TOSS THE CANDLES! BIOLOGICAL AGE IS YOUR NEW BIRTHDAY – RYAN SMITH – #883

Dave Asprey:

You're listening to The Human Upgrade with Dave Asprey. Today, we're going to get to talk about something incredibly exciting, aging. And you're saying, "But wait, I don't care about aging. I'm not old." I might have said things like that when I was 24 but by the time I was 26 and I had most of the diseases of aging, the arthritis, pre-diabetes, high risk of stroke and heart attack, cognitive dysfunction, fibromyalgia and a bunch of other stuff that I don't need to list for you guys again, stretch marks. Well, I realized maybe I could learn something from these anti-aging people. And it turns out that aging is another word, at least aging, as we understand it is another word for allowing systems to start to fail so that they become weak. They cannot make as much power and energy as they did before.

Dave:

If you're young and you're saying, "I kind I don't want to age the way we think aging is but really I want to go on a date with that hot person and I want to eat a burrito." It's okay. And I want to have a powerful career and I'll worry about aging when I'm old. And the Upgrade Collective, welcome guys. We have people of all ages in here and I see some of our more seasoned members going, yep. That was me. I'm just fortunate I learned from people three and four times my age when I was younger, hey, maybe I could have more energy now but then my aging path will be very different. And the problem has been for the last 20 years running an anti-aging nonprofit for many of those, how the heck do you measure aging?

Dave:

Is it the mirror? Oh look I have abs, I'm young. No. Then what's the quantitative way we do it? Well, it turns out we know more about how to measure age and what to do about it and it comes from something called epigenetic methylation. What the heck is that? Well, we're going to dive a little bit deep and not too crazy deep into gene function, gene expression and how that makes you age so you can do something about it. Our guest is biochemist Ryan Smith, who is talking about the top anti-aging diagnostic tests that I'm aware of called TruDiagnostic. He's a co-founder of the company and they're using methylation array based diagnostics to extend the human lifespan and tell you what's going on here. Welcome to the show, Ryan.

Ryan Smith:

Yeah, thanks so much for having me. It's a pleasure on.

Dave:

Is it true that you're a 170?

Ryan Smith:

It is. I started early on this anti. No, I'm actually 31 biologically, which actually is a little bit older than I am chronologically. And so I'm unfortunately a little bit advanced aging already.

Dave:

What do you mean unfortunately? With age comes wisdom. The world needs a lot more village elders right now. We need a whole big army of them, hopefully with pitchforks and the energy to use them. Now you said you're biologically 31 but what are you chronologically?

Ryan Smith:

I'm 30.

Dave:

Got it. You're already, so actually you're one year older than your biological age?

Ryan Smith:

Yeah, I'm one year younger than my chronological or I should say my biological age is one year older, which is not where we would want to be but hopefully that's why these investigations are happening to figure out what we can do to change that.

Dave:

Are you embarrassed that as a founder of a company measuring aging, that you're doing a crappy job of it?

Ryan Smith:

Oh, definitely. Absolutely.

Dave:

That was the rudest question I've ever asked anyone.

Ryan Smith:

Well, the good news though is that it used to be a little bit worse, so I'm making the right trajectory of change.

Dave:

Oh, that's interesting. My biological age as measured by TruDiagnostic actually before the last couple of interventions, I was five years. I'm chronologically five years older than my biology would tell you. I'm doing some stuff right. And it's probably closer to eight now, I have to order another test from you guys. But what I don't have is what was it like when I was in my twenties? I suspect I would've been in my forties if you guys had a test back then because I had so much inflammation. I had all the bad stuff going on epigenetically and I probably don't have the strongest biology. I feel like if I could come back from wherever the heck I was and be at least above average, hallelujah, that's awesome. But you're younger than I am. You're 30 and you understand all this biochemistry. Is it that you're not taking your own advice? Are you like getting drunk on weekends and doing that sex, drugs and power kind of lifestyle or what's up?

Ryan Smith:

I'm trying to live very, very clean and have been committed to I think a really healthy lifestyle for a while but I think that as we start to unravel the reasons by which people are advanced biological aging, we're

seeing a lot of different things. And so I think that it's an investigation to everyone's lifestyle. For me, I think probably stress and sleep are some two big factors that are probably.

Dave:

You're an entrepreneur. Oh no, who would've ever thought. I will tell you, Deborah from the Upgrade Collective says you look like you're 19, she's also winking at you. Deborah, stop that.

Ryan Smith:

Hi Deborah.

Dave:

Actually, they're also asking, how old was your worst or your highest score? How much have you shaved off through lifestyle so far?

Ryan Smith:

Yeah. Unfortunately, it's not a huge amount but I think hopefully I can explain why that is actually a good thing rather than a bad thing. But I was originally a 32.5 whenever I took it the test at my late 29 years of age. And so we've gotten it down pretty significantly over that period of time.

Dave:

And someone listening might say, "Well, that's not very much." Hold on a second here. If you are a normal, healthy 30 year old, by the way, there aren't that many of those given all the seed oils and other industrial crap that people think is food. But if you're a healthy 30 year old, you shouldn't have very much aging. And so the fact that you had more aging than you should have and in a small amount of time, as a young person, you've already been able to dial it back a meaningful amount, you've taken it back 1.5 years, how long did it take you to lose that 1.5 years of aging?

Ryan Smith:

Right around a year. And you don't want to test, I would say too frequently because you might get some noise there but generally over a year we feel pretty comfortable and with some statistically significant results.

Dave:

Wow. That's pretty neat. And I got to give you credit for that. That is harder to do it when you're younger. It really is. Especially if you don't have a lot of health problems and you look like you've been healthy your whole life. I'm assuming that you haven't had major weight loss and autoimmunity and all sorts of weird crap like that.

Ryan Smith:

Yeah. No, definitely. Relatively healthy but one of the things we're just seeing in general is that men first off age worse than women. Men are significantly more likely to have advanced aging and surprisingly, the amount of people who are advanced aging are actually pretty high, right around 50% for men. And so that is again a good proportion of the people that we're testing. And a lot of the people that we're testing are already self-selected to be relatively healthy, relatively affluent. And so I would say that our

group and population is actually probably a little bit healthier than most but still having some of those markers of advanced aging.

Dave:

Did you just say that half of men are above average?

Ryan Smith:

Half of men are above their own chronological age. They're at accelerated aging.

Dave:

I'm just messing with you. Yes, I believe that. In fact, I think what you said earlier about stress and lack of sleep is a part of the cause of aging in a lot of guys. You can say the world's changed but there is still a pretty strong bias towards you're the primary wage earner in a family, even if both people are working, this is how society works still today. And so there can be stress there. And then women, especially if there's kids in the house, an insane amount of work at home and a career. Both people have that stress but women do live on average, eight years longer than men? Has TruDiagnostic figured out why that is? Tell me there's some special methylation epigenetic mechanism in women that men don't have.

Ryan Smith:

I wish. I think there's a lot of different theories out there. I think that in particular, the interplay with sex hormones tends to be a relatively big impact on some of these aging markers. And that's something that we're continuing to evaluate. Right now I think a lot of the causative reason for aging are particularly I say the causative reasons for epigenetic dysregulation that we detect and categorizes aging are still a little bit unknown. We're still unsure of some of those causative mechanisms, even though we're seeing some really interesting data on treatments which can reverse that.

Dave:

All right. Let's talk about how you look at aging because many listeners are familiar with telomere aging and I'm going to do a real quick grounding for people who haven't heard of that. Telomeres are like wicks on a candle. They get shorter as you age. And when you run out of wick, then your cells can't reproduce and then the cell dies. If you can make that wick longer, you would theoretically live longer. My concern as I've written about in the books is that, it appears that telomeres at different parts of the body change relatively quickly, we always get blood, which is a relatively unreliable one. I've seen massive swings in people's age on telomere tests that don't reflect reality because of where they're getting it. And if you were to get brain telomeres, a punch biopsy of your brain is called a lobotomy so let's not go there. But we can't really get that. I'm a little skeptical but that's the one that most people know about. Tell me what I'm missing about telomeres and tell me how that's different than what TruDiagnostic is doing with methylation.

Ryan Smith:

Yeah. Telomeres have, as you mentioned, been the gold standard for a long time. However, if you look at some of these papers that look at all the different methods of biological age and sort of compare them, a lot of them tend to say that telomere length has been extensively validated, there's thousands and tens of thousands of studies on telomere length. The problem is that they're not necessarily predictive of outcomes. We don't necessarily know what having short telomere length does to your risk

of several other diseases. Conversely, this measurement of epigenetics is much more robust and much more predictive of different types of outcomes.

Ryan Smith:

And one thing I should mention as well is that this epigenetic mechanism where we're looking at this methylation and quantifying that, it can actually be trained to interpret even telomere length. And so we actually do report telomere length as one of the outputs. However, in some recent studies, they've sort of hypothesized the amount of variants that even twins can have and how that affects their phenotypic variation and they really attribute right around 2% of that phenotypic variation to be attributed to telomeres while right around 35% is usually attributed to things like epigenetic clocks and epigenetic regulation.

Dave:

You guys have looked at 13,000 patients. Tell me what it's looking at on patients, clients, customers, however you want to call it. What does looking at mean? All right, you send in some blood, what do you do to the blood to tell me how old I am?

Ryan Smith:

Yeah. We are extracting that DNA from the blood. And then instead of just doing a typical sort of genetic analysis where we might look at SNPs, what we're really looking at are locations on those genes and looking at the percentage of methylation. We're looking at 900,000 different locations. The locations themselves are entitled CPG locations which are generally found at the promoter regions of genes where those would be turned on or turned off, where those transcription factors would attach. And so what we're really doing is trying to quantify the amount of methylation at those locations. And typically methylation is thought to be a silencing of gene activities so sort of turning that gene off by making sure the transcription factors can't bind to that promoter region.

Dave:

Okay. How many? It's hundreds of thousands, I don't remember the exact number, hundreds of thousands of data points that you're looking at but how do you know what an older biology looks like versus a younger biology? What's the reference?

Ryan Smith:

It's a great question. And I definitely want to draw the difference between the actual data generation versus the interpretation of that data. Much like high cholesterol was back whenever they were first finding it in blood, they sort of can find this fraction of high cholesterol but they still had to associate it to outcomes. They still had to find out what types of health consequences were happening to those people who had high cholesterol in their blood. And so obviously they found out that that might increase things like cardiovascular risk, et cetera. And so we're doing a very similar thing where we're taking that data and then trying to see what outcomes are associated with it. And we do that via computer learning and artificial intelligence to create algorithms which are able to interpret that data for many different types of outputs.

Ryan Smith:

Obviously today we'll be focusing on aging and a lot of those age related algorithms but this methylation profile can reflect a whole host of things in your body. We can predict death, we can predict athletic

performance, we can predict hair loss. We just need the covariate data to then train those algorithms. And so that's sort of what we're trying to do here at TruDiagnostic is to build the biggest and largest database of methylation data. And also that phenotypical data where we can really understand the patient to create a multitude of predictive algorithms. This is a really exciting biomarker for that reason and will continue to expand over the next 10 to 20 years.

Dave:

What is the best score you've ever seen? The highest variance between your TruDiagnostic score and your actual age?

Ryan Smith:

It would depend on the algorithm and there are several of those different algorithms which would interpret age and we've seen different, I would say, variations in each different algorithm. If we're looking at some of the ones that have been most validated, we can see up to 19 years of age difference between someone's chronological and biological age. It usually tends to happen when individuals are significantly older. And so we've seen some pretty large variance and I would say we've seen about 15 years in the other direction as well with people being around 15 years older biologically.

Dave:

You can have a 50 year old who's 65 biologically and you can have a 65 year old who's 30 or whatever, math isn't, or is 45 biologically basically.

Ryan Smith:

Definitely. And it is, again, there's wide variance for every individual. And a lot of times it's not necessarily that intuitive I would say as well. You might think, why do I need to do this testing? I know that I'm healthy in all of these different other ways but the thought process and the reason that that age quantification is so important is because it's not intuitive and age is still the biggest risk factor for all chronic disease and death. And so we definitely believe that aging is a disease and should be classified and treated like one and now we finally have a way to quantify that process.

Dave:

Well, one of the things that I'm working to create a positive change for here is I just had Radha Agrawal from Daybreakers on the show and they have a survey on their website and they say, "Well, what gender do you identify as? And what race do you identify as? And they're like, how old are you?" And I'm like, I'm sorry but that's ageist because if I get to pick my gender and I get to pick my a race and those aren't actually quantifiable then what the heck? My TruDiagnostic score is what I would identify with more so than my chronological age. I felt like I was being judged and shamed because I wasn't allowed to identify as my correct age. Maybe we can get some changes where people can just identify their TruDiagnostic score or just whatever their age they want to tell their cells they are because chronological age is not a good marker because you see a 19 year variance, right?

Ryan Smith:

Absolutely. And it is sort of a societal concept. We define years as the number of sort of trips around the Sun and why that is the best method is anyone's guess. I think that this method is rooted in science, it's rooted in the biology of thousands of individuals who have been used to train these algorithms and it's

been proven to be highly predictive of these healthcare consequences. And so we know that by reducing your age, you can reduce all of those different outcomes.

Dave:

If I could get my TruDiagnostic age to under 18, do you think I couldn't be tried as an adult?

Ryan Smith:

I think if you want to go ahead and give that a go, I be happy to see how that was handled. Interestingly enough, they're actually already using, speaking of the intersection of epigenetics and the law, the first algorithms that were created were in 2013 and they were trained to predict chronological age, at least at first. And so their first application wasn't even in the medical space. They were used in things like forensic testing, where they could tell how old someone was at a crime scene and narrow down their suspect list. It was also used to date refugees to see if they were adults or minors and then therefore eligible for asylum.

Ryan Smith:

And so it already has had some real world application. And really, as these algorithms have advanced, where they've stopped training in trying to predict chronological age but instead have tried to predict outcomes of disease related to aging, they've gotten much better and much more accurate from a healthcare context. And then as a result, it started to be, I would say, implemented in different healthcare diagnostics. And so I I know your question was a joke but with that being said, it's already had some legal implications.

Dave:

And I think it actually should. One of the things I've learned, I've gotten to know from one of the states pretty well, a Supreme Court judge. Not US Supreme Court, so there's 50 states. There's lots of Supreme Court judges around but I never understood what the law really does until those conversations. But it's actually about being precise. End of the day, there should be no interpretation available where you're saying, "Okay, if the words are correct," it's like computer code. It says, "This is as it is." And so if we can say, "Okay, I would support before we say someone can be tried as an adult, let's look at neurological function, is their prefrontal cortex formed like an adult?" If not, I don't care if they're 25, they don't have an adult brain therefore they need more therapy or more whatever, instead of to be locked up in fed shit for 50 years, which is what we do to prisoners while we use them as free labor, which seems wrong but that's a different podcast.

Dave:

Where was I going with that? Anyway, the idea that there is mathematical truth is real but also there's algorithmic interpretation. You're getting hundreds of thousands of data points, this algorithm says, this one says this and then the courts would have to decide what algorithm. Are you worried about insurance companies getting your TruDiagnostic score and saying, "You're old. Biologically you're old therefore we want to charge you more?" Or maybe want to charge you less because you're young?

Ryan Smith:

I'm not worried about our data because I know our data policy is adamantly against that. But with that being said again, the applications actually already happened. There's one algorithm in particular by Dr. Horvath from UCLA called GrimAge, which is a sort of a death predictor. It's able to estimate death. And

that already has been licensed out to companies who will give you a life insurance based on your score on that metric. And so it's already sort of happening where people are offering that for life insurance and due to the predictive nature of these algorithms in terms of how, highly associated they are to disease, I think that that is definitely a reality where insurance companies might start to push for this.

Ryan Smith:

Just to give everyone an idea. If everyone in the world were seven years younger biologically than chronologically, so they were seven years younger than their chronological age, if everyone in the world was that way, we would cut disease in half overnight. 50% of people would no longer be sick. And so these have massive level health impacts. Even if we would just slow the aging rate in the United States by 20%, we'd save over $3 trillion in entitlement spending for the US. These things have massive impact. And the reason that we also obviously can talk a lot about the personal level and why everyone should be interested in reducing their age but even from a society level impact, I think it goes to show you what everyone can do, what we can all do for healthcare if we all focus on this as a primary measurement.

Dave:

I love the of cost savings there. It's almost like by slightly reducing the average biological, not chronological age of people, we could have paid for at least half the hand sanitizer that we've used over the last couple years, right?

Ryan Smith:

Yeah. The population level impacts are incredible. Especially as we consider an aging population, which we definitely have. And so I can completely agree and even some of the other metrics, I think that we might do. Things into the immune system we might read out or even the instantaneous rates of aging, all of those things have shown that if you show positive improvement, you can reduce health consequences and the health burden we might see in the United States or anywhere in the world.

Dave:

It's one of the are many reasons I'm at my core an anti-aging guy. It feels like anti-aging is one side of the coin but human performance is the other because we expect our performance will decline as we age and it doesn't have to be that way. I have the average brain response time of a 20 year old and I'm 48. I'm 48 chronologically, biologically I'm probably 43 right now. And actually, I would guess probably closer to 38 to 40, I'll tell you once I get my new results in from TruDiagnostic. I've done a bunch more work since my last thing. What do critics say? How do they say, "Oh, this isn't a good, TruDiagnostic can't possibly tell you your age." What is the argument that goes against this approach to measuring aging?

Ryan Smith:

I would say in the scientific community, there's a relatively strong consensus that epigenetic methylation is the best current method to detect aging. I think that generally, I think that most people would agree with that statement, as has been published in several different sort of overall reviews. However, I think that the majority of, I would say the critiques that can come from this come to the algorithms themselves and the variety of the algorithms and different things such as level of precision, the mean absolute error for some of these algorithms. And that's been one of the biggest restrictions I would say on this testing for a long, long time is the amount of noise on the actual diagnostic. Sometimes, we define that sort of as what we call the interclass correlation value. If we take two samples of the exact

same DNA and we test them at the exact same time on the exact same array, how correlated are they to each other?

Ryan Smith:

Ideally we'd see a correlation value of one. However, each algorithm has a different, I would say ICC value and therefore might be a little bit less reproducible. And so I think one of those questions is how sensitive and precise are these clocks? And that is an area of where we're seeing constant improvement on a daily basis and continues to see these algorithms become even more precise, which allows us to detect change accurately within a span of three months or six months instead of having to wait a year to really feel comfortable with the results of whether we're aging up or down.

Dave:

I think I can translate that into easier to understand. There's a plus or minus variance, a certainty on the age right now and you're going to be able to tighten that up and remove noise from the system.

Ryan Smith:

Exactly right. And great example is actually a study which is about to be released from Yale where they've taken all of these algorithms, which have been described. Things like the 2013 Horvath clock, GrimAges. We already talked about pheno age and made all of those ICC values above at least 0.9, which means that they're highly, highly accurate. And it also means that in order to do large scale studies where we're looking at what interventions are able to help our aging process, we can reduce the sample size needed for those investigations significantly as well. And so these algorithms are being improved by things like principle component analysis to make sure that these things are much more precise but already I think they represent a diagnostic which is able to give insight into every individual's aging process and then even make some recommended changes according to what you might find.

Dave:

I think that makes sense. I want to know though, so if I'm five years younger, what's the variance on that five years?

Ryan Smith:

It depends on the algorithm. If you look at the first ever algorithm published and the one that has by far, the most publications was the 2013 sort of pan-tissue clock by Dr. Horvath. That mean absolute error was around 2.9 years for every sample, which again is a massive error rate whenever most people are trying to get feedback within six months to a year. And so those have since been improved. Each of these have various degrees of standard deviation.

Ryan Smith:

One of my favorite outputs is one that has been developed by Duke and Columbia, which we've licensed and done a lot of work with called the Dunedin pace of aging metric. And so this one is one that is able to give you not an overall age but sort of a snapshot in time, sort of a speedometer of aging, how many biological years per year are you aging at this moment? And that one is incredibly, incredibly precise and accurate. And so that one is one that we might recommend more of every three months. Whereas some of the other algorithms we might say, you can only do it once every year to get really significant results on your individual level.

Dave:

I've seen a lot of good stuff coming out of Viome looking at gut bacteria and some mitochondrial stuff. Can you sort of compare and contrast the approaches that you guys have? I do both. I'm an advisor to Viome and full disclosure, all that for listeners who have probably heard, Naveen's a good friend, has been on the show lots of times. But they have an age as well. But they don't always match. In fact, I don't even off hand remember what the difference is there. But it's such just a radically different approach to the methylation approach. For listeners who are going, how the heck do I know? Should I get both? How would I know? How do I trust it? What's your take on it?

Ryan Smith:

Yeah. Unfortunately I'm not incredibly familiar with Viome's sort of microbiome testing. The one thing I will say is that going back to even sort of the letdown I think that some people felt with genetics. Whenever genetics was happening I think a lot of people thought this will solve all of the health problems that we could possibly ever encounter. And I think that a lot of people were let down because they're only looking at one piece of the picture. And I think now we've started to describe what some of those other pieces are. And we've done that through a term called the multiome where we can look at everything from, starting with DNA, to looking at the epigenetics or what DNA is turned on and turned off then going to transcriptomics with mRNA level profiles, those going into transcription to peptides and proteins, so the proteome. And then going into the metabolome where we're looking at metabolites of processes, ultimately leading to the phenotypic results or sort of the disease categories we might have.

Ryan Smith:

These are sort of all the different levels. Microbiome and cell cytology are also in there. And so each of these different levels of this bigger picture have each individually been investigated for aging clocks. There's proteomic aging clocks, there's transcriptomic aging clocks, there's microbiome aging clocks. And so I think the idea would be that at least eventually we'll have ways to interpret all of these data sets and have the most robust and accurate version of age. But right now, if you're trying to vet these things for the best way to look at your own biological age, what I would say is, look at the publication data. Look at the algorithms that are being used in the data and look how predictive they are, look how accurate they are. And then try and make a decision based on, I would say the data that's given. Are you choosing the most accurate method or are you choosing the method that is most predictive of health consequences?

Ryan Smith:

I think that there are a lot of different ways to make that decision. But the one thing I think is most important is making sure that these algorithms are published because otherwise it's like going to a fortune teller and just accepting their word for it. If you don't know how that data is translated and applicable to your own health, it's a little bit of a black box you can't see into. And so I would say that for anyone who's trying to vet these therapies, definitely look at the data and its predictive power.

Dave:

It feels like we're on the cusp of a big change in longevity research where historically we would pick an algorithm, we'd validate it, like some of the ones that you've got, then we get a bunch of samples and we say, "Okay, this algorithm appears to match reality," and then we tune in a little bit. And then there's another approach, machine learning based where we say, "We don't really know. We just dumped a

huge amount of data in here and let's see what comes out of it." And these are the people who appear to be younger based on some sort of thing, grip strength, let's say, which is a remarkably good marker of aging. How hard can you squeeze? And so you come out and go, "Oh, that's so weird. Who would ever thought?" But no one even knows why the algorithm does it.

Dave::

Same thing with all the, how do I say this in the right way? It rhymes with a sensor, a biological sensor but it's involved in traveling over the water in a ship. But if you actually say those words together, an algorithm will pick that up and then we'll magically very few people hear what you're saying. But if you were to go in and you were to ask, I don't know, Mark Zuckerberg or somebody, "Hey, did you do that?" They say, "No, we don't have an algorithm that does that." Because they're tuning a machine learning system based on very nebulous outcomes. Your approach is you're looking at GrimAge, you're looking at these other algorithms that are well proven but how do you add machine learning into that to know that in the future, who knows maybe people who smoke marshmallows live the longest and we just haven't figured it out yet.

Ryan Smith:

Yeah. The new algorithms that are coming out on a daily basis, which is both a good and a bad thing because the bar is always being set incrementally higher. And so that is a good thing because it means we're getting even better at diagnosing the real signal of age and getting rid of any association to disease and just actually getting the age values right. And there are a lot of different methods to do that but all of them involve computer learning. And that is exactly why we're seeing such a big, I would say, change in this aging research field is because now these computer learning platforms, which previously were unavailable, are being matched with diagnostic methods which are creating data sets, which were previously unavailable. And so we're sort of opening up and opening up these rooms of analysis.

Ryan Smith:

And that's exactly what we're doing is creating, for our epigenetic testing, as I mentioned, we measure 900,000 locations. There's no commercial competitor of ours that does even above a 125,000. And so we're getting nine times more data for each patient and also collecting a lot of that phenotypic data as well, where we're looking and asking about other diseases they might have, any reactions to medications. And so hopefully with all of that information, we can use these penalized regression modelings, we can use these neural nets to develop predictors of how someone for instance, might respond to metformin or for instance, how their bone health might be affected with aging or et cetera. And so we're being exposed to this huge data set and we're just trying to learn as much as possible, how to interpret that.

Dave:

Deborah from the Upgrade Collective has a question for you about that. Deborah, by the way, she's the one who thinks you look 19. She was winking at you earlier. Deborah, go ahead.

Deborah:

I was curious in your experience and I'll get you for that, Dave. I was curious in your experience, what interventions have you found make the biggest impact on improving the telomere age and the biological age?

Ryan Smith:

Yeah. Great question. And unfortunately I think that one of the things I'd like to sort of discuss is the fact that the first ever interventional trial showing a baseline measurement, a treatment and an outcome only happened in September of 2019. That was right before the pandemic hit and a lot of research has been stalled since then. And so there aren't, I would say a whole host of interventional trials where we can point to and say, "This is having a major impact." A lot of what we know is epidemiological based information. We know from large cohorts, we sort of investigate those to say, "Hey, the people who have great aging, what are their behaviors? And the people who have poor aging, what are their behaviors?" And then so I think that there's a couple ways to answer that question, one is, what do we know epidemiologically? What do we know about the treatments which have been published? And then what do we know about the treatments which haven't been published but we're starting to collect data on?

Ryan Smith:

And so, from an epidemiological standpoint, a lot of what we see are the things that are relatively intuitive. Avoiding disease, avoiding metabolic concerns, avoiding stress, avoiding any type of toxic insult. From what we know from these published trials, we know things like for instance, the first trial looked at metformin, growth hormone and DHEA and that was able to reverse the epigenetic aging process around 2.5 years in 1.5 years' worth of time. And so that was ever first proof of concept study. One of the restrictions is it only had nine patients. And so sample size in some of these interventional studies have also been a little bit of an issue.

Dave:

Also, sorry to interrupt. That study also ended up regrowing the thymus, that's as same study we're talking about?

Ryan Smith:

Yeah, absolutely. The TRIIM trial, which stands for thymic rejuvenation immunorestoration and insulin mitigation.

Dave:

Yeah. The founder of that is in one of the anti-aging groups I'm with so I spent a couple days with him and I've been wanting to do the protocol but it's so much lab testing I can't do it in Canada yet. It's interesting though because the entire aging may not have come from the drugs. It may have come from regrowing the thymus gland, which tends to be present in young people but what you are measuring with TruDiagnostic, Is you're saying, "Well, whether it was because the thymus grew back or it's because one of the drugs did something, it doesn't really matter because you got the results." And then other science would go in and say, "This led to this, led to this," kind of a perspective.

Ryan Smith:

Absolutely. And without getting too complicated, one of the important things to also think about there is the cell types that we're measuring because those are incredibly important. And so every cell on your body has the exact same DNA but your expression of your epigenetics is different in every type of cell. It's what gives your cell the identity that they have. It's why your skin cells behave like skin cells and your heart cells behave like heart cells. And so unfortunately every cell has a different epigenetic identity. And so when we're testing blood, the question goes to what type of cells are we testing? And as a result,

we're looking at a lot of different immune cells. We're looking at natural killer cells, basophils, lymphocytes. And so one of the things that can complicate these investigations is when people have different levels of immune cells. For instance, as we age, we might have more senescent T cells, less naive T cells and we have to factor that into these algorithms or otherwise we can't get a pure aging related signal.

Ryan Smith:

And so, controlling for immune system criteria are a very important part of this discussion. And we've seen this I think time and time again, especially in some of the interventional trials that we're doing. Currently we have 30 ongoing clinical trials, some are very, very large, others are relatively small looking at a wide variety of interventions to try and see what's actually working the best. And one thing we always have to worry about is controlling for those immune cell subsets to make sure we're picking up the correct methylation readings and we're not just picking up a change in immune cells.

Dave:

All right, let's talk immune cells. Ryan, there's a lot of people who are concerned that vaccines might make you old, have you guys controlled for whether people have had a vaccine, haven't had a vaccine? Are they aging faster, aging slower?

Ryan Smith:

Absolutely. And it's actually appropriate time to talk about this as we hope to be publishing some of our results in the next few weeks. But we have done a study looking at the longitudinal effects of COVID-19, as well as the mRNA based vaccines and how they might affect these aging rates. And we've definitely found some interesting things. In relationship to the virus, one of the things that we've found out is that age absolutely plays an effect in terms of how you'll respond from an aging perspective. Typically, people who are above 50 years of age chronologically actually have worse aging when they've been exposed to the virus. Whereas people under 50 tend to actually have improvements in aging and so the question might be, why is that?

Dave:

Hold on a second, let me get this straight. If you're over 50 and you get infected by COVID, it's likely to accelerate your aging but if you're under 50, it actually improves your aging, it makes you a little bit younger?

Ryan Smith:

Yeah. Correct. And so in terms of a hypothesis of why that might be, one of the things that immediately comes to mind is that younger people are more likely to amount an effective and hormetic response to the virus.

Dave:

There you go, like exercise for your immune system.

Ryan Smith:

Exactly, exactly. And so the idea then is that after a certain age, which we have sort of found in this study to be right around 50 years of age, what we might see is that people are less likely to out a

hormetic response, which is protective of that. And as a result, they get more inflammation, more of the negative consequences we see with a lot of COVID patients. And so we think that it probably has to do with the robustness of the immune system and the ability to respond to that insult. And so a very interesting thing there. One other thing that I would say we've seen with COVID-19 related infection is that almost everyone has reductions in telomere length, which I would say backs up several other studies, which have been done on across the sort of the scientific community, which COVID-19 tends to have a detrimental effect to telomere length.

Dave:

Younger people under 50, who get COVID still have a shortening of telomeres even though overall their net aging picture looks better than it did before.

Ryan Smith:

Correct. And the link between telomere length and biological aging, they're sort of measuring two distinct processes. I think that's very important to mention. If you were to immortalize telomeres in a cell, they would still epigenetically age and vice versa. If reset some of the epigenetic clocks, you'd still see the telomere length remain unchanged. And so they're two different processes of aging both that are separate and distinct and so we like to always talk about them a little bit differently.

Dave:

Okay. And this is going to be published? This is peer reviewed, statistically significant, P less than 0.01, all that kind of stuff?

Ryan Smith:

Yeah, absolutely. We've published in combination with an immunology group from Cornell and then a group from Yale who I already mentioned has published some really accurate algorithms called the principal component version of these algorithms. And so we hope to publish that with their help here in these next few weeks.

Dave:

Okay. That's really cool. Now that was just getting infected with it. Is that different than any other diseases you've looked at? I don't know, tuberculosis or other flus or I don't know, herpes, chicken pox, I don't know. But have you looked at other viral or bacterial diseases to see if they follow the same pattern?

Ryan Smith:

Unfortunately, not in a longitudinal method. Several other people have and it's a huge area of focus because we can actually see even some age related change for instance, cytomegalovirus, across populations who get CMV. We can also see that the age of monocytes in particular tends age more than any other type of cell when infected with CMV. And so we can start to sort of have these really, I would say, specific investigations into how this aging effect is occurring with different viruses. And so, we also have a lot of information on HIV and where that significantly ages an individual. And so some viruses have been investigated but nothing quite longitudinally like this, where we're looking at a before and an after.

Dave:

Not surprising. Many people have CMV and EBV and all, we just, we don't really know. That's really interesting but a lot of people are now sitting on the edge of their seat, do vaccines or at least do mRNA vaccine for COVID. I'm going to have to beep that out. I think we're allowed to have this conversation. Do they make you older? Or let me just ask this again, I'm kind of stumbling. Here's the golden question, Ryan, do mRNA vaccines for COVID show evidence of making you older or younger when you get them?

Ryan Smith:

The initial evidence we have, which is based on the population size of around 40 individuals. It is in terms of sample size, I think that's important we actually see a positive effect on aging with these mRNA based vaccines.

Dave:

That means that people who get mRNA vaccines are biologically younger, according to your diagnostics than if they had not had the vaccine.

Ryan Smith:

That's correct. And it tends to be irregardless of algorithm as well. And we do see some changes in these immune cell subsets as well. One of the reasons we might be seeing this change is due to the change to immune cells or we might be actually seeing a purely aging effect already. And so one of our next investigations to sort of try and answer those questions are to look at some of these booster shots before and after to see how those might affect the aging process. And then conversely look at more traditional vaccines as well, such as the influenza vaccine to see if we're seeing some similar signals and how that immune system change might relate to better or worse aging.

Dave:

How do you know that the data is good? You're sort of doing an intervention here, well if it shifted you said you mentioned monocytes earlier. If it shifted monocytes in one direction versus another, is that enough to just overwhelm the algorithm? Could I give someone a nice dose of lead that might suppress an inflammatory cell because it suppressed all the cells and then see a benefit? How certain are you given the sample size? Do we know the mechanism?

Ryan Smith:

We don't know the mechanism, unfortunately, but we're still fairly certain. As I mentioned, we're looking at several different algorithms and in terms of sort of the QA/QC data on the actual analysis, that tends to be fairly accurate and very well reproduced. And so we feel very confident that what we're seeing is that these algorithms are showing an antiaging effect, whether or not those algorithms are influenced by immune cell subsets that we aren't controlling for, then that is a possibility. We definitely want to leave that open and the ability to control for those immune cell subsets are continuing to get better. Right now, if you were to do some of our testing, you'd also in addition to your age, you would also get an idea of things like how many lymphocytes or CD4 or CD8 cells you have, T cells you have in your system as well. We control for those in some of these algorithms and the ability to control for those are going to become much more robust as we continue to go on to make these algorithms even more specific and to make sure that is not a confounding factor.

Dave:

That's kind of mind blowing information to be honest. I will say though, guys, I've been on the record even before COVID happened that I think mRNA vaccines are a major part of longevity in the future. And that means that when we have full data from independent third-party companies, I don't know, even like TruDiagnostic that are looking at things, I want very fine grain control of my immune response because the idea of inflammaging, the idea that in my mind, I would guess having written a book on anti-aging but not having a study on this, somewhere around 40% of aging is coming from inappropriate immune activation and inflammation. And if I could say, "Hmm, I know I have this and I whack that mole. I know I have this, I whack that mole. I'm going to have less inflammation over the course of decades and I'm going to live longer."

Dave:

And I'm totally happy to choose to take an mRNA vaccine that my doctor, my care provider, me and Dr. Search Engine, which is not Google because Google's full of crap. Well, that combination of things, I ought to be able to decide to do that so I can have my immune system work the way I want to perform as well as I want. By the way, also should be able to remove one of my arms as a weight loss strategy. It's stupid but it's my decision. If it's someone else wants to tell me that I have to age at a certain rate because of something that they want me to do, I believe that the only appropriate response to that is a lead injection at relatively high speeds in the reverse direction. I'm not sure what I'm saying there, some kind of a medical treatment from the 1920s, I think came after mercury in case you guys misinterpreted that. Ryan, have I offended you yet?

Ryan Smith:

No, not at all. I'm definitely a proponent of healthcare autonomy as well. But in that fashion, even speaking to the lead based treatment, I think it brings me an opportunity to talk about another area of even epigenetic analysis, which is particularly exciting, which is that in addition to being able to pick up aging rates and being able to pick up your immune cells subsets, being able to predict certain types of outcomes like death or cardiovascular disease, one of the really cool parts about epigenetic methylation as well is that it also tends to be a log of our entire history of health. We can actually tell you for instance, how much mercury or lead you actually have been exposed to by looking at individual locations on your genome and seeing how they're methylated. We have certain methylation patterns that are indicative of lead exposure or mercury or smoking for instance.

Dave:

That's not in my report though. Can you add that, likely lead exposure? Because lead is fascinating. We used to say 20 parts per million was fine going back to the seventies, this is the EPA who you should never trust with your health or your environmental protection, to be honest. Those guys, they don't even look at anything that lives in the soil. They just look at honeybees. Good God man. Anyway, different conversation. But you go back, it's 20 parts per million then, oh, we meant 10. Oh, we meant five parts per million. And the latest guidance is any parts per million of lead linearly increases cardiovascular risk and probably a bunch of other risks. But we just know if you have lead, you're more likely to die of heart attacks. It just isn't good for you in any amount of eating a fishing lead sinker once a week doesn't make you stronger. There's no hormetic response. But can you say, "Hey Dave, over the course of your life, you likely had this much lead exposure?"

Ryan Smith:

We can right now.

Dave:

Put it in my report, I'll pay you more. I really want to know that.

Ryan Smith:

Yeah. We're actually coming out, on our next series of reports is actually going to be called this exposome where we're looking at a whole history of exposures, not necessarily just toxic metals, which have been relatively well described but even things like particulate matter air pollution, things like the amount of smoke you've been exposed to across your entire life or how much are you been drinking right now. We can actually even tell you that. And so I think that hopefully just to give people an insight beyond aging, this is a diagnostic platform, is absolutely in its infancy. And without sounding too much like Elizabeth Holmes or Theranos the amount of data that you can get from just one drop of blood and the DNA that accompanies that is robust and very, very significant. Even in the GrimAge algorithm we discussed before, they can actually use that algorithm to predict protein levels of 12 different protein types.

Ryan Smith:

And so there's sort of a whole host of possibilities about how you might be able to interpret this methylation related data. Aging has definitely taken the forefront of most of the scientific research but over the course of the next decade, you'll see that this data set will be able to apply to many, many different things. Out of those 900,000 spots that we're measuring, we still report on less than 2,500. And just to give you an idea of the scope and scale of the additional data that we'd be continue able to report as we add new reports and new insights.

Dave:

That's ridiculous. You are the first person on the podcast that I can think of to use the word exposome and maybe the first year or so of writing my blog. And so that's 3,000 posts ago and it's probably still up on daveasprey.com. I wrote about it because Wired magazine had a brief thing about the exposome, which is the set of everything you've been exposed to over the course of your life. This is actually the real size or the full size, life size map of the United States. You can't use it because it's as big as the US but if you can tell what your exposures have been, then it's those things that then affect epigenetics, which then turn on and turn off genetics, which then determine if you have enough co-factors, vitamins and mitochondrial energy, whether you actually take what epigenetics told the genes to turn on, whether they actually get turned on and then produce something at the end of that. There's proteins, there's neurotransmitters, amino acid, some amino acids are neurotransmitters and hormones and all the other crap that your body does to stay alive, and electrons.

Dave:

But the exposome is the big thing that we're working as biohackers to discover. The definition, the art and science of changing the environment around you and inside of you so you have full control of your own biology. If TruDiagnostics can give me a reliable signal of what I've been exposed to that I don't know I've been exposed to so I can mitigate it, that's pretty exciting stuff, man.

Ryan Smith:

Absolutely. And then I think that again, the only thing that's been preventing us from doing that is a little bit more about precision. And so we're doing a lot of different studies because again, the only thing worse than no information is bad information. And so we want to make sure as we roll these things out

that they're highly accurate and still informative and actionable. And so we're definitely doing a lot of that research to help improve these things. And I think that our thought process is that this methylation platform can be used as one test to tell you a whole host of different things. And that's again, the beauty of methylation, it's not just something that pharmaceutical treatments can change. It's things that stress management and sleep, lifestyle changes and exposure changes. All of these different things can affect these methylation profiles. And so it gives you something to look at frequently to see how some of those interventions you're taking a part of are actually working and in a wide variety of levels.

Dave:

Well, people are now going, okay, I maybe at this point have learned that I can and most people don't believe this, listeners I think do, but I can change my biological age. You used to think, oh, I've had X number of birthdays. That's how old I am. And we have examples of people being 15 years older or 19 years younger. This should already be blowing your mind if you don't know about this but it's real. And it's been real for the entire source of human history. And there's always a few outliers. That's weird. He or she is 65, but their hair isn't gray and they still have hair and they aren't stooped. And they have the energy and the quick wittedness of someone much younger. That's so weird. It must be random but it turns out it's not. And so we're teasing out the randomness here to figure out what it isn't. But everyone now is wondering, okay, that all sounds great. How long does it take to measurably reduce my biological age? And you guys have some good data on that. What can you tell me?

Ryan Smith:

Yeah, we do. I would point to, again, the data here is still relatively limited. Most recently there was a study done by Kara Fitzgerald, a doctor from Connecticut, which actually showed epigenetic change over the course of eight weeks. And so even in eight weeks, Dr. Fitzgerald's study was able to reverse one particular algorithm done in saliva for around two years for each of those individual patients. And so I would say that's probably an outlier. And I think that the sensitivity of some of those diagnostic methods probably were not, I would say sufficient enough to pick up change in the eight week timeframe. But that also sets the precedent that there is some level of change in even shorts amount of time.

Ryan Smith:

And so I would say that for most people who are doing this testing, I think doing it more than once every six months, is probably a little bit too frequently for some of the precision of these algorithms currently. I would not suggest probably measuring under a six month timeframe, which gives you sort of six months to try and mitigate change if you're trying to take a before and after and really see a measurable difference.

Dave:

I love it that you're saying that. I get all excited to say, oh, you can reverse aging by two years in eight weeks. By the way, I think you actually can do that. But I also think it's very scientifically honest to say, yeah, but the needle wobbles a little bit. If you're doing 140 miles an hour, if you've ever driven that fast or faster, it's not like the speedometer super smooth, especially if it's giving the instantaneous speed, there's little wobbles. Those little wobbles are what would affect that. But we do know that it doesn't take very long to reduce inflammation radically, which reduces the rate of aging. And something else that TruDiagnostics does that's really cool. Can you talk about chronological age versus rate of aging because those are very different numbers and I think one is more important than the other.

Ryan Smith:

Yeah, absolutely. Well, so the idea is that I think, and even using a lot of physicians as an example, our biggest market is working with clinical providers. And a lot of these clinical providers have been through medical school and residency where they've had really poor lifestyle decisions, poor nutrition, high levels of stress. And so as a result, whenever they're first getting this testing, a lot of them might actually see themselves at advanced aging. And so they might see themselves as two or three years older biologically than they are chronologically. But one of the other measurements we have is, is I mentioned before is that speedometer of aging, that in the instantaneous rate and a lot of those same individuals who have now sort of been taught this anti-aging sort of health lifestyle. They might have great rates of aging but really poor biological ages.

Ryan Smith:

And so what that goes to show us is that right now they might be doing the things necessary to reduce their overall biological age with time. And so that rate of aging is one of my favorite metrics, not just because it's sort of a picture of what's happening currently, it's also very, very precise. And it also relates to a whole host of healthcare outcomes and a lot of outcomes I think sometimes people have a sort of this false dichotomy between living a long life and living a life worth living. And I think that false dichotomy because you can absolutely do both. And this rate of aging algorithm has definitely been proving that in these cohorts where we see, as you mentioned before, the faster your rate of aging, the worse your grip strength, the worse your IQ actually. We see it with even measurements of other measurements of physical function. We actually even see it with brain MRIs and even facial aging. We can even show you pictures of people at age 45 and show you what they look like according to their rates of aging.

Ryan Smith:

And so this algorithm is one of my favorites because it gives you an instantaneous look at how you're doing that isn't confounded by the other noise of what's happened previously in your life or what might even be transmitted to you genetically through some of your predispositions from a genetic profile. And so it's a really, really exciting algorithm and it allows you to differentiate the overall picture versus the immediate picture.

Dave:

That makes a lot of sense. I think of it also, if you're tracking your blood sugar, well, you just had some popcorn or oatmeal or something that you thought was healthy that wasn't and so you had a huge spike but your average blood sugar might be very different than your spikes. If you happen to measure during a spike, you're going to have a pretty big variance there. And if you were to measure your average and that's why for people looking at blood sugar and aging, you look at HbA1c, which good marker of your average blood sugar over time. And so you could look at that as the equivalent of your biological age. How'd you do so far? But then if all of a sudden, wow, I'm aging at three years for every year, I'm alive, you don't have much time left and your life's going to suck. But you go, that's cool. I'm now aging at half the rate. I'm only aging for six months every year that goes past. Okay, you're not necessarily getting younger, you're just aging more slowly.

Dave:

The first step, if you remember my book on aging, which was Superhuman, the first step is you want to live a long time? Don't die. Don't get the big four diseases of aging, which are all metabolic and diabetes

starts the whole chain. But the second thing you would do right after that is age less quickly. And the third thing you would do after that is actually age backwards. Which is something that you have just demonstrated. You've seen data from people aging backwards, where their rate is negative. How common is that?

Ryan Smith:

It is still early in this investigation. As I mentioned, we sort of started doing commercial tests in July of 2020. And so our organization has only been around a little bit over a year now. And so we're still trying to get data in order to say how common that is. However, we've seen some definitive things with certain types of protocols and procedures that show multiyear age reversals.

Dave:

In one procedure.

Ryan Smith:

Even with just one procedure.

Dave:

Stem cell related stuff.

Ryan Smith:

One of has been a stem cell related stuff. The other is plasma exchange or plasmapheresis, which looks to be incredibly positive.

Dave:

Were both of those written about in Superhuman, which came out like three years? Oh gee, they were. I love it that you're qualifying, mechanistically these have to work, here's why they should work. Here's the evidence in animals. And you're saying, "Well, the people who do those, we're seeing reductions in aging from a single procedure where you do a before and after.?

Ryan Smith:

Absolutely. And it's still definitely early in the process of investigation but the preliminary data does look very, very positive, especially if we can see multiyear age reductions. Again, remember that seven year as a delta, that seven year delta to be younger biologically than chronologically, if we're seeing multiyear age reductions with even single procedures, the idea that if this could be applied to a general population, we'd have massive positive population level health benefits. And so, we don't necessarily need to find the thing that reverses everyone's age to age zero, we're just looking for incremental change and changes that can be reproducible and consistent. And I think that we're starting to find some of those.

Dave:

It makes so much sense that you're going to be able to cherry pick the things that work. What is the largest drop in age you've seen from a single intervention of any type?

Ryan Smith:

Again, it's always hard to control for and because as I mentioned everything.

Dave:

I didn't stay statistically significant. I just want to get all excited.

Ryan Smith:

We've seen six year age differences, changes between one measurement of many different algorithms. I would say that the more precise algorithms tend to max show right around a three year age sort of reversal with just one treatment.

Dave:

Okay. It's definitely possible. And those are the types of treatments you talked about?

Ryan Smith:

Yeah, definitely. I think that the type and even the protocol of the treatment looks to be important. And again, we're hoping to even build this data out even more but I think the thing to take away is that we're getting a lot more data. And as the algorithms come out, we'll be able to interpret that data with the newer algorithms. As these things continue to improve, we'll be able to look at all that retrospective data and then update it to the most accurate diagnostic.

Dave:

I'm pretty excited about this world where we can actually see what works. I wrote about plasma exchange in the book because we're finding that plasma from young people, when you give it to older people, magically they test younger. And I presupposed some of the reasons for that. One is getting rid of all the toxic garbage that builds up in your blood, which you can do via a variety of ways. But the other one is that there are some anti-aging molecules like GHK or copper tripeptide that are present in young people's blood. Ideally in the future, we ought to be able to say, "We have 20 people and they all decided that they were just going to take an insulin syringe and inject GHK into their blood," which is entirely doable today.

Dave:

But you could actually see whether they got younger, if they did it and you could even see which doses work. Because right now we don't know, but we know you should have more of it as you age but it's all mysterious. Maybe with TruDiagnostic and a properly designed IRB approved, blah, blah, blah, test, you ought be able to tell in relative short order, people do this lose three, four years so maybe we could all do it.

Ryan Smith:

Definitely. Very hopeful for that. And actually, even with GHK, we do have even some data, I think that.

Dave:

Oh, tell me. I was discussing that. What's your GHK data? It's one of my favorites.

Ryan Smith:

Well, a lot of the peptides, I think we have some good data on. Warren Pickart is sort of the, I would say the godfather of the GHK molecule. And what we know is that right around in our twenties and thirties, we're right around I think 90 nanograms per essentially deciliter of this and it proceeds to go down to right around 20 nanograms as we get into sort of over 70, over 75. And so that's a precipitous drop and one that could be absolutely supplemented but that's one of many of these metabolites and molecules which change with age. We talked about immune system changes with age, we've talked about all of these different multiomes, the proteomic changes with age, the metabolomic changes with age.

Ryan Smith:

And so one of the things that we're trying to do is to put together that entire picture and we're doing that by doing a really, really robust multiomic study with Harvard's partners, Biobank, where we're looking at over 6,000 in individuals with full genomics, full proteomics, full metabolomics and then looking at how some of these people in their banked samples have proceeded to health outcomes over the course of 50 years. And so with this, we hope to have the most complete picture of aging, across many, many different platforms to sort of answer that question of first off, what are the changes in each platform but also then to elucidate why the mechanism is actually happening.

Dave:

We are right on the cusp of discovering so much cool stuff about aging. Are you at all worried that some of the results you find that are unpopular or less profitable might just never be reported in the search engines?

Ryan Smith:

I think we're already seeing some of that where the research is being done, is being done by groups that have the ability to profit off of the results. And so I think that we're doing some studies for a lot of private companies, a lot of private supplement companies even to look at the anti-aging effects of their products. And so I think that like unfortunately most areas of science, a lot of the data that will be generated in this will be driven by economic considerations. The good news is that I think that there are a lot of the work that's still being done is still being done outside of the private sector in these research based communities. And they're really following, I would say where the science makes the most sense. And so I would say you're going to see a little bit of bot, but that absolutely is a concern that we might neglect some of the intuitive and very easy treatments and prioritize, maybe some of those more exotic ones because there's an economic market behind it.

Dave:

I like that answer. Relatively long way of saying, yeah, you're concerned.

Ryan Smith:

Definitely.

Dave:

As I think you should be because some of the scientific inquiry things around aging, they're going to show that environmental pollution matters more than we thought. They're going to show that certain microbial things are way more important than we thought. And they're going to show that immune cross reaction, whether it's from egg protein or gluten or whatever the heck else is way worse than we thought, as well as things like mold. And am I saying this out of a sense of I just think it's true? No. Look

at the interview with Dale Bredesen who wrote The End of Alzheimer's, who's a very credible doctor. There's a lot of stuff that we already are seeing enough that you can write a book and say, "Here's the credible case and here's 50 or a 100 or a million people who got better when they stopped doing X."

Dave:

But I think you guys are going to quantify and say, "Did they get better is that they woke up and they didn't have bloating and gas, they woke up two years younger." And so we're going to have to have a very high standard of scientific reporting and credibility so that when you publish that data, we go, huh, maybe we should fix the world around us because the data says that if we do, we'll all live longer and better. And if we don't that we'll all get old really quickly and there's nothing wrong with being old, there is something wrong when old is a synonym for weak, which it is not, it is a synonym for wise. Which is what it's supposed to be. I look forward to being older so I can know more and being at exactly the age I identify as, which is 28.

Ryan Smith:

Definitely. And in order to even a little bit more credence to, I think that thought process and even to go back to one of the biggest, I would say concerns about some of these algorithms currently is that a lot of them have been trained off historical data samples, which so we might go back to the Framingham heart study where they've taken a sample from 1960, where that person was a certain age and that was used to train these algorithms. Unfortunately, one of the other big things that we can't control for in those data sets are the exposures that we might have as differences in population from when we lived. Unleaded versus leaded gasoline is a good example where younger individuals are probably less exposed to leaded gasoline but at the same time, they're probably more exposed to antibiotics.

Ryan Smith:

And so that's one thing that's really, really hard to control for and sort of a, I think a little bit of a weakness to some of these algorithms currently. But with that being said, as we get more data sets and particularly data sets of longitudinal patients, of people who measure multiple times across their life, we'll be able to factor some of those things out to get a pure picture of aging but then also to attribute how all those exposures or all those lifestyle factors are affecting that aging rate or health rates or health sort of prognosis.

Dave:

I love it. And I have one thing where I want you to explain for people because I've already done my test but what does the test look like? And most of the time you have to go to the doctor. Walk me through what it's like to get a TruDiagnostic specimen. How long does it take to get it? What do you send in and all that? And of course, guys, there's always a code if we have a company on here so you save 50 bucks, you can use code asprey, trudiagnostic.com. But what's the testing experience like?

Ryan Smith:

Yeah. This testing is actually really conducive to doing it outside of a clinician's office. And we do offer this direct to consumer. Although some of the reporting we offer direct to consumer is a little bit more limited than what we can give direct to those physicians.

Dave:

Shame, shame.

Ryan Smith:

Unfortunately.

Dave:

Come on. I can't get all of my own data? I need a permission slip? Dude, you got to fix that.

Ryan Smith:

I wish. I wish. One of the interesting things that allows us to do this direct consumer right now is that aging is not classified as a disease by the FDA. We're actually hoping it gets there but with that being said, we're not allowed to necessarily report on disease risk and considerations but we can absolutely report on aging. And so what typically happens first in the process is you might order a kit and it comes in a box with a couple fingerstick lancets. And what we collect is actually dry blood spot. Once you sort of prick your finger, you can drop a few drops of blood onto that dry blood spot card. And then you put that in a biohazard bag, you send that back to us, it takes around two weeks for us to do our full analysis.

Ryan Smith:

And then at that point, you'll get all of your results emailed to you in the portal that you use whenever you register that kit, sort of right after you collect that specimen. And so the reports that we have now are, I think a lot of the things that we mentioned everything from your biological age to insights into your immune system aging, to your instantaneous rate of aging, to telomere length, along with maybe some other sort of specific data sets. And actually we try and release that raw data as well because we realize that we're trying to get people control of their own data and we don't have all the algorithms. And so a lot of times what you can do is we actually even give you all of the algorithms, CPG codes so you can actually go and use that data with whatever algorithm you find.

Ryan Smith:

And so that is another sort of output we do. And we definitely believe that the people who do our testing, they own that data and not us. And so we want to give them as much access as possible. And so with that being said, generally two weeks after you'll be able to review your metrics. We do give some sort of light recommendations based on what we know so far. And one of the other things I'll say is we can continue to update. As I mentioned, we come out with new reports around every month. And so you'll continue to get updates about different readouts as we continue to update our platform. And so in the future, you might see things like how much have you smoked across your entire life? How much are you drinking right now? What is your propensity to be hypersexual or empathetic? We might tell you some cool stuff. We'll tell you even some of those exposome related information, about how much exposure you might have had to things like BPA or to toxic metals or some of those other things. It'll continue to grow with time as well.

Dave:

You get your report now and then if you get a new way to interpret the data in the future, you include that basically.

Ryan Smith:

Absolutely. It's important to realize that we're going to include that but we're still analyzing a point in time. We'll always be analyzing the time you gave us the sample and obviously these things are changeable. We do recommend trying to update or get a better idea of your aging process maybe once a year, maybe at maximum, as I mentioned once every six months.

Dave:

Okay. The URL, tru, T-R-U diagnostic.com/dave-asprey. They're not going to remember the slash, just use code asprey when you check out, that'll save you 50 bucks, trudiagnostic.com. And I want to give you a particular shout out for saying, look, you get all of your data, you can download it, you can save it. It's your data and you have a right to take your data and run it through any algorithm you want. There's probably someone out there who knows, maybe it's a member of the Upgrade Collective listening, who's going to take their data and they're going to compare it with cycles of the moon and whatever a commentator on CNN and Fox say simultaneously that matches and they're going to find that that totally reduces your aging. Maybe they're crazy. It sounds pretty crazy to me.

Dave:

It doesn't matter. You have the right to run your data past any professional or nonprofessional amateur you want and see what you learn and then take action on it. And I think there's something really cool about saying here's all of your data set. And one more question for you, Ryan, if I identify as my own physician and I fill out the registration form in that way, can I get full access to the interpretive results?

Ryan Smith:

Unfortunately not. We do have sort of a screening process where we look for a national prescriber identifier in that process.

Dave:

Are you preventing my ability to identify as whatever I want to identify as? You are a bad man, a bad man.

Ryan Smith:

That's a great way to end the podcast right now. I think no, no. I think that again, I think that just sort of go back to one of those terms we had earlier. I'm a big fan of healthcare autonomy and being able to analyze and look at your own data and we will take every step within our legal power to give you that ability as much as possible.

Dave:

That's abundantly clear. And let's be honest. There are many things that I would like to say back when I was involved with Bulletproof. I'd like to put this on the label. I'd like to send you a link to the study but I cannot because there's either a law or an insurance company that will not allow it. You're playing within a regulated field and even the fact that you're allowing people to do direct to consumer is very difficult. I'm not harassing you about that in any way, shape or form. I'm just mostly just pulling your chain because it's funny. The idea here though, is that if you did want to share the data with the doctor, then your doctor could then give you access to your own data. And we're all working towards a future where you can take your data and you do have rights to your medical records once they go to the doctor.

Dave:

But unfortunately you're not legally allowed to give me certain things. If you're doing your liquid biopsy thing and if I had cancer, you wouldn't tell me, you'd have to tell a doctor who would then tell me for my own safety. You guys are doing great work. We didn't get into the liquid biopsy but there's a lot going on there that you're doing. I think this is a really cool platform. It's very differentiated from anything else that I've done. It's complimentary with a lot of the other data sources. I think TruDiagnostics deserves its place in the biohacking labs you'd want to see if what you've been doing for the last couple years works or something you might do ahead of time. And then what happened over the course of years? I think people would be very surprised they can get younger. It works. Thank you, Ryan.

Ryan Smith:

Yeah. Thanks so much for having me. And hopefully we'll come back and update as we continue to hear what actually changes this process and make some more apt recommendations is to make everyone a little bit younger.

Dave:

I'm going to log into my results and see what other data I haven't seen since the last time I sent it in. Thanks man.

Ryan Smith:

Perfect. Thanks so much.