Diet Doctor Podcast
with Dr. Jason Fung
Episode 64

Dr. Bret Scher: Welcome back to the Diet Doctor podcast. I'm your host Dr. Bret Scher. Today I'm joined by Dr. Jason Fung, or I should say rejoined because if you've been following the podcast for a while you know we had a prior episode with Dr. Fung, episode number 23, so if you haven't listened to that, I highly recommend you go back and listen to that. Dr. Fung, he's a practicing nephrologist, but that just sells him short to say that's all he is.

He is also a best-selling book author, he's revolutionized the way we as people and as the medical community think about fasting as a medical intervention, he is the cofounder of the fasting method, he's written books about obesity and diabetes and longevity and of course fasting and now he's taken on cancer.

And it's so interesting to hear him talk about cancer and what he learned in his book and what he wrote in his book, because you can see his intellectual curiosity. I mean he is really like a little kid with knowledge. He is just so excited about it, about all that he's learned and what it means for potential therapies, where we sort of had missteps, what we can learn from it and how we can apply that to the future.

And I mean this is such an interesting interview because of the depth and the knowledge that he has and I really try to tie it in to what can we do about these things. And of course fasting is something he talks a lot about, but it's really putting it into perspective. It's not so simple to say fasting cures everything, just go and do it.

Everything has its place and there's a lot we don't know, we have to be honest about that, and he is honest about that and I think that's important. And he's trying to get his knowledge and experience, mix it with what we do know to see what could be coming in the future and what can we do to give us the best chance possible to live the healthiest life.

So that's really what I like from this interview, but there's a lot of information, a lot of detail about cancer. At one point we talk about nutrient sensors so I want to clarify, hopefully you're someone knowledgeable about this, but the nutrient sensors are anything in our body that sense nutrients coming in.

So mTOR, the mammalian target of rapamycin, is a big one, nutrient sensing protein, insulin of course is a nutrient center, which can sense both carbohydrate and protein and then AMP K or AMP Kinase, which basically just senses any nutrients in general and that's when it's really turned on by fasting. So those are the main nutrient sensors, so you're going to hear him talk briefly about that.

We talk about an atavistic theory of cancer which just sort of plays into what he's talking about with this evolutionary theory of cancer. Basically it's all about how cancers kind of are going back to how single cells function. So, I just wanted to clarify some of those terms so it's not too confusing when those come up.

Also there's little bit of a ruffle from his microphone in the beginning but we clear that up so stick with that and it'll get better in the end, but anyway to get all that out of the way let's get you on to the interview. It's a very interesting and very thoughtful interview with Dr. Jason Fung. Dr. Jason Fung, welcome back to the Diet Doctor podcast. It's great to have you as a guest again.

Dr. Jason Fung: Thanks for having me. Great to be here.

Bret: So first off anybody who hasn't listened to the first episode of our interview certainly should because here you are now probably a couple of years later coming back hot on the heels of your latest book, The Cancer Code, and I find it so interesting, because you're a nephrologist who has revolutionized the way we look at fasting as a medical community and from an individual standpoint, you've focused on diabetes and obesity.

And now you've made this transition to really doing such a deep dive on the history and the current status of cancer treatment and I'm really curious, like what was it in your experience and what was it inside you that made you want to focus on cancer more than what you've been focusing on before.

Jason: So I got into it from that sort of obesity and type 2 diabetes angle originally. So it was in fact one of these things that I've never really learned as a medical student, which is that cancer is actually a huge, huge part of obesity and metabolic disease. But this this is not something that was actually known prior or are appreciated I should say prior to about 2003 that obesity was a major, major risk factor for certain types of cancer, breast and colorectal for example.

And the other thing was that type 2 diabetes was the same. It was there but nobody recognized that it was actually a huge risk factor for cancer. And of course cancer as a topic in general is one of the most important health topics. It's sort of number two in terms of killers of Americans, right behind cardiovascular disease.

So, it's important. So we all about diabetes and heart disease, diabetes and stroke for example, you know, that's been known for 50 years, the link between those. But the link between type 2 diabetes and obesity and cancer had not been known. So, I start out approaching it from that angle. Then it took a sort of unexpected turn as I started to look into the literature, which is this much more interesting topic of what we actually think cancer is, that just sort of started coming out.

And I didn't know about this and my guess is that most doctors, even specialists like yourself and myself, just had no idea that there is this huge sort of revolution in the way that we actually think what cancer is. And because nobody has been talking about it, you don't hear about it on podcasts, you don't read about it in a book... and yes, there were some oncologists, like cancer specialists, who would say... You know, I'd been listening and yeah, cancer is an evolutionary disease.

And it would just be this throwaway terms like what do you mean by that? And it's like well there's a whole lot more to it than what we thought and that was just such an interesting topic. So I got into these things where I just start digging and digging and trying to learn more about it and that's sort of where most of the book sort of resides.

At least most of the first half of the book. So you know, what is cancer, what causes cancer, why does cancer exist, you know, where does cancer come from? All these sort of very deep philosophical questions about cancer that are actually very important because of the forms of treatment of cancer.

Bret: That's such a great point about the history of it. What it is and our philosophies and our theories of it, how that informs treatment. I think that's such a great point and the timing couldn't be better. Because there is just a publication in JAMA which you put out on Twitter, showing that... 92 cancer therapies between 2000 and 2016, there was an average life extension of 2.4 months between all those cancer therapies that were approved in that 17 year timeframe.

There was only one drug that showed life extension beyond six months and that was a drug that later a study didn't confirm that so the drug was pulled off the market. So basically it shows that the progress or lack thereof that we've had in some very expensive, very time-consuming medications to develop in terms of treating cancer. But it's not overall grim, as you pointed out in your book.

The cancer death has decreased 20% from 1969 to 2014. But it's sort of like the progress really isn't quite there and according to what you wrote a lot of it has to do with sort of a misunderstanding of what cancer is. So tell us, because I think one most people think about what cancer is, they think about toxins like smoking and they think about genetics. And that's sort of like the main framework which you go into great detail in your book. So tell us a little bit about why that's not the whole picture.

Jason: Yeah, this is the sort of the way we think about cancer is we started thinking about it as a disease of cells that just grow too much. It's excessive growth. And I call that the modern cancer paradigm number one. And it was very important, because if cells are just growing too much then the logical treatment is to kill them.

So we devised all sorts of ways to kill cells. So, either surgery, so you cut them, you can do radiation, you can burn them and you can poison them, which is what chemotherapy is. So, you can cut them, you can burn them, you can poison them. And that was actually a huge advance. And really still the basis of modern chemotherapy truthfully.

But the problem is that there's lots of side effects. People's hair fall out, they get nauseated, all the usual thing you think about with chemotherapy. But that's the logical treatment to cancer paradigm number one. And you reach a limit to what you can do because it doesn't answer sort of the more fundamental question of why are these cells growing too much. So you've answered the question what is it; it's a cell that grows too much. Fine.

You have liver cancer, a liver cell that somehow turns into a liver cell that grows way too much. But why? And that's the question. So then we started to get into the 60s and 70s and we started to learn about genes and so on and we said, okay we know there are certain things that cause cancer.

We knew this already, right? So sun causes cancer and asbestos causes, and tobacco smoke causes cancer and radiation causes cancer. But what is it that links all these things? Why are these things cancer-causing and some other infections not cancer-causing? I mean new viruses for example cause cancer. H. pylori which is a bacteria, it causes cancer and we knew ulcerative colitis cause cancers.

But we knew all these sort of disparate things. But we didn't know why something like tobacco smoke, to take the most obvious example would lead to cancer. So then we came to cancer paradigm sort of number two. Which is that the growth in cells is regulated by genes. So, if you have a mutation in that gene then it will grow too much. And all these different things, the viruses, the tobacco smoke, the asbestos, they are cancer-causing because they cause genetic mutations. Is they are mutagens and therefore they are carcinogens as well.

Carcinogens being the term for cancer-causing agent. And that seemed to tie everything perfectly together. So through the 80s and 90s we started developing a new type of treatment. Because now we no longer have to look for treatments that kill cells. We could now look for treatments that fix those genetic mutations. And so you're not going to get the terrible side effects that you are going to get.

So, the first new drugs that were developed... so there was imatinib for CML, which is a type of leukemia. And it was mind boggling. Like it is impossible to overstate how good that drug was for that particular cancer. And this was a very unusual cancer, very rare type of cancer. But it was practically curing these things. That was ridiculous. And then shortly after that you had trastuzumab, which was used for certain a subset of breast cancer. So this was for a new subset of breast cancer.

And of course only about 10% of people had this mutations, so they actually devised a test, they would test for this mutation in the cancer, then if you had it, they would give you the drug. So now you had a completely new paradigm of treatment which is a personalized treatment. So, not only targeted, so genetically targeted personalized medicine. And in 2000 we were like, this is going to cure cancer. Like this is it.

Bret: Right, when the first two examples are that good, it's sort of like game over... we got this, we finally figured it out.

Jason: Exactly, so huge optimism in around 2000. And just around the corner we had the human genome project. So, here we're going to get this map. We're going to say, there's growth in here, there's growth in here and in cancer we're going to see this mutation, this mutation; let's just fix them and that's it.

Bret: But it turned out to not be so clean, right?

Jason: Yeah.

Bret: It wasn't so simple.

Jason: So this was the sort of the two-hit hypothesis that I learned about in medical school in the 90s. So, it was that, you know, we had one hit, but that clearly wasn't enough. So, then you have two hits or three hits. So you had two or three mutations.

So then what we would do, this is what we were thinking in the 2000, is that well, we're going to find the two or three genetic mutations of breast cancer, two or three genetic mutations in colon cancer and just going to find out these drugs to fix these mutations and that's it, we're done... we've cured cancer. So, very optimistic and really everybody was very excited. But it didn't turn out that way unfortunately.

And so this is the somatic mutation theory. So this is the theory of cancer, the cancer paradigm number two... sort of that it's a genetic mutation in a growth containing region that caused this

excessive growth. And the problem is that when we did the human genome project even find what caused cancer, then we went on to something called the cancer genome Atlas, which was an even more ambitious effort. So they didn't just sequence one human being.

They sequenced 33,000 cancer samples and they compared them so that they could find out which genes are sort of important for colon cancer for example. Turns out that colon cancer, to take an example, didn't have one or two mutations. It had like 50 to 100 mutations. It was just terrible. So that problem is even worse than that.

Like the more with dug in, the worse this somatic mutation was, because if you had patient A and patient B, two people with identical appearing cancer, so colon cancer, stage is the same, you know, metastasis is the same, tumor size is the same, everything looks exactly the same, you would have 100 different mutations in patient A and 100 completely different mutations in patient B.

Bret: That's so important to point out though because it's not that the mutation there was totally wrong and that there were no mutations causing the problem. It's just it wasn't as clean as the CML example that there was one mutation you can target. There were just so many. How could you devise a treatment for this, if this is the only theory we have to go on?

Jason: Because in CML of course it was the exact same mutation in every single patient. So for like 80% of CML patients had the exact same single mutation that could be fixed for these are able gene And in colon cancer and other types of common cancer, breast cancer for example, that's not want you saw. You didn't see two people with the same mutations. You saw completely different mutations. And then the more you looked the worse it got.

Because patient A and patient B had different genetic mutations. But even if you took the same colon cancer and you profile the colon cancer compared to a metastatic colon cancer in the same patient, it would have different genes. And even in different parts of the tumor you had different genetic mutations.

So even if you got 100 different drugs, which you will never do into that patient, you may only treat, you know, a sliver of that colon cancer because the other part of the colon cancer has different mutations and the metastasis has different mutations. So, complete genetic bedlam. So in 2018, the last I looked for this book anyway, when they catalogued the number of genetic mutations that they have found in cancer overall, it was close to 6,000,000. Six million.

Bret: Mind-boggling.

Jason: It was mind-boggling. So the whole sort of somatic mutation theory that is one, or two, or three mutations per cancer was just out the window. And of course this is why we didn't have any progress in cancer medicine. Because if your paradigm is let's fix the genetic mutations, well, that paradigm has been completely invalidated and therefore you cannot make any progress.

So if you look at the number of genetically targeted treatments and they've done this in various studies that I cite them in the book, you can match like 2% to 4% of patients to precision medicine targeting. The number of drugs that are actually useful for precision genetically targeted personalized medicine is like maybe five.

That's probably generous, the number of drugs. And like I said, I had quoted an earlier study which looked I think up to 2016 or something, which show the same thing. Average length of

overall survival increased with these drugs. It was 2.1 months... here it was like 2.4 months. Very similar. That one extends out to 2020 of course. So it was just... you know we're completely in water by 2010; it was just terrible.

So the new paradigm had failed because it had failed to lead to new and better treatments. But now it was where sort of I had left the story, but it turns out that something very interesting sort of came through in the last 10 years, which was that the entirely new paradigm of cancer has basically taken hold, the story of which most people don't even know. Most doctors have no idea because I had no idea and most of the people I talked to had no idea.

And this was the evolutionary paradigm of cancer. So, you know, again none of this third sort of great paradigm invalidates what comes before it. It's simply building on top of it. So I'm not trying to say, oh, these people are so stupid. That's not the case at all. It's just that you know, you learn more and more.

You kind of peel back these layers of truth. So we know it grows too much, it's a cell that grows too much. So we ask why. Well, there's genetic mutations. Well why are there those genetic mutations? That was the crux. Because the previous theory had said why are those genetic mutations... and it was sort of this random thing. Tobacco smoke doesn't target any specific gene. It it's just like... just causes damage here and there, but it doesn't target one specific gene. So then if you say well why is this gene in particular affected? The answer according to the previous paradigm was it was just bad luck; it was just random.

Just like if you buy a lot of lottery tickets you will have a better chance winning the lottery. And in this case, if you have more damage, if you have more mutagens, you know, mutation causing agents, you're going to have a higher chance that one of them by chance is going to hit it. The problem with this is that the entire premise is wrong, because answer is not random. Like, you know, when they say okay, you get a genetic mutation and therefore you grow too much, your cells grow too much.

Well, that's not random because if it was random, you know, one mutation would have the cell grow too much. You know, one mutation might have me shooting laser beams out of my eyes. Why don't I have that mutation? Why don't I have mutation like Wolverine and I heal quickly? There's no reason a priori why you should have this specific set of mutations that is you grow too much, you metastasize, you use the Warburg effect, you know these are immortal cells.

There is no an a priori reason. So, therefore this cancer phenotype was not random. And that's a huge, huge thing you have to realize because if it's not random then you can say, what is driving it? And turns out it's evolutionary forces. And that to me is just an absolutely mind-boggling revelation because now you have something that's shaping these cells into cancer cells. But what's the destination?

And this is where the sort of this... Honestly, I think that this is one of the biggest leaps in cancer medicine is that if you look at the cells, it's not random. Like a lung cancer... If you take a lung cell and turn it into lung cancer cell, it's not random. There are specific attributes that it is driving towards. So, it doesn't matter if you're a Black man from 1920, or a Chinese man from 2020, right?

If you have lung cancer from tobacco smoke you could be a world apart, you know, a century apart, half a world apart, different races, different sexes and it's still going to look the same. So therefore there's nothing random about this. And what it turns out is just the totally unexpected fascinating answer is that the cancer cell that is driving towards is actually an evolutionarily primi-

tive version of our cells heading towards not a more advanced version of the liver cell or lung cell or whatever.

We are heading towards a more primitive thing. And it's trying to emulate not the multicellular organism but it's trying to emulate the unicellular organisms. Which like I said to me it's a completely fascinating thing to think about.

Bret: It is, it's so interesting to think about it, and you're going into great detail about it in your book. And you also talk a lot about the seed and the soil. That picture comes up a lot throughout the book. And I think that's such an important point to make. And I want you to just talk a little bit about the seed and the soil. We will get into a little bit more about it. But explain what you mean by the seed and the soil.

Jason: Yes, if this isn't a evolutionary process, then there's two things that are important. One, you have to have genetic heterogeneity. That is all cancer cells cannot be the same. That's precisely what we found, actually. So I remember in the previous version of cancer paradigm, which is what I learned. It turns out it's not. All those cancer cells are like a hodgepodge. Like it's a huge population of different genetics.

So you have to have the genetic heterogeneity, but then the other really important thing when we're talking about evolution is the selection pressure which is provided by the environment. And that's the sort of soil. So when you talk about cancer, you could think of it like a seed in the soil. If you take a seed, it doesn't grow necessarily.

If you throw it in the Sahara desert, it doesn't grow. You put it in a good soil with good water and sunlight and it grows. So therefore the seed can be exactly the same. And this is point with the genes. The genes, and looking purely at the genes of cancer... We're going to find all the genes in cancer. Well, we did. But it doesn't tell you about whether this cancer will grow or won't grow because you only know about the seed.

What is it about the soil that is going to allow this cancer seed to flourish? And that's the important thing. Because we can't do anything about those genetic mutations. But we can do a lot about the environment in which it finds itself.

Bret: Well, that's both a good and a bad thing, sorry to interrupt. It's both a good and a bad thing because on the one hand it says, we have the ability to do something about this, but on the other hand maybe there's something comforting about just saying it's a mutation that I don't have any control over. You know, not my fault versus all of a sudden maybe it is my fault. I've put myself in the environment where this cancer can grow.

So from a doctor standpoint it's easier to tell somebody random genetic mutation, it's not your fault versus maybe the way you've been living did have something to do with this. I mean, that's a different paradigm that's a little uncomfortable for the patient.

Jason: Oh yeah, for sure, it's certainly uncomfortable. And that might've been one of the reasons why we sort of flocked to that somatic mutation theory. But the evidence is very clear that cancer is not simply a genetic problem.

Bret: Yeah.

Jason: Because there's all this evidence. Yeah, we have evidence from as far back a long ago. But, you know, Denis Burkitt who went to Africa, discovered the Burkitt's lymphoma and so on.

One of the things that he noticed very early, this is the 50s I think, is that if you look at Africans who follow a traditional African diet and lifestyle they didn't get colon cancer. But the Whites did and so did the Africans that adopted the White of lifestyle... diet, you know, lifestyle.

They all got colon cancer. So it wasn't the seed because the Africans of course with the same genetic stock as the Africans living in a normal sort of traditional lifestyle... it was the diet and lifestyle. And you see the same thing over and over. A Japanese woman, if you move that Japanese woman to San Francisco and within two generations, the risk of breast cancer has approximately doubled or tripled.

Bret: Right so the main question is, what is it?

Jason: What is it? And you look at the Inuit of the far north for example. So in the 20s and 30s there were universities in Canada that were sending expeditions to the far north to see why these people were immune to cancer. It turns out when they changed their diet, they weren't immune to cancer at all.

So again it's not the seed of the problem. It's the soil of the problem. Which is the environment and how our genes interact. Even something like BRCA. We think of it as a sort of a cancer death sentence; BRCA gene it's very scary. Well if you look at the risk of breast cancer with BRCA, it's actually much higher now compared to sort of a century ago.

So if you had the BRCA gene and you lived in the 1920s your risk was about 10%. Now it's probably 50% or 60% of developing breast cancer in a lifetime. And again it's the same gene; it's the same genus there. But there is not the same soil and that probably has to do with their modern lifestyle much of which comes down to I think the nutrient sensors, insulin and, you know, eating too often and a lot of these other things, which are sort of new, what we talk about, so... It's such an interesting and empowering way.

Because, you know, on the one hand you say it's sort of comforting to say that is not your fault. But on the other hand, if you actually want to do something about it, then we actually can do something about it. Because again if you say okay let's take that Japanese woman in San Francisco. If we can understand what it is that's going to make a risk of breast cancer so high, we could drop her risk by a factor of 2 to 3.

So that's the goal... That's amazing. Like before 20 years ago according to the previous paradigm, we'd be like... What are you going to do? Right? You can't do anything. It's the genes, right? Now it's like we actually have a goal. We can see the goal. We should be able to get back there if we work at it and can understand it.

And that's what's so important about having these paradigms of cancer understanding what it is the disease we're talking about. And that's why it's so... this sort of... and there's new treatments to that that come along with that, but again it's one of these things that how think about the disease, influences so much the research, the public policy and all that kind of stuff. You know, people say, it's about genes, it's about genes.

Well, if were to ask you what causes lung cancer, would you be more correct to say it's a mutation in XYZ gene? But would you be more correct to say smoking causes lung cancer? Obviously, you want to know about the smoking not about the five genetic mutations that you found.

And this is the same thing. You got to get past that paradigm to say what's causing those mu-

tations and that's where we've already come, and we're just starting to scratch the surface and that's why think it's such an interesting topic.

Bret: So, that's a great sort of summary. I mean and it's so much there that you unpack in your book about where we were and where we are. And like you said it is a much more empowering philosophy because we can do something about it, but it's still not universally accepted among oncologists, the atavistic theory or the evolutionary theory.

There's still some people who think it's kind of not prime time. And I'm curious what you think about that? Like why are some people in the medical community still reluctant to sort of accept this is the new age of cancer? What have you come across?

Jason: I don't know. When I listen to some of these, it's not purely-- Like the atavistic theory, it makes a lot of sense. A lot of people are more willing to call it an evolutionary theory. So that seems to be fairly well accepted amongst oncologists.

And I've talked to a couple of oncologists and they say, yeah... I mean I've presented to cancer rounds and stuff. And most people don't think of it that way. They just think of it as an evolution, not thinking about the sort deeper... Because that part about trying to evolve towards that unicellular existence, that's what we're talking about for the atavism. It makes actually so much sense and you know, if you were to ask that question...

Because if cancer evolved sort of on a forward evolutionary basis, then there's no reason for cancers all to look alike. So if you have patient A with a lung cancer for example and patient B with a lung cancer which look identical under pathology I should say, well, those two cancers have evolved completely independently of each other; person A and person B. So why would they look exactly the same?

The odds of that are actually astronomically small. So how can you have 100 mutations in person A, 100 mutations in person B, and it looks like exactly the same? Like it doesn't make sense unless it's following a guided path. And that answers the question as to... you know, this sort of theory just answers so many questions that would otherwise be very hard to answer, such as why does cancer exist in every part of the body.

Why does every cell have the potential to become cancer? That wouldn't make sense any other way unless it's actually the very core of how we got here... sort of our existence. You can get cancer in your eyeballs, you can get cancer your heart valves, you can get cancer in your placenta. There's almost no cell in the human body that cannot become a cancer. And actually that goes much deeper than. Like every multicelled animal practically that's ever existed has the potential to get cancer.

Bret: But what are the problems--?

Jason: Maybe the naked mole-rat.

Bret: I don't know much about the naked mole-rats, so I'm going to stop you there. But one of the problems with the cancer also is that it's not one thing. There is thyroid cancer, testicular cancer, Hodgkin's lymphoma... those cancers are thought of as being treatable even with sort of the older paradigm and they are very different from colon cancer, breast cancer and lung cancer.

So we can talk about cancer as one thing, yet there are some defining characteristics that all cancer share which is sort of kind of a lot about what you're talking about. So using that, how

does that inform, controlling our environment in a way that's going to affect testicular cancer and breast cancer and colon cancer and prostate cancer? Are there certain patterns of life that are going to affect all cancers similarly?

And now that I asked the question we also have to have the caveat that we really don't have any evidence to show that certain activities prevent cancer because we're sort of like on the precipice of this type of theory and those studies take decades and decades, so how do you sort of formulate... how you've presented the evolution of cancer to where we are now, what we can do about it and what evidence do we have to support what we can do about it?

Jason: Yeah, and that's the thing. So, that was the big breakthrough sort of around year 2000 is that there is one couple of guys who published a paper called The Hallmarks Of Cancer. Which is sort of a total revelation, because prior to that of course everybody had said, here's breast cancer and here's leukemia and they're different. Yes, there are different.

They're both cancers but they are different. So people had always treated them differently but what they did which was different and what made it the most cited paper in all of oncology was that this was the first paper that really looked at how cancers were like. And that is what's sort of let us, that was beginning of the movement to figuring out what is cancer as a whole. Not as breast cancer and liver cancer, but what are these... what is the driving force.

So, we know there is genetic heterogeneity, but what is the selection pressure? And this is the thing that seems to be the most important is that the selection pressure is basically this chronic injury. It has to be very specific. It has to be chronic, because we're talking about a evolutionary process. It can't take a little bit of time. It has to be a continuous selection pressure.

And it has to be sub-lethal because if you have too much injury everything just dies. If you have too little injury, it just gets repaired. But in that sort of gray zone, if you have chronic sub-lethal damage of almost any kind your body now has to undergo some change. You can't just do what it's doing. So say take tobacco smoke, chronic sub-lethal injury.

Your lung cells if they do nothing, they will die. They have to evolve in order to survive and the way they evolve is to become more towards that unicellular pathway. So in fact it's not simply that this causes this cancer, this causes this cancer. Any type of sub-lethal injury... so if you look at ulcerative colitis... well, where is the causative agent?

Well, it's not an autoimmune disease; there's nothing unusual. But any chronic damage just can't cause that. Look at gastroesophageal reflux. Stomach acid is your causative agent, but it's not the stomach acid that does that sub-lethal damage. It could be the viruses work. But it has to be chronic. So you have a hepatitis B virus. Hepatitis B, hepatitis C cause cancer, cause liver cancer. So, those both cause chronic liver damage. Hepatitis A and hepatitis E do not cause chronic liver damage.

They cause acute fulminant liver damage and they don't cause cancer. Same thing with Hiroshima, the atomic blast. So if you have chronic radiation, you get cancer, but if you have a single huge dose of radiation such as the atomic bomb, you either die or if you survive, the outcome of those cases, those irradiated Japanese people, there's a lot less cancer than they expected.

They expected huge amounts of cancer afterwards based on the amount of radiation that these people were exposed to, but they actually didn't find it because there was no chronic ongoing selection pressure that is effective. So, it's a much more... It's much more nuanced in terms of...

you can't simply say this causes this... It's really any cause of damage.

So even the drugs that we use, you know, that chemotherapy, it causes, you know, from the original paradigm one, their way is to kill cells, but they can cause cancer too. So the very drugs that are used to cure cancer actually cause cancer. Isn't that strange? The very thing you use, radiation treatment for breast cancer for example, so you're trying to cure cancer with radiation, but that actually causes cancer as well.

And it's the same paradigm. What you're looking at is any type of sub-lethal injury to any type of cell will cause this selection pressure you have the genetic heterogeneity, you have the selection pressure and then you can get this evolution back towards a more primitive form. What I always think is interesting about... you know, people say, well it's not atavism.

Do you know like pathologists talk about cancer? That's precisely the term that they use for primitive. Hasn't then been for all of our entire medical careers that the pathologists have always said, oh, there's blast cells, which are early cells for leukemia, right? Oh, they're very primitive looking cells.

Bret: It's just taken a long time to get from the pathologists to sort of the frontline in the research and...

Jason: Yeah, and the word anaplasia means to move backwards. So everything the pathologists have been looking at in their microscope, when they look at cancer what they see, because that's what their eyes are telling them, is this is a not more evolutionarily advanced cell. It's actually a very primitive cell.

So it's like, we've been doing that for 50 years and yet people... I think there's a lot of people who don't know, I don't think there's a lot of people who are actively sort of against this. Like, they may not know the nuance. And what I thought was fascinating too about this is that in the last two years what they did was they looked at the genes that were mutated in cancer. So they didn't ask the question which genes are mutated in cancer.

They said when... from what evolution period of time are the genes that are mutated in cancer, when in evolutionary time was interesting is that you see this big spike right at the junction. So they took all the genes they divided them into 17 final strata which is sort of, you know, periods of evolutionary life, so from the most ancient to the most recent genes.

And there's a big spike right at the junction of unicellular and multicellular life. That's fascinating because it's like that is precisely what was predicted by the atavistic theory from 2010, which is a completely random thing that you'd say, okay if this theory of evolutionary cancer is correct and it's really backwards and the period you have to focus on is between unicellular and multicellular life.

And this is exactly what they found, what you'd never have found if you didn't have that theory. But you knew where to look now. And that's fascinating.

Bret: So, let's bring this around to some sort of treatment though, because let's face it, you're known as the fasting doc, right? You're the founder of IDM, you've sort of revolutionized how we think about fasting as a medical intervention.

So part of what I'm sure you believe, not to put words in your mouth, but that fasting is an appropriate indication for trying to prevent cancer, so why would that be and what kind of evidence do

we have to suggest that and where do you think the future should go for fasting as a treatment for either preventing or treating cancer?

Jason: Yeah, unfortunately there's not a lot of evidence. So there's actually very little evidence and the problem is that it's actually much more broad than fasting. That's what I tried to get out in the book is that it's actually not just fasting itself but this overall sort of nutrient sensors.

Because we have several nutrient sensors in the body and it's important because when your body senses nutrients, it wants to grow. So turns out that the nutrition sensors, insulin, mTOR and AMPK, which are the three nutrient sensors that our body uses, are actually growth factors, very highly pulling growth factors in fact.

So when you eat, your body says, hey, there's food available and then it tells the cells, you've got to grow, because you've got to grow while there's food available. So the thing is that if you don't have food, you're going to do the opposite way, your body is going to turn into a very sort of slow growth mode, which is of course less conducive to cancer. And that's part of what makes that sort of soil very fertile.

So this is why a disease such as obesity which is a disease of hyperinsulinemia... so it's a disease where there's too much insulin. So if I just pump somebody full of insulin, they're going to gain weight, because that's what you're telling the body to do. But the other thing you're telling the body to do is to grow. Grow as much as you can.

And that is going to tip the scales. It may not cause cancer but it's going to tip the scales towards favoring the development of cancer and realizing that those cancerous seeds is every single one of us every single day. It's just that our anticancer forces are strong enough to keep them all in check. But the minute you start to tip the balance in favor of growth versus sort of no growth, then you're going to increase your risk of cancer.

And that's why diseases such as obesity, which has too much insulin is going to be a pro cancer state. That's why a disease such as type 2 diabetes which is a disease of hyperinsulinemia is going to be a pro cancer state and that's the problem.

So now we have the disease of hyperinsulinemia, which we know as a society are actually growing, like there's an obesity epidemic, there is a type 2 diabetes epidemic... and in fact what we've been doing pretty well in terms of cancer, except for those cancers that are obesity related... so, you know, the biggest thing by far has been stopping smoking.

That's the most important thing... so, lung cancers are going down, oropharyngeal cancers are going down that kind of thing. But what's going up are breast cancer, liver cancer, pancreatic cancer, colorectal cancer to some degree... that's going down because of screening as well, but, you know, the point is that we're finding a lot more because we are having a lot more hyperinsulinemia. So what does fasting have to do with it?

Well if you are overweight then you can use fasting to lower your weight and presumably that will lower your risk of these obesity related cancers. Same with type 2 diabetes. If you use fasting to reverse your type 2 diabetes, which you can, then you're going to be at lower risk of developing those obesity related cancers. That's about all you can say right now. I mean I think it's a very useful tool.

Bret: Yes, so in your opinion is that the most potent intervention or how would you compare it

to weight loss surgery which can help you lose weight and lower insulin and glucose or to a ketogenic diet which can do the same? You know different versions to sort of achieve similar goals. Like how do you see the difference between all those?

Jason: I think that they will all actually benefit. So it would be very much the same for ketogenic diets, because the ways it benefits people is that it reduces your insulin. So if you're eating a high-fat diet, then fat has very little insulin effect compared to carbohydrates or proteins. So therefore it's a very sort of low insulin diet.

Same thing with the bariatric surgery. If you manage to keep the weight off and there's issues there of course because even if you narrow somebody's stomach, cut up their stomach, they can still drink soda and you know all this bad stuff. So, a lot of people do regain it but if they can successfully keep that weight off then you will lower the risk of those diseases. So there's many ways to do it. It's not like fasting is the only thing. It's just that one of these easy things to incorporate into your lifestyle.

Bret: Then how about a higher carbohydrate but still relatively calorie restricted diet where someone is losing weight? Would that have a similar effect because the weight is in check even though the insulin response may be different?

I mean I guess it's an unknown question, but you know, when you see people like in the blue zones, you don't get cancers eating a relatively high carbohydrate diet, they're not going to have maybe the same insulin response. So it's not all carbs; it's carbs as part of the whole picture I guess.

Jason: Yeah, I think it is all part of the whole picture because what I thought was interesting from some of the data from the Kitavans, is that the Kitavans, which was this island in the South Pacific, and years ago they did the study... So the Kitavans eat somewhere around 69% carbohydrate diet.

But a while ago they measured the serum insulin levels of these Kitavans compared to a reference Swedish population and that's only because the researcher was from Sweden and it turns out that these Kitavans, which are eating this very high carbohydrate diet, had serum insulin at the 5%.

Meaning that 95% of the Swedish population had higher insulin levels. I remember Swedes are amongst sort of the fittest people on earth. This was done in the 80s when there's practically no obesity there. Even now they are doing better than most North Americans.

And even compared to those these Kitavans were eating all kinds of carbohydrates; 69%, 70% carbohydrates. But unprocessed, not eating all the time, you know... you can still do extremely well. I mean I think that part of it... a lot of it is due to this intricacies of what the carbohydrates are, right?

So, if you're eating boiled potato all day long, you're not going to eat much after a while, because there's no sort of... you know, there's two reasons why you eat food. One is you're hungry, and two is that it tastes good. So, this is probably what the Kitavans are doing. They are eating a lot of boiled roots and, you know, low, low, low sugar foods. But it's not tasty enough that you're going to say... wow, you know, boiled potato for the third time today. For the last 35 years I've been eating...

Bret: Yoo-whoo!

Jason: Yeah, it's like... it might be high in carbs, but if I had to eat boiled potato and I had to eat it day in day out, I'd be pretty unenthusiastic. So the minute that I wasn't hungry, I'd probably stop eating that boiled potato if it was my 10,000th meal of boiled potato. So it's a lot more intricate than just carbs and fat and there's a lot to do with variety. If you restrict foods you will generally do well because you probably take away.

Like if you eat the same food day in and day out, like Chinese people for example ate a lot of white rice in the 80s. Very little obesity, but a lot of white rice. I don't know if they really enjoyed it that much, because it was every single day. And as soon as they were full, they just didn't want to eat more, because there was no pleasurable sort of stimulation as opposed to what we eat now.

We're going to go out to this and McDonald's and Burger King and... you know, all these things which are sort of made to taste very good and we add the variety and we eat foods from all over the world, so therefore we never lose that sort of zest for that which is good in one sense; we get to enjoy life. But on the other hand we have to be careful because a lot of times I think we stop eating just because we're hungry and we eat because it's a pleasurable activity.

Bret: Right, I think that's a great example of how different societies eat, very differently than the way modern industrialized societies do. So it's not just about the food necessarily but it's about the whole atmosphere of the eating; that's a great example.

So, one question then... let's take a couple of different people. I mean I have to talk about fasting with you because you probably know more about fasting for health than anybody... but someone who is following a ketogenic diet and a whole foods diet versus someone who's following a more Western-style diet, if you're going to take them and say what benefits are they going to get from a five-day fast, you know, every quarter or something like that, do you think it's going to be drastically different between those two?

The potential benefits they may see from fasting because of their baseline diet and their baseline lifestyle?

Jason: Yeah, because the point about fasting is that you're going to lower your nutrients sensors. So if you are suffering from diseases of too much insulin, then lowering insulin is a very good thing. So therefore, if you are eating a ketogenic diet which is relatively low, you don't necessarily have to go on a long fast for example.

If you're eating a standard diet, which is super higher... eating six, 10 times a day and you are eating foods that are very high in refined carbohydrates sugars, well, your insulin is super high, so lowering is going to be a good thing. Whereas with a ketogenic diet you may not need to do that. You may not need to do it at all.

And I always look back at the 1960s in the United States. There was a period of time where there was very little obesity and yet people were still eating three times a day almost every day. It's just that they didn't eat in between. So they stopped eating at six or seven and they didn't eat again until seven say.

So we're talking about a 12 hour automatic fast every single day. Now, of course, that sort of doesn't even exist anymore, but the point is that even if you weren't that careful on the foods that period of fasting still certainly reset yourself because you allowed yourself that period of low insulin. Now, of course, you finish dinner and people have dessert and a snack... Oh, you should eat a bedtime snack. That was like classic dietitian advice for 25 years. All through my medical

school, all the way up until three years ago.

Bret: Because otherwise you would wake up hungry as if that's like some tragedy.

Jason: Right. And then the minute you get up, make sure you eat right away. I probably gave the same advice for the first 15 years of my career. I didn't do it myself, because actually just don't eat breakfast.

Bret: So this brings up sort of the threshold question which I think is a fascinating question; is its own topic. But if a paper came out showing that all you need to do is fast for three days to get life extending benefits and nobody in the world is ever going to fast for four days. Everybody wants the minimal effective dose.

So what is that? Is a 16-8 going to get you similar results of a five-day fast? And how do we know? How do we measure? What kind of markers can we look for to sort of get an idea of are we hitting a minimally effective dose for weight loss, for blood sugar control, but also longevity and cancer prevention and some of these harder to measure things?

Jason: Well, I think the only way to look at it... so I don't think there's a minimally effective dose, because I think you can do say 12 to 14 hours, like all the Americans in 1960 and 1970 and still do reasonably well. But there's two sort of things that you can play with. You can play with sort of the foods that you eat and you can play with the timing of your meals. And I think you can adjust the two so that you get an optimal balance.

Like if you eat really bad foods, like fast food all time, then you probably have to ratchet down the number of times you eat per day. If you're eating very, very sort of healthy foods then you may not need to fast so much. So there's different ways that you can play around with it and I think that there's also things that are... you know, different foods are sort of different levels of fattening ability.

So sugar is probably on the top there. So you don't need that many calories of sugars to get a lot of damaging effects. As opposed to vegetables for example. I think you could eat a lot of vegetables and not worry about it. Whereas sugar, if you start eating a lot of it, you should probably start worrying. And then there's the duration.

So if you've been doing it for a long time then it's going to take a lot more time to reverse. So therefore the best thing I think is to simply go with those markers which you can well validate. So something like your weight for example, so things like waist circumference, blood pressure... so this is the metabolic syndrome which is part and parcel of this whole hyperinsulinemic state.

You've got HDL, you know, not LDL, which is always very interesting to me... But we look at the metabolic syndrome; there's five criteria according to the ATP, right? LDL is not one of them for all that we talk about. It's HDL and triglycerides and those are those things that dietary carbohydrates are really going to worsen.

But then also sugars, blood pressure, waist circumference. So, again not even weight which is again really interesting to me. So the BMI does not calculate... as one of the criteria for metabolic syndrome as waist circumference. Because again there's a difference between the fat in your abdomen, liver, intra-abdominal area compared to the fat elsewhere. It's much more metabolically dangerous.

So those are well validated. Like we know that if you have type 2 diabetes, your risk of cancer, your

risk of heart disease goes way up. Therefore you should target that as opposed to saying, I want to hit this macro of whatever you want to do. It's like well you could do a high carb diet as long as you're getting towards... you know, your blood pressure is good, your triglycerides are good, your HDL is good, your sugars are good, your weight circumference is good and hey, crazy, right?

You know because again in the 80s you had like literally 1 billion Chinese people who were eating 300 g of refined carbohydrates a day. That was the study that they did in the 1980s. There was 300 g of carbohydrates, almost all white rice, almost zero sugar, which is very interesting to me too. But most of them were metabolically healthy, because there's no obesity, their blood pressures are low, that kind of thing.

So that's what I mean like you know sometimes we make things too complicated, oh, we need to hit this macro or that macro or this or that. To me as a physician I'm always like, well these things are well validated. Nobody really denies those things for metabolic syndrome. So, target those.

Bret: Yes, that's interesting. I mean it's the markers to follow are the markers for overall health. If we're talking about longevity, which includes cancer, it's about being healthy it's about weight, it's about blood sugar, it's about insulin, it's the metabolic syndrome, it's about the things that we can measure and we talk about but don't always think about in terms of cancer.

And I think that's a big part of sort of like about what this book is. About how the other theories have evolved and how it does in some way relate to weight and insulin and diet. And although it may not be proof of causation, it's certainly highly associated and suggests that addressing those will reduce the risk and hopefully we're on sort of the forefront of having studies to show that.

And in the book you have a chapter, A New Hope, which I love the Star Was reference by the way, but A New Hope which is a good way to sort of finish it, that you're optimistic for the future. So tell us about your optimism and what you see for the future.

Jason: I think it stems from sort of a deeper understanding because I think that sometimes we get so blinded by these, sort of, let's do an RCT on this... We all have to think about what it is you are doing, like trying to understand the root causes of your disease so that you can come to sort of rational treatments.

And this is by this whole new paradigm it's actually unleashing all these new treatment potentials that we never considered ages ago. So because we see it now as an evolutionarily driven disease, there's implications for example for screening. Like you can't get rid of that cancerous seed. It's everywhere.

So if you can more you look for it... the more you will find it. Which may actually lead you to overdiagnosis and overtreatment. Which has been the story of mammography for a large part. Whereas before we were sort of expanding the indication for mammography, that people have now been moving back on that. So, the US preventive task force for example was saying don't do it at 40. The other implication is that there's these other new treatments that we've never even thought about.

So, immunotherapies, this new sort of way of targeting things. So again if you look at sort of this new evolutionary paradigm what you say is that the cancer has actually basically evolved into essentially a foreign invasive species. So you might that's ridiculous, right? You know, your breasts cells didn't turn into an invasive species, but yes, did.

Because that's not the way that I look at it. That's the way that your own immune system looks at it. So you know that the immune system which kills cells, is very powerful, but it has to distinguish between foreign cells like bacteria and fungi. It wants to kill them, but you don't want to be killing your own cells. That's why you have foreign cells... you know, they're called self- and non-self cells, you have ways to distinguish them.

Well, the cancer cells are identified by your immune system as foreign cells. You have natural killer cells which without even having seen them before will target these cells and kill them... so it's identified by your own immune system as a foreign invasive species. So now, if we understand that you have to treat this as an invasive species, but we have a whole system, the immune system that actually is designed for that.

So now if we simply boost it we can actually do things like immunotherapy. So, we have these great new treatments and they're just starting. So I don't want to judge among them, but the check point inhibitors have been very successful in a number of treatments like melanoma, you have CAR T therapy, which is almost brand-new. So maybe it will work, maybe it won't work, but it's a whole new way of treating cancer that's just incredible, because again you're not trying to kill cells.

That's paradigm one. You're not trying to fix genetic defects. That's paradigm two. Now what you're doing is you're trying to boost your immune system to fight an invasive species much like a bacterial infection. And interestingly we use the exact same terms in infections; the metastatic infections. Because they are going where they don't need to go.

Only two diseases are referred to as metastatic - cancer and infections. And that's not by coincidence because they are actually very similar in many, many, many respects. And in fact the other treatments, for example I talk about there's adaptive therapy, which is this way of treating say prostate cancer, instead of giving maximally tolerated doses or MTD, which is the standard way... So, the standard way we've always thought about chemotherapy is give the most drug you can without killing the patient.

That I was remember the whole scandal, the autologous bone marrow transplant, which is a whole sordid story that I didn't actually get into, but... I don't know if you remember this but the autologous marrow transplants were once very popular for various diseases because some guy said... you know he was getting great results and it turned out it was all fabricated. So they were just...

And I did this myself when I was doing my oncology rotations, giving people maximum, super maximum doses and then rescue autologous bone marrow. It turned out there was no evidence at all for that. But anyway that was always the way you treated with chemotherapy.

Turns out it may not be the best way, because again you don't have to kill every bacteria in your body. You have all these good bacteria in your gut for example. So you should actually just give enough to maintain a good balance and that's this idea of adaptive therapy which is what you're going to do is you're going to give less treatment and only give it when you need to, so that you just suppress it rather than try and kill it out right, because you will never kill cancer completely out right, because the seed lies in all of us.

When you give too much chemotherapy what you do is you now have a selection pressure on those cancer cells and you will select out the most drug-resistant cell. Because now you're applying evolutionary biology to cancer, which you never did before because you didn't know it was an

evolutionary disease.

So it's like okay that's another completely fascinating area which we are just scratching the surface on and there's another one called the abscopal effect, which is again where these checkpoint inhibitors, this immunotherapy drug, may actually unleash this sort of hidden potential of radiation treatment.

So if you radiate a cell, so if you give checkpoint inhibitors, which is one of the immunotherapies, in combination with radiation therapy, say you radiate a metastasis in the liver, if they are on immunotherapy it turns out that sometimes you see a reduction in the cancer not just where you radiate it, but elsewhere in the body.

And it's like that's interesting... what happened there? What probably happened there is that the radiation sort of broke up these cancer cells with the immunotherapy sort of almost like a vaccine. It exposed these sort of antigens to your own immune system and now the immune system can identify say a metastasis that's not in the liver that you radiated but say in the bone.

And the bone meta will start to shrink and it was like, that's fascinating. What's interesting is that prior to the immunotherapy age, it was very rare. But since we started using immunotherapy you've had sort of this... you know, whole bunch of case reports coming out where it was like oh, we had this patient, we radiated his liver and his bone mets got better or his spleen mets got better. I was like, that's fascinating.

And you can't understand it until you understand the sort of cancer paradigm 3.0. But again points to the fact that we have all this potentially game changing stuff in front of us still. And to me it's like I'm very optimistic because now have a whole new way of looking at things as opposed to 2010 where we were sort of at rock-bottom, you know, and we had nowhere... what are we going to do? The genetic paradigm is dead, right?

Bret: Well, your passion and your intellectual curiosity about this is very clear. I mean it's clear that you are excited about this, about where the future will bring us because of all these... this fascinating progression of how we've understood cancer.

And it seems like the future is going to be a combination of better targeted therapies, immunotherapies, but also withdrawing the growth factors, withdrawing the glucose, the insulin and that combination may be the strongest of all and we didn't even talk about how fasting can impact radiation therapy and chemotherapy, you know, fasting around those.

So I think you're right, I think the future definitely is going to be very interesting for cancer therapy and hopefully we will make much more progress in the next 10 or 20 years than we have in the past 40 or 50 years. I mean, I think the curve is going to be pretty steep and I think that's the hope that your book sort of leaves us with.

It was such a great and detailed description of the theory of cancer, so I definitely recommend it for everybody. And where else can people find you to learn more about you and what you're doing and all the other great work you are providing?

Jason: Yes, you can follow me on social media, on Twitter or Instagram, it's @DrJasonfung, that's D-R Jasonfung. You can find me on my website which is thefastingmethod.com. We have a whole bunch of blogs that have been written over the last eight years or so, so there's a lot of information there. And you can find on YouTube as well posting a lot of new videos these days just going

over some of the basics of fasting, trying to help people in terms of trying to get them better, so you can find me on any of those places.

Bret: I really appreciate you taking the time to be on the show once again and hopefully we will have you back again in the future because it's always a pleasure to talk to you.

Jason: Great to talk to you too, Bret.