Transcript – Saying GeNOme to Cancer with David Haussler - #342

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Dave: Do you feel like you're stuck in life? Like your creativity's blocked? You need to check out the Unmistakable Creative Podcast. Think Ted Talks and Oprah put together on a podcast show. They recently talked about the art of strategic gifting and how you can make someone feel appreciated with a simple gift. To listen and be creatively inspired, go to podcastone.com or download the free mobile app now.

Speaker 2: Bulletproof Radio, a state of high performance.

Dave: You're listening to Bulletproof Radio with Dave Asprey. Today's cool fact of the day is that there are about 37 trillion cells in the human body and if you unwound all of the DNA encased in each cell and put it end to end, you would have enough DNA to stretch from the sun to Pluto and back seventeen times. That is actually kind of profound. It's also totally, totally not true because the orbit of Pluto is not circular, in case you're into astronomy, but anyway, it's a good analogy. That's about right, if you look at the average orbit of Pluto, so let's just be precise here.

Before I get into the show today, which I might have just hinted has something to do with DNA, if you're a regular listener of Bulletproof Radio, you've heard me share the top ten list of biohacks. Let's talk about number nine, Fun Hacks for the Bulletproof Mind. It may sound weird but hanging upside down is a great way to hack your brain. Regularly inverting trains your brain capillaries, making them stronger and more capable of bringing oxygen to your brain. It's a pretty straightforward thing. More oxygen to the brain means better performance for you.

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If you don't know about the Bulletproof Performance Kits, that's probably because you haven't been to the Bulletproof Store in a little while. If you're new to Bulletproof or you're just looking to figure out what works for other people, we've got a bunch of new performance kits. More than a dozen of them to choose from like the coffee kit, the brain kit, the detox kits and these are based on what the Bulletproof ambassadors do that helps them perform better. Head on

over to bulletproof.com and check out how you can pair these products up to get more performance out of your brain every single day.

Today's guy is a guy I'm really looking forward to having on the show and you may not have heard of him before but he's done some pretty amazing work. He's also a little bit diverse. He actually studied psychotherapy for a little while back in the day and today he's a distinguished professor of biomolecular engineering at University of California, Santa Cruz. He's also a bioinformatician combining math, computer science and molecular biology to develop new algorithms to understand the human genome. He's pretty well-known if you're a genetics focused person, for his work on the human genome project where it was his team that made the first publicly available computational assembly of a human genome sequence on the internet. His name is Professor, Doctor, it's not right. Anyways, his name is Dr. David Haussler.

David: [Inaudible 00:04:18] the professors and the doctors. It's wonderful to be here. It's great to have a chance to talk with you about the exciting potential for DNA. We can probably use it for other things than reaching to Pluto and back. I think the analogy though is [out 00:04:39]. There is an enormous amount of information in our genome and we're just now beginning to understand it.

Dave: I was intrigued at your very early work with the human genome. Back in my career in Silicon Valley I ran the web and internet engineering program for UC Santa Cruz, the extension of Silicon Valley. I used to teach working engineers how the internet work instead of how computers pre-internet work. It's the first wave of eCommerce companies. Google's first server is on our data centers. We also had a company called Double Twist. I did work on their infrastructure. You know who these guys are, right?

David: Double Twist, yeah.

Dave: Literally I've been in the data center Double Twist for people listening was the company that held the data as I understand it for the work you were doing, computational analysis and they were doing the storage for the human genome. It was a whole floor of a data center in Alameda, if I remember right. I did architecture for them.

David: Double Twist was one of the early bioinformatics companies in the upsurge leading up to the combination of the human genome project in the year 2000. They were built by the venture capital community in view that here's an opportunity and it surely to work out but I think being conceived and created by the venture capitalist rather than an independent genius who really had a passion for it, they were doomed, I thought they were doomed to failure from the beginning. You can't create these companies out of whole cloth. You got to have individuals that are passionate about ...

Dave: You need your Craig Venter.

David: Yeah, you need somebody like Craig or one of the other great thinkers.

Dave: Who are the other maybe less famous but other great thinkers in the field that you would name the other two or three people worth following?

David: George Church, Eric Lander, there are a number of really fascinating people in this area. I'll get into trouble if I make a long list and leave somebody out.

Dave: I understand, that's why I asked for two.

David: There are dozens and dozens and I'm just giving the very big names that are probably household, somebody that's been on [Cobear 00:07:00], that level. For instance, Collins, George have been on so it's a great area. We do exciting things and we're thrilled to be able to ...

Dave: One of the things that you do that's particularly interesting is you focus a lot on human genome and cancer. Talk a little bit more about what you're doing to map our genetic predisposition for cancer. People listening may not know a lot about genetics so give me the entry level view but a little deeper.

David: Absolutely. The quest to map the human genome started out early on we had actually a meeting here at Santa Cruz, the chancellor Sinsheimer called it in 1985 and had some of the great experts come and say, "Is it possible to map the three billion different bases of As, Cs, Ts and Gs in the human genome?" Figure out what a typical person's genome looks like by hardcore biochemistry to sequence this and it was initially thought that that would be impossible but it turned out that by 2000 as you said we've had the first draft and we were very proud to do the computational analysis.

There were a bunch of little snippets of DNA that were produced by the genome sequencing machines and we did the key assembly to put them together into a coherent first draft of our human genome. Posted that on the internet on July 7th 2000. This was simultaneous with the production of the genome by Celera so Craig Venter's company and my good friend and colleague Gene Myers. We went to school together. Led the assembly of that version of the human genome. By 2000, suddenly there were two versions of the human genome and that set the stage for a subsequent development in thinking about, "Okay, now if this is the overall map for the human genome and we're all 99.9% identical at the DNA level then what about the differences and how did those differences affect our health?"

The primary differences that people were thinking about in the initial stages were the differences that we have in our genomes that we inherited from our mom and dad. You get one copy of a gene from mom and one copy of the gene from dad and little variations in those genes in the DNA can make a difference in your health and in your propensity to get various diseases. Actually, there is a disease, cancer, in which new changes happen as you grow older. Not in those trillions of cells that you were just mentioning in this intro, they all start essentially with the same genome that you got from mom and dad but as you grow old they accumulate changes and so when cells divide they naturally don't make a perfect copy of their genome for the daughter cells.

That's a main source of differences but also you can have various chemicals that are carcinogenic and increase the amount of mutation that occurs in particular, smoking creates these compounds and they can cause mutations in the cells in your lungs. Some light can cause

mutations in the cells of your skin and those are then significant events rarely do they do anything bad, most of them make no difference whatsoever but with trillions of cells the odds are that if you keep going on long enough, if you live long enough then you're going to have a bad combination of mutations that causes that cell to grow into a cancer tumor.

We now have confirmed through careful investigation over the last few decades that cancer is actually very much a genetic disease. The cause of cancer is mutations that happen in some of the cells in your body that cause them to go rouge. Treating cancer is all about killing the cells that have those dangerous mutations and it is an enormous effort and we are learning so much more about it now that we can read the DNA of the tumor cells.

Dave: I'm working on a book about mitochondria right now. I'm going pretty deep on krebs cycle. It's a book meant for lay people and frankly I'm not a university grade researcher on mitochondrial benchtop chemistry but I'm pretty good at what I do. I've interviewed guys like Dominic D'Agostino looking at the mitochondrial angle on cancer and the mitochondrial DNA mutations which happen more quickly than the human genome DNA.

David: Nuclear genome. The human genome has a nuclear component in the mitochondrial genome.

Dave: Thank you. That is exactly what I was thinking. You have the nuclear DNA which is where we focus all of this and we're developing this view, I am looking at Wallace's research on mitochondrial epigenetics and what gets expressed from the nuclear side of things. I'm wondering, your take on this, you are one of the top people in the world looking at the nuclear side of genetics and cancer and I'm talking to other people who are looking at the mitochondrial dysfunction side of cancer. How do you line those two perspectives up? I don't know.

David: I think mitochondria have now been shown to be involved in a number of diseases including cancer. They are of course the energy factories of the cell and such. That among the other key roles they play in telling a cell whether it's over, basically, you should commit suicide or whether you should keep going. All of these information and energy processes that are rooted through the mitochondria are important to the cell and important to disease so we certainly appreciate the value of the mitochondria even though it has a tiny genome 16,000 bases of DNA compared to the three billion bases of DNA in the nuclear genome.

The nuclear genome contains more of what we are just more bits of information about what we are but the mitochondria, tiny as it is it's very important also to our health. There are number of new studies that show mitochondrial effects in cancer and how that can alter the course of the disease but again, there's more going on in the nuclear part of the genome in cancer than there is in the mitochondria and that's not surprising just because there's so much more complexity in the nuclear part.

Dave: Just given the size there.

David: Yes, just given the size.

Dave: How far are we from being able to look at someone's nuclear DNA and saying, "Based on this we

have a very reasonable likelihood of what kind of cancer you're going to get if you get cancer"?

David: We'll never get to that point where we can be highly predictive because the progression of cancer depends on random and inherently unpredictable events. It could be a cosmic ray that comes down and hits the right place in the genome of the right cell at the right time or wrong place wrong time if you want.

Dave: You could start smoking, right?

David: Yeah, you can start smoking so we won't be able to predict it in that sense but I think the largest hope for the future is that we would be able to catch it earlier than we are now. The most difficult problem with cancer today is that patients are coming in after the cancer has progressed to a point where it's very difficult to unwind and get rid of all the cancer cells. The hardest thing about treating cancer is that you need to get rid of all the cells. If you leave some behind and they grow back and that's the problem.

On the other hand, the good thing about cancer is that you only have to kill the cells, you don't have to fix them. If you have cells that you need, your neurons or something and you're trying to alter them to work right, that's very much harder than killing cells. The good part of cancer is we only have to kill, the bad part is we have to kill them all. There are challenges.

Dave: There's a whole bunch of things I want to ask you based on that. I've looked a lot at the respiration of cells. It seems like there are pre-cancer cells that can be fixed where you haven't kicked off that cell death process called Apoptosis. Do you ascribe to that? I'm not a cancer expert. You are, so I'm asking questions without meaning to question what you're saying there or to challenge what you're saying there but just to get an understanding. I know a lot of people who've listened to the show have had heard several guests talking about increasing electrons in mitochondria and reversing hypoxic states in cells and turning anaerobic cells back into aerobic cells thereby preventing them from further progressing to become cancerous. Is there meat on the bone for that theory in your experience or was this more of a nuclear DNA problem?

David: There definitely is a metabolic shift that occurs in cancer and it does towards anaerobic from aerobic. That is part of the cancer switching into a metabolism that is optimized for tumor growth. Cancer of course is an evolutionary struggle within your own body. The cancer cells are competing for real estate against your normal cells. Growing faster and being more vigorous in stealing resources like blood vessels are characteristics of cancer because that's characteristic of who wins this battle for real estate in your body. Part of that is shifting metabolism and that brings again in the mitochondrial aspect because mitochondria are so fundamental in this metabolic process.

Again, that's just part of the story. The overall cell cycle is critical and that's been the most extensively investigated in cancer. You have to start dividing and you'd have to divide a lot and rapidly to be a bad and dangerous cancer. What happens is that when you're an embryo, your cells are dividing a lot and then that process slows down and so when you're adult, most of your cells are senescent. Basically they finish, they are dividing and they are occupying their place in your body and they shouldn't start dividing again. When they revert to this, "Wow, I think I'm

like a stem cell like thing, I'm going to divide again." That's a symptom of cancer that is more central and profound than the energy shift but it's all part of the story. There are many hallmarks of cancer that we look at.

Dave: What do you do in your life to minimize your chances of getting cancer?

David: I try to use sunscreen. I don't smoke. I watch some of the foods that I eat so you don't want to eat moldy peanuts for example. Aflatoxin is one of the most potent carcinogens known. There are number of chemical carcinogens that aren't necessarily just from industrial processes. They are so called organic, natural carcinogens the aflatoxin grows peanut mold grows if you're an organic farmer or not. You can't just say I eat organic and so I'm safe. You have to be very, very cognizant of the molecules that you're exposed to, make sure that they are not cancer-causing.

As I said before, really the most important thing is detection and early prevention because no matter how careful you are, there's still this increasing probability that you will have that unlucky event that will cause mutations in your cells as you grow older. There are really no amount of diet and lifestyle can prevent that risk because it's an intrinsic fact of the way cells divide and how they age that will force us to be exposed to cancer. In fact, many have said that there's a dual relationship between cancer and longevity. We may alter our mitochondrial if you're an NAD+ person and so forth.

Dave: I am.

David: A lot of us are so we may alter our lifestyle and even our chemistry to live longer but that will have the effect of increasing the amount of time that our cells are waiting to mutate. Ultimately, your chances for cancer will just accumulate. If we are going to be successful in very high longevity situation then we will have to do better with cancer. It won't be diet that will save us from cancer. It's going to have to be detection and prevention and rapid treatment. We'll need that more and more as we age.

Dave: No doubt, if you live longer you have a greater incidents of cancer.

David: That's it, yup. Nothing that can change that completely.

Dave: When we talk about NAD+ there for listeners, when your mitochondria are making energy, you add electrons NAD+ and they could end up NADH and what's going on there is if you can change the ratio of those two molecules you can change the efficiency of your mitochondria and thereby have more energy right now which is one of the big topics of my upcoming book. Also potentially change your risk of the mitochondrial side of cancer at least that's what some of the research I've seen says. By improving the efficiency of the Krebs Cycle reducing oxidative species in the cells, it appears to have a cancer-reducing risk. For some compounds it even appears to make chemotherapy work better.

David: Chemotherapy is a hell of a toxic thing. All the organic fruit and so forth that you're eating has a little effect compared to the dramatic effects of the chemotherapy compounds that are commonly used to treat cancer and radiation of course again which is still commonly used to

treat cancer. One of the goals of cancer research based on our knowledge of the DNA and the DNA mutations is to try to get beyond some of these more toxic methods for treating cancer. If you're faced with cancer that is so much more important than the healthy diet or the NAD+. It really is important that we get to the point where we can have therapies that are precision targeted towards the cells that have cancer and have little collateral damage on the other cells.

That's been a major goal and it's a major hope. The Vice President has announced the moonshot and there's optimism. A lot of this optimism is based on the idea that maybe we can coax or induce your own immune system to fight off the cancer cells and this is an idea that's been around for decades but only become really operational within the last few years and has resulted in some spectacular results for certain types of cancers. We're still trying to understand why it works for those cancers and doesn't seem to work for other cancers at least in the incarnation we know about this immune approach we sometimes call immunotherapy.

That would obviously be a terrific approach to cancer if you can just get your own body to eliminate the cancer by targeting your immune system to it. That's terrific. Part of that in combination, a lot of people are talking about doing that in combination with crippling or killing many of the cancer cells. The immune system is drawn into a fight sometimes that is started by either chemotherapy or some other kind of targeted therapy and if the immune system can lock on and finish the job, that is terrific in cancer.

Dave: The immunotherapy you're talking about there actually saved my cousin's life. I wish I knew exactly what kind of cancer it was. I believe it was a brain thing, some kind of pretty aggressive thing. This is not a cousin I'm close to. It's wife's family in Europe but he flew to Israel and did a very advanced form of immunotherapy where they essentially in layman's term made a vaccine to some cancer cells, injected it and he's perfectly healthy with no signs of cancer today. This wouldn't have happened five years ago. It's just shocking.

David: No, it couldn't. It's spectacular. That form of treatment where you're actually using an inactivated virus or something like that to draw attention of the immune system to the tumor. You can do this with bacterial molecules that bacteria create or viruses. They do this in bladder cancer for example. They'll use these kind of molecules that activate strongly activate the immune system to then recognize the tumor. We're very interested in the actual molecules that the tumor displays that allow the immune system to distinguish the tumor cells from the normal cells. We know a lot about this from immunology. We know in fact that all of the proteins that are made inside the cell and make the cell work and do all its stuff are essentially ground up into pieces.

Some of those pieces are representative set of those pieces of protein are actually displayed on the surface of the cell as if to say to the rest of the body, "This is what's going on in me right now. Here's a sampling of pieces of my proteins." In a sense, the cell in your body is telling the rest of your body, "Here's what I'm about right now." Your immune system is acclimated to recognize those signals and it's constantly surveying your cells and saying, "Looks like this one is okay. Yeah, this one is okay." When a cancer cell comes along it gets DNA mutations and some of those DNA mutations then cause the proteins to be mutated and so you get little snippets of mutated proteins on the surface of a cell and that's what the immune system uses to recognize

that something wonky is going on on that cell.

A vaccine essentially functions to alert the immune system that this is the kind of thing you should be looking for in attacking the cell. This whole system evolved over millions and millions of years of evolution. For example if a cell gets infected by a virus, the virus will make its own viral proteins and those will show up as foreign proteins and then be recognized by the immune system and the cell will know to attack. It's a regional phenomenon so you want to get a hot zone around the tumor where the immune system is highly active. It turns out that in the last few years we've learned that tumors have these tricks for shutting down the immune system.

Everything in biology is about balance and so over these years of evolution actually human cells have evolved a way to say, "Hey, I'm in trouble. Hey, I'm really in trouble, you should attack me. Hey I'm only kind of in trouble, shut down the attack." That ladder message is used by cancer, the cancer will actually distort this natural biological process and make the cancer cells such that they are saying, "Yeah, I'm kind of in trouble but not so bad so don't really attack me." New drugs that shut off that signal are the most exciting thing in immunotherapy. They are trying to make so the cancer can't hide from the immune system anymore but it requires two things.

It requires the inhibition of these, "Don't kill me, I'm really okay," signals but it also requires that there will be at least something, some different protein on the surface that the cancer is displaying that the immune system can latch on to to distinguish it. Actually, that is from… I made this long story so we could get back to why we care about DNA sequencing cancer because we have programs about a dozen other labs now have computer programs where we can take a sample of your cancer tissue, sequence it in a DNA sequencing machine and then use computer analysis to infer what kinds of abnormal proteins are in the cancer.

What kinds of pieces of them might be on the surface and hence, what the cancer cell might be telling your immune system. We also look at whether it's sending out these special signals about, "Don't really harm me." If we can tell whether a cell is actually displaying that it's different and also maybe shutting down the immune response then we know that by reversing the shut down of the immune response, the immune system should be able to recognize it because it is displaying something different. If it doesn't recognize it, we could actually in principle customize a vaccine because we know how, what kind of different signal we need to train the immune system to recognize that cancer.

It's a very, very exciting potential coming up here. We're still years off from actual routine use of vaccine related cancer. Your cousin was in a very, very special program that's not routine in all hospitals. The new drugs, the so-called PD1 checkpoint inhibitor drugs, checkpoint blockade drugs which shut down this PD1 signal that the cancer is using to hide from the immune system are now in almost routine use for many different cancers in particular, melanomas. They were proved recently for non-small cell lung cancer and so forth. We are getting to the point where this is not exotic anymore but becoming part of regular clinical practice but before the vaccine stuff is regular, it's going to require more work.

Dave: There's a set of genes that have been identified that make people more prone to auto-immune conditions. They are on the HLA-DR. I'm one in four people who has a tendency towards auto-

immunity. I'm sensitive to toxic mold in the environment. I actually did a documentary about that because it absolutely just causes inflammation neurologically and throughout my physiology which also increases my risk of cancer and all. At least according to some of the stuff I've read it does. Now, that's irritating because my plan is to live to 180-years-old.

I said it was my plan. I'm doing everything I can to get there. I don't know if I will or not but I'm sure I'm going to do everything possible that normal people would never think about. How quickly am I going to be able to use CRISPR or some other technology to just go in there and get rid of those few annoying genes and some meaningful substantial subset of my cells? Over the course of seven years as I replace my cells, I can just be done with that.

David: Very interesting that you bring up the HLA genes because they are the scaffolds that actually hold the proteins to show the immune system. The HLA genes are amazing in the sense that they are generic proteins that will load on a small piece of random protein from some protein that's being made in the cell and then carry it to the surface and display it to the immune system. The immune system comes along and recognizes it by these cells called T cells. They are part of your white blood cells. The T cells have these receptors and they are constantly looking to see whether the peptide that's being displayed by your HLA molecule is of the normal kind or whether it's something weird that they haven't seen before. That is the key event in immunity. It's the key event in deciding whether it's okay or whether something is wrong.

Now, if something is wrong, genuinely wrong like a virus has invaded the cell or is a cancer cell then you want the T cells to respond. You want the T cells to go into emergency mode send out the cytokine signals and all of these other signals that say, "Something is wrong, we've got to start killing." This ultimately the killers so called literally killer T cells are very powerful in terms of attacking cells. It's a very powerful system but it also has to be carefully controlled and so the auto immunity problems that you refer to come in when there's a mis-adjustment of the immune systems so that you have propensity now for the immune system to make a mistake and think normal cells need to be attacked. Then, once your immune system starts attacking certain of your normal cells then you have problems. You may have arthritis if it's attacking the cells in your joints.

Dave: I had arthritis when I was 14 in my knees. I don't have it anymore but I did.

David: Yup, you may have multiple sclerosis if it attacks the sheets on your particular axons and your neurons and so forth.

Dave: I've never said this on the air but I am reasonably certain that I would have ended up with MS had I not radically changed my biology using the lifestyle and all the other things I've done. I've never been diagnosed with it but I could see what was going on in my nervous system with neurological inflammation. I'm friends with Terry Wahls, Minding my mitochondria and I am stronger now at 43 than I was at 23 because I'm aware of the problems and able to take action to turn that off. Most people aren't but I suspect I would have by the time I'm 50 I probably would have had MS. I don't think there's a chance in hell that's going to happen to me now.

David: Good. That's the most important thing is the health thing. I could say actually I'm stronger now

at 62 than I was at 43.

Dave: Good. Wow.

David: It's possible to keep it up.

Dave: That's powerful.

David: Mainly because I've started working out in the last five years. You get to a certain age and you think, "Oh my God, if I don't do something," I'm not really paying any attention and not really doing anything for regular health. Now I am but back to the immune system, I think it's not so much that you want to actually go in and try to genetically change your HLA molecules. I mean, every cell in your body has the aversion of HLA genes that you got from mom and dad and my suggestion is that you got to live with that. It's not going to be easy to change all those cells, they make up your whole body. You don't want to start changing your fundamental genetics.

Dave: Sure I do, why not?

David: Okay. Let's not go there right now, you may want to do that but that's not going to be the easy route.

Dave: Agreed. Okay, I'm with you there.

David: What happens is then there's got to be some particular peptides that these HLAs are expressing to your immune system in particular cells that where the problem is arising, right? There's some particular mis-recognition phenomenon that's happening, it's not all over your body. It's only under certain circumstances that these certain HLAs will produce an inappropriate immune response that causes autoimmunity. If we could target just that, just like we do cancer, if we can target that inappropriate immune response specifically without messing with any other part of your body or your immune system, that would be in my mind a more appropriate approach to autoimmunity.

The beautiful thing about this is now we have billions of dollars being poured into immunotherapy because cancer is a huge, huge topic. We are learning about the molecular details of the immune response at an outstanding rate because it's driving billions and billions and billions of dollars of investment in new immunotherapy drugs. Part of that we'll have and I'll make a prediction here that might be a little comforting, part of that will have the side effect of greater understanding and greater technology that will allow us to manipulate the immune system. We can imagine a world in a decade where we can measure exactly what your immune system is doing at anytime and we can say, "Okay, this looks great. All right, you had a cold two weeks ago and your immune system reacted to it.

It looks it's appropriately calming down, right, then so we're not having T cells that are reacting to that rhinovirus anymore, we don't need them," and it's great. What we want to be able to say is but if this is indeed the case we're starting to see an autoimmune reaction in certain tissues where you have these particular T cells with this receptor that's recognizing this displayed

peptide and that is an inappropriate interaction between the T cell and the normal cell. We need to stop that interaction. On the other hand you may also have a tiny, tiny cancer that's starting somewhere in your body and your immune system is not recognizing the abnormal protein.

These events are two sides of the same coin, in the one case you want the T cell to recognize the protein and the other case you wanted to stop recognizing or stop reacting to the protein. That's the autoimmunity case. Because cancer and autoimmunity are two sides of the same coin, the more we understand the system of how the immune system recognizes the peptides that are being displayed and the more we have technology to manipulate it, the better we'll get on both sides. I think the enormous investment is going to payoff within a decade where we'll be able to have more precise manipulation, more precise surveillance and then more precise manipulation of the immune system which could save you a whole world of pain in the future if you have an autoimmune disease and it's well worth the investment. I mean international investment in research.

Dave: It is one of the most important things you can do because this stuff affects at least one in four people and probably more than that if you look at just subsets like Hashimoto's and things like that that are almost rampant at this point. Now, I'm debating, I want to talk about the Global Alliance for Genomics and Health, the computer hacker side of me. I'm really intrigued at sharing this volume of data securely. Before we go there I've said I want to see if I can either freak you out or offend you given what you just said about immune presentation. One of the things that reduced my autoimmunity and I haven't talked about this on air either before but I just want to pick your brain.

Tell me if I'm crazy. When you're having autoimmune reaction you release a lot of antigens in your urine and there's discussing Ayurvedic practices of drinking urine and things like that that don't work but are meant to work via this pathway. However, when you take those antigens, collect them from urine when you're having an immune reaction. These are the inappropriate immune molecules. They are immune molecules created by an inappropriate response. If you present them to the immune system as foreign molecules you can make antibodies to your own antibodies and cancel them out.

When I have a big autoimmune attack I actually, now this is going to sound crazy, I didn't invent this, I will take the urine, I'll mix it with Lidocaine and I'll inject it through a 50 micropore filter into my muscle tissue. It presents those antigens. I can eat foods I couldn't eat before and I have a lot less reactivity even to the things I'm most reactive to. It seems to be working and it's like completely caveman level immunotherapy but I'm kind of liking my life. Am I nuts?

David: You're nuts. I'll tell you a story. Before I went back to graduate school I work at a ranch. It's an old family ranch. We've had it in near Paso Robles we had in the family since my 1920. My great uncle started it and he got ill and died and there was nobody really there to take care of the property. In between undergraduate school and graduate school I spent a couple of years managing the property, the farm, where we grew almonds and walnuts and dozens of different varieties of fruit. It's a little organic farm.

Dave: Gorgeous.

David: I had a hell of a time with poison oak, very reactive to it and being out in the field I was always seeming … It was seeming an annoyance and you couldn't get away from it. I was downtown one time when Paso Robles was a little town and not the wine mecca that it is today. I was talking with an old farmer there, Charlie Yearwood was his name. He did a lot of tractor work around the area. I had noticed him on a job burning poison oak and then actually driving his tractor into it to compact it and breathing this poison oak smoke. I just couldn't believe. That's the worst exposure that you can have.

Dave: You could die from that.

David: You could die from that. You could definitely die from that. The oils of the poison oak coming in and I said, "Charlie, how is it that you're not allergic to poison oak?" and he said, "I was when I was young. I had a horrible reaction to poison oak but I found this woman down in Paso Robles. Some people call her a witch but she said all you have to do is go out there in the springtime when the leaves are just about the size of a squirrel's ear and you just eat one of them. Come back the next day and eat another one of them, you do that for seven days, you never have a problem with poison oak again."

Somewhat the same principle, right, you're kind of overloading your system at some point and trying to get your immune system to switch. I don't know. I was stupid enough at this point. To think that this should might work and I was living there with my best friend Don and I went out one morning in the spring, picked the leaf, chewed it up. What the hell? Here we go, right. Got back home, spent the night worrying about it. Nothing happened. Got up in the morning, told Don what I had done and I said, "Look this is proof, I feel great.

This is great. Day one I'm tip top." I went down, ate another leaf. Second day I came back and so forth, went to bed. I woke up in the morning my whole system was swelled, my whole mouth was swelled up, my whole internal digestive system was on fire, I was a total mess. I got very little sympathy from Don, the only thing he said as I recall is, "I guess you don't know how big a squirrel's ear is, do you?"

Dave: This was all a joke to see if he could get you to do it.

David: Right. Charlie, yeah. Charlie's good joke. I don't know. I think you're crazy.

Dave: I have been called that before and I might sustained one or two biohacking injuries. I appreciate you both sharing the story and rendering your opinion there. I figured I was unlikely to do a lot of harm and I'm always curious. I think if it's not going to really, really cause permanent negative effects in my work, someone's got to be the guinea pig it might as well be me.

David: Right.

Dave: Let's talk about sharing the human genome because now that we've got this data and the data is relatively affordable. I just had my entire genome sequenced at HLI. I didn't have the results

yet but the full thing which is pretty cool that a mere mortal can get it done. It's still reasonably expensive.

David: Price is still coming down.

Dave: It is.

David: My genome sequencing.

Dave: How much is the current price?

David: The cheapest price is a couple of thousand bucks if you just get the machine to do it and without the interpretation and so forth. That's getting to be within range of larger and larger number of people and then of course if you just want to snip it. You want to look at the tiny fraction say one out of a thousand different positions that are the most informative positions in your genome, you can just go to 23andMe and 95 bucks I think you can get a glimpse I would say, a snapshot of some of the important parts of your genome. Whether you want the whole thing done or just a little bit, it beats the price, it can range from a hundred to several thousand dollars but these are not undoable numbers.

Dave: What are the big barriers of sharing this data? We have a world let's say where now thousands of people have their full genome sequenced then soon hundreds of thousands or millions of people. What are the barriers to doing this and what are you doing at Global Alliance for Genomics and Health to solve this?

David: When we did the first genome as part of the public human genome sequencing project we were very proud to be a public effort that was going to share all of our data. Really the day July 7th that we posted that, July 7th 2000 was the best day of my life, I mean it's the day I'm most proud of. We shared that first glimpse of our genetic heritage free and unrestricted as open source, open data on the web. That was part of the whole structure of the public effort that it was scientist all over the world just trying to help humanity making this information fully open and available so that we could most rapidly advance our medical research and our basic biology.

Let's face it the understanding of who we are. Evolution is the process that created our genome over billions of years from our distant, distant ancestors and the results of that are really the product of untold numbers of stumbles and triumphs by our ancestors through the eons. This is a fundamental script for humanity that has been sculpted by so much pain and triumph that you have to make it in our opinion public and something that we can now cherish and understand. What happens as we got now into medical sequencing, clinical sequencing is that the tendency is just the opposite, the tendency is to lock data up immediately and not to share. Part of that is just HIPA and the whole tradition of medical privacy.

Dave: HIPA, for people listening define HIPA?

David: Yeah, this is the Health Information Protection Act that make sure that when somebody asks about your medical information they don't tell that person unless it's you or a designated

relative so that people cannot go spying or snooping around on your hospital records. Now, there are very good reasons why we don't want to let arbitrary people have access to our medical records and the DNA is increasingly part of the medical records. We're not arguing that the DNA and all of the rest of the medical record should just be named public. The problem is that when you start to not even make this information available for research then you're losing an enormous opportunity and cancer is a great example.

We know that there have been mutations in cancer tumors from the very beginning and we know that there are untold millions of different combinations of mutations in those tumors. We will not be able to figure out the important ones that we need to develop therapies for versus the unimportant ones sometimes called passenger mutations that don't do anything. Unless we have a large number of cases to study. I often say that if you just have one genome you can't learn anything. It's only by comparing genomes to each other that the patterns emerge. Anybody who knows statistics also can understand that there's a signal to noise ratio problem when you have only very little data and a lot of variables, a lot of things to look at.

The genome is a classic example of that, there's three billion bases that can change. There are a lot of variables to deal with and in order to do that we need to look at a lot of genomes. The focus of the Global Alliance for Genomics and Health which I co-founded three years ago is to create a mechanism so the world can share these genomic data. There are certain types of genomic data that can be shared openly and publicly. For example it's reasonable that even if you don't share your genome that you got from mom and dad, your so called germline genome technically. You may still want to share the changes that happened in your cancer tumor because you're not going to pass those onto your kids, they are not private to you, they are like any other medical symptom.

We need to account for the frequency of all of these medical symptoms including the genetic variance as well as the other measured variance. We have a program right now that we're trying to push called the Cancer Gene Trust where we're trying to get people to share the genetic variance that occur only in their cancer and just publish them openly so everybody can research those. If we do this right there's no privacy problem there, the problem is that the general public doesn't understand the distinction. It's a scientific distinction, right, between DNA that's changed in the tumor versus DNA that's part of your cells that you're going to pass on to your kids. That gets complicated to explain that but if we can get that kind of thing to be shared that would be great.

Now, there are also are cases though where we want to share information from your germline DNA, information that you will pass on to your kids. Another project we have is a the BRCA challenge. You may know the gene BRCA. Many people know it because Angelina Jolie made the famous announcement that because she had a genetic variant in her BRCA gene that made her highly prone to breast cancer she was going to have a double radical mastectomy. That certainly was a wake up call all over the world to be the importance of this particular gene and the importance of genetic testing when it comes to thinking about and planning for your future.

The problem is that right now when women go in to get tested for BRCA, a very significant percentage of those women are told, "Yes, you have an unusual variant in the gene BRCA but it's

a variant of uncertain significance. Go away and worry about it but we can't tell you anything about it." What a horrible, what a horrible report for a woman to get and there's one and only one reason for that is that we haven't shared the data, we haven't accumulated enough observations of that variant to be able to decide whether it is associated with breast cancer or not. If we only been sharing the data we probably could be able to tell. The BRCA exchange is about getting the world to share that data.

Now, in this case we're sharing it with experts, we're not publishing it openly on the web. We're not asking women to publish their BRCA, full BRCA gene sequence that the same one they will pass on to their kids. We're not asking them to publish this, we're asking them to share it with the experts and let the experts help classify the variants so that everyone gets a better diagnosis. Those are two projects, one where you're publicly open, one that we're trying to at least share the genomic information with the experts.

Dave: In 2011 at the big data conference called the Gigaom Conference in New York I proposed a system like the one that you're talking about, a policy basis to expose some of your genetic or lifestyle information for instance your fitness tracker information so that you could share it with your community, you can share with your doctor, you sell it to a drug company, you can sell it without your name on it, you could associate different things, do it all by policy. Essentially create a marketplace for your data because a lot of people also react, "I don't want big pharma doing research on my genes." Basically most people that I know now kind of look at big pharma as not necessarily honest like one step away from big tobacco and frankly if they're going to patent one of my genes I get a cut or you guys don't get my genes.

David: That attitude has got to change. The solution to that is to prevent patenting and this is very relevant in the breast cancer area because there was one company Myriad Genetics that had the exclusive patent on BRCA gene testing and that was thrown out by the Supreme Court two years ago.

Dave: What a win.

David: Hallelujah. There's a step forward. I think the goal is not to keep information from the pharmaceutical industry but to make sure that they're not misusing it in the sense of exclusively patenting genes because we do need people to develop drugs. You're really going to cut yourself short if you completely cripple the pharmaceutical industry. I intend to take a less radical view of that but go ahead.

Dave: I'm speaking for a lot of people listening to the show and I have no fundamental problem with drugs. Drugs who save lots of people's lives probably including mine when I had a really bad infection or something.

David: That's right.

Dave: No problem there. Some of the business models and behaviors associated with these companies are ethically challenged. For instance we make drugs that reverse the effects of the pesticides that we sell from the other arm of the company. That kind of crap has to stop, Monsanto I'm

talking to you, all right. There's other disturbing things like that that I think people have woken up to and they're not willing to contribute to that system. If you put them in a hospital and say, "There's a tumor this big inside your head," they're going to gladly consume whatever cocktail of things is going to get rid of that. Assuming that it is a cocktail of drugs that are going to do it. We haven't talked about vitamin D in cancer, we haven't talked about ketosis and cancer, some of the other things that we probably won't get to in the time we got.

David: You have to talk to my brother about vitamin D, Mark Haussler. He is one of the major discoverers of the hormonal form of vitamin D and really, really is an expert on how it increases longevity and may help with cancer and so forth. He's devoted his life to the study of vitamin D, brilliant.

Dave: What's his name?

David: Mark Haussler, my brother, my older brother.

Dave: Would you facilitate an introduction?

David: Sure, I'll have him on. Yeah, he's great.

Dave: I would love to. I've been using vitamin D and looking at that in the various interactions with light for a long time. That would be fantastic. What a neat family. It must be amazing. Let's talk about what you're doing with the block chain which for people listening this is what Bitcoin uses and this is the idea that you can take data that you want control over who sees it and who does what with it. You can encrypt the data with the data that came before, the data that came after so you can sort of track whether anyone has accessed it or if anyone has messed with it. Do you have this rolled out for genetic data? Could I share my stuff today on block chain?

David: We don't have this rolled out. We're just working with the system, for the cancer gene trust we have one version that uses block chain and one version that doesn't use block chain that's even simpler but just as a start. What we want to do is make sure that we get people starting to share right away with a little overhead and just get it going and then add more bells and whistles as we go on. The block chain would be important for transparency, we're using it as a public ledger which you can record all of the transactions that have taken place. Simplest transaction is Sue decided to share this genetic information and Billy used that genetic information and then Bob shared this information and so forth.

All of these things being transparent and being available in a public record that can't forged or cheated or something like that is very, very important. In sense when you say share the data this is the other part of this, most people are thinking share the data with who and who has control of the data. What to share the data? We give it all to Google and they distribute it or we give it all to the US government they build a big database that the world can use and so forth? Most people are unhappy with those solutions, they really want something that's organic like the internet itself so that we are essentially posting that data onto a shared database that is essentially a globally shared database.

In that the block chain maybe one mechanism for keeping track of who does what in terms of submitting data and using the data. If it's transactional then you can actually use that to create an economy of the type you are talking about, right. You can keep track of who's using your data, you can get various types of feedback or even value back from the data. I'm highly discouraging of the idea of selling your genomic data at this point, I think that will hold research back.

Dave: Agree.

David: I would like people to first consider contributing data to science for the purposes of knowing that you did something good for the world.

Dave: I fully agree. I support that.

David: We run a pediatric cancer program and I'll tell you briefly about it. The Governor of California announced the precision medicine initiative. In California there was a serious competition for that about a year ago and of all the applications we were thrilled that ours was one of two that were picked. The program is called The California Kids Cancer Comparison, it is idea of introducing DNA comparison into the treatment of kids with cancer. A kid comes into one of the hospitals that treats kids with cancer and they're only about a dozen in California, less than a dozen in California. They would be referred from a smaller clinic up into one of these larger hospitals.

Even the case as the kind that there is a standard therapy that's very likely to work, in which case the kid gets this therapy or the child has a type of cancer that we really don't know how to treat or the child, the worst case is the child is coming back with a recurrent cancer that was treated before and now has emerged resistance or is re-surging again. Those are particularly hard to treat. The proposal to the governor and the state of California is every kid either the latter to the categories if their cancer is hard to treat from the get go or they're coming back with a second cancer. They should have their genome sequenced.

We should look at all the mutations in the tumor and try to come up with a precision medicine treatment for this child. This was accepted, we are well into it, we have three clinical trials which is a mechanism for trying to do creative, more creative things with treatment. One is in the Pediatric Cancer Group at Stanford with Alejandro Sweet-Cordero, fabulous pediatrician who works in the area of pediatric cancer. He's now invited us to participate in the weekly tumor boards that they have where we discuss the individual hard to treat cases. We present all of our genetic analysis along with regular cancer analysis and all of the best minds at Stanford think about, "Okay, what can we do for this kid who's failed the original therapy and now we're looking for an alternative?"

This is just an enormous opportunity to have an impact at this stage. What we're mainly suffering from into this and a similar program at UCSF and a similar program at UC Irvine, Children's Hospital of Orange County. We're all involved in these things and we're finding that the biggest frustration is that these kids have different combinations of mutations and there isn't a database out there that we can look up to find similar kids. I'm getting back to this, this is

why the Global Alliance is so important that you know there are other kids that have had mutations like this.

God damn it why can't we find them and understand what happen to them and allow it to treat the next kid. If we talk to parents do they want to share this information, yes they want to share this information and purely for the satisfaction of knowing that their child's struggle helps some other child.

Dave: Absolutely.

David: That's enough. They don't want to get paid.

Dave: Not at all.

David: They don't care whether a pharmaceutical company is going to make a drug out of it. They would like to just help other kids and they want to share this information. We are trying to help them share this information so every kid has a fighting chance, every kid can learn from every other kid who's ever had cancer. Obviously I get a little agitated about this but that's really important.

Dave: That's what this is about is helping people. A friend of mine Alexander Carmichael started a company called Patients Like Me.

David: Yes, I think it's great.

Dave: Okay, and I love Alexander, she's unique and she has autoimmunity, right. In fact I would argue she probably had mold exposure given all of her symptoms but she and I have talked about all kinds of stuff and I have no idea if mold is it or not. She's been very open about this, I wouldn't talk about it. Anyway, she said, "Okay, there's tens of thousands of people who deal with all these stuff everyday, why don't we get together and run our own trials because things are too slow." They did exactly the same thing but they didn't have the genetic data because this was five years ago.

David: Exactly.

Dave: What we're talking about now is patients like 2.0 with genetic data and you're putting the structures in place in a profit to facilitate, actually control for parents who have sick kids. Find the other three sick kids like this, find the genome therapy that work for one of them and maybe it'll help me. We owe that to each other as human beings, I support that all the way.

David: I love that line. Can we use that line?

Dave: It's yours to do it.

David: "We owe this to each other as human beings," that's exactly why we need to share this data.

Dave: That's the motivating factor for why I share all the biohacks I do too. No one gave me an instruction manual and I weighed 300 pounds and I had arthritis and all these other things. I'm irritated that I spent 20 years and almost a million dollars hacking it but hey I'm happy I'm here. It's been a fascinating interview and I've got one question for you, David.

David: Okay.

Dave: If someone came to you tomorrow and they said, "Based on everything you've learned in your life not just in your academics but in everything, I want three pieces of advice. I want to perform better at everything like I want to kick ass at everything I do. What are the three most important things I need to know?"

David: This goes back to the classic kind of response to the genome skeptics, right. The classic story is you get your genome sequenced and you get the total quantified self and you know everything about it and you ask the biggest guru in the world and he says, "Yeah, there's three things you need to do. Exercise, eat right and get plenty of sleep," "Thank you. I pay $30,000."

Dave: Those come up remarkably often as answers to that question.

David: Yeah, and this parable is actually had some essence to it that's important to understand is that the human body and or physiology and our health is a very, very complex process. We are only gradually starting to understand it and part of it is because we were working with it as a black box for so long. That those the previous medicine just simply was in this hopeless state, I'm not being able to open the box and see what's going on and we're only now starting to make that transition to where we can start to understand the complexity of what's going on.

In there it's still incredibly daunting and there's still lots of things we can't measure and there are a lots of modalities that we can't model. Until we get a lot more data and a lot smarter, it's still going to be difficult to give a very precise plan for maximum health. All I can say is the only way we'll get there is massive sharing of data, massive data of analysis and engagement of everybody. I welcome citizen scientist for getting involved and they've been shut out completely up until now. There was no way they can get access to any data that they needed. We need to bring the best minds to bear on this.

Dave: Some of those best minds are probably biohackers who are dealing with these conditions and are unwilling to keep dealing with it and I'm one of them.

David: Yeah, that's great. You have the strong motivation and brilliance and so we need to make an avenue through a global sharing and internet based infrastructure where we can share these data. Still protect the privacy of the individuals information but nevertheless share with individuals who can help.

Dave: David, where can people find out more about the initiatives that you're working and how can they support them?

David: Go to Global Alliance and Health, globalallianceforgenomicsandhealth.org, you can ga4gh.org is

the kind of the geek site. If you just Google Global Alliance for Genomics and Health, just Google that phrase you will get the main web pages. It's all about our projects and our leadership. We have an enormous participation more than 400 different institutes from 40 different countries are members and are participating. Our scientific advisory board is very illustrious, Francis Collins the director of the NIH here for example is on our scientific advisory board, just to drop one name there. We do have a substantial investment in data sharing at this point and if you're a geek you can go directly to the github site where you can see all of our open source code.

Anyone can participate, it's a classic open source culture, if you start actually making creative enhancements to the code all you do is … You can come out of anywhere. We don't require membership or anything like that but if your code change or pull request as they say gets thumbs up from three different other existing engineers on the project then it will be incorporated into the code base and you've now become a developer for the Global Alliance. This is the Apache voting rules of open source, right, three plus ones and no minus ones and your pull request is accepted. It's an open embracing, welcoming community of geeks that are trying to make a difference and we want everybody to join.

Dave: David, thank you so much for being on Bulletproof Radio today. It's been a very illuminating. I appreciate you taking a really complex topic and making it something that all of us can understand.

David: Thank you. All right, all the best with your health quest. We'll celebrate when you're 180 and I'm 200.

Dave: It's a deal.

David: Okay, thanks.

Dave: Thanks for watching. Don't miss out. To keep getting great videos like this to help you kick more ass at life, subscribe to the Bulletproof YouTube channel at bulletproofexec.com/youtube and stay Bulletproof.