

Crusonia Conversations – Bruce German and Carter Williams

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The following has been lightly edited for clarity.

Sarah Mock: [00:00:00] I'm Sarah Mock and a welcome to Crusonia Conversations, a forum bringing together entrepreneurs, innovators, and experts in ag, food, and health, a group passionate about the fundamental belief that food is health.

Carter Williams: [00:00:23] Thanks, Sarah I'm Carter Williams, CEO of iSelect. We focus on hard problems. One of those hard problems is Americans spend \$1.6 trillion every year on food, but spend nearly \$2 trillion on diet-related illnesses like Type 2 diabetes, obesity, cardiovascular disease. Each of these is fatal in their own rights. They're more fatal when they're comorbidities for COVID-19. These are tough problems. At iSelect, we believe if you want any hard problem solved you give it to an entrepreneur. We believe that you cannot solve the healthcare challenge we face without the evolution to a new, better and more nutritious food system.

Our work at iSelect, and the broader work we're doing with Crusonia, is focused on bringing the right people together to make this happen, to affect the change, to bring entrepreneurs forward, large corporations, healthcare systems, and patients, together to make real progress; to solve the problem associated with healthcare; to introduce better food; to make it so that food and health are combined as a solution to improve our quality of life. Our hope is that results are measured not only through the traditional financial metrics. But through a fundamental and positive impact on reversing the footprint and impact of diet-related illness.

Sarah Mock: [00:02:16] Hello, and welcome to Crusonia Conversations where entrepreneurs, experts, and investors explore change in the global food system. I'm Sarah Mock, your host for today's discussion. Today, we're talking about the role of the microbiome in shaping health and immunity, with particular applications in the time of COVID-19. Here to help us dig into the links between gut life, overall health, and nutrition is UC Davis professor and chemist Bruce German and Carter Williams, CEO of iSelect.

Bruce German joined the faculty of the University of California Davis in 1988 and is currently Director of the Foods for Health Institute. His research interests include the role of milk components in food and health and the application of metabolic assessment to personalizing diet and health with the goal of building and launching knowledge necessary to improve human health through diet. And Carter Williams is CEO of iSelect Fund and founder of Crusonia.org. iSelect is investment with impact and Carter believes deeply that investment at the nexus of food and health will both contribute to social good and create significant financial growth opportunities.

I think a helpful place for us all to start is just talk to us a little bit about the research you've done and what you've learned about how these big topics of the microbiome and gut health tie into the overall health sector?

Bruce German: [00:03:37] Sure. Thanks, Sarah. We started looking at diet and health from a very specific focus about 20 years ago. Using lactation, this remarkable process in mammals where a mother literally dissolves herself to make a complete comprehensive diet for her infant. And we're trying to understand milk so we can understand how diet can work, not just for mothers and babies, but for all of us. And one of the things that we

discovered that that caught us completely by surprise was that human breast milk is full of fiber. So, this made no sense, right? And it wasn't fiber from the mother's diet. And that's when we realized that evolution had come up with a remarkable strategy, that mothers recruit another life form to babysit their babies. And as a result of this combination of the right bacteria and food for this specific bacteria, breastfed babies are full of, in the lower intestine, a very specific strain of a bifidobacteria.

So the question: what does the microbiome do for you? And the studies on breast milk and bifidobacteria taught us that, A) the microbial community in us is very important. It protects us from pathogens. It fuels us. It nourishes us. It educates our immune system, even our metabolism. So clearly throughout the evolution of higher organisms, we have been surrounded by, in essence, bacteria. We live with bacteria on an, in us all the time. And if we get the right ones, life is good. If the wrong ones, not so good. And it opens up the possibility for people to literally control the microbial community in them. So, of course, protect them some pathogens, but also to guide your immunity. To suppress inappropriate inflammation, but to support the appropriate response to an infection or a vaccination.

Sarah Mock: [00:06:00] You know, as people become more sensitive to foods, whether because of an allergy or because of just increased interest in their health, what kind of technologies, or where do you think there's an opportunity for more technology and investors to play a role in helping bridge some of the gaps that might exist in people taking on health in these new ways?

Carter Williams: [00:06:21] We look right now in terms of things like RNA and DNA, longitudinal data that would be gathered from Fitbits and Garmin watches and Apple watches. Those are sort of the first steps in this direction and trying to get more span-wise data, instead of you going in and getting a blood test with your doctor once a year, and trying to determine what's going on by monitoring that data on a more regular basis. And very specifically, in terms of our investments, that's been around the areas of imagery data and RNA data, and gathering that and trying to drive more causation.

The other part that's going to start to come on— we've looked a lot at assays that test people's biome and their various efforts to sort of say, just like you'd get your gene sequence from 23 & Me, I'll get my biome monitored, and make some causation.

We're not at a point where we can make those connections, but I was listening to a podcast recently, actually was fascinating. Ben Greenfield, who's a sort of a biohacker, actually went in and got a continuous blood glucose monitor and monitored himself for a year. And in that process, he found that he would get, for example, a glycemic spike when he ate green beans; he loves green beans, eats them all the time. And that called glycemic spike was ultimately related to an allergic response. And he determined ultimately that unbeknownst to him, he was allergic to green beans. And so now he mediates how he eats green beans because that allergic response ultimately has a longer-term effect on his immune system in various ways. And he's trying to actively manage his CRP down. Which, in that whole jumble of mess that I just said, most people wouldn't I do. But the think that somebody is at that step on the front end: a human being, who's not a doctor, is using a continuous blood glucose monitor for something other than diabetes to start doing evaluate himself, it automatically becomes clear that the two or three years — just like how we have a watch that now can measure your EKG and can measure pulse rate variability... pulse rate variability also can be an indicator or whether you have COVID, that was discovered that was sort of realized and reduced to practice just recently through the whole COVID scare — it totally makes sense to me to think that we will somehow package up

continuous blood glucose monitors to be a small thing that everybody wears. And then, start to get some more information about these correlations

Sarah Mock: [00:09:26] As a lay person who's learned about the microbiome and who's maybe read some articles and learned about the importance of bacteria. I think the obvious solution seems to be – the easy silver bullet – is I'll just take a probiotic. Are probiotics, whether it's pills or yogurts or drinks, is that the solution we're looking for is that it's like addressing the right issue there?

Bruce German: [00:09:49] Probiotics are an interesting case of a field in development early. So gradually we're beginning to realize that we don't have all the bacteria that we'd like, and they're not functioning the way we would like, and so eventually we're going to have to deliver the right bacteria to people. That's a compelling idea. And then the first generation of probiotics are aware of that idea.

However, it is much more complicated to actually introduce a bacterium into the intestine that will persist and remain as a stable part of that community. Growing, dividing, multiplying, and influencing the overall community. That's a very difficult challenge for a bacteria and the current repertoire of probiotics have been screened for two basic criteria: 1) safety, they have to be safe, and one of the most remarkable success stories in food history is the safety of probiotics; they have been proven to be very safe, and 2) industrial stability so that you can have live viable bacteria in a product. However, those bacteria, though safe and stable in a package, do not contribute significantly to the population of bacteria in your microbiome.

So we know where we're going scientifically and therapeutically. We're going to have to alter the microbial community in us and on us. What we don't know yet is exactly how we're going to do that. Unfortunately, we do know that the current generation of probiotics don't do that. But in one sense, that's actually good news because if you took a living organism and it established itself as a permanent colony in you, and it did anything you didn't want, how are you going to get it out?

There's a double edge sword to probiotics. We have to develop bacterial ingredients that will alter the microbial community in us, consume complex carbohydrates from our diet, and grow and function as part of that community, and provide us therapeutic advantages; but, when we don't want them anymore, they leave. So it's a tall order, but we're getting very close.

Carter Williams: [00:12:37] My sense is the opportunities in the most immediate-term are really to sort of bring us back to nature to some degree on this. I am unsettled on the biome and probiotics. A biome is a wide complex, area. And in as much as somebody finds one instance where one dataset maybe overlaps with that probiotic applying to that particular case, has so many different components to it that I... maybe, maybe it works. I'm not a scientist, but I'm a little, I'm a little uncomfortable about that: that probiotics is a good first step. But I think that we're going to learn a lot more in the next five years in this. I think, as we think about, immune response... immune response is becoming a really important field of study, both for cardiovascular disease – half of cardiac arrests are related to people that have no known cardiovascular disease, other than inflammation – and inflammatory aspects to diabetes. There's clearly a more important thing showing up. Its connections to CNS disease like Alzheimer's is becoming more present. And I think that the amount of pressure that's going to come in, in and around the area of understanding inflammation as a broader topic, has always been fascinating from an investment standpoint. We don't have perfect data on it yet, but I think that the, the present case of COVID is going to cause a lot of PhDs to think harder about, "Hey, maybe I want to go work in

this area." It's sort of that period of time where our understanding of inflammation and the immune system is really going to yield a lot of interesting opportunity over the next 15 years.

Sarah Mock: [00:14:47] There's a movement right now happening in the agricultural space around soil health and the importance of paying attention to soil health as part of an agricultural cropping system. Talk to us about how that might translate all the way through the food system into the foods we eat. You know, how directly related is soil health to human nutrition?

Bruce German: [00:15:07] The scientific community has been completely changed over the past 10 years because of the advent of mass sequencing. And with that sequencing, we can tell what microorganisms are there as communities. And as we've been able to look into communities, literally from the plants and the soils they grow on all the way to us and the bacteria in us, we realize it's not in essence simple, it's complex communities. When you get them right, things flourish.

And so, if the soil community is appropriate then, the minerals that are in the soil get taken up better by the plants. And so the plants tend to have higher nutritional quality they're healthier plants that grow better, and they're literally healthier for us. It all relates to understanding a very complex community structure; not possible 10 years ago, very possible today. And that's why you're seeing this explosion in scientific knowledge. All of these bacterial communities and increasingly the application of that knowledge as utility: healthier foods, healthier people, more delicious foods, more delighted people. It's genuinely all coming together as we understand these microbial communities.

Carter Williams: [00:16:28] What we have seen, certainly in the food system, is as we've boosted yield – we've really backed the yield and things like corn and soy – we've really backed down on the nutritional qualities. What we're seeing from the consumer marketplace is a lot more pressure to increase in nutritional qualities.

And so, certainly in terms of micronutrients and core nutrition, it is absolutely clear connectivity between how we grow these things and how they end up in our food and what happens. And it's just, so it's a reasonable, logical connection. Understanding the connectivity between microbiome and soil health and crop nutritional performance is certainly a... we're well-invested in that area and paying a great deal of attention to it.

Sarah Mock: [00:17:14] Is there lessons to be learned from other places that can inform maybe technologies going forward or business opportunities or the science as we move forward and understanding the biome?

Carter Williams: [00:17:25] The analogy I make, or the things I pay attention to in regards to the biome, is, 1) if we think just back to genetic sequencing – we really started understanding how to do genetic sequencing in the early seventies as we saw Legionnaire's disease and HIV come online – we just started sequencing viruses in and understanding them in a greater detail. And that sort of led over time to a wider application of solutions and immunotherapy in sort of the 2005 timeframe. So, I sort of see that as a cycle of you 1972-73 to 2005, where we really saw connectivity of how we understood how viruses and immunotherapy interact around cancer.

The discovery that bacteria can affect ulcers, that was originally discovered, I believe, in the mid-eighties, but not really recognized as a practice until the mid-nineties, represents a period of time in which the world changed his viewpoint of is bacteria killed in the gut too is bacteria a much more complex system and. Along that same kind of footprint, if we sort of think through the years, it'll take 30 years to sort of sort through it.

But in the near term, there are specific things that we will discover, that as the rest of the world runs around with probiotics and says, "take probiotics," it's sort of that first noise that comes up with any new technology. But then very specifically, we have really clear evidence of what's happening with babies and sterile birth and its effect on early childhood immune disease that we can sort of go early into that market and see that as an opportunity and then learn from it. And then at some point later on, we're going to understand a much better perspective on how biome choices affect somebody over a 20-year period. And we'll have more comprehensive solutions that come down the way.

Bruce German: [00:19:48] Carter, great points. If I look at where we're going with the science and what history can teach us let's take the essential nutrients, the vitamins. The nutrition community did a wonderful job in identifying these rare molecules and their role in us. The public health translation of that knowledge: magnificent. Put vitamins into foods, make sure we didn't process them out, monitored the entire food supply. Magnificent public health success, commercial disaster. We basically don't pay anything. Iodide protects you from a horrible disfigurement of your throat, of goiter, and catastrophic neurological damage to infants during pregnancy, if you don't get enough iodine.

How much did you pay for the iodine salt? Nothing. So, magnificent public health success, disastrous commercial value creation. So we need to realize that if we're going to invest and capture what's necessary to take the next big step and diet and health – improving the kinds of diseases that diets today, obesity, diabetes, heart disease, hypertension, allergies, all of the problems that are destroying our quality of life – we're going to have to get the public health right and we're going to have to get the commercial side right. And you've already alluded to the concept of us measuring our health better. And so you're going to see the proliferation of cottage industries that give us better information about ourselves.

So the more we understand the relationship between food and our health, the more we can swing that entire process, not just to less disease, but more performance. And from a commercial perspective, I'd be happy to pay for it.

Sarah Mock: [00:22:05] Now we want to go and turn to the audience for a live Q&A with Bruce and Carter. A few notes on how this session will work. If you have a question for either of our speakers, please write it in the Q&A box, which is located at the bottom of your screen. If you submit a question to chat, please go ahead and also submit it in the Q&A. That's where we'll be pulling questions from. Our moderator will put you in the queue as soon as you've added your question. And when you're up. I'll recognize you by name and you'll need to unmute your microphone. And we ask that you please introduce yourself and your affiliation. So, we will dive right in. It looks like we have a question from Horace Nalley. Horace, are you ready to ask your question?

Attendee: [00:22:49] Yes, I am.

Sarah Mock: [00:22:50] All right. Go for it.

Attendee: [00:22:52] What do you gentlemen think is the future for postbiotics?

Bruce German: [00:22:57] If we define postbiotics as the metabolites produced selectively by bacteria, under particular growth conditions – and much of the research emerging suggests that they are many of the effectors of the microbiome in us – they constitute the potential to, at least in the early stages, achieve some of the benefits of shifting the entire microbiome by providing, in essence, metabolite pools that are produced

naturally within you by the microbiome. It's very attractive. What we don't yet know is just how critical the concentrations of those postbiotics are, the time their delivery, and the location of their delivery.

They're unique in that they're delivered to a particular tissue as it were in a particular timing. But as a therapeutic option, they look very attractive. And, especially for specific therapeutic applications, I think it's going to represent frankly, a whole new therapeutic opportunity for interventions.

Carter Williams: [00:24:16] Bruce, I've got a question for you on that. How do you investigate the correlation?

Bruce German: [00:24:25] Very painstakingly. There are, now, beginning to be initiatives in which the metabolome of the microbiome is being measured. So we in essence capture all of the bacteria within a particular ecosystem, the intestine of healthy and not so healthy individuals, and then, capture all of the metabolites that are being produced by those bacteria as a sample. And then you start taking those metabolites and studying them both as individuals and as ensembles for their therapeutic efficacy. So the tools of modern science, genomics, metabolomics proteomics, are ideally suited to these ecological questions. Absolutely.

Sarah Mock: [00:25:19] Carter, did you have any follow up on your perspective on postbiotics?

Carter Williams: [00:25:25] Now, it is a top area at this point. We haven't been really investigating it that much. So we've been sort of tracking perspectives.

Sarah Mock: [00:25:35] Absolutely. We have another question. How do you separate human genetics and predispositions to chronic disease such as Type 2 diabetes from whatever affects, either positive or negative, come from the microbiome?

Bruce German: [00:25:52] Sure. I'll jump in on this as well. This is a great question. This is genuinely what the scientific community and the National Institute of Health are racing to try and understand because complex diseases that take decades to develop in a population and don't afflict a population homogeneously represent the massive challenge that science is facing in the same environment. Some people are lean, mean fighting machines and some are overweight and on a trajectory to, frankly, diabetes. And it's a multifactorial problem. One of the things that's helping is the new development of this cottage industry of health measurement. Carter alluded to it, that it used to be that sampling blood and measuring glucose was a painstaking process that you really only undertook if you were a diabetic, but now devices are emerging so that you can follow the time course, in real time, of your blood glucose. And so you can begin to explore in individuals, what are the perturbations in their diet, their lifestyle, even their microbiome, that have the ability to start bringing glucose control under a, in essence, a set of efficacy variables. And, we are confident that's what precision health is all about. Precision medicine is already going there. Precision nutrition, that's its next step. And the microbiome is going to be part of that, in part because we now know we can genuinely affect the composition and function of the human microbiome within individuals.

Carter Williams: [00:27:53] Building on this a bit, one way.... we concentrate a lot on what's going on with diabetes. We've certainly had...Robert Lusting talked about that in the past, certainly in some of his most recent commentary, he's really suggested quite heavily in regards to COVID that dramatic reduction of ultra-processed food makes a lot of sense right now.

I think the concept around the biome... there are some first order things we can do right now that improve health that are obvious. Reduce ultra-processed food. The second step or third step down row will be these tighter correlations to try to understand how does the biome interact with other disease states. Main case, we got to take the noise of obesity out and then inclusion, in the midterm, having a better understanding of biome will help to sort of help further refine and keep people on track. So there's a time series issue of when these things are going to come true.

I think that the thing that is going to happen first is really, more around the longitudinal data area in which, and this is an area that we have not – I made an attempt to try to sort of say, "Hey, can we open up HIPAA, can we make it easier for people to get this data? Can we deepen the quality of the data around them?" It's sort of a public service kind of function that we're thinking about. And maybe after the elections, or when we get back with some of the policymakers and free that up.

But, I think we got to dramatically increase the depth of data that we have, and that there are both venture business opportunities near term in that realm and also public opportunities in that realm that I think we all need to sort of contribute to help augment the hardcore data that folks like Bruce are working on, to try to correlate in their laboratories.

Sarah Mock: [00:29:55] I'll take the moderator's prerogative here, but just to ask a brief follow-up.

So I'm curious, from both of your perspectives, so much of nutrition science has just been changing so quickly, to Bruce's point, especially in the last 10 years. Is there any risk that we're going to learn things in the near term about the biome – build technologies around addressing or integrating that piece of knowledge and then find out 10 years from now that we didn't have it quite right and that we actually were causing harm? Or something along those lines. I think that's not uncommon in the nutrition space. In example, like taking all the fat out of food, which was a trend in the seventies and eighties and replacing it with sugar. You know, what's kind of your perspective on... what's the risk of moving too quickly?

Carter Williams: [00:30:43] 100%?

Bruce German: [00:30:50] Well, I would say there there's two perspectives on that. One is: the situation is actually pretty bad right now. And, so there is a true urgency to build an understanding of, of the relationship between diet and health. Because as, as Carter mentioned, we're basically destroying the value of agriculture as an enterprise with the health that it's destroying.

So there's a true urgency, to this. What I think is, is, has been driving much of the misinformation is actually the vagueness of the information. And we've been pursuing a nutritional model for a century that suggests that we treat everybody as if they were the same. And we were lulled into that sense of confidence by the essential nutrients. The vitamins and minerals that we need. Every single person needs to consume. Vitamin C. There's no variation. There's not some people who can make it or not. So we had this wonderful ability to reduce diet and health to these single molecules and single actions. And that was wonderful, but we've solved that. The next generation of diet-dependent health conditions aren't that simple.

And, the problem is some people thrive in an environment that causes other people to have considerable health problems. Those are genetic variations, those are lifestyle variations, age variation. And so, as we begin to realize we cannot make these generalized recommendations and have everyone in essence benefit the

same, precision is an absolute requirement. But that's the way the world has gone anyway; a hundred years ago, if you wanted to listen to music, you went to the town square on a Saturday afternoon and listened oompa band. Today, there are technologies in your device that bring you the music of the world that you specifically prefer. And that not considered wildly, in essence, technology-dependent. It's just the way it works today. So imagine being able to deliver diet and health with that kind of precision. Then we'll be able to see health become something we can control.

Carter Williams: [00:33:23] When I look back, even at the shift away from fat that occurred in the dietary standards in the late seventies, nobody said eat more sugar, but once fat was taken out as a marketing function, it was easier to sell ultra-processed and it had its own kind of natural addictiveness to it, so the market sort of moved in a different direction. But it wasn't like the nutritionist said, "Eat more sugar, and your reduction of fat..." So I think that the core scientists have a pretty good understanding of directionally what is correct, and that things in the marketplace caused some confusion. I think that the venture opportunity is to take these complex subjects and reduce them.

I've often thought that even something like cardiovascular disease, that you can go become a cardiologist, and it's a lot of effort to be a good cardiologist. It is possible educate people around the major factors they need to pay attention to. And to simplify that. And the analogy I might make is I remember when DVDs and MP3s first came out, it was a complex process of ripping DVD and fiddling with the data. And people started building databases to automatically index them, and a whole bunch of things. And now pretty much it's all pretty straightforward. Right? Talk. Nine, 10, 15 years to simplify that. In a similar way, when I look at my HRV data and I measure it and it's telling me that my total power frequency and low frequency... those are very, very complex subjects that I can't understand, but it seems to be a matter of time before somebody, an innovator, sort of steps up.

These are the kind of people we're looking for. An innovator steps forward and says, "yeah," – a complex subject – "we can streamline this, put it into an app, make it available on top of Garmin, make it available to people, to guide them in a more personalized way." That's, that's the type of innovation I think we're going to see in the near term and what those innovations will do will really normalize people and get people to execute what Bruce already knows as best practice.

The error will be people that read some goofy article on, I don't know, Google somewhere and decide that they're going to completely changed their diet because it worked for one person, and really has no relevance to them.

Sarah Mock: [00:35:53] I think we'll come back to that question of personalization versus generalization, but I want to first send it over to Mark Connolly.

Mark, are you ready to answer your question, ask your question? Sorry. Go for it.

Attendee: [00:36:04] So, Dr. German, you talk about the need to create a sustainable change in the microbiome and probiotic supplements are not doing that. Given what we know now, how do you think about current technologies for making those kinds of changes?

You know, eliminating green beans from your diet is not that difficult. Adding foods isn't difficult, but supplements don't seem to work. I wonder if this ultimately becomes a pure drug delivery- type mechanism, or are there more pieces to that to create that sustainable change?

Bruce German: [00:36:43] Great question. And, that's really what is facing this entire scientific and therapeutic communities: how do we go about influencing the community in ways we want? And actually our work on human breast milk and what it does for babies is very instructive.

So human breast milk contains an impressive array of complex sugar polymers, oligosaccharides. It's like your mother's putting fiber in the milk and, and it's not from her diet. It's, literally, she's making it. So, why does she do that? We originally thought it was to feed bacteria in general and clearly that was not true. These all go saccharides are sugars held together with glycosidic bonds. The bacteria need to be able to cleave those bonds, to get the sugars. Bacteria can't cleave them either.

But then we found one bacteria, a bifidobacteria. And this specific bacterium has a repertoire of genes that encode enzymes that release all of them sugars and make it possible to consume those sugars and live on it. As a result, a breastfed infant that acquires this bifidobacteria from its environment, then... it's amazing what it does to the microbiome. Over 90% of the bacteria in that breastfed baby is a single strain of bacteria, and that bacteria fuels the baby, it drives out pathogens, it drops inflammation. It provides a wealth of benefits to the baby as long as breastfeeding proceeds. But when breastfeeding ceases, then the advantage to that bacteria of that unique and selective food supply is gone. And now all other bacteria begin to populate that, that community. So we know what's possible from breast milk.

But the problem is, of course, it took millions of years of evolution to achieve that in a breastfed infant. Now science has to consider: how should we proceed for the rest of us? How do we get that combination of the right bacteria, and its metabolism, and the food supply that will encourage that bacteria to be an essence and important member of the microbial community? But, mothers have given us a really nice path to get there.

Attendee: [00:39:34] So, if I could continue to... in essence, what you're saying is that the bacteria that the mother is providing does not in fact necessarily sustain beyond the breastfeeding stage, but it sort of sets the stage for what comes next.

Bruce German: [00:39:52] And, actually, we see considerable evidence that the immune system in infants is educated through the first months of life. And that education is highly sensitive to the microbial community. So you can have, we'll say, two alternatives. You have a baby that's breastfed and it has the right bacteria. There's very little endotoxin. There's very little activation of the innate immune system. There's relatively little inflammation, even detectable. So that immune system is being educated in what we'll call a very positive environment. Now, a baby that doesn't have those bacteria – they now are gradually being populated with a gram negative enterobacteria, producing endotoxin causing in essence explicit activation of the immune system.

And now that immune system is being educated in a very different environment. Many of those educational steps persist lifelong. And you get them wrong, evidence is increasingly compelling you yeah things like allergy, asthma, eczema, and those autoimmune conditions appear to persist your life.

So, the things you do early in your life have effects. And so the bacteria and that, that unusual microbiome is critical in those developmental educational steps. The question everybody needs to answer of course, is can we fix it? If developed inappropriately can restoration of a more protective microbiome recover your immune system? We don't know.

Carter Williams: [00:41:46] So Bruce just put a finer point on this, because I'm not sure the audience knows some of this research; the process of a sterile birth that's fairly conventional on Earth today, your work has determined, may very well be the reason why a kid has a peanut allergy. And that by reconnecting the biome, you can get rid of, notionally, the peanut allergy or diabetes or certain autoimmune diseases that have expanded that your work suggests is closely tied to the fact that we're having more Caesarian sections. And trying to keep the baby clean at birth. Is that fairly accurate?

Bruce German: [00:42:34] Yeah, exactly right, Carter. And actually it's a multiple-faceted problem. Throughout human history, one of the – in fact, mammalian history – one of the advantages of life birth is that it's a bacterial transfer step. And so the mother transfers her bacteria at birth and over those few first few hours and days, quantitative, it's an ingenious idea. And with the best of intentions and very successful outcomes in many respects – antibiotics and Caesarian sections have saved literally millions of mothers and babies from pathogens – however, that has a consequence. We didn't just eliminate pathogens; we've eliminated in essence these commensal beneficial organisms.

The great news is: you can put them back. The bad news is: that has been a medical experiment; our evidence suggests that well over 90% of babies that have been born in the last three generations, never got the right bacteria. And what the consequences of that are, is an explosion of autoimmune diseases, allergies, asthma. And so, again, we've discovered it, we know what went wrong and we can now put it back.

Carter Williams: [00:44:01] Is it fair to say – again, I'm going to push out here a little bit. When we look at things like higher CRP ratios and people with higher inflammation related to the cardiovascular disease, is it a legitimate inquiry to sort of say that same effect, even at birth, of making more sterile, births may very well relate to an increase in cardiovascular disease and things of that sort? – or is that unfair?

Bruce German: [00:44:29] Inflammation has gone up in a population to the best extent that has it's been measurable. And inflammation drives a lot of adverse conditions and virtually all of the chronic degenerative diseases have a significant inflammatory component.

And so yes, one of the immediate goals of fixing everyone's microbiome is to get the endotoxins out of our gut and drive it out with bacteria that are our net protective. How to do that is something that clearly was a goal of, the result of the selective pressure through Darwinian evolution of lactation. It was vitally important to protect the baby from not only over pathogens, but from the chronic inflammation that gram negative bacteria provide. And that's one of the things that that breast milk does. And it's really a spectacular idea emerging from evolution: how do you reduce inflammation in your baby? Recruit the right bacteria and feed them. What scientists would have thought of that!

Sarah Mock: [00:45:48] I don't want to bring this conversation to a close, but I feel like we could go on on this topic forever. And we have some other folks who need to ask some questions. So I'm going to go ahead and ask Rob DiBella. Rob, are you ready to ask your question? Go for it.

Attendee: [00:46:03] Carter you recently mentioned the correlation between the reduction of highly processed foods and improved nutritional health. And I wanted to get your thoughts on the plant-based meats. And is that an exception to that comment? Because they're highly processed programs yet they're growing in, in trend and in popularity.

Carter Williams: [00:46:33] Yeah, I should reserve my comment; when I say ultra-processed, I really mean higher content of carbohydrates. But that does not... I do wonder, in terms of... as we think about something like, for example, if you're referring to something like Impossible, the degree to which that is processed, I think that there is one natural pressure that I think will start reducing the number of ingredients on something like Impossible.

As we look at SPC, you know, soy protein concentrate – and one of our portfolio companies, Benson Hill, is very involved in producing a higher protein soy that when it comes off the field can be processed into a high concentration of protein without requiring a substantial amount of later stage processes – I think that with some of the cost pressures that, as Impossible and Beyond try to reduce their cost, you're going to see that some of that processing disappears. An interesting area of research is, in terms of venture activity, can we improve that food science so that we might be able to reduce the amount of ingredients in a product?

And my just general intuition is fewer ingredients is better, but very specifically when I – well, I use the term ultra-processed perhaps a little too liberally, and I really mean high sugar content, high refined sugar content.

Attendee: [00:48:10] Very good. Thank you.

Carter Williams: [00:48:14] And one final point on that, I'm sorry. The sort of issue is – Bruce is talking about sugars I think that are more extracted out of the bowels – when you've got a highly refined sugar it's really just going right into your system and, and firing up your insulin and everything. And just is a shock to the system.

Sarah Mock: [00:48:36] Thanks for that question, Rob, we have time for a couple more questions. So if you have asked one in the chat and we don't get to it, I'll give you some information on how to join our Slack channel and we'll continue answering questions there. But next I want to ask Richard Miller. Richard, are you ready to ask your question?

Attendee: [00:48:52] Yes. Thank you. I've followed Carter and iSelect, and we're finalizing a business model. And my question is derived from some of the research. One of my advisors, my PhD son, researched, in tribal communities, breastfeeding up to the age as high as eight years old versus alternative feeding methods to children. We're seeing at each stage of our lives, whether it's in the birth in a stage or early childhood to young adults to middle aged adults to seniors that the way that commercialization of food has changed our diets and biome, it's disrupting every stage of our lives. And we're wondering if there's a method in the science that allows us to evaluate each stage and develop a nutritional process during those stages that allows a consumer and the medical community to work in concert. And if that isn't available right now, is there money available to put in to that process? So we can begin evaluating one's diet as early as in the mother's womb, based on the mother's diet all the way through their development stages.

Carter Williams: [00:50:50] Bruce, that one's for you.

Bruce German: [00:50:53] Actually, I would love to see you as a visionary and a thought leader in the investment and science support community. This is a great vision you have. From the perspective of this life

stage approach, in fact, when we look at breastfeeding itself, we see evidence in essence and in many respects of exactly what you're saying.

So breast milk changes, literally not just day to day. Hour to hour, from the beginning of feeding to the to the end of the feeding. It's profoundly different throughout the period of lactation. Early milk is supporting especially the immune system of the infant and getting in essence the maturation products to the gut and all the things that were, in essence, very naive because it was just born. And then milk gradually changes as, as the baby itself. There's a slight difference between morning and evening milk. Babies sleep a little bit better. There's a slight difference between the milk that a mother gives to her son versus the milk that a mother gives to her daughter. So mothers who have daughters have slightly different, so there's boy milk and girl milk.

So, so as we begin to use the consequences of evolutionary, selective pressure on lactation and milk, we start to see not only we should measure people throughout life stages, but what we should measure to see how they're doing. And then for those where we see an early trajectory going in that direction we would not like, we can act early in preemptively to reverse that trajectory before ever gets to the point where we're seeing overt, inappropriate health conditions. And ironically the best answer we've, we've developed from all of this is, when you have a question, go ask your mother!

Attendee: [00:52:58] You know it's interesting because if we analyze the process foods – and I know Carter you've studied this tremendously – and we introduce organic and natural foods it enhances the immune system, not only in the soil, but also in our humans.

So if we can develop a synergy between our growth in plants and growth in animals that we consume and then interject it into the human life stages, we can enhance the immune system which has been seen by our advisors as beneficial in the breastfeeding stage versus, in the United States, weaning them off of even starting breastfeed and putting them on commercialized formulas. So we can get that start early.

Bruce German: [00:54:09] Yeah, you're absolutely right. But I want to emphasize that not all processing is bad. There are some plants and biomaterials that need to be processed in order to make them safe. So it's not processing that's the problem, it's inappropriately processing. And we have learned how to process foods to make them almost pure rocket fuel. And humans don't have a lifestyle today that's consistent with having rocket fuel is a food supply. So, so we have to learn how to process for each person.

Attendee: [00:54:46] Individually.

Bruce German: [00:54:47] Yeah.

Carter Williams: [00:54:48] Yeah. Sugar is not necessarily bad for you, but how and where you absorb it in your body, and how it processes into your body can make a big difference.

Sarah Mock: [00:54:59] Well on that note, Richard, thank you so much for that question. This has been an enlightening conversation. Thank you, both to Carter and Bruce, so much as well as to iSelect Fund. And we want to offer a big thank you to all of our partners in producing Crusonia Conversations. A big thanks to Benson Hill, a partner of the Community Foundation of Greater Memphis, Cushman and Wakefield Commercial Advisors, EY, and United Health. As we wrap up, we just want to remind everyone that Crusonia Conversations are free to attend but, unfortunately, not to produce. So please consider donating to the Crusonia fund. Go to crusoniaonthedelta.org to donate or click on the donation link in your follow-up email.

And please join us for our next Crusonia Conversation which will feature Vonnie Estes, VP of Technology for the Produce Marketing Association. That'll take place on Wednesday, September 16. You can register at crusoniaonthedelta.org. And if you're looking to revisit today's conversation or to keep up with Crusonia Conversations going forward, or for folks who didn't hear their questions answered in today's conversation, follow along on LinkedIn, Twitter, YouTube, and on our very lively Slack channel. You can go there to keep up with this conversation as it moves forward, both online and offline. It's a very lively group. Until then, links to all of these resources will be available in the follow-up email you receive after this event. And also, registration for Crusonia on the Delta Digital Forum on Wednesday, September 30th, broadcasting live from Memphis, will be open now. Please be sure to check your inbox for an invitation. Thank you all so much for joining us and sticking with us today. We're looking forward to seeing you again in September. Thanks!