#### Dave Asprey (00:01):

You are listening to the Human Upgrade with Dave Asprey. You are listening to the Human Upgrade with Dave Asprey. Today is an interview about what's going on inside your cells. In the last oh four or so years, there has been a surprising and unprecedented surge in the speed of some types of cancer proliferation that I've been hearing about from a variety of friends in the field. And cancer is one of the big four killers, if you've read Superhuman, which is my big book on longevity, that sort of set a framework that a lot of longevity books are using now. There's four things to do to not die, and then there's a bunch of other things you do to support the systems that are in your body. And not getting cancer or at least surviving cancer because you detected it early, is one of the biggest things you could do to live a long time.

#### (00:56):

That's easier said than done. Support metabolic health. Don't expose yourself to toxins, don't have too much sugar and don't do a bunch of other things that are not so good for you. But how do you know if it's working? Well, I've got a guest for you who has spent a long time about 15 years working in biotech as president at Grail. Dr. Offman is pioneering early cancer detection technologies, and we're going to talk about multi cancer early detection or something called a grail test. Something I first did almost, I want to say seven, eight years ago, because regular cancer screenings are part of my longevity strategy. It used to be just sort of a scary thing, wait till you see a lump, which means it's really big. Or get a blood test and see what happens if you can detect something way before you could see it and well, let's talk with the world's expert on this kind of stuff, Dr. Often welcome to the show.

Dr. Josh Ofman (<u>01:49</u>):

Thank you very much for having me.

Dave Asprey (01:51):

So GRAIL's been around for how many years now?

#### Dr. Josh Ofman (01:54):

It was founded in 2016, so it's been around for about a little short of eight years now. And it was spun out from a company called Illumina, which is a sequencing company, and we've been independent now for about since then, since 2016.

#### Dave Asprey (02:11):

Well, I am grateful because being able to know whether you have cancer or not can be a huge source of relief for people, especially if you had some sort of cancer in your family, which is not really common. You're saying, well, do I have higher risk? Is it genetic? Is it environmental? We don't really know or I used to smoke. How many types of cancer can you detect now with the GRAIL test?

#### Dr. Josh Ofman (02:37):

So just to take a step back for a minute, and you mentioned this in your introduction, cancer is soon to become the number one killer of men and women worldwide. And why is that? Well, it's because we're finding most cancers too late. So the way traditionally in healthcare we have screened for cancer is by looking at one cancer at a time. So for women, we look for breast cancer, cervical cancer, colon cancer, and if she happens to be a smoker, also lung cancer. And we're looking for those single cancer. So we call those single cancer screening tests, right? A pap smear or a PS. Well, grail was invented and kind of

founded some really breakthrough technology that looks at DNA that is being shed by cancer cells into your blood. And we figured out a way to combine genomics and artificial intelligence and machine learning to read a pattern in that DNA that you see very commonly in many different kinds of cancer and importantly, that you almost never see in patients without cancer. So far, this pattern recognition technology has enabled us to find well over 50 different types of cancer, and we're grouping them so we know it's well over that we know probably 60 to 70 already. And because we're not looking for any particular cancer, we're looking at whatever cancer the individual may have because there's a shared signal in that DNA that we're reading, and then we can localize that signal to where in the body that signal comes from to tell the doctor where to go look to find that cancer if it exists.

## Dave Asprey (04:30):

I've read that there isn't a lot of genetic overlap. You take two different pituitary tumors and they could have entirely different genetics in them. How do you know what cancer DNA looks like given that a lot of cancer looks like it might not be DNA caused?

## Dr. Josh Ofman (04:45):

When most people are talking about DNA, they're talking about mutations changes in the code of the DNA. And you're exactly right, Dave. You and I may have some changes to our code or mutations that are exactly the same mutations that you see in cancer, but we don't have cancer. So that does happen, and you can be fooled. Mutations are uncommon. They occur in cancer and non-cancer and they get fooled by clonal hematopoiesis and other things. We're not looking at that. We did a very, what GRAIL did very uniquely, which is quite interesting, is they asked a very unbiased question. They said, okay, we know that DNA is being shed into the blood. We know we can find that DNA, what is the best way to interrogate that DNA to find a signal of cancer? And they studied all of them mutations, chromosomal changes, fragment lengths, proteins, RNA and methylation, which is the epigenetic changes. Those are those little molecules that attach to the DNA that turn genes on and off, but they don't change the code. And when that study was completed, grail determined that these methylation changes were the most powerful way to find cancer signals, and they're the most specific.

#### Dave Asprey (06:06):

It's interesting. Other colleagues both at UCLA and other schools are using DNA methylation for something a lot of listeners know about, which is DNA methylation aging tests. You can see speed of aging or aging clocks, Steve Horvath's work. And so these are really the same sets of genes. You just have a different lens to look at them, right?

# Dr. Josh Ofman (06:27):

Yeah, they're molecules basically when from the time you're in embryo, these little molecules, they're called methyl groups are attaching to the DNA and they're actually regulating the DNA. So the genes are actually the codes within the DNA, but these molecules turn those genes on and off. And so when you're an embryo and a certain type of cell says, I now need to go become a liver cell, it's usually those methylation markers that are telling the genes to differentiate those cells into liver cells. So there's a little fingerprint that's always left on those cells to tell you where the body they are. And so we read that fingerprint, but we read a much broader pattern also that in cancer, those molecules are in and around tumor promoter and tumor suppressor genes turning them on and off. And so in cancer, you see this hypermethylation of those tumor promoter and suppressor genes and kind of a global hypomethylation of other informative genes around cancer. And that pattern is what we're reading.

# Dave Asprey (<u>07:38</u>): How do people go about getting a grail test?

# Dr. Josh Ofman (07:42):

The grail test is called gallery, and you can get it in two ways. Right now it's been on the market for about, since mid 21, and it's right now can be ordered by a physician. It must be ordered by a physician. So someone could go to their doctor and say, I would like GRAIL's gallery test or the gallery test, and it's usually because it's not covered by most insurance yet, usually an out-of-pocket expense at this point. Or they can go on the gallery.com website and order it through a telemedicine provider and the kit, it's a small kit with two tubes will get shipped to their home and they can go to any Quest labs or any local labs or have a phlebotomist come to their home and draw the blood, and then they'll get their results in about seven to 10 days.

## Dave Asprey (08:29):

And what's the cost when you go to the website?

# Dr. Josh Ofman (08:32):

A retail cost is \$949. And obviously if you're part of an insurance company or a self-insured employer or a life insurer that offers the test, it'll be far less than that. And some of the prices are discounted in certain health systems and other provider organizations, and we have line of sight to getting those costs down over time with future versions.

# Dave Asprey (<u>08:57</u>):

People can also use in the US anyway, FSA and HSA where you can set aside some pre-tax dollars for this, which basically saves you 300 bucks in taxes or something when you do it. And just thank you for making it direct to consumer. Right now we're seeing this, what I think is a really powerful shift where you used to have to go to the doctor and say, what test do I need, doc? And now people are saying, well, I just want to do this so I know what's going on in there and it's not because sick, it's because I'm going to not get sick. And sometimes you just need to go online and order what you want and get your own data and then call a doctor if you need it. So the telehealth way is I think a way of reducing friction for people to have access to their own data.

# Dr. Josh Ofman (09:42):

Couldn't agree more. We have a breakthrough device designation with the FDA, we are seeking FDA approval, but before that, we don't really do direct to consumer advertising or marketing. We do awareness raising, and then a physician does need to prescribe it, whether it's a telemedicine provider or a provider in an office. But what's beautiful about this is that gallery is a really important proactive tool. It gives people the power to be more proactive about their health because the only chance that we have to bend the cancer mortality curve is to find many, many more cancers much earlier before symptoms present. By the time symptoms are present, those most cancers have already spread. And if you can find it in an asymptomatic state, generally at an earlier stage, most cancers are very treatable and they're often quite curable. So we have already found in many of our studies and in the real world, we are finding early stage of the deadliest cancers. And surgeons are saying things like, I've never seen a gastric cancer this early or a pancreatic cancer this early, and they're undergoing curative intent treatments.

#### Dave Asprey (<u>10:57</u>):

How does the GRAIL test compare with whole body MRI for cancer screening?

#### Dr. Josh Ofman (<u>11:02</u>):

Well, whole body MRI for cancer screening has never been studied yet. So we don't know. We know there's never been a formal study of MRI for cancer screening compared to other forms of cancer screening. So I think there have been some studies done outside the United States and those studies did not look particularly favorable. MRI whole body imaging is an interesting technique. It can find early cancer, asymptomatic cancer, but it doesn't visualize some of the areas very well, like the hematologic compartment, for example. And it doesn't visualize inside your GI tract very well. So there are limitations. And the other problem with MRI, although it's a very good test, is that you find all kinds of things in the body that people don't really know what to do with that aren't suspicious of cancer, but there are other things that you find. And so that's been a challenge, but I think it is in use, and I think we're hearing more about whole body MRI, but there's no direct comparison that I'm aware of because I don't know the performance of whole body MRI for early cancer detection.

#### Dave Asprey (<u>12:14</u>):

I've done a few podcasts on whole body MRI in combination with ai. And there is some early, I will say early growth detection, but you can't tell what it is. I mean, you can get some indication of the size of it or the density of it, but it may just mean you need to explore what it is, but you don't know if it's cancer or not. And if you're doing a grail test, it's very specific for cancer versus you have something going on in there, right?

#### Dr. Josh Ofman (12:41):

Both are useful and I think time will tell about cancer detection. The other thing we know is that we're getting, what's unique about the innovation that GRAIL has developed here in the test called gallery is that it's highly specific for cancer. As you know, it's got a false positive rate of less than, it's about 0.5%. That's an order of magnitude better than anything that's ever been seen in cancer screening before. Wow. And it also is very accurate in telling you where in the body that signal is coming from, which is tremendous and it's very sensitive for the deadliest cancers. The issue with after you get a positive gall test, if it says, so Dave, let's say we did the test on you and it said, cancer signal detected predicted origin, liver or pancreas or stomach imaging is imperfect, right? We've already had many cases where imaging didn't detect the cancer that was there.

#### (<u>13:44</u>):

I'll give you an example. A woman got a positive gallie test that said gallbladder is the predicted location. MRI of the liver in the gallbladder showed a gallbladder that looked fairly normal, but it was filled with gallstones. So the doctor didn't want to do anything. The woman was asymptomatic. She insisted on having her gallbladder removed, and the first surgeon didn't want to do it. She wasn't having any symptoms. The second surgeon did it, and when they went in there, the gallbladder was stuck to the liver. And when they took the gallbladder out and opened it up, there was a cancer inside the gallbladder that was being obstructed by all the stones. So imaging missed it. And we've had many, many cases like that. And so what we're used to using for cancer screening is we're used to using shadows, images, and directly visualizing tissue with either a pap smear or a colonoscopy or upper endoscopy. And we know that those are not perfect. Now, what we're seeing are direct biological signals being shed directly from the cancers, and that's teaching us a lot about cancer.

#### Dave Asprey (<u>14:54</u>):

That means that we'll be able to see it earlier and earlier, the more data we have coming in from people as well, right?

#### Dr. Josh Ofman (15:01):

Yeah. The more data we have, the more we'll be able to teach our machine learning algorithms to get better and better, to get more biological noise out of the assay so that we can detect smaller and smaller amounts of this tumor, DNA, that's being shed into blood. Now, there are some tumors that just don't shed DNA into the blood brain tumors, for example, are protected from the by the blood brain barrier, very early melanomas there. They're too superficial to access the bloodstream. The slow growing tumors like encapsulated prostate cancers are not shedding a lot of DNA into the bloodstream. So not all cancers can be detected this way, but many, many cancers can. And importantly, 80% of the cancer deaths today are caused by cancers we are not looking for. And so this gives us an opportunity now to look for all those cancers that are causing the vast majority of cancer deaths that we are not screening for today.

#### Dave Asprey (<u>16:02</u>):

That's incredible. So retail price, about 950 ish dollars. It's almost like if you looked at some of the, what, 160 billion that the government sent overseas. If you took the number of people in the country and multiplied times \$960, assuming no volume discounts, it looks like we could have afforded many times over to do early cancer detection for the entire population of the us including anyone who's in the country, whether or not they're a citizen or not, green cardholders and everyone else. And if we did that, our \$1.4 trillion or whatever it is, national spend on healthcare would drop precipitously, right? Because the amount of money you spent on cancer is insane.

#### Dr. Josh Ofman (16:50):

Yeah, we do. Late stage cancer is very expensive to treat and isn't very effective. Early stage cancer, obviously much easier to treat and much more effective and much less costly, often five to 10 times less costly to treat early stage cancer than late stage cancer. The other thing that's really important to know is that so often we get asked the question, is this affordable? By the time this gets to population wide screening, the cost of this test will be much lower than they are today. But remember all the screening we're doing today, we spend about 25 billion a year screening for these five cancers, and most of that money is being spent on working up all the false positives. So those screening tests are only finding about 14% of the incident cancers in elevated risk adults. And we look at risk, age is the most important risk factor, and that's not enough cancer. We're not going to bend the cancer mortality curve finding so few cancers, and they're generating an enormous number of false positives, and that's what's consuming all the money. We're suggesting that gall be added to those standard of care single cancer screenings, and we can create a much more effective and efficient cancer screening system to find way more than just those five cancers, but all the other cancers that people are dying from. And to do it with a much lower false positive rate.

#### Dave Asprey (18:22):

That sounds like that would be well life changing for a lot of people. And that was why I wanted to have you on, because this is a new way of thinking about cancer. It was very much an imaging game or a symptom game like you're limping, let's find the bone cancer, but by the time you're limping, you're kind of screwed, right?

#### Dr. Josh Ofman (18:43):

That's right. And it is very different. It is a paradigm changing type of technology to be able to transition from only looking for individual cancers now to also look at individuals for whatever cancer they may have. So let me give you an example. You're a man. You get prostate cancer screening, colon cancer screening, and let's say you use a stool-based colon cancer screening test like Cologuard or the FIT test, and let's say you're a smoker and you also get low dose CT of the lungs. No doctor has ever told you that across those three tests, your false positive rate for you the person, not the false positive rate of the test, but for you will be almost 40%. Wow. Nobody would ever recommend a test like that, right?

Dave Asprey (<u>19:31</u>):

It's almost like you could flip a coin.

#### Dr. Josh Ofman (19:33):

Well, that's at the false positive rate level. Now, if you think about positive predictive value, which is if you add a positive test, what's the likelihood you have cancer? That's going to be less than 2% because cancer is very uncommon. In general, it's about 1% incident. So the positive predictive value for the gallery test to look for 50 or more cancers is somewhere between 40 and 50%. So an order of magnitude higher than anything that's ever been seen before with cancer screening.

Dave Asprey (20:05):

Wow. So you're finding all this stuff that nothing else can find. That's

Dr. Josh Ofman (<u>20:09</u>):

Right.

Dave Asprey (20:10):

Do you have enough data over the past year since you started doing testing to look at incidents of cancer, have you seen anything in this signal that says cancer is getting better or getting worse over time, or is this just we're detecting more?

#### Dr. Josh Ofman (20:23):

We haven't. We're going to be detecting more. We haven't seen any data on any particular cancer as to whether the incidents is changing. But what was good about, I joined Grail about four and a half years ago, and they had begun investing in a very large evidence program that's considered to be probably the largest clinical genomics program ever undertaken. We're studying over 380,000 individuals in all sorts of studies, including the largest randomized clinical trial ever conducted for a multi cancer early detection test in England where we randomized 140,000 adults with no signs or suspicions of cancer. And that study is fully enrolled, and they've done their third consecutive screening round, and that study will weed out in a year or two. We've done real world interventional studies in the United States where when we added gallery to standard of care screening, we more than doubled the number of cancers found in the population, and half of the cancers we found were in stage one and two 70% of the cancers had no recommended screening.

#### (<u>21:36</u>):

And again, the positive predictive value, if you had a positive gallery test, the likelihood you had cancer was 43%. Again, order of magnitude higher than anything that's ever been seen. And we found some of

the deadliest early cancers that have been found, and we continue to study in the real world. We've done over 150,000 commercial tests now. We're seeing a signal detection rate of about 1%. So about 99% of the people who take Galler will get a result that says, no cancer signal detected. Please keep getting your single cancer screening tests because we don't want to replace those. We want to add to it. And about 1% will say, cancer signal detected, predicted origin, ovary, or uterus or stomach or pancreas. And those doctors will go work them up for cancer. And we're finding those early cancers,

#### Dave Asprey (22:32):

And most cancers if you detect them in stage one, are highly curable, right?

#### Dr. Josh Ofman (22:38):

That's right. Even stage two, stage one and two solid tumors are localized. They haven't spread. And so those are very well treated. They're more treatment options. And even if they're not curable, the life expectancy is much higher than it would be in later stages, and it's often surgery with or without radiation is the treatment.

#### Dave Asprey (23:04):

If Steve Jobs had access to the Grail Gallery test, we would've spotted that way earlier than we did, right?

Dr. Josh Ofman (23:12):

Probably. Yeah. Yeah,

Dave Asprey (23:14):

Yeah. That's what it looks like. And so people fear pancreatic cancer ly because of Steve Jobs, plus it's a really severe, relatively fast moving and highly fatal cancer. But if you get it at stage zero, stage one, it's pretty darn untreatable. That's right. I know 950 bucks is a lot of money for people right now, half the country in the US doesn't have a thousand dollars for an emergency medical expense, and you may or may not have insurance, and it's not supposed to be like that in the country, and it wasn't always like that, and it won't always be like that, but it is right now. And so if you're listening to this, this is one of those things to ask your insurance company and your doctor about. And if you are someone who's in a fortunate position to say, all right, I'm spending proactively and avoiding the four killers. Don't get diabetes, don't get cancer, don't get heart disease, and don't get Alzheimer's. If you can just do that. And there's so much information now about how to just reduce your risk by orders of magnitude with some simple lifestyle behavior things, and you can measure whether you're making progress. This seems like one of those things that ought to be on your list of what, every two years. How often would you do a Grail Gallery test?

Dr. Josh Ofman (24:29):

Actually, we're recommending gallery be used annually.

Dave Asprey (<u>24:33</u>): Annually,

Dr. Josh Ofman (24:34):

Okay. Because what we're learning about the rate of growth, the pace of change of these cancers is faster than what most people have come to understand because now we're looking at this biological signal being shed from the cancer itself. And so most of these deadly invasive cancers are moving really quickly. And so if you don't do it annually, you run the risk of missing that early stage detection. Most of our studies are with annual testing. In fact, Medicare has just worked to approve a study that we are doing called the Gallery Medicare study or the reach study of 50,000 Medicare beneficiaries who will get tested for three consecutive years and Medicare will pay for the test and the workup. And so we're going to really study this in the Medicare population. And again, an annual test. And to your point, \$949 is a lot for Americans right now, but we're in a transitional period. We have every intention of getting FDA approval as soon as possible, and then payer coverage and payer reimbursement will occur so that patients won't have to bear the burden of that cost. And we can get to population-wide screening much faster

## Dave Asprey (25:54):

For those interested in getting a gallery test done, you can go to gallery.com/dave, again, that's G-A-L-L-E-R i.com to see if you're eligible for \$50 off their test. If you live outside the US and you want the Grail Gallery test, can you get it?

#### Dr. Josh Ofman (26:11):

No, it is not available. The only place right now where it's available is in the England as part of that study, and the UK government is going to think about whether they would do an early implementation pilot in a million Englanders over the next couple of years. And we'll hear about that probably over the summer, whether they're going to do that or not.

#### Dave Asprey (26:33):

I was just down at uc, San Diego at Dr. Patel's office, lithium mitochondrial biology, and he's getting amazing results from just getting blood on dry blood samples now. And I've seen so many companies with mini lancets, and it seems like there's a big revolution of not having to go into Quest or LabCorp to get liquid blood. Are you guys close to being able to use better sampling so that the cost could go down?

#### Dr. Josh Ofman (27:03):

The sampling is not a huge part of the cost, but right now, no, we need two tubes of blood. You do? Okay. We run the test on one tube and then we keep a backup tube in case it's needed. And we're always looking for ways of improving our test, and we may come to something like that, but for now, we're trying to collect two tubes of blood on every individual who takes gall. We want to make sure we have that extra tube in case something happens.

#### Dave Asprey (27:30):

Got it. So you could rerun the test. That makes sense. And do you mix all the blood up at the end of salt of vampires? Just checking.

#### Dr. Josh Ofman (27:36):

No, no. But the way our test works is pretty straightforward. We isolate the DNA out from the plasma, so we spin down the blood, get the plasma, isolate the DNA, amplify that DNA, and then sequence it using bi sulfite sequencing, a very proprietary chemistry that gives us that ability to see the methylation pattern, and it's that the machine learning classifier is taught on. And then if there's a signal scene, it

goes through a second machine learning classifier to pinpoint where in the body that signal came from. There's that little, yeah. Wow.

## Dave Asprey (28:11):

This is groundbreaking stuff. Another question for you. The history of medicine, at least in all the 19 hundreds has been, let's do it on college age, mostly white dudes because that's who was going to college. So you look back in seventies, eighties, and even early nineties, there was way more sampling of men, but the population is 51% women, at least in the west, and it's a little bit stilted of less women in some parts of Asia, mostly because of birth practices. So that means that you're sampling though. Now, is it an equivalent? Are you getting 51% women samples, 49% men, and is there a difference in the way you have to analyze cancer and women versus cancer in men?

## Dr. Josh Ofman (28:58):

That's a great question. No, we're not. We're trying in our studies to get as representative a population as possible ethnic representation, racial representation, and socioeconomic representation. So traditionally, so the Medicare reach study is a good example where we're really aiming to get into those populations that are traditionally underserved. The UK trial that I mentioned in England is very well represented with a diverse and is socioeconomically deprived population. We're trying to get as broad a population as possible. We know that age is the most important risk factor for cancer. So the studies are typically done in adults the age of 50, and we know that adults over the age of 50 have about a 13 times higher incidence of cancer than adults under the age of 50. But there are younger populations like a 30 5-year-old smoker or a 30 5-year-old cancer survivor where a 30-year-old who may have a hereditary cancer syndrome or a carrier germline mutation. They're also at that elevated risk of cancer. So in clinical commercial use, it's being applied to all of those elevated risk groups, but our studies are typically in adults over the age of 50.

# Dave Asprey (<u>30:14</u>):

Makes sense. I feel like if I was to just apply what I know about the world, I would guess that the second biggest predictor after age would probably be poverty level.

# Dr. Josh Ofman (30:26):

Yeah, I mean, we do know that socioeconomically deprived populations and ethnically less diverse, diverse populations, excuse me, if you're in a black community or a Hispanic community, that they do have a higher death rate from cancer. They get less cancer screening and they have a higher incidence of cancer. And so that's a sad state of affairs. The truth is, Dave, there's just nothing acceptable at all today about the status quo in cancer screening. We are not finding enough cancer, we're not screening the population enough. We're not looking and screening for the cancers that are most deadly other than colon and lung, and we need to do a much better job. And we have technology now that can help us get there, but we've got to get through this period of pre reimbursement to get there.

#### Dave Asprey (<u>31:25</u>):

It feels like when Medicaid has the ability to say, oh, you turned whatever age 50 because there's a big peak there, or when you first go on Medicaid, just you get a grail test automatically, they would reduce cancer care costs enormously, but they might have to pay benefits for another 10 or 20 years. So maybe it doesn't pencil for the bureaucrats, but for those of us who want our grandparents around it, pencils very, very clearly, which is why this is so critically important and why I wanted to have you on the show,

if you put on your future hat here, you have so much data, is there ever going to be a day where we can say, you know what, we're pretty darn sure that these three environmental things or these two food things, those are smoking guns for cancer.

## Dr. Josh Ofman (32:13):

It would require quite a lot of population data. And I think still a lot is being learned about the exposures. You've got first responders and firefighters you've got in the military, people who are exposed to burn pits and other chemical warfare agents that we know are getting early cancer and are dying of early cancer. And so there's a lot we need to learn and a lot we can still do, but it will require novel technology like GRAIL's technology to get widespread use if we really want to make a dent inness and to figure all of this out, but at a population level, we need to get there and it's just going to take us time. But traditionally, Dave, it's taken decades from the time you had a validated technology until the time it was widely used for screening. Cologuard is a good example. Colonoscopy, mammography, low dose CT for the lungs, decades from the time studies showed they were good and valid to the time it was widespread.

## (<u>33:18</u>):

We can't afford to do that any longer. We have technology today that can find cancer in people who have no idea they have cancer, and we refuse. At Grail, we have a huge sense of urgency to get this into the hands of providers and their patients, and we're doing everything we can to do that today. That's why we launched it as a lab developed test. That's why we're pursuing FDA approval. Medicare, as you know, doesn't even have the authority to pay for tests like this. The only reason they pay for colonoscopies and mammograms is because special laws were introduced, giving them that authority. So we're hopeful that Congress will do what's right to give Medicare the authority to pay for tests like this in the future once they're FDA approved.

#### Dave Asprey (<u>34:08</u>):

It sounds to me like the grail tests should just identify as a virtual mammogram and confuse the heck out of the attorneys. That's

Dr. Josh Ofman (34:14):

A great idea.

#### Dave Asprey (<u>34:18</u>):

Nothing like wordplay to get bureaucrats all in a tizzy. Now, when we talk about in the future we'll have more data around cancer going back historically, it feels like you can see various points where there's a change in the slope of the curve. Like in the nineties, early nineties, cancer rates just started going through the roof and the age at which people got cancer started to go up a lot. And I've seen various people say, well, there's new chemical things. There's mobile phone things, there's compact fluorescent light bulbs, and whatever cosmic ray is, there's lots of different theories about that stuff. If you had to, we'll say with all the disqualifiers you could say saying, I'm not sure, but as an expert in the field, if you had to guess at what would you hypothesize if you were just going to say, let's experiment and see if I'm right, where would you throw that dart?

Dr. Josh Ofman (35:11):

That's a great question. I think what we're seeing interestingly is an age shift in the incidences of cancer. For example, colorectal cancer as you'd seen over the last five years, seems to be showing up in younger people now more often than it used to. And we don't know why that is. Is it food related? There are a lot of hypotheses, but you've got to suspect that if that's happening in colorectal cancer, it's probably happening in other cancers as well, right? The relationship between our exposures and the incidences of cancer is just something, maybe the National Cancer Institute, maybe people need to really take that up and help us learn a lot more about that. But I do see colorectal cancer as a leading indicator of what we may see more frequently, which is as we live longer, you're going to see more cancers in the elderly population.

## (<u>36:07</u>):

They're not going to be dropping dead heart attacks, but certain cancers showing up more and more frequently in younger individuals, and we need to be able to figure out how to screen them so that they're not showing up with late stage cancer. The other opportunity I see is that this technology that we've developed looking at these epigenetic patterns is also going to be very applicable for those who have symptoms suggestive of cancer. And for those who have diagnosed cancer, we can look at the amount of DNA that's been shed from those tumors and get a very prognostic look at how aggressive they, and then after treatment, see if that treatment was complete or they have minimal residual disease left, and then look for early recurrences. So I see applications even for our technology, not well beyond just cancer screening, but throughout the whole continuum of cancer. And then if you look even further into the future, you could see this whole approach that grail has taken to cancer to potentially be used in neurodegenerative disease or cardiovascular disease or autoimmune disease because there are those epigenetic signatures that are sure to be found in those conditions as well.

# Dave Asprey (<u>37:25</u>):

That makes so much sense when you think about it. A good number of people listening to the show are probably in the camp that says, I don't want to use chemo or radiation or things like that for cancer. And frankly, I don't want to use those either. However, there are some forms of cancer where those work exceptionally well in somewhere they don't work that well, and we actually have good data on that. And so there are some people say, well, I want to treat my cancer metabolically. And I've seen shocking results from that where people shrink tumors and they can be operable. But I've also seen the flip side of that in the functional health community, sometimes people don't want to talk about suppose as I'm going to ignore my stage four breast cancer and meditate on it, and then they die, right? And it's not okay either.

#### (<u>38:10</u>):

So here's a call to you. If you are a believer in functional medicine, and I do a lot of functional medicine, I'm a believer in that stuff. I like to make my mitochondria so healthy, they can't even think about cancer. So I like to think my risk is lower than average, and it probably is because of all the lifestyle stuff I do, but I could be wrong. So I'll test it and prove if I'm deceiving myself. So if you're on the path of healing yourself, which I fully support, and is your God-given right to heal yourself however you want to do, it's also something that you might want to test and see if you're on the right path. So if you decide you're going to meditate your cancer way and you get a grail test and you have more cancer, DNA, not less, your meditation isn't working, so then you need to change your meditation or change your treatment.

# (<u>38:54</u>):

And some of the Western therapies for cancer are shockingly effective, especially for early stage cancers, and they aren't going to harm your body as much as a late stage cancer. So I would just say be

very level-headed. There is nothing good or bad about pharma. There's nothing good or bad about nature. A spider venom and bean toxins can both kill you from mother nature and some pharmaceuticals can extend your life and make your brain work better. And some of them have a lot of side effects. So I would just say get the data with grail. You get data on 70 or so kinds of cancer, and if that's something that you're looking to hack in your body, prove it to yourself that whatever you're doing, if you have cancer, that it's working. So this is now the speed of aging test that I've talked about so much. What's my rate of aging? I age at 72% the speed of normal people because of my longevity practices. That's the same as Brian Johnson, by the way. And if you had cancer, what's the rate of reduction of cancer DNA in my blood? That's proof that what you believe and what you are doing is an accurate reflection of reality. And as far as I know, the grail test is the only thing you could do besides in imaging. Look at the size of shrinkage, which is less quantitative, I think. Right? That's right.

#### Dr. Josh Ofman (40:11):

Well said.

# Dave Asprey (40:12):

Any further comments on that? I mean, it's a bit of a lecture versus a question, but just for listeners, this is so important. So fill in what I missed on that conversation,

# Dr. Josh Ofman (40:20):

Just that there are a lot of technologies that are emerging like ours that still are being validated in all the different types of cancer settings that can be used to track the progression of your cancer or track the effectiveness of your treatment. Some of them look at tumor informed signals from DNA, others look at DNA in the blood. There are other molecular tests that are out there that can help you make good decisions about whether your cancer is being effectively treated or not. The issue that Dave's raising is that imaging, while that's been the standard, is imperfect. I can tell you many personal stories of family members who've thought they had a very localized tumor based on imaging and in surgery it was found to be widespread. And I can tell you the opposite, where it was thought on imaging to be widespread, and when they got in there, it was pretty localized. So it can happen and you just need to take, think about these more biological signals from your cancer that might be more accurate over time, time will tell. We have to prove that. But the proof is coming,

# Dave Asprey (<u>41:33</u>):

The work you've done with cancer and cancer detection so far, and I want to thank you for coming onto the show to talk about this because this is the first time in history that you could say, I'm not really worried about cancer because I can get the data. I am now changing from ideally doing this every couple of years. Full disclosure, I've done it twice since you guys came out with it, and I think I had early access before it launched through one of the groups I was a member of, but it's been a little while. So I would encourage you if you're listening and it's in your budget, given what I've seen over the past three years, especially with soft tissue cancers, I'm getting reports from physicians in clinics that they're seeing more of this in younger people than they have before. But I don't have hard numbers on that.

#### (<u>42:20</u>):

So I would just say it's a good idea to do this every year or if you feel like you're lower risk maybe every couple of years. But I just sent a note to my people saying, all right, it's time for me to do it again, and I will get the results. Hopefully they'll be the same as last time. If they're not, I'm not going to lose my

mind. I'm just going to get more data. Because as you said, if you get a positive, it doesn't mean that you have it. It just means you have a great chance of having it.

## Dr. Josh Ofman (<u>42:45</u>):

That's right. And what's interesting, Dave, is for you and I, I've had three consecutive tests now. All the data, as spectacular as it is, and as impressive as it is, is really based on a snapshot of an individual at a point in time. And now we're beginning to get enough body of evidence of people who've had multiple consecutive tests. So we're now going to start being able to layer in the movie at the individual level, and that will even be more informative. And so I expect our performance to even improve more as we do that.

## Dave Asprey (<u>43:15</u>):

Wow. I guess the other important thing as we're just helping people who might worry, I've got a friend who's in our late thirties and just lost her mind. She had a lump in her pelvis and two CT scans. Just really, really huge amount of stress. It's a knotted muscle and damaging people, we don't know it. We don't see anything there. The amount of emotional stress because of fear over cancer. Guys, if you're worried about this, you order a test and then you can stop being afraid. It's that straightforward. But every bump is in cancer, and if you do have cancer, it's way more treatable than it used to be, and it's not something you want. So catch it early. And just the lack of panic available. Any words of wisdom for people who are just fearful of this?

## Dr. Josh Ofman (44:08):

It's a great question, Dave. And I'll tell you a personal anecdote. My doctor who prescribes Gall quite often hasn't taken it himself. And I asked him why he hasn't. And he said the classic words, I don't want to know what, but that's the old mindset. He grew in clinical medicine for the last 40 years thinking about cancer as a death sentence. And it's hard to shift that mindset, but you have to because now we're in a moment where technology can enable us to find all of these deadly cancers early. So you do want to know, because if you can find them early, you can be effectively treated and potentially cured. It is not a death sentence. And so that's the mindset shift that has to happen. And it is happening, but it takes time.

#### Dave Asprey (<u>45:02</u>):

It's something that in my world, which is a unique biohacker world of my own creation, admittedly, cancer is primarily a mitochondrial disorder that comes from my environment, and it's something that's manageable like any other health parameter. As long as I can get the data, we probably can do something about it. And it's not knowing that would be a cause for concern, right? Because the more data I have, the better decisions I can make. And so I have a hard time with it. But your colleague reminds me of Dr. Paul Newhouse at Vanderbilt. He's studied nicotine since 1986, multiple major trials showing it either prevents or reverses Alzheimer's disease, pharmaceutical, nicotine, not smoking. Smoking causes cancer. It's bad for you. And at the end of the interview, I said, Paul, what form do you use? Do you use a patch or a gum? He goes, never tried it.

#### (<u>45:58</u>):

How is this possible? So there you go, one of the guys who prescribed grill but doesn't do it for that reason. I think we're going to see a lot more people just saying, I want my data. I don't need permission. I don't need lecturing. Just like prove it's real. And that's where I'm putting all of my attention right now, personally and even professionally with Upgrade Labs, which is a franchise company, not medical lab testing. It's go in and you are your own laboratory. Let's do the things that change your metabolic function. I don't want to believe picking up heavy stuff works. Either it does or it doesn't. And I'll show you what the data. And when we become data-driven and we become very personalized, all the data you're generating at Grail going to tell you over time, huh? People who do this, and if they get a grail test every year for five years, we can tell you with almost a hundred percent certainty, you should probably go for a walk and stop smoking because the numbers don't lie. And that's when we start really understanding the manual for being a human being that runs for a long time. That's

Dr. Josh Ofman (46:59):

Great. Great advice.

Dave Asprey (<u>47:01</u>):

Well, thanks again for being on the show and for your research.

Dr. Josh Ofman (<u>47:04</u>): Thank you very much for having me.

Dave Asprey (<u>47:06</u>):

Visit gallery.com/dave, that's G-A-L-E-R i.com to see if you're eligible for a \$50 off limited time online only offer. This is worth it, and maybe it's worth getting it for your parents instead of yourself or maybe for both, because the older you are, the more important it is that you get a grail test.

Dr. Josh Ofman (47:25):

Dave, thank you for having us on the show. We really, really appreciate what you're doing as well.

Announcer (<u>47:31</u>): You are listening

Dave Asprey (<u>47:31</u>): To the Human Upgrade with Dave Asprey.