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Robb: Howdy folks, Robb Wolf here, another edition of the Paleo Solution podcast. I'm very, very excited for today's guest. I would say that one of the large drivers of me being involved with health and getting a Biochemistry degree, getting into cancer and autoimmune research was actually a very close loss in my life with a 16 year old girlfriend that was also 16 years old at the time due to a metastatic brain tumor.

And so this has influenced my thinking right from the get go I still kind of keep a finger in that area a lot of the time that Squatchy and I spend throughout our week is actually involved with trying to match people with a variety of diseases including cancer with practitioners that will actually help these folks. And we find it incredibly frustrating because very few people are really knowledgeable about some of the unconventional methodology that exists out there.

And today's guest Travis Christofferson is the author of the book Tripping Over The Truth: The Metabolic Theory of Cancer. Travis, how are you doing man?

Travis: I'm doing fantastic. Hi Robb.

Robb: I have a really deep personal connection to these stuff. You know my girlfriend Stacey, she had an astrocyte brain tumor which she went through the normal rounds and found it grade 8 and then she survived until sophomore year of high school. Things were getting really bad, grade 9, went into remission and then came back full force.

And something that haunts me with all these is in my reading and understanding of say ketogenic diet and restricted diets for various types of cancer, astrocyte brain tumors have one of the variety that respond the best to these therapies. And I've got to tell you that it has haunted me and will haunt me to the day of my death. But I'm kind of rambling on

a little bit. Travis, give us some of your background and then we'll talk about your book and how this thing came to be.

Travis: First, your story, personal stories like that, it's hard to find anybody that doesn't have a very personal story like that. And you know I was just thinking about this the response, the burden is enormous for cancer. This year alone, 600,000 Americans will die of cancer. One in three women, one in two men will be diagnosed in their lifetimes.

And you know I was thinking about the response to this data is kind of funny well not funny but it's sort of highlights human misjudgments because I was just watching a Youtube video of Dr. Mukherjee The Emperor of All Maladies. And he was saying how since 9/11 we've spent 4.4 trillion dollars on wars because of the twin towers. The twin towers killed 3,000 people.

Every day the equivalent of one twin tower collapsing on society is how many people cancer kills. And like your story, it's not – we tend to think of it as disease of old people. It's not. It's a disease, it's leading killer of children. It's the leading killer of 30 something and everybody in between. Age groups 45 to 65, it's the number one killer ahead of heart disease, accidents and stroke combined.

So it is a disease of all people but it's an enormous burden on children as well. You get this sort of capitulation response, you got to die of something which is true. But cancer it's a problem. And it's a problem because just the fact how carcinogenic we've made our lifestyles. The price to pay for ease of existence is cancer.

Robb: So you don't actually have a cancer therapeutics background. Tell folks about your background. You have a really interesting background and then how you became acquainted with Tom Seyfreid and kind of the outgrowth of that story.

Travis: Sure, yeah. Non-linear is my background. After finishing my undergrad, I was awarded this private foundation fellowship for research. The largest one on the side of South Dakota. So I went on to graduate school. I was accepted in Med school but I decided I was really more attracted to the science.

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So entered grad school and then the non-linear part stepped in where I met a girl, started some businesses, two kids later and 15 years later is when I went back to grad school. And that's when I sort of found myself immersed in this scientific detective story with cancer because I picked up, I have three credits left, they allowed me to do an independent study class. And so I picked up cancerous metabolic disease, this masterpiece book by Tom Seyfried. And it just struck me between the eyes.

As you are a biochemist, as you learn, as every doctor learned, as I learned cancer is through and through a genetic disease. So all of a sudden I picked up this textbook that laid out this beautiful, comprehensive theory that stated that it was not genetic that it was perhaps metabolic in origin. And luckily I was at this time in my life where I could really pursue this. So I flew out to see Tom. You know I've read the book twice and compiled a list of questions. And Tom is generous enough to see anybody.

So I was in Boston, I met him in the hallway early in the morning and we started talking. And he had a graduate class to teach and so he invited me in. And I'm sitting in class and Tom has got a dynamic lecture. He goes through his gears and sort of works himself up into ladder. In the middle of class he stops and he goes alright, how many of you students have so and so from molecular biology. And half the class raises their hands.

And he goes now when you go in that class he's going to tell you everything I say is wrong. And that was the sort of epiphany moment for me, this is the book. At this world class institution, you can have these two brilliant minds that completely conflict about the origin of cancer.

And if you step back, the general public doesn't know this. They have this sort of impression that we've been at this a long time, we're mapping this critical details out, therapies are around the corner. But in reality the real science is in this incredible flux at the moment.

Robb: And you know – I'm just thinking so many things here. So I want to say it was 1969, 1970 that Nixon declared war on cancer.

Travis: Yup, 197…

Robb: And if you want to guarantee the perpetuation of anything, just declare war on it. Drug war, terrorism, whatever you know. That will solve the fucking problem. Just declare war on it and it's guaranteed that the thing will stretch into ad infinitum that will never be dealt with. But there was even some cocksureness that was thrown around like five years, five years we'll have this thing lit.

I think a lot of this was coming off of the success of antibiotics and vaccinations. We had really transformed the world through chemotherapeutics applied to infectious disease. And there was this thought that cancer was more a kind to an infectious disease than actually us and that it would be reasonably easy not to crack and that's been entirely wrong.

When you look at the data, it's been just somewhat stable across the board. When you look at rates within populations, cure rates and what not, and what you would just for earlier detection, it kind of looks like people are living longer but really we're just finding the cancer earlier and we really haven't with a few exceptions testicular cancer and some bladder cancers and a few other things, we really haven't made all that much progress in dealing with cancer and throwing billions and billions of dollars at the problem.

And from my perspective, that means that we're probably going after this thing wrong. I would say that after 40 years and billions of dollars and we really haven't turn the dial all that far, I'm going go out on a limb and say maybe we're looking on the wrong direction. And that direction has largely been you know genetic based elements and the chemotherapeutics that we have been applying has basically been trying to bugger the DNA of the rapidly replicating cancer cells and try to find a way of doing that you know and not kill ourselves in the process.

I really love the chapter that you have where it was talking about Watson, co-discoverer of the DNA molecule talking about how the sharpest people in Biology used to go into the Biochemistry side looking at metabolism. And that was true up until the point that they discover DNA and then all the hotshots went in to more molecular biology and DNA research.

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And metabolism has been kind of a redheaded stepchild since then. And I've heard Tom Seyfried the number of people mentioned that in the ketogenic diet kind of research world, Volek and some of these other folks, I'm forgetting the guy who was the grad student of Hans Krebs but the really deep metabolic research has kind of run a ground. And I guess my point with that is that you know our bestest and brightest may not be looking in the right place on this topic and may in fact be looking in a complete dead end street.

Travis: Yeah, I mean well said. That to me was the theme of the book right there, the most interesting part was you know the historical perspective of how we viewed cancer throughout the century and of course dictates how we therapeutically attack it. And one of the re-occurring themes was any given point in history when you're in a middle of the forest, you tend to get lost. And you tend to not – you have this perspective that we are on the cutting edge of technology, of course you are. But you don't know how wrong you are.

If we can get a time machine and go back to the Greeks, we would be sitting there and they'll be telling us cancer is caused by an abnormal amount of black bile, an imbalance in the humors and they'd be dead sure that that was the reason. And of course now we look back and this is silly but as we stand right now, we don't know how wrong we are.

And instead, you enter this sort of new realm of human misjudgment and how we get things wrong in a large scale. When we really tend to screw things up humanity, we tend to do it on a large scale. And so you're right. I mean we've viewed cancer as a genetic disease since the 19 – well most of the 20th century. But really in 1976 is when it got locked down, a series of experiments just drew the sharp conclusion that it's a genetic disease.

And so we've been attacking it through the paradigm of targeted therapy since then. And it's not hard to look at the data to see how disappointing this approach has been.

Robb: Just compare it versus antibiotics. Just as a baseline. Compare it versus aspirin dealing with a fever.

Travis: Right, exactly. And so many diseases are like I said in the book, they're just presented to us in such a simple way. Aspirin you know inhibits one enzyme to bring down fever and inflammation. And cancer is this complex beast that clearly it's hard to know where to begin. But we thought we had it mapped out because we found certain genetic anomalies that we can target.

And so we've been at this for a long time this paradigm of targeted therapy and to date, over 700 targeted therapies have been developed. And only one, Gleevec has been a real homerun. And most of them have marginal efficacy at best. You might get a month or two, some offer no increase in survival at all. And so that was the question of the book, to me why are we losing the war? And there's no doubt we're losing the war.

And the conclusion that I came to or you know that I presented was perhaps we've mischaracterized the nature of cancer that's not exclusively a genetic disease. It might in fact the origin might be more metabolic than genetic. And so if that's the case and we've lost two decades of chasing you know betting on the wrong pony.

Robb: Travis, you mentioned Warburg here, what's kind of the insight of Warburg's research with regards to this potentially metabolic underpinning of cancer?

Travis: Otto Warburg was this brilliant German scientist that did his work right at the beginning of the century 1900s. And he existed in this time of the scientific golden age where he was a member of this institute the Kaiser Wilhelm Institute of the Advancement of Science where they would deem certain people worthy of getting membership status and then they just shower him with zero responsibilities and almost unlimited funding.

And you contrast that today with an American scientist who spends over half of his time fighting for grant money. These guys were just allowed to think and do research. And so he was remarkably productive scientist. He was nominated for the Nobel Prize three times for three separate achievements and these guys were viewed as rock stars back then.

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So Warburg, he wanted cancer to be the thing that he attached to his name forever. He wanted to find out the origin and hopefully cure it. And so when he turned his attention to cancer, the first thing he noticed was his metabolic anomaly that cancer cells produce lactic acid in the presence of oxygen. And this is something that normal cells never do.

So if you remember back to your biology 101, the cell can produce energy in two ways. It can produce energy aerobically with oxygen and this is a highly efficient method of energy production. It's 90% of the cells energy is produced this way or can produce energy anaerobically through a very inefficient pathway that produces a waste product lactic acid.

And so Warburg noticed that cancer cells in the presence of oxygen reverted to this antiquated pathway of anaerobic energy generation. So the question is why. And then throughout the century he had more experimental evidence that led him to conclude that there is an injury, the cell had an injury to the ability to produce energy aerobically and this was the prime cause of cancer. This injury to we now know is mitochondria and it can reversion to anaerobic energy generation.

So he made this simple observation and until his death he staunchly believed this was the prime cause of cancer. And as a century wore on more evidence accumulated for a genetic theory and Warburg's theory was cast aside and almost ridiculed. But then as you know it sort of behind the scenes the evidence built up and built up.

Robb: Could you explain a little bit how – this is where correlation and causation or chicken and egg type stuff come in because as my understanding of this has grown over time, it's damage to the mitochondria that then causes kind of a cellular stress response and it's kind of almost a microevolutionary process where the cell then start shuffling DNA like crazy trying to figure out a way to survive.

And this could be the oncogenesis kind of process. And so we do end up having all kinds of aberrant effects in the DNA but is that the causative factor or is that an after effect of the mitochondrial dysfunction. And that led into chemotherapeutics. What was kind of the process of folks thinking about okay, this is DNA related so we're going to find things like cisplatin and taxol which really aggressively attack DNA. And we're going

to go after these hopefully rapidly dividing cells and this is going to be a wink. Could you talk about that process a little bit?

Travis: Yeah, the first chemotherapy drugs they're largely indiscriminant poisons. And they were born if you remember from the book they were born out of this accident in the Bali Harbor in World War 2. And what happen was the Germans bombed the allied forces and unknowingly released the contents of one of the ships which had 120,000 pounds of mustard gas.

And so this horrific scene right went on throughout the night where all these soldiers were burned and lost their sight and of course the high command knew what was going on. They knew that this mustard gas spilled but there is this tenuous agreement between the two sides to not stock pile mustard gas but each side was stock piling it just to be ready.

And so they flew in an expert and he gathered samples from these soldiers. And he took them back to the United States to Yale and when they analyzed the tissue samples they noticed that the lymphoid tissue was depleted. And that's the tissue that get's packed with rapidly dividing cells from lymphomas. And so they began this conjure up this sort of crazy idea that well maybe this compound can be used as a chemotherapeutic agent. And up to that point there was not one.

Before that there was only two ways to tackle cancer which was surgery and radiation. And so desperately people wanted, doctors wanted a third line where they could get two cancer after it metastasize or of course to the liquid cancers like lymphomas. And so they tried it and low and behold they achieved this flickering remission and it worked. And so that began this process of looking for agents that just like you said they went out after cell division. That was the only functional difference that they do between cancer cells and normal cells was this rapidly dividing behavior.

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So born out of that rudimentary logic was this chase to find this indiscriminative poisons that just inhibited cell division and that's how we know chemotherapy today this cisplatin like you said. And what they do is they go through the cell and they lock up DNA. It covalently binds DNAs

so it can replicate. So of course it's indiscriminant and it does it to all the cells in the body…

Robb: Mucosal membranes, hair, all those silly things.

Travis: Right. And that's why we know the side of chemotherapy that we know today is still largely associated with all these side effects. But yeah it was born out of a very rudimentary understanding of cancer. And then it morph into this huge government effort to find more and more. And the hubris of like you said earlier the war on cancer sort of merged with these new drugs. And they went too far. I don't think anyone would argue that what the NCI morphed into in the 70s was a trial and error and sort of a mass scale.

But they ran into a stumbling block when they try to do real hard cancers. Of course they fell, some of the easy ones like testicular but when they try the real hard ones, solid cancers they ran into a stumbling block and the efficacy of those drugs was realized.

Robb: So we've kind of gone through this process where we had surgery and radiation and then we found these largely indiscriminant you know, buggerers of DNA replication. Some of them interpolated DNA and sliced it up when it's replicating, others just lock it up and make it inaccessible for replication. You can't unzip the DNA.

And then we've been moving more towards this promise of targeted therapeutics and maybe even looking at the genetics of the individual and the genetics of the cancer and then trying to find some targeted therapeutics from that direction. But unfortunately, I forget the title of the paper but it was describing one woman who had a stage two or stage three metastatic breast tumor.

And it moved throughout the body and when they started looking at the genetics of these cancer cells, it was as if there were 50,000 different organisms. It was not hey cancer, it was cancers. And these different like you literally – there was enough difference between these cells that you could have speciated and separated them out. And so this is one and still is interesting to me because that information seems to get very, very little airplay but they're still a lot of talk about targeted chemotherapeutics and clearly lots of companies, lots of people, the

government have enormous amount of money and reputation you know kind of driving down these directions.

Slowly hearing some story about immunotherapeutic interventions which I find interesting because our body does clear cancer reasonably well when all those systems are functioning. And so it's always been a little bit curious to me that the immunotherapy side even some of these things I think like the COX vaccines and stuff like that where you get the immune system fired up in general. And then you might get some other therapeutic effect.

But for me, reading that paper and again it depends cancer to cancer but it really looks like once the cancer cells start getting into this microevolutionary stage that you are never going to track down a chemotherapeutic, it's kind of the problem with the flu virus to some degree. Influenza virus replicates or mutates in such a rapid rate that the likelihood of getting an immunization that fits exactly with the variety of virus that's out and about starts decreasing rather rapidly. And you know the efficacy starts dropping off.

So you do talk about that a bit in the book. What are your thoughts on that as far as this targeted chemotherapeutics? I know a lot of people hang a lot of hope on that. I just think it's pretty much a dead end.

Travis: Incredibly important. Right. And I've noticed a rift in the community between about that topic. Even if you believe in the genetic theory of cancer, you're right it leads you down this cul-de-sac. And there's two from this massive government project called the Cancer Genome Atlas which began in 2006. And the goal was to sequence the genomes of various cancers and compare them to normal cells thereby cataloging all the mutation anomalies thought to precipitate and drive the disease.

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And luckily in 2006 the sequencing technology had got to that point where we could do this. It's almost science fiction the fact that we can even do it. So if you step back what researchers were sort of expecting to see when the sequencing began was the sequential model of tumor evolution. And doctors in the clinic had noticed for a long time in the 80s,

90s that cancer didn't just appear. Right? It went through this graded series of steps.

And then they attempted to match genetic anomaly to each step. And what they found hinted that there are certain genetic anomalies that draw the cancer step by step towards full blown malignancy. So as the sequencing machine started in 2006, that's what they sort of expected to see was this each cancer would have this sort of finger print that defined it.

Now instantly, right away the first year they noticed that model was a scrapped. And it was because of this phenomenon called intertumoral heterogeneity. And all that is is a quantification of variability from patient to patient. When you sequenced a tumor of one patient and compare it to the next, you see like you said this astonishing degree of variability. So that's one problem.

Now the second problem and that's even more ominous is the phenomenon called intratumoral heterogeneity. And that describes the difference in genetic anomalies from cell to cell within the same tumor. And this intratumoral heterogeneity that leads us down to sort of therapeutical checkmate, one reporter described it trying to cure cancer that way is a game of whack-a-mole. Because if you do find the target within one patient, there's likely a mutation within the same tumor that renders that drug ineffectual.

Robb: And then you just selected for this more aggressive variety of tumor, more robust variety of tumor.

Travis: Right. It's just cancer is clonal in origin so as it grows it morphs, expands in to this increasing complex monster. And it's just the nature of these genetic mutations that they get scrambled in a way that it scraps the approach of targeted therapy. But there is this rift in the community I've noticed like Dr. Mukherjee who wrote The Emperor of All Maladies, this widely influential book and I just saw a Youtube video where he was talking to Washington policy makers how to move forward.

And his idea was to just we got to keep going down the genetic path. We have the sequence, target, sequence, target. And there's others within the same community Dr. Watson is one who said we can't do that. It's

just we're thrown into a therapeutical checkmate to keep going down that pathway is futile and others have said the same thing.

So there is this kind of growing disagreement on which way to go. And you're right, looking at the data I don't know how you would ever attack some of the more complex cancers through targeted therapy.

Robb: You know, it's interesting this maybe gets a little bit far down the rabbit hole or off to another side but the whole evolutionary process has been this seemingly very, very complex story. And one of the things that has made a lot of sense for me with that is this guys Stephen Wolfram who developed Mathematica. And he's really kind of championed this idea of cellular automata which it's these very simple rules end up going together in a way that creates incredibly complex patterns and systems.

And when you think about it we've really tried doing the reductionist, tear it all apart to understand it at least on the genetic side. But it looks like that is like trying to catch quick silver in your hands like it just forks right out and it's off and running. And you know I think to address that is it possible to make sense out of this complexity part of the book. For me it's take a big step back and looking at the metabolic factors the metabolism is not going to change at the rate or the complexity that the genes change.

Substrate utilization, you know we're not going to magically start using mercury or something as a reducing agent in the cell. Probably not, not at any time really quickly. So we have to meet the potential of looking more at the metabolic side and also the immunology side, we have kind of a macrosoft focus kind of look at this process which interestingly I think offers a lot more therapeutic potential on the long run. What do you think about all that?

Travis: Exactly. When you view cancer as a metabolic disease, one of the beautiful things is that all of a sudden you're not targeting this morphing mass. You're targeting one problem which according to Seyfried is damaged mitochondria.

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And so you have one target and you have the defective metabolism. And you're right, I think in the end what this will look like is attacking this for many angles. Just the first few attempts to attack cancer metabolically, of course Tom came up with this idea the restrictive ketogenic diet. And now that it's metabolic, it's thrown into your world. Diet, nutrition, so many other ways that we can manipulate cancer.

In the restricted ketogenic diet, it's beautiful in concept for a cancer cell because a cancer cell has damaged mitochondria. And the data to me is just clear about this. You can look at cancer cells in vivo and just count the mitochondria and invariably the aggressive ones have less. They have about 50% of their mitochondria. And the mitochondria that you do find are rife with a host of abnormalities, proteins, fats. They're not right.

In Biology, structure equals function. So when the structure is that altered, it's clear that the ability to create energy aerobically is altered. So the ketogenic diet restricted, all of a sudden when you drag down blood glucose. And that is cancer cells that is their preferred fuel. They have this voracious appetite for glucose and that's what you see when you look at a PET Scan is their insatiable appetite for glucose.

And then at the same time you raise ketone bodies which have to be burned in functioning mitochondria. They have to be burned oxidatively which is something cancer cells don't have. So you put the cancer cells in this tremendous energetic stress. And also you put it in an oxidative stress because it has to use glucose to generate an intercellular antioxidant called glutathione. And when it can't do that the cancer cell is left uniquely vulnerable to free radicals.

And like I said in the book Watson had this epiphany moment 2012 when he realized that the generation of free radicals maybe way, way more important to cancer therapy than we've ever thought. And then maybe one of the best avenues to get to the cancer cell because they are purged in this oxidative state of chaos.

And so this diet when you look at it it sort of preps the cancer cells in super unique way where it's left in its vulnerable state while at the same time it turns healthy cell or normal cells in to this robustly healthy state

that packs them with glutathione. And they're energetically they're pack with ATP.

And so there has been, there's been clinical studies in humans where they put people in a state of ketosis and then they give them chemotherapy. And the side effects that you can measure the objective ones nausea, I'm sorry vomiting, hair loss are al diminished. As are all the subjective ones like tingles, neurological problems, things like that.

So it appears like this diet is able to uniquely diminish side effects well at the same time leaving cancer cells in this vulnerable state. Exactly. And that's just the first attempt. That's a first sort of paradigm of targeting metabolic damage in the cancer cell. And there's other ways and they'll come fast but it looks at this point to be extremely promising avenue.

Robb: One thing that's fascinating to me and you know, when I saw Tom Seyfried I'm thinking like 50 things here and I want to spit them all out. To figure out which one it is I want to say to you.

Travis: You've been out with Tom for a long time. You've interviewed him 10 years ago, is that right?

Robb: I interviewed him in 2004 and we published it in the Performance Menu in 2005. So I didn't even know that he was speaking at AHS in Boston. And so I showed up at that gig and then saw the speaker's list and I was like oh my god. And I literally I think I stiffed arm an old woman to the floor. Like get out of my way honey. And ran up to the podium and I don't know if I scared him. Probably if he was carrying a concealed weapon he might have tased me or something.

But I was just you don't understand like you literally are one of my life's heroes. You know once a week Google alert you're seeing what this guy was up to, what he was publishing and all the folks that he collaborate with. And like you said when he speaks he just gets so spun up on this stuff. But it's fascinating to me that – my point here is we don't want to perpetuate quackery which you know there's lots of stuff that could potentially fall into that category as you know like governing body.

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And for physicians and what not, where do you draw the line between trying things that have maybe sort of a mechanistic potential versus this is just preying upon people's ignorance and all that stuff. I get that there needs to be a quality control within all that story. But it is almost impossible to get an okay to use a restricted ketogenic diet as a first line intervention or as a co-intervention with more traditional therapeutics. And I just find that incredibly frustrating.

Again the times are changing. That stuff is all morphing as we get more information and so that stuff will change. But it's incredibly frustrating to me. Part of the argument that's made with this is that people won't change their diets to do this. And I agree, a lot of people will not.

But would it be unreasonable to say hey, there's this nutritional approach and then maybe plus something like Low Dose Naltrexone which is this modulator of opioid receptors and also modulates the immune response which also has this really interesting effect on cancer. It seems to be both cancer and autoimmune disease interestingly. Is it just crazy to try these interventions which have very low side effect, very low risk as the first go. Like is that a crazy proposition?

Travis: You know that's an interesting area. And anytime you bring diet to the table with conventional western medicine, it instantly gets lump into this debate. And there's no doubt the restricted ketogenic diet, how it's going to work best. It's got to be done in a clinical trial. And diets are brutally tough as you know for clinical trials it's because compliance is hard.

But luckily you can measure ketones and glucose. So you do have some tangible variables that you can measure. And there's a lot, there's nine I think currently recruiting. And a lot of them do they combine the diet with other therapy so we will answer soon enough. But at this point right, what do you say to somebody who's just been diagnosed with glioblastoma? They're going to die.

Do you say hey, well this thing is not proven yet. Or do you say hey, go for it. Chemotherapy might give you a couple of months, the standard therapy. So you are, you're put in this moral dilemma and physicians are and as I highlight through the book there has been case studies with the ketogenic diet but there has been no large scale clinical trials but they all

allude to that the diet does slow cancer growth. They strongly, strongly suggests that.

And so if somebody is dying, I think it's the right thing to do is to give them that option. It's free. It's not going to hurt you. So why not put it on the table if you want to do standard therapy or forego standard therapy which is I probably, debatable whether it's worth it or not for some diagnoses. And again other ones like testicular cancer, you'll be crazy not to do the standard of care because it works. But you can do it with the diet in hopes of mitigating side effects.

So yeah it's a tough line and Tom has certainly been has its detractors. And he has a lot of people that would lump him into the quack community which is unfortunate because he's anything but. And if you just read his book and you walk away with a ketogenic diet, it is the most important part of the book you missed the whole point.

Because the book is about what is the origin of cancer. And until we pin down the exact molecular events that start the disease, we're really not going to be able to design therapies that work.

Robb: Travis, so if somebody is – again one of the things that I actually spend a remarkable amount of my week and Squatchy helps me with this, we are deluge with folks. And you get these just gut wrenching stories of I've got a glioblastoma, I've had a malignant melanoma whatever the case is and I just want to try something different or I want some sort of a supported you know intervention.

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And we've got the Paleo Physicians Network. That thing is largely on you know, no QA QC on it like I don't really know how folks practice medicine in that scene. But we do the best that we can trying to match some people up with oncologist, rheumatologist, folks that are at least open to and a little bit knowledgeable about some of these other approaches.

But can you think of some hot beds of where people could go if they want to give something a different shot? I mean clearly reading your book is a great spot for folks even if they want to jump right back into the

intervention site which you have in the appendix talking about how to put together restricted ketogenic diet.

But can you think of anywhere you know a clinic? It's not Cleveland clinic, it's not scripts, it's a place where there's a group of people – so I'm asking that question then I'm going to do a little side here. This is one of the interesting things and I'm going to toot my horn a little bit here about this especially health place.

Everybody in that clinic, all the doctors, all the nurse practitioners, all the PA's they get this whole Paleo diet gig. They get this evolutionary medicine gig and we're on the same page with you know sleep, food, exercise, ketogenic diet maybe therapeutic here. They may be inappropriate there. Gut biome, resistant starch blah, blah, blah and I think at that to some degree why we're going to be able to go out and kick a bunch of people's asses with this. And I hope a lot of people. But I don't see anything like that specifically cancer related. Where do folks go?

Travis: Right. I do not know the place like you said where it's just about that. But in appendix B I listed the doctors that I did know that are treating people, are helping them implement ketogenic diets and maybe hyperbaric oxygen with it which has been shown in a very good study with metastatic mouse samples where the ketogenic diet, the restricted ketogenic diet alone slow the growth of the cancer by 56%.

And when you combine it with hyperbaric oxygen, it went up to 80%. And the reason for that is simple. As I said earlier, the cancer cells put in the state of oxidative stress. When you saturate the body with oxygen pressure, you sort of tilted over the edge. There's enough free radicals to kill of the cancer cells. They can't fight it.

It doesn't take a lot of internet search to find stuff about the ketogenic diet cancer. But to do it right and how to do it best like I said those things haven't been mapped out yet and as you said this holistic approach where it's all about the gut biome diet and all these things are inter-combined no doubt because if cancer is metabolic in origin then now it's all about the mitochondria.

And everything you're talking about is about restoring mitochondria. Intermittent fasting or just a good diet, low carbohydrates stimulates mitochondrial biogenesis. And so that falls in to the prevention area. That's the way medicine is going without a doubt.

Robb: Travis, in this kind of Paleo land scene I would say that low carb diets were very much the vogue for a long time and then we started looking at some issues like adrenal fatigue and thyroid dysregulation and maybe people are doing a low carb diet wrong or maybe they were doing it right. We still again you know lots of anecdotal stuff not any type of clinical trials and probably never going to see clinical trials to fair it that stuff out.

But what in your mind is – is there an argument for doing three months a year of a ketogenic diet? Doing a block of time each year where you're doing some intermittent fasting plus a little bit of a calorie restriction or ketogenic diet. And all of these again has to be overlaid with the caveat here. The people that I've seen that are willing to do these more onerous interventions are doing CrossFit six times a week and CrossFit endurance on the weekend because that doesn't count because it's just endurance work. You know they're just type A nut cases.

And so those folks, the ones that I actually see that are generally willing to do this or willing to do everything and typically do and then it ends up being too much but you know the people who should be doing this somewhat sedentary desk jockey it's kind of hard to get him to do it. I mean what do you think about all that stuff?

Travis: Yeah, I mean how do you get somebody interested in their own health? It's got to come from them you're right. And to go back to the idea of what's the right approach, Richard Veech was a scientist you alluded to earlier that was the student of Hans Krebs who was Warburg's student.

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Veech is this brilliant Biochemist and his mapped out biochemistry behind ketosis more than anybody. And you know he's quoted in the New York Times article saying it's normal to starve occasionally it's not normal to have a McDonald's and a delicatessen on every corner of every street. And periodic fasting or fasting, the only thing that's been shown to increase the longevity curve and you find that this a periodic fast is

incredibly restoring. You induce this thing called autophagy where all the sudden your cells digesting all of its defunct proteins and even in whole organelles like whole mitochondria that are damaged will get consumed and digested. So this incredibly restored of cleaning out process.

And Dr. Seyfried has maintained that the best way to prevent cancer is just do an occasional fast. And he said, I heard him say once in seven days because that's when he did a math from a mouse model to human to equal that the benefit they assigned mice, you have to do seven days as a human but then he sort of retract it. He said you could probably get the same benefit by doing a two to three day fast maybe twice a year.

And evolutionarily right, I think it's of safe bet to say that humans had tough times getting food once in a while. So it's not normal to be just saturated with food all the time. So I think it's safe to say that this idea of occasional ketosis or an occasional fast is an incredibly healthy thing to do.

Robb: Right. I'm really glad that you mentioned – it's something that you said made me think about the energy throughput of this whole system. So if you do some poking around, cancer is very tightly related with insulin levels. And there's some theory out there related to obesity is only an insulin driven, if you keep insulin levels down and the amount of food that you consume is kind of irrelevant and I've kind of been in that camp.

And then I've had what I deemed to be my eyes open and you know it's actually you know macronutrients matter but total chloric load matters. But my best understanding of the development of type 2 diabetes specifically and this is what's really, really interesting to me is that it becomes a metabolic dysfunction due to the body trying to figure out how to deal with a toxic load of nutrition.

It's literally trying to – first you see the body temperature go up in these folks and then you see all kinds of reshuffling, repartitioning and people start gaining body fat and that is an attempt to just basically sequester nutrients in a low metabolically active tissue and reduce reactive oxygen species and then at some point, the signaling mechanisms and that whole process are lost.

And even though the individual is a wash in nutrients, deliver things that it's starving and so it's pumping out glucose, it's pumping out triglycerides. This is combined with the dietary glucose and triglycerides and things kind of go to hell rather quickly after that. But when I look at some of the mechanisms there, it looks stunningly similar to the mitochondrial damage that occurs and potentially some of these cancers.

It's still intriguing to me like childhood cancers. Like some of these leukemia's and is that more of a xenobiotic you know xenotoxins kind of deal that's damaging the metabolism or was that something possibly in utero or what's the story with that?

But that aside, it's interesting that I see some parallels between these over nutrient flux flowing into say like metabolic derangement in type 2 diabetes but also just sniffs really similarly to me to the mitochondrial dysfunction that occurs from two great a throughput a constant throughput you know not really letting the machinery rest and retool itself in some sort of a fasted state.

Travis: Yeah. Exactly. And the overlap is where this gets interesting. And like you said diabetes type 2 is a huge problem. I think right now it's one in 10. And the curve if you extrapolate it, it looks like it will go as high as 1 in 4. So it's a modern plague and right like you said it's just probably due to this constant consumption of too much food.

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And the way I view the insulin the response kind is it's kind of a 911 call that says okay we have an abundance of food, let's eat and store fat so we can get through a lean season. But certainly it wasn't meant the signaling pathway wasn't meant to be on all the time. And that's when you run into these problems obesity and type 2 diabetes.

And incidentally obesity rates correlated with higher rates of cancer. And diabetics, high blood sugar levels correlate with higher rates of cancer. And the drug Metformin which is used to treat diabetes incidentally surprised everybody when they found out it caused a reduction in the probability of getting cancer.

So clearly all these things are overlap and are very related. And it's going to take time to sort them out. But the general principles I think we can safely say are already been mapped out like too much insulin like you said is clearly a bad thing.

Robb: Travis, what have we missed? What did we miss on this thing? For folks that I just recommend everybody read this, all the listeners read it. Buy two or three copies to keep handy because the unfortunate reality as Travis alluded to at the beginning of the show, we all know people who are affected by cancer. Maybe we ourselves are affected by cancer.

The book is technical. It covers the technical grounds spectacularly but it's incredibly accessible. It's written in kind of a story format so the technical pieces drop in amidst the framework of the very, very well written story like I'm very impressed by the whole book. But primarily from a geek standpoint it really spun my wheels that way but then from a fellow author I was really impressed with the story quality of the book. And it just makes it incredibly accessible. But did we miss anything? Is there anything else that you want people to know?

Travis: First, I'll thank you. You saying that means a ton to me. I just hope – the ideal outcome for the book for me would be to hopefully just stir this debate to get to this core scientific issue about what is cancer? And we get lost in the woods. I mean when you type in cancer to a PubMed search, you get 2.8 million hits. So we've beat this disease to death experimentally. And all these things just create a sort of lose image of cancer where we still have not gotten to the core.

And until we do, we're not going to follow the right drug design. It's just absolutely important that we elucidate these seminal events that are the cause and whether it's metabolic or it's some chimerical monster that combines metabolic with genetic, we have to get to that before we go forward.

Robb: And you know some of my thoughts along that line, we really need to give up this idea of a magic bullet. Like there's probably not – even the restricted ketogenic diet itself is probably not the end of the story. It is but a part of the beginning and we need to look at immunotherapies and combined therapies like hyperbaric oxygen plus a restricted ketogenic

diet plus possibly standard chemotherapeutics used at remarkably lower levels just act as reactive oxygen species generators. There's just an enormous opportunity with that.

And there is a reality that there would be a lot of people who would be unwilling to take on the lifestyle changes necessary to enact this and we need to be okay with that. But god we also need to be okay with providing this opportunity for people. Like if you want to try it then absolutely god damn it we're going to do it and we're going to check this stuff out.

We definitely need to vet the science. We need more studies. But when we see the numbers such that they are I think that we also need to provide a little bit more latitude for our boots on the ground practitioners to look at some of these stuff, look at plausible mechanism, try intervention and to keep very good clinical notes on what the outcomes are and that also is going to very powerfully steer what direction we should take our randomized control trials.

We have an opportunity to have tens of thousands of laboratories occurring in parallel instead of waiting for laboriously you know moving political entities to make a decision about what direction this stuff goes. And I really think we need to decentralize it.

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Interestingly when I'm describing that it sounds a lot more like the evolution of cancer. Then you know it's interesting so we need to use some of the very things that make cancer so effective at what it's doing and apply that to the solutions in trying to help people.

Travis: Well said. Absolutely right. I couldn't agree more.

Robb: Thank you and Travis, just very stoked that you wrote this book. It's fantastic again the title is Tripping Over the Truth: The Metabolic Theory of Cancer by Travis Christofferson. We're going to have that prominently in the show notes. This is also going to become the first book which is permanently affixed on the front page of robbwolf.com. Not even my book, I don't even think I have a link to my book on the front page of robbwolf.com.

So this thing is going on the front page. And again maybe the metabolic theory of cancer applies to some cancers, maybe it applies to all cancers. But we've really studied the other story pretty extensively and so I think like you said we need to start having the discussion, need to be open to thinking about these things in a different way and we don't know what the end story is.

And I hope that folks don't take from our conversation that this is being presented as the end-all, be-all. But hopefully it's some place to start looking in a different direction.

Travis: Exactly. And Robb, thank you for everything you've done. I put you in the acknowledgements because there probably wouldn't have been a book if you weren't brave enough to publish the article that I wrote a long time ago that you know kind of kept me going when I needed to.

Robb: That's awesome. Well you know based off that article we had feedback from people that are undergoing cancer treatment and on their own and in work with their oncologist they enacted restricted ketogenic diets. And again these are anecdotal reports. We need more than that but these folks, they got notes from their oncologist saying hey, I'm very interested by these stuff. And they ended up buying Tom Seyfried's book and reading about this.

So your article could have saved lives already. And so that's really powerful stuff. And when you – I'm 42, theoretically about the halfway point of this life you start thinking about legacy and what you do and how it affects the people around you and what you're going to leave to the next generation and the world after us. And this is some really powerful stuff. If we could start looking at this disease process in a different more efficacious way then it could really benefit a lot of people in that change.

Travis: Yeah, I've been thinking along the same lines. I'm 43 and I've been thinking legacy. And you just hope that what you do is in that benefit in the end. And it's tough to say but it's just it's all you can hope for.

Robb: Yeah. Well we'll keep fighting a good fight. And hopefully, ironically just getting people to have a conversation shouldn't involve an Irish beer brawl, but if they need it then we'll bring it.

Travis: Alright.

Robb: Alright man. Maybe a couple of months down the road, we can get you back on the show. Open you know do a blog post, get some questions and then bring you back on the show and talk about this stuff some more.

Travis: Absolutely, I love to.

Robb: Awesome, Travis. Well take care and we'll talk to you soon.

Travis: Okay. Bye bye.

Robb: Bye bye.

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