

Global Wellness Summit

**11th Annual Global Wellness Summit
DNA and Biomarker**

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[background music, noise]

FEMALE VOICE: Good afternoon everyone. Thank you for joining us in the salon. We're going to start momentarily if everyone can take your seats.

DR. KEN PELLETIER: Okay, good afternoon. My name is Ken Pelletier and I'm just chairing this session and what we did collectively is I asked each of the participants to send me six or seven questions and then we kind of pooled them together and came up, you know, I came up with roughly six or seven topics that we are interested in talking about, but what we want to know is what are you interested in talking about, and I thought if we could just take quickly, just go down the panel here because these they really are experts, and that way you get to know who we are. We'll talk a little bit about a few questions that we've thought of, but really, for the majority of the time, at least half of the time, we'll open it up to you to address questions and thoughts that you might have. Does that sound like a good use of the time? Okay, great. So, Alyssa, could you?

MS. ELISSA EPEL: Sure. I'm Elissa Epel so thank you for coming. This'll be an interesting discussion. It's a special year with an explosion of companies, of us having testing in our hands. Can I ask how many people have been tested here with genetic testing? A highly select group. I am a health psychology researcher and I am an expert on telomere testing, which will eventually get to you and I'm a consumer of genetic testing and I have lots of opinions, but the genetic experts are near me, and I'm making up, for being short all my life, I adjusted my chair up and it wouldn't go down.

[laughter]

MR. SIMON CHIN: Yeah, I'm Simon Chin and it's a real honor to be among the distinguished panel here, so my background is that I am the president and CEO of IRIS Wellness Labs, so what we do that is different than any other company out there is that we look at the end to end solution from you know your whole genome sequence to your epigenetics and your micro biome, as well as in-depth analysis of your family medical history and lifestyle. So we ask questions. There are about 20 pages,

so we dig really deep into it, but most, most importantly, we work with the patient and their physicians so we can help them if we need help with treating cancer or other diseases. We also help, you know, healthy people.

MS. LORENA PUICA: Hi, my name is Lorena Puica. I'm the founder of CEO iamYiam, an everyday and lifelong preventable health platform, so I've spent about a decade of my life in the investment management, investment banking space. I've messed up my health in more ways than one and more ways than doctors can fix and after about five years of hormonal therapy and different approaches, I decided to take things in my own hands and take control of my health, and that has been the inspiration of looking at health very differently and looking at health as an everyday activity, rather than a one-off, repair shop approach and that's what we aim to do, besides of enhancing the health of a billion people by 2025. But that's all. Nothing more than that.

DR. PAUL LIMBURG: Good afternoon, I'm Paul Limburg. I'm a gastroenterologist at Mayo Clinic. Early on in my career, I saw way too many patients with colon cancer, which is the area I focus on, so I did advanced training in preventative oncology. As we start to learn more about family history and its effect on chronic diseases, cancer and otherwise, was interested, became more interested in the role that genetic or genome testing would play. Our organization has recently invested in something called the center for individualized medicine, where we apply many of these assays and the data that come out of them to real-life clinical scenarios.

MS. RAYA KHANIN: Hi, I'm Raya Khanin, and I have over 20 years of experience in computational genomics, and even before that, it was called computational biology so, and I've been working the last eight or so years in Memorial Sloan Cancer Center analyzing data from cancer patients in the hospital and developing methods, figuring out why some drugs work on the one group of patients and not the others and really looking at these comprehensive data sets with genomics, micro-biomics, micro RNAs, everything and then with kind of this growth in energy. I just thought that it would be really good to apply the very same techniques again to prevention and to wellness and I co-founded together with Alamaster Sheri [phonetic], we cofounded LifeNorme and our goal is to bring prevention and wellness and to personalize products and services in the wellness industry.

DR. PELLETIER: Very nice. Thank you. Just taking from what Paul said about preventative oncology, it's kind of an oxymoron in the preventative medical specialties, preventative oncology, cardiology and so I'm curious, any speculation about the difference between healthy biomarkers approach and epigenetics and genetics versus disease predication. Any thoughts that you have about that? That distinction, if it's a meaningful distinction, which one do you pursue, which one has the greatest future, et cetera? Thought?

MR. CHIN: I think, you know, looking at the epigenetic aspect of it, as well as your DNA is kind of like asking which hand is more important, your left hand or your right hand. You need both and not one or the other. You know, you can function with one hand, but if you have two, you get much more information so they can help you in making better decisions and then a lot of people in this audience have gotten their genetic tests. So, let me ask you this question. How many of you think that you have one unique DNA? Please raise your hand. Okay. How many of you think you have two unique DNA? Please raise your hand. Okay. I don't see too many hands.

What I mean is, a lot of people think, as a person, my DNA is unique and you think you only have one unique DNA, but in reality, you have two because you have one from your father and one from your mother and they are not identical, so that is something to keep in mind, number one. Number two, a lot of different tests are out there. You have, some of you have gotten the tests done by IM or by LifeNome, and the amount of things they look at, correct me, if I'm wrong, if your DNA is like a book with 1,000 pages, what they look at is about one page, so they give you a quick snapshot on things that are important to you, you want to know, but the other 999 pages has a lot of information that is really crucial to your life, either now or in the future, because if you have your whole genome sequenced and let's say you have things that happen in the future, you already know where your baseline is and you know what changes, so I just kind of bring that to the front so that you have a better idea, because the panel, the question to ask us is are the DNA tests ready for primetime. So, the way that I look at it is are you ready to discover yourself? In a way, it's like asking can you use a Stradivarius violin to make good music. The answer is, depends on who's playing it. Okay, and likewise, you know, when you look at your genome, the DNA test, you really need

to know who is really looking at your data and what do they really know they can help you with.

MS. KHANIN: So, going back to the question whether one should look at healthy structures or disease predisposition, from our perspective is, what, what is the goal? What are you trying to do with that information, so there is a combination of healthy data points and predisposition to disease, so from our perspective we look at things and at data points that help us provide the relevant information so that the individual can take action and take a set of steps that help limit the risk factors that build into their genetic structure. At the end of the day, the DNA, we understand less than five percent of it, so we are a long way to go. However, the strength and the weakness of DNA structure is that it's a fixed data point. However, the epigenetic factors as well as the lifestyle factors are dynamic, so looking at both the fixed data set, which is the DNA or element, as well as the lifestyle factor and epigenetic factors and look at the interactions between these two, that is what I think is helpful for the individual to be able to take action and informed action to be able to face risk factors that are in-built in their genetic structure.

DR. LIMBURG: Yeah, I would just follow up on that, too. I think in some ways, we've gotten smarter in clinical medicine, which, again, is not necessarily the consumer-facing piece, but as you talk about the diagnostic ability of some of these markers that we're looking at, chronic disease is not a light switch. So, you don't wake up one morning and develop a chronic disease.

In the area that I work I, disease is carcinogenesis. It's not cancer. So, at some point, a normal cell becomes an abnormal cell, which becomes more abnormal and eventually meets the definition, technical definition, of cancer, so, I think as we start to think about these chronic conditions are processes, then it becomes how do you change the risk? How do you minimize the risk. How do you maximize the benefit of whatever it is that we're trying to do as an intervention?

And I do think it's a combination of all of the different technologies. What's running through my head is technology, biology and the art of medicine, which sounds like a bad book title, maybe, but I think that is reality. So, is it epigenetics? Is it genomics? What is it? I don't know, but I think if we start to think more about the model is

carcinogenesis, it's got a genetic component. It's got an epigenetic component. There's the transcriptome. There's the metabolome. There's the environment. We need to put all of these things together and find those measures that are most useful, and to me, those are the ones that are most actionable.

MS. EPEL: What did you have in mind for positive biomarkers of health, not disease?

DR. LIMBURG: Well just the pre-disposition, so for instance, lipids would be moving in, in a positive direction, depending on their profile and that's one way to look at the testing. Another is to say you've got this percent of chance of coronary heart disease or MI in the next year. That's what I meant by the disease prediction model, using the data, but using one that is modifiable and emphasizing that it's a healthy marker, you can change it, versus this is your fate. You have an X percent change of heart disease. That's the, it's not binary.

MS. EPEL: No.

DR. LIMBURG: It's a matter of emphasis, like left hand, right hand.

MS. EPEL: I mean, for true prevention, I'm still waiting for that list of health markers, not disease markets. There may be such thing as resilience genes. There's people like Eric Shatt [phonetic] are looking for people who have genetics, strong genetics for a disease and never manifest the disease. These are usually genes that have extremely strong penetration and manifestation of phenotype, and some people never get them, so there's resilience genes. There's probably other environmental ways of interacting with that genome that create resilience but for a real paradigm shift toward prevention, it raises the question, it's kind of not on the table here, but what if you took someone who is a young adult and they have their whole, or, you know, even a teenager, their whole life in front of them. What should they monitor them to even think about prevention? They're not thinking about disease yet. Right? That's not motivating. That's so far off, but with this kind of achievement orientation that is rampant, how can I stay well and maximize my health and thrive and have, you know, live to 110. So, what are those markers?

You know, I think that we know in general what to measure in the short-term for thriving and positive physiology, heart rate variability, DHAA. There are all sorts of wellness indicators in the moment, but we don't know that those are long-term resilience factors. They're a starting place.

DR. PELLETIER: You're raising an interesting question. So, maybe we can have some thoughts on what do you tell a patient? What do you tell a person and what are the plusses and minuses of disclosing this information, given the state of the art right now. Five years from now, that's a question we'll get to, is I think it's going to look very different. But given the state of the art right now, I think that's going to look very different - -

MS. PUICA: Okay, I'll start. I'm not a physician, so I think it really depends on the patient. It depends on disease, as well. I mean, it's kind of common knowledge that mutations in BRCA1 and 2 genes, so immediately, you know, people test for that and talk to their counselor, state talking to oncologist and take immediate action and personally, I think that in many cases some of these mutations are of borderline functional significance in terms of the risk may be a little bit lower. We don't know that. But here is a balance between risk of getting, you know, metastatic breast cancer in this case or playing a waiting game, and on one hand, we don't have enough knowledge to act on that. On the other hand, if we don't do that, then everybody with these kind of mutations will take immediate action and we will never, ever know.

So, you know, and this, this is a kind of, a question for patients to decide, the physician and probably also for the society are large. Is it like the binary, there is a mutation in this gene, there is a surgery, or there are some other factors to take into account. And what are these factors, as well.

DR. LIMBURG: So, I do think it's important. I think Simon touched on this already that your genetic code is not your fate, so again, we're talking about risk and how do we alter risk over an individual's lifetime. There are clearly carriers and states for specific genes and specific issues where that information is useful and actionable where someone has a BRCA 1 mutation, they may choose to have surgical preventative operations to try to reduce their risk, et cetera. There are also very real situations where that

genomic profiling can be extremely useful in a clinical setting, pharmacogenomics. Should I take this medicine? What is the risk to me if I take this medicine at this dose? Pharmacogenomics can be enormously helpful in that context. Other chronic conditions where you can do a targeted panel of genes to try to identify or risk stratify, and then in our center, we also sometimes see patients who have been to multiple physicians, multiple extremely good healthcare institutions and they don't have an answer. The Center for Individualized Medicine has called those cases diagnostic odysseys. So, but nobody can quite figure it out. In that situation, again, a more expanded panel of gene testing can be very informative, can look for some of those rare conditions where there is an action plan both for that individual and their family members.

MS. KHANIN: I think Elissa briefly touched on the science element, and from my perspective and from our perspective, the science, what is the scientific backing of all of these different approaches is key. The wellness industry, I think it has struggled for the past couple of decades with the right scientific backing for different types of approaches that are available in the market, so looking at the situation very much from a preventable disease perspective, first question is, is one focusing more on the acute conditions? Is one focusing more on the narrower percentage of the population or on the broader population that is facing day to day challenges, everything from stress anxiety to depression, diabetes and cardiovascular disease, and for that audience, then the, the question is what are the most robust and scientifically backed set of tools, approaches and protocols that in combination with and understanding of the genetic data and the respective risk factors and the epigenetic data can provide an indication of what the person can do about it.

So, the powerful element here is in an understanding of where science is on these different barometers and when it comes to cancer, Alzheimer and Parkinson's, there is, while research is being developed now and there are clinical trials that are taking place, there is a smaller body of data in clinical trials to be effective and actionable, long-term protocols for people that have these conditions, so from my perspective, it's also a question of how many clinical trials and how many people have been involved to show efficacy and efficiency of those protocols for specifically that approach for that condition.

MR. CHIN: Yeah, I mean, you know based on all the published literatures on all the genetic stuff, current the recommendation is that there are like 59 genes, you know, so if you find one of these 59 genes incidentally to test that we were running. Then, the recommendation is to share this information with the patient. And one thing I think most of you would be familiar with is what Angelina Jolie did after she got tested for breast cancer. So, the BRCA gene is something that, you know, they say if you are positive, it means you have like 87 percent chance of getting disease, and there are many women that, after Angelina Jolie went ahead with a mastectomy, many women followed suit. So, if you look at the traditional curve in terms of how many women get a mastectomy, the curve was like this. It exponentially came along and went up like that. But, within like, something like three or six months, it came back down to exactly where it was before. So, there was no change, you know, in long term.

But let's say looking at the BRCA genes, new research have showed that instead of just looking at BRCA genes, some of the mutations, if you look at more deeply, then instead of just telling a patient that you have 87 percent chance of, you know, getting the disease, you may be even able to narrow it down into telling them, okay, you have somewhere between 30 and 87 percent and you're actually close to 30 than 87 percent, so then that will allow them to make better decisions, so that is, you know, what is currently published, but a lot of people don't know about this yet.

But Elissa talked about what can we tell the young people who aren't worried about disease yet, but the thing that's very prevalent today that wasn't prevalent 40 years ago is that the kids today have a big problem with obesity, and obesity is a gateway disease, and because, from obesity, you will get diabetes, you will get heart disease, you will get neurological disorder. You can go blind, you know, alone, people have to amputate because of diabetes and so on. So, obesity leads to many disease, heart disease would be an obvious one. So, what we can do, I think is help educate the children, maybe at the school level and maybe the parents somehow so that they understand what is really happening and what, It's not just saying, you know, it's the soda or eating fried food. It's really, what it comes down to is a lifestyle. The way that we like, we like to work is that, instead of dealing with things short-term, we like to engage

on like a lifelong type relationship where you help families or you help companies that want to have healthier employees, but focus on the long-term so people understand the consequences and the choices that they have.

MS. EPEL: Thank you Simon. Very interesting data. I have a question for the panel, which is, what does that data tell us. We know that people know what to do and have trouble changing, and especially kids. They didn't choose to be obese and so we have, so the question is, when people know they're at risk for diabetes or Alzheimer's, does the health behaviors or eating behaviors and more actually change? Testing positive, does it change behavior?

DR. PELLETIER: Even without genetic testing, if you look at the evidence for sustained behavioral change in medicine, it's almost none. I mean, there's almost no evidence that sustained change is easy. It's very difficult. So, for example, hypertension is the most ubiquitous condition for which we have clear pharmacology. We have excellent behavioral change programs, and yet, it's one of the most pervasive, highest risk factors and has been for 50 or 60 and I haven't seen any of it, at least in cardiac technology general practice, that hypertension incidence is changing, despite that. So, I'm skeptical that no matter what information a person is given, that it's going to motivate them to change.

If there's a related kind of, you'll appreciate this, variant of what you're asking, which is any outcome, you have a type one, type two error, so you have a positive outcome and in fact it is not accurate. A person is saying, you know, predisposition to Alzheimer's, you don't, despite what the genetic evidence shows, there's a countervailing genetic interaction somewhere in the sequence that negates that. Then, you have a type two error, which is where you have a positive and you don't have that risk, and you never will manifest that risk. And how do we sort that out in conveying to that person, and the only think I've thought of is we'll maybe transition to asking for you questions and input and thoughts is that it's a tri-part type conversation for everything we've been hearing, which is you have the genetic testing. You have the wishes and interests of the person, patient, critical, critical ailment and then you have the counsel of the physician or a genetic counselor, or nutrition, so, but when you have that tri-part type group in place, then you've got that way to create the conversation

and create some conversation about predisposition and moderation. Without that, you're really adrift kind of in the science of sampling, so I'm okay with it, can we open the floor? Okay. Is that good?

Okay. I'll try to, say your question loud enough and I'll try to repeat it to make sure everyone can hear it. This is now your time.

FEMALE VOICE: And if you have a question, if you'll say your name and introduce yourself and make sure you speak into the microphone because we are recording.

DR. PELLETIER: Thank you.

MS. CHRISTINE HOFFMAN: Hi, my name's Christine Hoffman and I'm a consultant that helps bring wellness programming to spas and other properties. My question is, are they researching with genetic correlations to find the genes that make it more likely that people will engage in change behaviors, like behavioral genes that will identify that if you give this person this information that they're going to embrace change or what might make change more successful for a given genome type?

DR. PELLETIER: That's a great, great question, because I said the great bane of medicine is how do you, you can illicit change. How do you sustain it? And Elissa and I were actually talking, and so if you would field that?

MS. EPEL: I think, I from what I understand and know, this is the edge of behavioral genetics where people want to understand what genes predispose people to better lifestyle behaviors, particularly exercise and there are a set of genes, there are already companies that are counseling people on exercise genes, et cetera. I personally am someone who's very skeptical because any one gene predicts, oh, Jay Williams actually taught me about this. I just noticed she's here, so she should comment after me about these exercise genes, but any one gene predicts, I mean jeans are different, but for most of the genes for behavior, we're talking about tiny, tiny tenths of a percent or thousandths of a percent's of variance to predict. Same with obesity, right? I most of obesity, 95 percent of obesity, we can't predict. We only know the genes that predict five percent of obesity, so these are complex behaviors that are developed over a lifespan that are shaped by life experience, and I think the biggest things are helping people enable them to do the right thing by

helping them, their, they need to be supported. They need to have a supported environment to do the behavior, and then they can be motivated. Motivation doesn't just overcome all barriers. That's not, we're more animals than we think, so we can predict a lot from these rat studies, for example about impulsive eating and what happens with predicting and understanding binge eating is another are. Jay?

MS. JAY WILLIAMS: Yes, I actually have been using some of these testing methodologies to work with clients and I've set up batteries of tests, actually, that were part of both initial conversation and ongoing behavior modification for people. Lifestyle, of course. I don't do disease. I do lifestyle. And, the way that I see them best used at this point, because I think everyone will admit we're tip of the iceberg. Every day. You know, there's a couple companies I work with. I work with fitness genes and a couple of other predictive genetic fitness companies and every day they send you new information. Every day there's new research and so the way that I see them best used is a start of a conversation, a part of a consultation that then involves, as Elissa says, there has to be some handholding because you can tell somebody that their genetic makeup says that they should best work out in the morning, not in the afternoon, but if they don't have time to work out in the morning, or they don't like to work out in the morning, they're not going to, so it doesn't matter what their report says, so there has to be the element of, here's what we know about you at this point in time. There's more coming, and there has to be the lifestyle piece, the emotional piece, the what are you capable of doing if you want to move the needle with somebody.

So yes, I love these tests. I am using these tests, but it has to be a part of a bigger picture.

DR. PELLETIER: Thank you. Yes, sir?

MR. JOHN FERNSTROM: John Fernstrom, University of Pittsburg.
What exactly do you mean, or, no, what do you sample when you sample for the microbiome?

DR. PELLETIER: Oh, basically, the question is what do you sample for the microbiome. It's a stool sample.

MR. FERNSTROM: Right, so, I've seen studies and discussed this with some people in the area and it is basically a continuum running from the beginning to the end of the small intestine and what you see are very different levels of population

densities of different microorganisms, so the question would be, what would, and this one person I talked to is stool is the last thing you would be interested in measuring because you're already looking at a post-body modified version.

So what actually do you want to look at as a reasonable representative? Do you want to look at different parts along the length of the colon? Or what?

MR. CHIN: Well, you know, you're absolutely right.

DR. PELLETIER: Well, just a sec. The, yes and no. I mean, you have, you do have. Oh, mike, sorry. Mea culpa. So, you do have cells, in fact, along, the mouth to the anus and in the case of women, you have the reproductive tract is also part of the microbiome environment, the trillions of cells, so you do get trace cells no matter where you're sampling, so even in the stool sample, though the bulk of it might be fiber, might be dead cells. You're getting samples all the way through the gastrointestinal tract, so it's not really accurate that we're only getting, if you will, by-products that don't really tell us much about what's going on in the total intestinal tract. I mean, certainly you don't want to biopsy any aspect of the tract, and I think the quest now, and again, Paul, chime in. I mean, now the issue is that we have maybe 300 to 400 biomarkers that you can detect in the biome, so the question is, what do they mean? It's like looking at a barcode in a supermarket, and if you don't have a scanner, you go I have no idea what that means. And how many of us, have you really looked at your own genetic map? I look at it and I have no idea what this means and it's like that with the microbiome. That's why it's the last and most difficult of the tri-partied measures to--

MR. FERNSTROM: [interposing] People now make a whole lot out of a stool sample, so all kinds of stuff show up in professional journals based on somebody interpreting what's in a stool sample and generalizing way beyond what's reasonable, and talking to folks that actually work with the microbial populations of the gut don't think very much of that, and basically, I'm not a good interpreter because I don't work there, but I've listened to some of this and they don't agree that a single sampling of anyone is enough to be able to say what the actual function of microbial population is.

DR. PELLETIER: Yeah, this is a, this would involve a multiplicity of samples, actually, more stool mass than we'd ever care to

think about, so at this point in time, that's part of the problem, which is how do you, obviously you can draw X number of vials of blood and you'll find something, but what is the minimum number that will give you a complete CBC, and again, with the microbiome, what is a reasonable stool sample that will give you cellular activity.

MR. FURNSTOM: What I'm thinking is, if you're taking a patient and giving a sample and read the entrails, if you will, is it appropriate just to have a stool sample to make a reasonable statement about what's actually going on.

DR. PELLETIER: Yeah, I think, and again, I don't want to take up too much time here, but Paul, you're the gastroenterologist.

DR. LIMBURG: It's all about the colon. I think we all realize that. I'm kidding. So, I, I think like with all cutting edge questions that affect health and well-being, I just feel like we don't quite know enough yet, so can we find variation throughout the intestinal tract in the types of microbes that are habituating? Absolutely. What does it mean? I don't think anybody knows that yet. Even if you measure a stool sample and you measure repeated stool samples, nobody quite understands what, what the implications are for health or for disease, so I think we have to kind of take it in a stepwise process.

As Simon and I were chatting prior to the summit, the analogy to me is, don't throw the baby out with the bathwater. It doesn't mean that none of these technologies are good or useful. We just have to understand how to apply the data. We can measure a lot. We just need to know what to do with the information.

DR. PELLETIER: Also, you're not looking at it in isolation, so you're looking at genetic markers, the blood markers and the biome markers, and sometimes these align and you have a strong predisposition. Other times, they're contradictory. What you see in the genetic coding and what you see in the blood markers in terms of is that being manifest in the blood and then you see if in the biome and it's completely missing and you say where did it go? We don't know. You're absolutely right. There's so much right now that we don't know, and you concern, your caveat is well taken because it's accurate.

MR. CHIN: Let me comment on some of the nuances associated with it. A lot of the microbiome tests out there today are

practically useless for different reasons. Number one, you know, the stool sample that is taken, you know, you are right that along the track that, the small intestine through the large intestine to the colon, the microbiome populations have different microbes in there. That part is true.

That you know, when you have the stool that pass through, you know, you can actually get good data from that. The problem with the way that people preserve the stools made a big difference, because if you use the wrong reagent, then it will favor some bacteria surviving compared to the others, so that is a number one big problem, because a lot of the firms don't look at that carefully, number one, and number two, when you do the microbiome analysis itself, what you have is that people look at things at the species level. If you're only looking at the specie level, it doesn't tell you a whole lot. It could tell you how things change over time, so you can take your microbiome test and you watch it over time, then you can see how it actually changes, so there are over 1,000 different species of microbes in your gut, but more importantly is the genes, you know. What are they doing in your gut, because there are 10 million genes in your gut and you know, our own DNA only have 23,000 genes, okay? So those 10 million genes product a lot of different proteins that go all over your body and into every organ, and what is important about the micro biome is that number one, is helps you to digest the food and number two, it helps, you know, it produces the vitamins that you need in order to be healthy, and also, your microbiome trains your immune system. So, for example, let's say you have breast cancer and then you get treated with chemotherapy. If you don't have the right microbes in there, your chemotherapy is not going to work, so there are a lot of things about the microbiome that's very important because the micro biomes, let me regress one minute.

You know, we're all sitting here thinking and listening and talking. Our brain, the way it functions is that it uses neurotransmitters, and 70 percent of the neurotransmitters are produced in your gut. So, this is an area that you absolutely have to see because the microbes are, especially if some of them get passed through the blood brain barrier, because as you get older, the barrier gets more porous and it gets into your brain. So, let's say you have bacteria get into your brain, the way that the brain fights back is to produce these beta amyloids that surrounds it and kills it.

the problem with all these beta amyloids, it's like chewing gun, so it sticks to your cell and kills your brain, so you know, that's one contributing factor to Alzheimer's. You know, similar things associated between bacteria and Parkinson's disease in any way. So, if anything that medicine needs to do today is to focus on really studying and understanding the microbiome. That is really the next frontier in terms of helping to complete the understanding and enable physicians to help.

DR. PELLETIER: Let me just jump in, Simon, to make sure we get time for people.

MS. PATRICIA LATTICE: Hi, my name is Patricia Latt--

DR. PELLETIER: [interposing] I'll get to you sir, I'm sorry.

MS. LATTICE: Hi, my name is Patricia Lattice and I'm the co-founder of Chema Wellness in New York City. We're a physical therapy and wellness center. We're also linked with the functional wellness community, people like Dr. Ornish and the like. And what I find is that these physicians who are doing a lot of this testing are starting to back off doing some of it. One, because it's just not suiting their patient population. It's not creating their behavior and change. What we do is that behavior changes long term do happen in community, and so pairing patients together, having groups, having some sort of online chat or something like that really does lead to behavior change, but you know, some of this testing, even as a physician, you can't do. It's not legal in certain states, depending, so you can get a very detailed micro biome test but you can't for, if you're a certain physician, so now naturopaths are starting to come up and are able to do these things, and it's a lovely thing, but what my question is, is it okay just to have this DNA testing alone? Or do you really need to do a metabolomics testing, like you said before. So, you have the BRCA gene. On average, that gives you 80 percent, and I don't even know how you come to that average, but for me, it might be five percent because of my lifestyle because I have no cancer history in my family, et cetera, et cetera, and I'm not saying that I have the BRCA gene, but what I'm saying is, I think that's ore what people want to hear is more their percentage, not just that they have the gene, and I think that's more of an ethical thing.

But, I also think, how about food sensitivities. That's what everyone wants. They're like, okay, great. I have these

genes. I have these percentages, but what are the foods that I should eat. I want to make the lifestyle change. Why does this food affect me a certain way and this food doesn't. How come my friend can eat carbs and not sleep and the minute I have a crouton, I'm sleeping. You know, things like that.

DR. PELLETIER: Some of those things are easy to answer and there are good answers. Others are very complex and probably have no answers. Seriously, from the question you've just rattled off. Okay, go ahead.

MS. PUICA: I'll have a go at this. I think there are two ways of looking at it. One is the scientific debate which is where the micro biome and the metabolic analysis I perfectly, it's a perfectly valid conversation and it's a science that's still in its infancy and we're going to discover a lot more in five years' time.

When it comes to the DNA side of things, as well as the epigenetics, there are things that an individual can already take action on, and that's the other side of the debate and from my, from an ethical as well as from our ethos perspective, the question is always what is the purpose of the test, of the respective test or of that specific engagement with a naturopath or a platform or expert, and then what is the desired outcome. What are you looking to get out of it. From that perspective, we've made a strategic decision not to go into the micro biome space because it's still in its infancy, and it will prove very effective, once we actually know what the correlations are between the data points that we have and the outcomes that we want. But, at this point, we don't have that.

And on the behavioral side, I think it's been touched on by Dr. Ornish and a few other presenters, over the past few decades and maybe over the past 200 years since we've been in this medical paradigm, it's always been in a negative conditioning, as in, if you don't do this, this will happen, so the fear was the driving factor of behavior. And now we've developed and understood that's not working and that positive conditioning in conjunction with the right community involvement at the right time and making that journey fun and exciting and just enjoyable, because health is supposed to be fun, I think that will be the key game changer in this space, in my opinion.

DR. PELLETIER: Sir, in the back?

MR. SIMON ALAD [phonetic]: Yeah, my name's Simon Alad. I'm a rheumatologist working in the UK and I can see my practice increasing tremendously with all of this because I already spend a lot of time allaying fears of patients who attest that they don't understand, particularly immunology tests, which have taken many years to standardize, so my question really is about standardization of genetic testing. I would hope that the genetic information would be the same in different laboratories, but we've heard about epigenetics. I suspect that even the genetic code is different in different laboratories. Will patients get different messages from different laboratories, increasing anxiety, increasing my workload.

MS. KHANIN: It's a good question, yeah. So, even in the medical community, there is annual evaluation of specific mutations in, let's say cancer related genes and yes, those guidelines change, so, it's, this is a dynamic area, so it's not like we can just, we as a community, can kind of make decisions now and freeze them for forever. It is changing, so maybe, you know, there could be false positives and false negatives here, so of course their goal should be to standardize things, but again, on one hand, we know a lot, but we still don't know so much more--

MS. EPEL: But Lorena and Raya, would he get the exact same result going to your two companies for the known genotypes?

MS. KHANIN: Oh yes, yes.

MS. EPEL: Is there 100 percent accuracy? And you're just talking about the nuances of decisions about what is, has been shown is going to be a risky SNP.

MS. KHANIN: So from, the first question is what SNPs and what type of barometers one covers. We don't go into cancer, Alzheimer's, Parkinson's--

MS. PUICA: Neither do we. This was more kind of, yeah.

MS. KHANIN: So, from the SNPs, obviously there is a body of research that is unified across the universe to the extent of my knowledge, so for those specific barometers, as long as one communicates the same message, it would be the same. Now, a lot of the companies in the space decide what group, how to interpret those SNPs for specific predisposition, and in that case, the results would be different if the wording as well as the parameter name would be different, and those

are nuances that probably the end consumer is not immediately noticing, but that is what will give the differences in outcomes for the end consumer.

Whether everything that's out there is very end consumer focused, I have my opinions about that, but I am obsessed about what is the purpose of the end consumer of engaging with anything, and for me, the question is what are you trying to achieve with that. Do you want to have a healthier lifestyle across the board? Happy days. We can help with that. Do you want to prevent cancer, Alzheimer's? We can't do that, and I think that messaging and that overpromising and under-delivering is the key questions.

DR. PELLETIER: Thank you. And over here, please.

MS. LIZ TERRY: Hi, Liz Terry from Spa Business Magazine. I'm interested in the state of flux that we exist in. So, I understand that gene expression changes constantly. Every millisecond of the day, your gene expression is changing, so if you ask yourself every second of the day, what can I do right now to help my health and wellbeing? Do I drink that drink or this drink? Do I sit up straight? How do I breathe? Do I get sunshine on my face or not? That will actually change your health. I wonder if we're communicating the urgency of this to, to our customers and to the world in general, whether we're looking at this as something that can be tested and is it the same today as it was last week, rather than thinking about it as something that is constantly in a state of flux.

DR. PELLETIER: Well, I'll leave that to everyone, but there is a stability over time. So, there are fluctuations, but they're in relatively limited parameters, so if you look at lipid sub-fractions as an example in a blood sample or you look at predispositions to metabolite lipids in a genetic test, it will fluctuate within a narrow window, so yes, you're influencing it, but it's not clinically significant. However, if you have a hyper reading or a hypo reading that's really out of range, that's when you can focus and begin to think of environmental exposures or stress management or dietary influences that will bring that particular parameter within this narrow range band.

MS. TERRY: But given how many people get sick, because generally those small differences all add up and you can go on a downward trend, which is when chronic disease and serious

illness happen, so although it might be a small oscillation, if it's on a downward trend and it does change every second, then is that significant?

DR. PELLETIER: So, I mean pharmacology, pharmacokinetics use pharmacology at that point, depending on how out of range a reading is you want to intervene with pharmacology. Foods, nutraceuticals, botanicals are not necessarily going to be powerful enough and that's where the typing, if you will, of pharmacology came in. Go ahead.

DR. LIMBURG: I was just going to add, sounds like there's a lot of comments that are pending here, but you know, again, there's a genetic blueprint and the genetic blueprint is fixed. Then, there's the gene expression. The gene expression is influenced by multiple different factors, including epigenetics, whether you methylate a gene, you turn it on or you turn it off, so the genes stays the same, but the expression of that gene can change dramatically given all the factors that you mentioned.

Then there's the host response to whatever is being made in, you know, too much or too little or just right amounts. The whole immune reaction, the whole immune response to any of these things, these triggers that are affecting gene expression, you know, then there are all the other things that are on top of that, the socioeconomic status, so disease is wonderfully complex. I think when you get to the gene testing sort of the core of what we've been talking about here, the standardization from a laboratory level, no disrespect to my colleagues who spent year working on this, is the easy part from my perspective. It's the standardization of the interpretation and what we do with that information that I think we still don't know.

MS. EPEL: Well, so this isn't supposed to be a debate, so kind of like, should I say this or not. That was my disclaimer. In my opinion, the genetic testing is going to be critical information that people should be empowered with and we will learn as we go along what to do with it. Everything else, when we get to big data, to me, is in the scientific discovery stage, and if I were running a business, I would only, the only reason I could see doing some of this and having your customers get all this alarming information and trying to interpret when it's really a swamp is because you need to do that because all the competitors are doing that, but a lot of it is really, really not helpful.

So, gene expression, we have a few disease signatures, a few out of all of the diseases. I don't want to know my gene expression profile unless, you know, I know it's going to be something I can monitor. I have IBS and we actually have a genetic gene expression profile that I can then monitor. And the rest changes. I've studied. I've been studying gene expression and I have a lot of colleagues who do, and I can tell you that it's a moving target and so when we talk about stability and the meaningfulness of clinical biomarkers, you have a lot to already worry about and I'm gone. So, genotyping is one thing, and then you get into big data and I personally think the more years you wait, the better, so that's my you know, sorry, my skepticism.

MR. CHIN: Yeah, so let me comment on that.

DR. PELLETIER: We need to wrap up because we have five minutes.

FEMALE VOICE: We have time for one more question, and I'd like to go to this gentleman.

MR. PAUL EVANS: My name is Paul Evans and I'm with the international Research Institute for Wellness and Prevention. We're located in Atlanta, but for the last four years we've been doing work in Thailand. Thailand has a significant problem that has one of the most rapidly aging populations in the developed world. The economic studies there suggest that they need to keep the people alive and healthy longer in order to fill the jobs that they currently have, so in agreement with the last speaker, I think what we're focusing on there is the Thailand health spans study along with Thailand NIH and universities. We're looking at a longitudinal study, which we think is really important here, over the next several years for large populations to take a look at lifestyle and possible changes in genetic markers.

DR. PELLETIER: Yeah, it's an excellent observation. As an example, the Republic of Singapore is an example of what you just pointed out, which is they have no natural resources, just intellectual resources, and they as a nation state have committed to creating the longest lived, healthiest workforce in the world. That's a stated objective of the republic of Singapore because they realized they don't have enough young people to support what is in effect an aging population, so they need to have that population maintain a high level of health and outcomes and they've just begun to add, I think last year or the year before, I haven't kept up with it, but

they've just begun to add in some of the genetic markers and begin this longitudinal tracking over time, so yeah, I agree with what everyone has said.

I thank all of you today. We're really at the beginning of this, and I think that's what the takeaway message is. We know some and I think anything that we find out through genetic testing with our clinicians and in discussions with them is what it needs. We need genetic counselors. We need individuals who can interpret the results of this testing, so thank you all for being here, thank all of you for participating.

[Applause]

MS. EPEL: One more comment. We didn't get to telomeres, of course. It's on my website. If you're interested in telomere testing, Elizabeth Blackburn, who is a Nobel laureate who discovered them and I wrote kind of, here's what you should know if you're going to test them. It doesn't say do it or don't. It's really complex, and if you want to help people interpret their test, please read this FAQ. It's aging metabolism, just my name and UCSF would probably bring you to the website. It's called aging metabolism - - oh, no, I don't do self-promotion. If you're interested in learning about telomeres, we did write a book about all the research from the cell to environment and neighborhoods and relationships and how they're associated with telomere length. It's called the telomere effect. He made me promote it. I didn't mean to.

[inaudible female voice]

[END RECORDING]