot of carbohydrate. It's not going to mess up your metabolism. But if you're just sitting around the couch, a little bit can be bad. So, it really depends on you, your metabolic health, your body fat.

Dave:

Do you really see people who eat only meat and fat do healthy in the long term?

Mark:

I don't know because I haven't seen people do that very much. The only thing I would say is the plains Indians at the turn of the century had the largest amount of centenarians. People lived to be 100 years old, and they basically survived on bison.

Dave:

But they ate small amounts of carbs too.

Mark:

Yeah, they did. They ate berries, and they foraged for plants, and so they did eat.

Dave:

They did eat the plants for at least polyphenols.

Mark:

I mean, there are cultures that were more carnivorous, but I think we have these built-in systems to regulate carbohydrate metabolism, so it's not bad. It's just when it gets flooded. The second is mTOR. This is a long conversation.

Dave:

I love mTOR.

Mark:

mTOR is a really interesting pathway that is regulating protein synthesis. It can be overstimulated by eating all the time, by not giving it a break, by eating too much, in general, carbohydrate or protein. If you don't give yourself a break from eating, you can't give this pathway a rest, which is needed to actually create one of the key central things that makes you live a long time, which is autophagy. It's essentially self cleanup. Self-cannibalism is your recycling, repair, regeneration mode. It's where you take old parts, and you get rid of them. You digest them, and you break them down, and you build them into new things.

It's like a recycling plant basically. We desperately need that to function, and to be turned on every day, and to maybe have longer periods where it's turned on by more periods of fasting. We saw, for example, people who survived the concentration camps. They live really long time, and it's fascinating, and not a genetic thing. They just seem to live in their 90s, hundreds. It's like, "Wow, they're still around," and it was 75 years ago. So, a lot of that had to do with this shutting down their systems through starvation.

Then that actually activated on these longevity pathways. We'll talk about mTOR and what to do and everything, but that's where you get time restricted eating, intermittent fasting.

You've got drugs like rapamycin. There's other plant compounds and things that can actually affect mTOR. C15 is a fatty acid that actually stimulates the inhibition of mTOR. Then you've got these two pathways that sense not enough, which is AMPK and sirtuins. So, if you have a low nutrient state, you're basically... Well, AMPK means adenosine mono phosphate kinase. Essentially, it's a... You run on ATP, which is your fuel. You run on carbons and gas. You run on ATP. When the phosphate molecules are given away, instead of adenosine triphosphate, it becomes monophosphate, meaning one phosphate molecule instead of three.

Then your body goes, "Wait, I'm starving." Then it kicks in all these beneficial switches and pathways to conserve energy, to make your system optimized, to reduce inflammation, to improve your mitochondrial function, to do all these really beneficial things, which is great. That's where metformin comes in. I'm going to answer your metformin question. Then the last pathway is the sirtuin pathway, which has been highlighted by David Sinclair and Leonard Guarente, from MIT, who basically found that you could extend life by a third by giving huge amounts of resveratrol to rats or mice, and that was amazing.

They found it increased their metabolism, and improved their fitness level, did all kinds of things even if they were eating crappy, and not exercising. So, it was a very powerful pathway. This pathway is actually important, because actually, when it's activated, it stimulates DNA repair. One of the hallmarks of aging is damaged DNA. So when you stimulate sirtuins, it activates DNA repair. That's a good thing. It also improves mitochondrial function, reduces inflammation, improves insulin sensitivity. Those are all the things. So, all the things do all the things basically when you look at it.

That's where NAD is being used. So, you might have heard the NAD and metformin, rapamycin, and insulin. They all work through these central topics.

Dave:

I think, listeners of the show, at least for a long time, have heard at least one episode on each of those topics, right? But now, you're putting them all together saying it's-

Mark:

It's not all separate. It's like one system.

Dave:

So, what do they all do?

Mark:

They're regulating your body's entire biological systems. They're regulating mitochondria, which regulate energy. They're regulating immune function in the inflammation. They're regulating your antioxidant systems. They're regulating your insulin sensitivity. They're regulating the autophagy process. All these things that have to be dialed in if you want to prevent and reverse disease, and live a long time, you have to dial these things in. Metformin is being touted as a longevity drug. Now, I have a huge problem with it.

Dave:

You and me both. We got to... Let's slam on metformin a little bit.

Mark:

I wrote about this, and I tried to create a balanced conversation in the book. I said, "Here's what the data show. Here's why I think it's problematic." There's a large trial coming out called the TAME trial, which will help answer some of these questions. Recently, Dave, a new study came out that put a little bit of warning signs on the metformin craze.

Dave:

Another study that does that you mean?

Mark:

Well, so metformin is a drug that is beneficial towards AMPK. So, it optimizes the AMPK function, which is good, which is all we just talked about. So, you think, "Okay, that's good, but it also has some side effects." It has some mitochondrial side effects, which I really worry about, because mitochondria are key to healthy aging. It can cause digestive upset in some people, improves insulin sensitivity. I think it's fine. But when you look at a large trial, it's very hard to do randomized controlled trials in nutrition, very, very hard because you need thousands of people. You got to give them the same program, and you got to have control groups.

What they did was this very, very big famous study called the Diabetes Prevention Trial. What they did was they took pre-diabetics, and they gave them three different interventions. One was nothing. One was metformin, and one was lifestyle change. The metformin reduced the progression to type two diabetes by 31% benefit compared to the control group. Lifestyle was 58% reduction. There's that, but it was a shitty... I know people who were in this study, so I had patients who were in it. I was like, "Wow, this is really nuts," but it worked because people cut out all the crap in their diet. They exercise. They support each other. They were accountable. A lot of reasons for it.

But my point is this, if metformin doesn't work half as well as a crappy drug, I mean, as a crappy diet and a lifestyle intervention, what if you put people on a ketogenic diet, and I mentioned that, against Metformin? Then what?

Dave:

It dominates. Just completely changes everything.

Mark:

I'm not a big Metformin fan at this point. I'm more of a rapamycin fan, but I think Metformin recently was reviewed in another large study, and they found that the original results seem to show that type two diabetics who were on metformin died at less rates than people who were not on Metformin, I think, has been challenged. So, I think it's still an open question, but it's definitely not on my list of things to take for aging at this point. That patient, who I just mentioned, was an advanced type two diabetic on insulin every day.

Within three days, she's off her insulin. She's off all her medications. Her A1C is normal. Her insulin sensitivity is high, because of the food. There's no more powerful drug. So, I'm just saying like-

Dave:

So, they put her on beyond burger and impossible burgers and all that. Is that what she was doing?

Mark:

Definitely not, but think about it. It's like-

Dave:

Those are highly-processed foods. You have to take those out.

Mark:

It's like if I can give you 1,000 milligrams of aspirin for your headache, it's going to work better than if I give you two milligrams of aspirin, which probably won't work. So, I think of these drugs as two to five milligram doses compared to 1,000 milligram doses, which is lifestyle. That's how big the order of magnitude difference is in terms of the effect. You just can't get... You can get... Every diabetic, every drug, every treatment is conventional for diabetes. You will never reverse it. You will never... With every single drug piled on, you will never see the disease go away.

But with food, you can go away in three days. So, how is that not such a headline news on every major news outlet?

Dave:

I love what you're saying. It's one of the reasons with Upgrade labs, and since we last talked, we're opening dozens of locations all over the country, and it's a non-medical facility. If any disease is reversed, that's a side effect of lifestyle. All we're doing is saying, "What's the lowest dose of lifestyle that will get you there?" Because I'm a little disturbed by the pharmaceutical sales engine right now trying to say these things.

Mark:

Ozempic, let's do that.

Dave:

Well, I actually think Ozempic is exciting. Isn't there an anti-aging angle for GLP agonists?

Mark:

Because of its effect on body weight or on insulin sensitivity?

Dave:

Not just body weight, on insulin sensitivity. It seems like Ozempic might not be a bad thing if you're obese compared to the alternatives.

Mark:

You show me a single patient who took Ozempic and reversed their diabetes.

Dave:

I have no idea.

Mark:

It doesn't exist. It's the same-

Dave:

I will tell you, I did do one injection of Ozempic, because I interviewed one of the lead researchers in the trial, so I always try everything I can. I felt like I had morning sickness for a week. I didn't want to eat, and then I lost muscle mass because I didn't want to eat.

Mark:

Well, that's the other thing. Well, that's the other thing.

Dave:

There's that.

Mark:

That's the other thing. What concerns me about Ozempic, and this speaks to really one of the key central features of healthy aging, is muscle. You've got to maintain, keep, build muscle as you get older. It's harder to do as you get older, but you can, and when you take Ozempic, 40% of the weight loss is muscle, which means-

Dave:

Wow. Even if you're lifting?

Mark:

Yes, you can avert some of it by aggressive strength training-

Dave:

And a whole bunch of testosterone.

Mark:

... and a whole bunch of supplements and testosterone.

Dave:

If I weighed 100 pounds, I would take Ozempic though, just to be really clear.

Mark:

If you weighed what?

Dave:

If I weighed 100 pounds more than I do now, so if I weighed 300 pounds like I did, I would've taken Ozempic, and not regretted a minute of it, lost the weight, and then worked my ass off, and made sure my hormones were [inaudible 00:27:41].

Mark:

That's fine. That's fine, but people have to understand the minute you get off it, your metabolism is slower than when you started it-

Dave:

Because of caloric restriction.

Mark:

... because of the muscle loss that happens. Unless you really are aggressive while you're taking it in strength training, you'll see that. Even if you don't, you'll see that. Also, I would say that 65% of the weight that you lose gets regained for the average person if you stop it. So, this is a lifelong drug unless you radically change everything in your life. I think if... Like you said, would I say if you were 100 pounds overweight, instead of a gastric bypass to take Ozempic for a year, lose the weight, and then be aggressive in the taking of it, changing your lifestyle and after? Yes, I can understand that, but not as a solution.

I mean, think about it. New England Journal just came out of an article last week, and it was about Medicare Part D. Now, Medicare part D for those listening who don't know is basically the drug benefit. The entire budget for the drug benefit, the entire budget is \$145 billion. If just the people in Medicare who are obese, not the overweight ones, just the obese ones took Ozempic, the entire bill would be \$268 billion, which means it would be almost 85% more than we currently spend on all drugs for all Medicare patients. The bottom line is that when we think of interventions that have orders of magnitude of benefit more than medication, there are so many of them.

Dave:

You're totally right.

Mark:

I think diet, exercise, certain lifestyle practices, and certain supplements, and even certain medication can be useful. I think rapamycin works on mTOR, which is interesting because that-

Dave:

Let's talk about rapamycin.

Mark:

I am fascinated by this, because when you start to see... I don't know. You can see pattern recognition. I've been doing this so long, so I see when I read this stuff, I go, "Oh yeah, this is how everything connects. This is how it works." The body's like a system. It's like a network, and you start to see an ecosystem. It's like tripping on mushrooms. You see how everything's connected. So, it's like, "Whoa," and I begin to have this excitement and epiphany as I begin to unpack this science around this. mTOR is a very important pathway, because we need it to build muscle. If you shut off mTOR all the time, you are going to not be able to build stuff, and make proteins because you need mTOR to activate protein synthesis.

But if you do it all the time, you're going to build too much proteins. You're going to get cancer and all kinds of other stuff. So, overstimulation is not good. Inhibition of mTOR in a cyclic way is so critical to longevity, because it's the way we activate this pathway of autophagy or self-cleaning up. So, when you think about, "Why did this all there? Why did we have these pathways?" Because historically, we didn't have Whole Foods or grocery store or 7-Eleven on every corner. We didn't have an abundant sea of food carnival around us to eat every kind of crap at every minute of every day.

Dave:

No skittles.

Mark:

No Skittles, no. We basically had to go through periods of starvation, where we're, "Oh God, I can't find anything to eat, or I can't kill that." I was watching some Instagram feed of a puma chasing a guanaco in Chile. Guanaco is like a llama. The poor puma was jumping on in. The guanaco throw it off, and jumping on, throw it Off. Finally, he couldn't get a meal, right? I'm like, "God, it's tough out there." So, somebody just can't catch that buffalo, and so you go hungry. We had these ancient systems to make sure we don't die when we're not eating, and that not only don't we die, but we start to really fix everything.

Oh geez, I'm in trouble. The body kicks into gear, and has these ancient systems to repair, clean, rejuvenate, use all proteins, old proteins, build new things. You don't stop making proteins when you're not eating. Your body uses the body's proteins to start to fix it. So, that's what mTOR inhibition does. It activates this process of repair cleanup. What's so fascinating to me is in the pathways named mTOR, which means mammalian target of rapamycin, rapamycin is the drug. So, why would you name a pathway to this drug? Well, that's how they discovered it. This rapamycin is named after Rapa Nui or Easter Island, which is where they found this compound.

These scientists in the '60s were scraping the soil ,and trying to find cool compounds. I don't know. Maybe the aliens they thought dropped some good medicines in the soil. So, they basically got this compound. They put it in a lab. They tested it for antifungal purposes, didn't really work that well. The guy's boss said, "Just throw it out. It's garbage," and he didn't. So, the lab guy was like, "I'm keeping this stuff." Then they found it actually modulates immune function, so they used it in transplant medicine. Then they found out that it actually inhibits this pathway called mTOR, which can extend life dramatically in animals, and reverse a lot of the biological aging phenomena.

So when you look at the one thing, the one thing that almost all scientists agree can reverse aging, and actually extend life, so we don't really have many interventions that can extend life by a third. That means if you lived to 80, instead, you lived to 120. That's impressive, right? So, it's not like you're getting a couple extra years. You're getting a massive increase. If you eat a third less calories, you live a third longer. Now, that's pretty miserable. I met a guy once who was in the calorie restriction society.

Dave:

I know some guys like that.

Mark:

I said, "What did you have for breakfast?" He's like, "Oh, I had five pounds of celery." I'm like, "You must have very strong chewing muscles."

Dave:

I'm still trying to get a date.

Mark:

I'm like, "What did you have for lunch?" "I had 12 pounds of tomatoes." I'm like, "Okay."

Dave:

It's not sustainable. It's just not going to happen.

Mark:

So anyway, but in animals, they can do it because the animals can't complain, and so they find it really works. So, what we're trying to find... You hinted this. What are the things that mimic calorie restriction? What are the things that can make your body pretend? Fasting is actually calorie restriction. So, time-restricted eating is a form of calorie restriction.

Dave:

Works great.

Mark:

Ketogenic diet's another form of calorie restriction in the sense of how the body perceives it because-

Dave:

Because it's the insulin effect.

Mark:

Well, it's like... It's basically what happens when you don't eat. You go into ketosis. So, the body... It's actually doing the same things. Fasting mimicking diets where you have low calorie diets for five days periodically, all these things work in a very similar way. The active-

Dave:

Even soluble fiber when you think about it, or sorry, insoluble fiber that it's calories that you can't absorb, so that's calorie restriction, even though there's calories, right?

Mark:

Right. Right. Right.

Dave:

It's another to add list. Keep going.

Mark:

Basically, you basically can, through many different doorways, turn on these ancient starvation systems, these ancient survival systems. When you do that, you actually can really have a dramatic impact. So, rapamycin seems to do all these things. It inhibits mTOR, which then turns off inflammation. It activates mitochondrial biogenesis, it increases antioxidant systems. It increases autophagy. It increases DNA repair, has impacts on all the other things, so it may activate sirtuin activity. So, they're all interacting. They're not separate things. So, it's a cool thing to say, "Oh, I'm going to take this drug once a week," which is the protocol, six milligrams a week.

Some people are taking it two milligrams three times a week for eight weeks or five weeks off or eight weeks on. Everybody's guessing, honestly, but the data's really fascinating, and I'm optimistic about it. I started taking it.

Dave:

How often do you take it?

Mark:

I take it once a week.

Dave:

Do you fast on the day you take it?

Mark:

I take it at night, so I do an overnight fast, so 16-hour fast. It's not too fast. I'm too skinny. If I fast, it can be a problem.

Dave:

I'm the last guy who would ever be saying it's a problem, but I did get too thin even without taking that stuff. But if I over fast and all, it's to the point... Having that metabolic control is incredible, but you've always been thin, right?

Mark:

Yeah. I've always been like this. I mean, I've always exercised, but basically, I was 40, and I was running. I was eating healthy. I was doing functional medicine, but it was an era where we thought more carbohydrates, less fat, less protein was better.

Dave:

[inaudible 00:36:49].

Mark:

So, I was eating whole grains. I was eating beans. I was eating... I wasn't eating junk food, and I wasn't eating a lot of sugar, but I definitely didn't have the muscle mass. I was shocked when I was going through pictures, and I saw this whole picture of me when I was 40. I was thin, but I just looked like nothing. Then I looked at this picture of me when I'm 62.

Dave:

You're ripped.

Mark:

It's like, "What?" So, the body has that amazing ability to do this at any age, so it's never too late to start.

Dave:

I've got to ask you the mTOR elephant in the room question, given that elephants are made out of meat, not that I would eat one.

Mark:

Oh, meat. Meat is definitely bad because meat causes mTOR to turn on, and that's really bad, so we should never eat any meat, right?

Dave:

I mean, Dr. Gundry was just on. Dr. Gundry's a friend, and I respect him greatly. We talked about it. He's all these plant-based proteins and all for that reason. That's an area we don't agree. We agree on many things. But, what is your take, Dr. Hyman? Meat or no meat and mTOR.

Mark:

Well, I've written about this a lot in Food: What the Heck Should I Eat? I basically locked myself. I was in Austin actually when I wrote that chapter. I locked myself in a room in a hotel with a pile of paper this big-

Dave:

Next to a barbecue shop.

Mark:

I'm like, "I'm not going to listen to every stupid blah, blah, blah guy, influencer, doctor, scientist. I want to know what the data show." I'm like, "I'm a doctor. I can read papers. I understand how this works. I can evaluate how this is." I'm trying to... The one thing is to read the headline. Another thing is to read the abstract, another thing to read the methods and then to read the supplementary material, which has all exactly what they ate, and what they did, and what the other factors were. Basically, my conclusion was that meat is not bad for you, that yes, we should not be eating feedlot meat for many reasons.

Dave:

Lunch meat and hotdogs are not meat.

Mark:

Oh my god, Dave. I was down in Florida. I had to do this show, a TV show. My flight was late. I got in late. I didn't have dinner. I woke up, had a bunch of stuff to do, didn't really have breakfast, didn't really have lunch, had a little few snacky things. I finally got to the airport on the way home, and I was really hungry. I'm like, "I'm going to try to find something to eat." It was like-

Dave:

At an airport?

Mark:

Fort Myers, Florida. I'm like, "Oh God." I looked around, and found, "Okay, this place looks good." It had, it said, carved turkey, black-eyed peas, collard greens. I can go for that. I get the turkey. I'm thinking carved turkey means it's carved from a turkey.

Dave:

No. No. No.

Mark:

It was turkey-leg substance. It was like-

Dave:

Carved from a loaf.

Mark:

I don't know what the hell this was, but it was some weird soggy sponge like-

Dave:

Did you eat it?

Mark:

I was so hungry. I ate it, but it shreds some turkey in it, but sometimes you just got to deal with what you got to deal with. I think, it was fine. Basically, the meat question is really around aging has to do with mTOR.

Dave:

Yes, it does.

Mark:

So, the idea that if you overstimulate mTOR, you're going to age faster is true. Logically, if you eat anything that stimulates mTOR, that's bad. Well, that's wrong, right? It's like Goldilocks. You need just the right amount the right way. It's like you need to sleep, and you need to be awake. You need both, right? So basically, the body has a need to build protein, so you need to have a construction crew and a building crew. You also need a demolition crew and a cleanup crew, and so you need both of them.

If you just made dinner in your kitchen, and never cleaned it up, it'd be a freaking mess. That's what happens when you overstimulate mTOR. But if you didn't ever cook, you'd serve it. So, I think it's really about how to properly activate and inhibit mTOR. Let's talk about how do you turn on protein synthesis, because this is really key and has to do with the quality of the protein?

Dave:

It does.

Mark:

When you look at the PROT-AGE study, I'm not a protein expert, but I had read what protein experts have written. There was a group of protein experts. The world's protein experts got together, and they wrote a paper to review all the science about muscle, protein, aging called the PROT-AGE study. It was a really in-depth study that looked at and review of all the data, and they came up with a number of conclusions. One, you need two and a half grams of leucine to activate mTOR. If you don't have that in a meal, mTOR will not turn on to simulate muscle synthesis.

The idea basically is that if you don't have enough of the high-quality protein, then you can't turn on mTOR. You can't build muscle. So, you either have to eat meat or chicken or fish and turn on mTOR with 30 grams of high-quality protein with two and a half grams of mTOR in it, or you have to have some highly processed plant protein with jacked-up amino acids. I don't like that. I wouldn't do that.

Dave:

It sounds like an ultra-processed food product to me.

Mark:

It absolutely is. I met these guys who were the game-changer guys, and these guys were super jacked. They're ripped, and they're strong. I'm like, "What is going on?" So, I met some of these guys. I'm like, "So, what do you do? How do you this?" "Oh, well, I have 12 vegan protein shakes with branched-amino acids and extra leucine." I'm like, "Okay, so you basically cheat the system by actually having highly-processed food." If you want to get this from eating greens and beans, good luck. I mean, you're going-

Dave:

Look like Buddha.

Mark:

To get 30 grams of protein, of usable protein with a piece of chicken or meat, it's like four ounces, which is not very much. It's a small amount. If you want to get that from brown rice, it's six cups. From beans, it's two cups. Good luck eating that, and don't be in the room when you're doing that.

Dave:

There's something else that raises mTOR more than leucine, more than tryptophan, more than methionine. Sugar.

Mark:

Oh, wait a minute, we're supposed to quit eating animal protein, because it raises mTOR, but sugar raises mTOR more than animal protein. How about I eat the highest quality animal protein out there, because it works best, and eat less sugar, and I'll still have less mTOR? So, anyone who tells you to go vegan, who doesn't tell you to also eat no sugar and no starch.

Dave:

By the way, there's no food left on a vegan diet after that.

Mark:

The tofu.

Dave:

That's a fair point, Jesus. Oh my god, kill me now. This is an impossible thing. So literally, if you're restricting animal protein because of cancer, and you're having any sugar at all, you're doing it wrong, because sugar is way stronger than animal protein at raising mTOR.

Mark:

Yes. Yes.

Dave:

This is why bodybuilders, you lift hard if you're not doing this stuff in my new book, in Smarter not Harder, which is a lot better than lifting. But let's say that you lift really hard, what do old school body

builders know what they're doing to? They take maltodextrin, which is to spike their blood sugar and a ton of protein, so they get insulin, which acts just like insulin-like growth factor. They get a huge mTOR effect from the carbs and then the protein, right? You have to have both of those.

Mark:

But also, I had some shocking discoveries when I was practicing at Canyon Ranch, because we had a DEXA machine, so everybody got a DEXA scan. I love those machines because if you're looking at a biomarker for healthy aging, you've got to look at your DEXA. This is a way of measuring your body composition, amount of muscle, amount of fat, where the fat is, but you can do a total body comp thing with those bioimpedance things, and you're not going to know. I had a guy who, I guess, was 12% body fat in his arms, and 30% in his gut. The DEXA was interesting, but this guy was a bodybuilder. He had super high body fat, but it was all marbled meat.

It was like all marbled meat.

Dave:

Wow.

Mark:

His muscles were just marble, and because he ate a lot of carbs and protein together, like what you're saying.

Dave:

You don't want to do that all the time. It's interesting. Charles Pelouquin was on the show. I would call him one of the OG biohackers before biohacking had a name. He taught me that when you see someone with a ton of fat in the front, like the Buddha belly, that that's usually a cortisol issue. Still, doctors get mad at the... He said, "Look, you can look at the pattern of fat deposition in a body, and it'll tell you the hormone status of the body."

Mark:

Well, that's true. I mean, with Cushing's disease, which is a cortisol-reducing tumor, you get certain fat distribution.

Dave:

You're like a moon face, right?

Mark:

You get a moon face. You get a buffalo hump on your back. You get big, big tummy, waist muscle. You get skinny arms and legs.

Dave:

What I wanted to say for your friend there, the body builders, if you're always eating a ton of high-glycemic carbs and protein together, it's not a good idea. High-glycemic carbs and fat together, not a great idea all the time. But if you wanted to have the croissants, and you're not gluten sensitive, and you're in Europe where there's no glyphosate on the grains, and you did that every now and then, it's not going to harm you at all if your metabolism is healthy.

Mark:

Well, that's it. I think the whole point here is this idea, and it's central to functional medicine is that health is about metabolic flexibility and resilience. Most of us are metabolically inflexible and metabolically not resilient. So, for example, if I have a can of Coke, my insulin might go up a little bit. If some Sally over there who's been chowing down on two-liter bottle of soda for 20 years, her insulin's going to go through the roof. Same input, very different biological response. I think people don't understand this, that you can eat the same thing, and have profoundly different effects depending on your own biological software, and how well you're functioning.

If you want to maximize muscle synthesis, load up protein on a fastest state. So what do we have for breakfast in America? Bagels, muffins, sweetened coffees, pancakes, French toasts. Bottom line is if you eat typical American breakfast, you are killing yourself. Most of us, unless we have eggs and bacon for breakfast, don't have protein. So, having protein in the morning and a load of protein, probably 40 grams, and it depends on your weight. If you're a five-foot tall, 100 pound little lady, it's different than if you're a six-foot five, 250-pound football player, right?

Dave:

Right.

Mark:

It's different, but you need to look at the recommendations around protein. I'm going to get into a minute, but you need a big load of protein in a fasted state so that you actually activate mTOR in that way after a fasting. That's the best way to build muscle. That's a huge thing to understand. I think if you're looking at what the recommendations are for protein... This is what a lot of people talk about is 0.8 grams per kilo, and it's what the RDA is the recommended dietary allowance. Now, what those are minimum amounts that if you don't have, you will get a deficiency disease.

So, how much vitamin D do you need to not get scurvy? 30 units. How much vitamin D do you need to not get infections and flus and COVID and everything else? Maybe 5,000 units. So, it doesn't mean-

Dave:

Why do we still look at RDAs?

Mark:

Well, it really was around... It was really around the era when we had massive nutritional deficiencies in this country, but the idea that we need 0.8 grams is basically how much protein do you need to not get protein malnutrition?

Dave:

But even then, it depends on what protein, right, because different levels will still give you protein malnutrition.

Mark:

Right. So, in developing countries, protein malnutrition is a real issue, and so it's a problem. That's the minimum you need, and that's okay, but it's not the optimal you need to live to 120, or to build muscle or to do all the things you want to do. That's probably more like double, 1.6 or up to two depending on how active you are.

Dave:

That's the real challenge. If you wanted to live a long time, go a while without eating, and then when you do eat, have adequate protein. Does that match your perspective?

Mark:

Totally. Totally. I would say also I would challenge you on this nomenclature of anti-aging. I'm not anti-aging. I'm for healthy aging and for optimal aging and for reversing our biological age. I'm not against chronologically getting older. I don't... Right? That's going to happen. I can't do anything about that.

Dave:

This is a branding problem for anti-aging.

Mark:

It is.

Dave:

It has been for the... I ran an anti-aging nonprofit group that was started in 1993, and in the late '90s, I ended up being chairman even though I was the youngest guy there. I'm like, "Can we name it anything but anti-aging, because being against something into-

Mark:

Right, and for something, I'm not... I think it just gives a whole field a little bit of a bad rap definitely.

Dave:

I've worked for 20 years on finding a better name. I had... There isn't one that means healthy aging.

Mark:

Young Forever.

Dave:

Okay, Young Forever Association.

Mark:

I mean, no, I think it's healthy. It's whatever. I don't even want to call it healthy aging, but I think it's for understanding how to optimize our health as we age, and to prevent and reverse diseases, and to extend our life. Whatever you want to call that-

Dave:

I want to be time resistant.

Mark:

Time resistant, that's good, time resistant.

Dave:

I think Young Forever, you actually nailed the name of your book, because that's what we're talking about. The forever part, the time actually doesn't matter, and the age doesn't matter. So, you're not against it. You're not for it. It's irrelevant, because I get to look and feel and act in the way I choose.

Mark:

I want my physiology and my body's capacity to be getting better as I get older, and matching the wisdom and increased understanding of the world that happens as you get older. That's as opposed to having a great mind, but I can't walk up the stairs, right?

Dave:

Right.

Mark:

I think that's what happens to a lot of us is we can't function. I'm doing stuff that I just wouldn't have imagined that it would be possible for a 63-year-old. I'm skiing like a maniac down super steep mountains. I'm playing tennis, and improving all the time. I'm constantly getting better.

Dave:

Love this.

Mark:

I'm riding my bike and being faster than most of my 30, 40-year-old friends, and who basically can't keep up with me. The body has that capacity if you understand how to work with it. Most people are just not running things properly. So, if you put in diesel fuel in a gas car, it ain't going to run very good. So if you understand what is required to optimize the function of your car, you'll know how to run it better.

Dave:

Wow. I love that, and it's entirely possible. What we're working towards is normalizing that.

Mark:

Exactly. I agree. I agree. There's things that are, I would say, out of reach for the average person without enormous amount of money, which is stem cells and exosomes.

Dave:

We're going to make those available. By doing them now, in 10 years, they will be available for everyone.

Mark:

For sure.

Dave:

We are building a society where just like cell phones came out, and they were only for rich people, and now the poorest people and the remote parts of the world, it's changed their lives.

Mark:

That's right.

Dave:

We're doing that with anti-aging. I'm sorry, with healthy aging. I want to ask you about one thing that's on your list of 10 hallmarks of aging from Young Forever. This is a really good book, Mark. You write about inflammaging, which I did not have as a separate part of the seven pillars in my view on aging. I had that as mitochondrial dysfunction creates inflammation, because when mitochondria don't make electrons or proteins, they can make inflammation. So, I thought it was mitochondrial dysfunction, but I have new thoughts that I didn't know about when I wrote that book. Tell me what inflammaging is, what causes it, and I want to go deep with you on inflammaging.

Mark:

This is not actually a relatively new idea. This is something that's been in the medical conversation for a long time now around all the diseases of aging, so heart disease, cancer, diabetes, Alzheimer's, depression, obviously, autoimmune disease. All these are inflammatory diseases.

Dave:

They're also all mitochondrial diseases though, right?

Mark:

They are. They are, but you can have a mitochondrial dysfunction, and that'll drive inflammation, but you can have inflammation that's primary, not driven by mitochondrial dysfunction.

Dave:

That's important.

Mark:

I think if you have, for example, your microbiome being a problem, that can drive inflammation. That will also mess up your mitochondria-

Dave:

Because of lipopolysaccharides, right?

Mark:

Right, but it's not the only mechanism. The body has multiple mechanisms to create the same thing. There's only certain final common pathways in the body that I always say the body only has so many ways to say ouch. You have pain. You have inflammation. You have certain things that happen that create all these symptoms, but there're these common roots. So, inflammation is this common root that seems to accelerate as we get older. So, we can measure biomarkers of inflammation that are highly predictive of mortality. David Furman at Stanford has done amazing work around this called the Immunomes Project, 1,000 immunomes, and took people, looked at their 50 different cytokines, which are inflammatory, or I mean, not always, but their immune molecules that are often inflammatory.

He measured 50 different cytokines across the 1,000 people from little kids to very old. He found that there were four very highly predictive inflammatory markers that none of which probably, anybody including me, ever heard the name of. That's in some obscure medical textbook somewhere on immunology that are the more predictive than the things we do measure like CRP.

Dave:

Are you talking about IL-6 or interleukin?

Mark:

No.

Dave:

These are not a thing with cytokines.

Mark:

No, you would not have heard of, I promise.

Dave:

I love this.

Mark:

I can't even remember, because it's so weird. It's like CMX12 192 or something like that.

Dave:

So that you can't get a lab test on anyway, right?

Mark:

Right, exactly. But now, there are ways to test this, and using high throughput testing and screening, and looking at an AI analysis according to how it correlates with all these chronic diseases. They found that these four things were the most predictive. So, there's going to be ways that we can map inflammation, and everything that happens as we get older drives inflammation. They regulate a nutrient-sensing mTOR dysfunction, sirtuin dysfunction, AMPK dysfunction, mitochondrial dysfunction, microbiome dysfunction, epigenetic changes. All these drive inflammation, so it's like the downstream effect of all these upstream causes.

Inflammation can be we call it chronic sterile inflammation. It's not an infection, but it's inflammation. That is super important to track to measure, to look at, and to understand why. So, I always joke. I say, "As a functional medicine doctor, what's my specialty? I'm an inflammologist." I'm really good at figuring out the root cause of inflammation, and reducing inflammation in the body by using all my functional medicine tricks, removing the bad stuff, putting in the good stuff. So when you look at all these different pathways, you end up with accelerated inflammation.

One of the ways that really accelerates this is the formation of zombie cells, which are senescent cells, which you wrote about in your book, which are essentially these cells that when your cells are done doing what they're supposed to be doing, they usually die. We have a whole system for that. It's called apoptosis. They blow up. We recycle the stuff, and we... It's great, and we have a recycling plant, but

sometimes these don't die. They basically live forever, but they don't do anything useful, except they spread tons of inflammatory stuff all over your body. So, they float around your blood and your tissues, and they create inflammation.

Then they literally infect other zombie cells. Other cells make them zombie cells, and you end up with this fleet of zombie cells that creates this inflammatory phenotype that creates just this accelerated inflammation. So, it's like putting fuel on the fire. You want to make sure you can treat those zombie cells. There's a lot of ways to do that. One, don't live a shitty lifestyle that makes them form. Two, you can take things like Fisetin, which is from strawberries. It's senolytic, so the whole class of compounds now being researched that are senolytics like quercetin and things you can get from vegetables and plants.

Then also, there's drugs that might do this. But what's really interesting is the hyperbaric oxygen therapy was more effective at reducing senescent cells or zombie cells than any other treatment.

Dave:

It's funny. I have a hard shell hyperbaric chamber at home from OxyHealth.

Mark:

You do?

Dave:

Absolutely.

Mark:

Where? Here in Austin?

Dave:

Yeah.

Mark:

No, you don't.

Dave:

Absolutely.

Mark:

I'm coming over.

Dave:

All right, come on over. Anti-agers got to anti-age as we say.

Mark:

Oh my god. I'm coming over next week.

Dave:

See, that or a Tesla. So, I drive a 10-year-old Jeep, but I have a hyperbaric [inaudible 00:58:28].

Mark:

Is that your black funky-looking Jeep out there? Oh my God, that's got to be Dave's car. Are you such a weirdo? It's got to be his car.

Dave:

It's painted with Kevlar.

Mark:

I'm like, "This is weird. This looks like a military vehicle."

Dave:

I bought it that way. It's so cool.

Mark:

It's like a military vehicle.

Dave:

It's so upgraded. It's better than a new Jeep. We'll put it that way. I'm all about the upgrades. Hyperbaric works really well. I have a theory for you that I want to run past you. I'm pretty sure that a major portion of inflammaging is actually mast cell activation.

Mark:

Interesting. I think what Dave's talking about, for those of you non-medical people, you have a lot of different kinds of immune cells. One of them are called mast cells. When they're activated, they release histamine. Histamine, we're familiar with when you get hives, or you get a beef sting, or you get a rash. That's histamine activation, allergies, if you have seasonal allergies.

Dave:

But they also do heparin and about 100 other inflammatory cytokines, probably including the four nasty ones.

Mark:

Yeah. So, there's an awareness that there's a subset of humans who are very allergic and who have what we call mast cell activation syndrome, which makes you really miserable, and you have to learn how to figure out what's causing it. Remove those things. You have to figure out how to regulate histamine production with various kinds of plant compounds, drugs, whatever tends to work, and there's a whole treatment pathway.

Dave:

There's a whole huge regimen for them.

Mark:

I think mast cells do play a role, and so some people need to be on low-histamine diets. Some people need to be taking antihistamines that are regulating their histamine production.

Dave:

Not everyone needs to do that. What I'm seeing it is that when people get sometimes a car accident, sometimes, emotional stress from a narcissist or a sociopath or from bullying or toxic mold, environmental bacteria, sewage fumes, these all take the... I like to describe them as landmines in the body. They're sitting there waiting to stop something bad, but once they get programmed to think there's something bad that's not actually bad, they keep setting it off, and that's a major cause of inflammaging. It's not the only one. But I feel like if we can learn to reset immune sensitivity, we're going to age a lot less.

Mark:

See, this is essential point, and I discovered this as a functional medicine doctor. People are like, "Oh, I have to eliminate this. I have to eliminate that. I'm going..." Well, yes, you're sensitive to all these things, and all these things trigger an inflammatory or immune response or some other adverse effect. The real question in what should you eliminate is why are you so sensitive?

Dave:

Let's fix that.

Mark:

People come in with all these environmental allergies.

Dave:

How do you reprogram those?

Mark:

People are so overstimulated by environmental allergies or food sensitivity, or food allergies, and they're a mess. When I fix their gut, when I reset their immune system, they stop being allergic. I hear this over and over again. "Oh gee, when you did all this program, I don't have my seasonal allergies anymore."

Dave:

That's cool. Is that fixing the liver and gallbladder kind of stuff or?

Mark:

It's fixing the gut and the usual functional medicine mambo jumbo, hocus pocus magic tricks.

Dave:

It's funny because we don't exactly always know which pathway caused the allergies to eliminate. Was it the gut or the liver or some spleen thing? I think there are some question marks in it, but we know if we do this, it works. But exactly why it works, we haven't figured out yet. That's where science is interesting. Speaking of interesting, I just have to say Young Forever is a great book, and it's very

actionable, which is something that I really look for in books. It's easy to write a book, especially now with ChatGPT, for God's sake, which regurgitates nonsense, pretty much.

Mark:

That's pretty much how I did it. I said, "ChatGPT, please write a book called Young Forever on Longevity," and it was amazing. In five minutes, the book was done. It was the best ever. You're right. My book is very practical. I did it. I'm a doctor, so I'm not like... You can read a lot of longevity books, and they're very interesting. They talk a lot about the science, and they give you an understanding of the field. But then you go, "Okay, now what?" So, this book is now what?

Dave:

It's making it usable. That's the hardest part as an author is saying, "Okay, what do you do?" It's full of things like, "Okay, take note of these things, add up your score, and then figure it out." So, this is the thing that says, "All right, if you're not going to go see you at Ultra Wellness Clinics, which not everyone can do-

Mark:

No. No.

Dave:

Read the book, and you're going to get 80% of what you need right there.

Mark:

For sure.

Dave:

They'll probably fix it.

Mark:

Totally.

Dave:

If it doesn't, you go find a specialist. I just think you've done a great service to people or for people with the book.

Mark:

Thank you. Thank you.

Dave:

Guys, it's called Young Forever. My friend, Mark Hyman, who is definitely a modern master and also knows that plant-based protein's a joke. Thanks, Mark. I look forward to having you on when you're 16th New York Times bestseller is out.

Mark:

When I'm 16? My life 2016.

Dave:

We'll meet when we're 16, and we'll make fart jokes. It'll be great.

Mark:

All right, buddy. Thank you.