EP.126 – Dr. Hood and Dr. Price

Narrator: You're listening to *BioTalk* with Rich Bendis, the only podcast focused on the BioHealth Capital Region. Each episode, we'll talk to leaders in the industry to breakdown the biggest topics happening today in BioHealth.

Rich Bendis: Hi, this is Rich Bendis, your host for *BioTalk*. We have a special treat for the listeners today. We have two renowned scientists who are releasing a new book next week, but I understand there might be some advanced copies on Amazon that you can purchase already. We have Dr. Leroy Hood, cofounder of the Institute for Systems Biology. He's a pioneer in the fields of systems biology, proteomics, and P4 medicine. He has won the Kyoto Prize, Lasker Award, the Heinz Award, and the National Medal of Science. Dr. Hood, welcome to *BioTalk*.

0:00:55

Dr. Leroy Hood: It's a pleasure to be here.

Rich Bendis: Thank you for joining. He's also coauthor of their new book, by the way, which is called *The Age of Scientific Wellness: Why the Future of Medicine Is Personalized, Predictive, Data-Rich, and In Your Hands.* His coauthor is Dr. Nathan Price, who is the Chief Scientific Officer of Thorne HealthTech and Professor of the Institute for Systems Biology. He was also selected as an Emerging Leader in Health and Medicine by the National Academy of Medicine. He's received the Grace A. Goldsmith Award for his work on scientific wellness and has coauthored over 200 peer-reviewed scientific publications. Dr. Price, welcome to *BioTalk*.

Dr. Nathan Price: Thank you, Rich. It's great to be here.

Rich Bendis: Thank you both for joining. Traditionally, what I do—I've done the big intro of you, the stuff that you probably wouldn't talk about yourself, but what the listeners really want to know is the stuff—how you would introduce yourself, rather than my introduction.

0:02:00 I'm going to start with Dr. Hood—Nathan, if you don't mind—and Dr. Hood, let's get a little self-introduction of yourself from as far back as you want to go to bring us up to current day with those things you feel are relevant in your life.

Dr. Leroy Hood: I think the things that are relevant in my life are really teachers that I had at a very small school in Montana that inspired me to go on to science, to Caltech, and later to medical school. I've always had a fascination with human health and its complexity. My younger brother was born with Down syndrome many years ago, and I remember asking the doctor why that happened, and no one had the faintest idea what it was about, and I remember thinking, "My goodness, something like this, and we can't even begin to explain it."

0:03:00 It was 30 years later before we discovered chromosomes that we at least could describe what happened to a Down syndrome individual. Finally, I would say I have a lifelong passion for sports. I played football in high school. I was quarterback on the team that was undefeated the three-and-a-half years that I was there. I went to Caltech, and was on a football team that was many times defeated, but our home field was the Rose Bowl, so we'd have 50 people on one side of the field cheering us on, and 100 on the other side in a Rose Bowl that held 105,000 people. It was a great experience, but probably the pinnacle academic experience in my life was climbing, with a close friend, the East Buttress of El Cap, a 22-hour climb, incredible physical feat.

0:04:02 I just look back now and marvel at the fact that I could even do it. Anyway, it mixes science, people, mentors, and a fascination with human complexity.

Rich Bendis: Thank you for the introduction. I've watched the video on the gentleman who freestyle set the record up El Cap. It's just unbelievable how quickly he did that and how perilous it is, and you really just don't think about as you're climbing—he did a little shorter time than 22 hours, I think, didn't he, Doctor?

Dr. Leroy Hood: He did a much shorter time than 22 hours. He's probably a one-in-a-billion athlete. There aren't many people that even could do a fraction of the things he did on that climb.

Rich Bendis: It was amazing. I think it captivated the nation to watch him do that. Congratulations on your feat, though. I think that would also be something that could be on a lot of people's bucket lists.

0:05:01 Now we're going to hear about Dr. Price's background. Did you have any sports that you want to talk about that you're as proud of as Dr. Hood, Nathan?

Dr. Nathan Price: Not as much as Lee, certainly. I did a lot of running and cross country when I was younger, and I was a very avid basketball player—loved doing that. I was always vertically challenged, so I didn't rise terribly far in the ranks, but loved to play that a lot. Probably my best sport is ping-pong. I'm actually quite a good ping-pong player. It's been several years since I lost there, but that's not with a ton of games, but it's pretty rare I play someone who's better than me. There's one person so far who really is, but Mark, if you're out there, you know who you are.

Rich Bendis: Let's talk a little bit more about, other than your ping-pong prowess, what else is there in your background?

Dr. Nathan Price: I grew up being trained primarily in academics by my grandma, who was a private-school teacher who then sort of became a live-in tutor. Her house burned down in California, and she moved in with us.

0:06:00 She had a huge impact on my early life and reading lots of books about science, and I just became really enamored of science and wanted to get into that. I'll fast-forward several years to not go through all of that, other than just to say I come from a large family, so I'm the eldest of nine children, and most of the others are all musicians, and I'm the lone scientist. It is fun because when I go home for Christmas, they do a big concert for the whole neighborhood, and people come by and comment on—I guess I got missed in the talent gene of the family, [laughs] so that's pretty much me.

Rich Bendis: You have another talent, though.

Dr. Nathan Price: A different talent that doesn't show up. I became really interested in science—so, I went to grad school at the University of California in San Diego in the bioengineering program. I got started by building these large-scale computer models of how, first, cells, and then humans, taking all the different chemicals that are in our food—how do we create ourselves?

0:06:59 Just going through a lot of that kind of information. I did well in grad

school, got a faculty job straight out of grad school, which was unusual, and deferred it for two years, actually, to go work with Lee. I was pretty convinced that Lee was the top person in the world in personalized medicine, and I had been a fan of his from afar, and had met him briefly in 2003. I like to say I met Lee in 2003, and he met me in 2005, because he would never have remembered me from this nobody kid that ran into him, but it was really fun to reach out to him. Then I deferred my faculty job for two years. University of Illinois was kind enough to let me do that to go work as a postdoc with Lee. That was a wonderful two years. I then went back, was a professor in Illinois; grew a group there of about 25 grad students and postdocs in about four years, so it was growing and thriving, and then Lee and I would get together in his place out in Montana every summer, and were talking on the phone early mornings all the time.

0:07:58 He got this amazing $100 million grant from the government of Luxembourg, which helped enable me to move my lab back. He gave me a call and he's like, “Just move back. We should just do things together,” and I loved that and ended up saying yes to that, came back, and then I'm sure we'll get into all this, but basically, we developed a lot of this notion of scientific wellness, worked at ISB together for about a decade on all the stuff that's in the book, and in the later stages actually merged our lab groups together to form an integrated effort, started a company together, cofounded Arivale, which I'm sure we'll talk about as we go along, and basically got into this area and just became very convinced that the whole structure of how we do health and medicine needed a really big reframing because we interface too late, and we need to do it a lot earlier, and I'm sure we'll get into a lot of those ideas as we go forward.

0:08:53

Rich Bendis: Nathan, you just mentioned four different areas we're going to get into. I think we're going to be here about an hour and a half on this podcast, so I hope you both have time. Dr. Hood, let's go back to when you first met Nathan and a little bit about your scientific background and research. There's probably a lot of postdocs or people who aspire to be postdocs and work with renowned scientists around the world. Talk a little bit about that process, how you came in contact with Dr. Price. What did you see in him to say, “Let's give this guy a shot working with us here?” Talk a

little bit about that postdoc experience and how you got together.

Dr. Leroy Hood: Nathan's mentor, Bernard Paulson, was a close friend of mine. I remember I first met Nathan when I went down and gave a lecture there. Bernard said that he had someone he thought was very good. What was exceptional about Nathan was he was enormously productive as a graduate student. He had, I don't know, I think up to that time, the most papers that ever came out of Paulson's lab and everything.

0:10:01 He clearly had a deep, integrated synthesis and understanding of them. I think for me, what was always important in selecting young colleagues was finding people a) that had ideas and b) that had the independence and the courage to take those ideas on and carry them out themselves. I didn't like the idea of hand holding people, and it's not how you learn to do science. You learn to do science by formulating ideas and then really carrying them out, and Nathan was obviously superb at that endeavor. It was a real loss when I was hoping he would stay on as a senior fellow in the lab, but he was insistent on going back to Illinois, and I think from his point of view, it was exactly the right decision. He built a group; he was very successful. He created his own vision of going forward.

0:11:00 When he came back, we were equals, not student and mentor. When he came back was a very propitious time because we'd started this Institute for Systems Biology which pioneered this whole new view of science. It was holistic, global, and very data-driven, and when he came back, we immediately started thinking in terms of human biology and took the radical step not to focus only on disease. We did a lot of disease-oriented kinds of things with systems approaches, but to use the systems approach and focus on wellness was an entirely new endeavor. I remember, in fact, in 2013 when we were thinking about a bold project which involved 100 people that we would fund and study in enormous detail, their genomes and their phenomes. We'll talk about what those things are a little bit later.

0:12:06 Going back to NIH and making the proposal to the director there that, "This is a new direction, a new area; would NIH be interested?" To my amazement, he said, "No, NIH is really interested in disease. We would never fund anything in wellness." So, Nathan and I figured out how to get

the project funded, how to get started, and that 108 people, then positioned us to start a company called Arivale where we could think about bringing what we call scientific or quantitative wellness to ordinary consumers. We collected over a period of four years, 5000 people, and had data on them, and it was that Arivale data that utterly convinced us and continues to convince us.

0:13:00 Because from that came more than 25 different papers, and they each validated different aspects of scientific wellness, so it opened up the field of what we now call precision population health, and it led to Arivale—and we can talk about Arivale and the observations that came from it, and a particularly fascinating question is, why did such a great idea fail? And I'll just say, in my history, I started 17 or 18 different companies. I would say my most important company was Arivale because it gave us a vision of what the future of healthcare was going to be.

Rich Bendis: Sometimes we learn more from our failures than we do from our successes, and you probably had been able to apply that into the other 16 companies. Hopefully some of those have been very successful, which we'll learn more about.

0:13:58 I'm going to go back to Dr. Price, but before I do that, you've been a mentor to Nathan, I would imagine, during those early formative years, and I'm going to go back and ask you, who inspired you? And who would you consider your most prominent mentors you've had in your life, Dr. Hood?

Dr. Leroy Hood: I really had terrific mentors. In high school, I had three teachers that I think were among the best teachers I ever had. I think the most important thing they did for me is they treated me as an equal, and they gave me a vision of what I could be that I never would have gotten otherwise. In fact, one of them really encouraged me to go to Caltech as an undergraduate, which I'd never heard of. I never would have applied without his pushing. At Caltech, I would say I had three mentors that really made a big impact on me.

0:14:59 They were less mentors than they were teachers, but one was Richard Feynman. I was in his freshman physics when he was writing this three-

volume series on physics, and it was an unbelievable experience. Here was a guy who could talk about the most complicated aspects of physics, and you knew you understood everything until you went home and tried to work a few problems out, and you realized that somehow you didn't quite get it all. The second person that really impressed me at Caltech—and he wasn't faculty there; he came and gave lectures to the undergraduates—was Linus Pauling. I would say Feynman and Pauling both taught me how to teach and taught me how to speak in the sense of pushing this idea: Feynman was famous for saying, “There is a lot of complexity in the world, but you don't understand it unless you can explain it to an ordinary person and have them understand it.” There's enormous truth in that.

0:16:04 I think the third person for me at Caltech that made a difference was Ray Owen, who was a very famous immunologist who should have gotten a Nobel prize. What he set a standard for is being a mentor and being personalized and caring about the individual lives of young freshmen, sophomores, and juniors at Caltech. That really had a big impact on me.

Rich Bendis: Thanks for that background. I think all of us are looking for those inspirational people to guide us through our lives. I'm going to go back to Dr. Price now. Let's talk a little bit about the Institute for Systems Biology which Dr. Hood mentioned earlier, and also systems biology in general. Talk a little bit about the creation of the Institute for Systems Biology, why it was created, what inspired the creation of it, and what its primary focus was that led you two to your collaborations.

0:17:08

Dr. Nathan Price: I can certainly speak about systems biology. I feel like maybe we'll let Lee talk about the founding since he was there and I wasn’t. [laughs]

Rich Bendis: Oh okay, we’ll go back.

Dr. Nathan Price: I had not heard of systems biology at the time as I had just barely finished college that month, [laughs] so I had not yet pioneered that Institute, let's say. Systems biology is the study of biological complexity, so it is an approach to biology that, rather than trying to figure out all the different constituent pieces, which is what molecular biology does, systems biology

is about taking those pieces and understanding how they integrate together to create what we recognize in life, emergent systems, and so forth. It involves computational analysis, typically, high-throughput data analysis, so this is things like genomics—which Lee was a massive pioneer in—proteomics, metabolomics.

0:18:04 These things just mean measuring all of the DNA, all the proteins, all the RNAs, and so forth, but as you take that information, you build computational algorithms to try to understand how those pieces fit together, and then make predictions, and then those predictions have to then be validated by experiment, and you iterate. One of the interesting things in systems biology is that these computational models themselves are hypotheses. They're very structured hypotheses about how biology functions, and they're falsified in parts, not typically as a whole, but you falsify the different pieces and iteratively make it better until you gain a much deeper understanding of how the whole fits together. So, that's really what that's about. Later, you should talk about the founding of ISB and why you did that. I can; I know the story well, but it's best for Lee—

Rich Bendis: We're doing his backwards, so Doctor, let's talk about that founding of your institute.

0:19:00

Dr. Leroy Hood: Caltech was a wonderful place to do science, and I got interested in two things that my colleagues at Caltech were not so interested in. One was the Human Genome Project, and initially many scientists opposed it. The other was the development of technologies, and the senior faculty of biology at Caltech felt that should be done in engineering and not in biology. Fortunately, the chairman didn't move me, but there was a bit of tension. I decided then I would explore whether there were more fertile places to do these two things I really cared about. Without making the story too long, the University of Washington in Seattle turned out to be that kind of place, because I'd wanted to start a new type of department that was cross disciplinary in nature.

0:20:01 It had all kinds of scientists, and they could work together, both to envelope new techniques, strategies, computational tools, and then apply

them to biology. This department worked very well, but what I'd really wanted to do was build on top of it a brand new area that hadn't really been pioneered before, and that was called systems biology. I found at the University of Washington, the bureaucracy made it really challenging to get something really new started. There were just lots of hurdles. A simple example is when I talked to the head of computing at the university, he came by and showed me this really small janitor's room, and he said, “That's all the space you'll ever need for computing. I'm sure we can get that for you.” I tried to explain it wasn't.

0:20:58 Then I wanted to hire a surface chemist in my department, and the dean refused to let me because he said surface chemists had no role in a medical school. I decided it was time to go someplace where I didn't have the constraints on what I needed to build. In 2000, I resigned, and with two colleagues, Alan Aderem and Ruedi Aebersold, started the Institute for Systems Biology, and we brought many of the people from my department there. They formed a cross-disciplinary core environment, and it took off, and it really pioneered a whole new way of doing science now, and there are probably 100 centers or departments or Institutes of Systems Biology around the world today, so it's become a very powerful tool for dealing with all the complexity we face in biology, as Nathan nicely articulated.

0:22:00

Rich Bendis: Talk a little bit about the funding for the Institute at the beginning. When you left the academic institution, it was going to require some funding to do the startup from an entrepreneurial perspective for your new institute, so what was your vision for how you were going to fund it and grow it?

Dr. Leroy Hood: My initial vision was very naive. Bill Gates had brought me to the University of Washington. I went to him after I decided to resign, and he actually was very disappointed. I don't think he really understood why I had to resign and start something all over anew. But, he asked me that same question. He said, “How are you going to fund this? This is going to take a lot of money. You're starting all over.” I said, “Well, that's part of the reason I'm here.” I remember Bill just shaking his head and saying, “I never fund anything I think is going to fail.” [both laugh] But, I scraped

and put things together, some from philanthropy, some from companies who put in $6 million to get a started in proteomics.

0:23:05 Foundations put in money, and then ten years later, Bill made a really bold match. It was really funny. He said, “Well, I finally decided to fund you, but I have one condition on the funding. It's a ten-to-one match. I'll give you $10 million, but you're going to have to give me $10 million for each million you gain.” It turned out to be very fortunate that within the year, I struck a bargain, as Nathan had mentioned earlier, with the government of Luxembourg for $100 million to fund P4 medicine and helped set up an institute like ours in Luxembourg. So, I was able to use that and match—I'm sure Bill did the match tongue in cheek, and he never expected me to perform.

0:23:58

Rich Bendis: [laughs] So, what is Bill's attitude today?

Dr. Leroy Hood: I can't ask. I do not have a lot of interactions with him in recent times. I think Bill really respected what we’d managed to do in systems biology, and then, of course, started his own endeavor, the Gates Foundation, in dealing with third-world medicine and things like that. It was really an exceptional experience meeting Bill, because what the University of Washington had me do was give The Dance Lectures, which were three lectures on the future of something, so I gave on the future of biology, and Bill came to all three, and we had a dinner atop the Columbia Towers, one of the highest buildings in Seattle, and we kind of settled the future of this new department and the money he would put in to fund it and get it started and everything. He was enormously curious, inquisitive, and masterfully critical about things. He really knew a lot of biology, so I have the greatest admiration for Bill.

0:25:04

Rich Bendis: Congratulations on your determination.

Dr. Leroy Hood: I’ve always said, in science and administration, determined optimism is the most important characteristic of success, plus having good ideas.

Rich Bendis: Well, anybody who can conquer El Cap has quite a bit of determination.

[laughs]

Dr. Leroy Hood: Yes, physical determination I do have. I agree, yeah.

Rich Bendis: That's one of the things I read about both of you, is that the scientific principles that you've been studying about, you really look at in your own personal health habits, especially the things you've learned through systems biology. So, Nathan, talk a little bit about what you see in systems biology and how you relate that to your everyday life.

Dr. Nathan Price: Systems biology just gets you to think about how you can interface with your body and make a real difference.

0:25:55 One of the things that I'll point out is, for various reasons, when we do randomized clinical trials, for example, we're typically isolating one variable, and then you test it to see if it has an effect, and you measure it, and you do this over and over; it's how we come up with drugs and the whole bit. That's all very well and good in good statistical models, and we do a lot of that, but when you start thinking about, "How do I solve a problem in my life?" You're much more likely to think, "Okay, I know there are all these levers that I can pull," but if you want to make a big systems change, you've probably got to do those things together. So, when we launch this, the Pioneer 100 Project that Lee mentioned, and then Arivale, what that meant is that we were able to generate, really for the first time on a significant population, lots and lots of layers of data—so, this was genome, proteomes out of the blood, so hundreds of proteins out of the blood, hundreds of metabolites out of the blood, hundreds of species in the microbiome out of your gut, about 1,400 of these in total out of the blood, and then plus the gut.

0:26:58 So, when you did that, what we found was that we could learn a tremendous amount, which is what the book is really about, about how you could modify your health. I'll give a couple concrete examples. For one, let's take a very common molecule that people use clinically, LDL cholesterol. People know that they have high cholesterol, a lot of people are on statins—millions of people are on statins. What we found is that we took people through a lifestyle program over the course of about four years, and some of them were able to lower LDL cholesterol, and some

not, and there's many papers published in the literature that say, “That's kind of a mixed bag; you can kind of do it.” But then when we took all these different layers of data, it turned out it was totally predictable who could do it and who couldn't, and the key variable was that when you built a genetic predictor—so, given your genome, not knowing anything about your lifestyle or anything else, I can make a prediction about what the likely level is of your cholesterol.

0:28:00 What we found out was that if you took a person’s actual level on this genetic prediction, if there was a gap—in other words, your genome predicted low and you were high—you could lower it by lifestyle; and if the genome predicted high and you were high, you couldn’t. Just think about that for a brief moment. We give millions of people statins, and as far as I know, essentially no doctors today utilize information from the genome. They treat your high cholesterol, your high LDL cholesterol, as exactly the same, whether or not you're there for a genomic reason or for an environmental [reason]. Yet, when we do deep studies, we find that is the most predictive variable of why it would change, and it's not only true of LDL cholesterol. It's true of HDL cholesterol, the so called good cholesterol that you're trying to get up higher. It's true of hemoglobin A1C. Genetics is predictive at the same clinical level—everyone in medicine treated exactly the same—but at that same level, the genome predicts who's more likely to go into diabetes or not, and I could go into mechanisms for that.

0:29:04 So, as you get into all these different areas, you find that you can look at the body as a deep system and optimize the way that you’re interfacing with your body. By the way, that's just one example, or the tip of an iceberg. There's 1,000 more examples, but it's the point of layering that really dense data, analyzing it, pulling the AI approaches on top of it, and it just gives you very simple, actionable results. The one other thing I'll add on that is that this introduces a completely new category of variable into all of healthcare, which is to take all these biomarkers that we already use all over the place, all these clinical diagnostics, and ask, “Well, what's the genetic predictor for each of those?” And then that delta, or that difference between the prediction and the actual becomes a road map to all the things that you can change where your genome will work

with you rather than against you. It's different for every person, but we can do that in spades now.

0:30:05

Rich Bendis: So basically, you're going to create new scientific wellness [?? 30:08] using different principles to modify lifestyles.

Dr. Nathan Price: To modify lifestyles, and it relates also to how responsive a person is likely to be to a supplement, how likely a person is to be responsive to a drug, in some cases, and definitely how responsive they are to lifestyle, and that's probably the order that I would say you want to try to deal with things: Lifestyle, if not that, then maybe there's a natural product or something like that that you could nudge a system in a certain way, and if not that, then you can do heavy duty drugs, and you do the trade-off.

Rich Bendis: I would imagine these new findings you have led to the inspiration for your new book, *The Age of Scientific Wellness*. Dr. Hood, talk a little bit about the evolution of this book that you have, and what difference do you think this is going to create to educate people about what they can do to change or modify their lifestyles and their predictive health for the future?

0:31:03

Dr. Leroy Hood: The book, *The Age of Scientific Wellness*, was a two-year-plus attempt on the part of Nathan and I to capture the wisdom that we'd revealed in these various studies that we've already talked about, and to convey the idea that a data-driven approach to health really looks at three different aspects of health. It looks at wellness, and we believe for the ordinary person, you're at 30% or so of your wellness, and we can enormously elevate that with bona fide, actionable possibilities. The second part of wellness is you move from wellness to disease, and you go through a transition.

0:31:58 In Arivale, we were able to demonstrate that this transition can actually be detected anywhere between one and three or four years prior to clinical diagnosis. It raises the really attractive idea of, if we had a large enough population, not 5,000, but a million, say, could we make

predictions about these abnormal proteins that told us what the transition to a given disease would be? And could we actually reverse the disease at that early stage? And of course, the third aspect of wellness is disease itself and its progression, and of course, the systems approach that Nathan talked about gives us very powerful new tools for approaching disease.

0:32:53 This data-driven assessment of the individual then lets us deal more effectively with each of these three aspects: wellness, transitions, and disease. It's our belief that in the future, as we bring this data-driven wellness to more and more individuals, it will be able to catalyze a paradigm shift from a healthcare that's focused virtually entirely on disease now, to one that focuses entirely on wellness and actually prevention, the two things we've talked about. The really critical question then gets to be, how do we go about doing this? I think both Nathan and I agree that we need a much larger demonstration of the power of data-driven wellness. I've really been pushing a million-person project that, in a sense, is a second genome project where over a 10-year period, with government support just like the first Genome [Project], we'll be able to do a genome/phenome analysis of a million people.

0:34:07 And that will do two really important things: 1) Unequivocally, we can demonstrate the improved quality of healthcare for individuals that are undergoing this data-driven approach, and 2) we will unequivocally be able to handle the five major challenges of healthcare today. One is quality, so scientific wellness and so forth. The second is the aging population. One of the things maybe Nathan could talk about is the fact that out of the Arivale data came a metric to identify an individual's biological age and make predictions about how you could optimize aging.

0:34:55 And number three is the explosion of chronic diseases. Suppose we could detect them early and reverse most of them, and that 86% of our $4 trillion healthcare dollars, suppose you cut that by a five-fold factor. You can save enormous amounts of money. Finally, there is the idea that you can reduce the costs as I've indicated. Another aspect that's emerged much more recently, that is the knowledge that it is really important to know your racial origins because the genome has a big impact on your ability to respond to diseases and so forth. We think the data-driven

approach in this program would be absolutely transformational in that regard, and we think in 10 years, we can see a real shift beginning to go toward a wellness and prevention that is going to improve the quality of healthcare and enormously reduce its cost.

0:36:02

Rich Bendis: You mentioned a million-person study. I think there's an ongoing program at NIH related to a million-person genomics study that they're doing to study the genomes of a million different people to create a broader database. Are you talking about something different, or that would be complementary to that study, Dr. Hood?

Dr. Leroy Hood: We're talking about something that would be complementary. As you mentioned, the major focus of that very important program is on genomics, healthcare records, and so forth, and it is basically a research project to make available data to many researchers, and already we began to see returns on it. What we've proposed to do with our million-person project, which we call The Human Genome Initiative, is to do the genome/phenome analysis with focus on wellness and prevention so as to catalyze this transformation we've talked about.

0:37:04

Rich Bendis: Super, thank you. That would be nice to see that our tax dollars are used to enhance studies rather than to start from scratch with everything brand new again, and I think what you're talking about would be very complementary on data-driven because when you look at AI, machine learning, and quantum computing right now—and I don't know if you noticed it, the name of the firm that I created was called BioHealth, not biotech, not life sciences, because we have the convergence of the science and technology coming together today, but we're not applying it to the extent that we should be.

Dr. Leroy Hood: The analogy I make is, if we just give up four B-2 Bombers, we have enough to do the Human Genome Project with the cash to spare.

Rich Bendis: I would imagine there are many other things that we are funding today that we could give up to apply to this scientific area in the future, but

that's another topic, and it would take a little longer than we have on this podcast, doctor—it might be a little more controversial, too.

0:38:06 Nathan, Dr. Hood threw it back to you to say that you were going to explain something or expound upon something related to this for the future, and I'm going to throw it back to you now.

Dr. Nathan Price: Yeah, so we talked about where he's really leading this out on the million-person project, so for me, where I'm really trying to drive has been my jump fairly recently from academia into industry, so taking over as Chief Science Officer of Thorne HealthTech, which we took public on the Nasdaq a couple of years ago. Really what that's about is trying to take all these different things that we're learning in scientific wellness, and try to turn them into products that make it easy for people to take action on the kind of things we're talking about. That's an ongoing process. Some of those things, we certainly have.

0:38:56 Thorne has had 5,000,000 customers and works with about 50,000 healthcare providers, so there is a network and a starting place, but it really is about trying to pull together lots of the findings and the discoveries and make it easy for people to do something about it. It's not just us, of course; there's a whole ecosystem of companies that are emerging that I would put under this umbrella of scientific wellness that are mining the microbiome for discoveries, that are driving natural product discovery by massive mass-spec efforts from plants and, and things of this nature, and just this whole burgeoning enterprise. I think it's really important, because while we think that there's this huge vision for what healthcare should be and that we're working towards, that will be very radically different from what we have now focused on disease such that you're really working to optimize your healthspan, maybe indefinitely, being able to focus on ways to slow down the aging process and so forth.

0:40:01 I also don't want people to walk away from this with the notion that there's not a lot that you can do, even now, to start to take advantage of, “Well, what does your genome actually tell you about health? What are the measures that you can do that are out of your blood that are related to that? How can you get a gut microbiome?” All those kind of things. So,

that's really one of the big focuses that I have, especially currently with the move to Thorne, was really motivated by an excitement about so many of these things that we've learned, and just trying to make it into a form that millions of people could take advantage of if they so choose.

Rich Bendis: Let's talk a little bit—it's a little off track, but it's related to what you both have been doing, and that's: If you look at patents, publications, and products, most scientists are very active based on the incentives that have been established for them to get involved in doing publications and patents, but a minority of scientists actually have the entrepreneurial spirit to actually go into business or create businesses.

0:41:03 You've just made a transition to go into Thorne. Dr. Hood's talked about 16, 17, 18 companies he's been involved with. Let's talk a little bit about that transition from science to business, how both of you have been involved in it. Talk about the challenges that are there and what motivates people to actually look at: How do you get that science from the bench into the bedside to the patient where there's an actual product that can benefit human health in the future? So, you just mentioned Thorne. Why don't we start with you, Dr. Price, on Thorne, your evolution into Thorne? We also talked prior to starting today about how the timing of your public offering couldn't have been better, then what's happened in the bio and the financing world over the last two years. Talk a little bit about your entrepreneurial experience from the science going into that entrepreneur world. Then I'm going to talk to Dr. Hood about that a little bit.

0:41:57

Dr. Nathan Price: Yeah, it's been really a fascinating experience to jump from academia into the business world. Lee and I, of course, had cofounded Arivale before, so had been involved in entrepreneurship. Lee, of course, as you'll hear in a moment, is one of the most famous academic biotechnology entrepreneurs of all time. From jumping into Thorne and building up products, the really interesting thing is just how far away you are from a functioning product when you write the paper and you make the discovery, and that can be a sometimes-painful process of just going through, “How do I actually get this to check off all the various boxes and

the regulatory?" And then you get into mundane things that relate to, how do you get collection, for example? So, I'll give an example. We've done all these big papers on the microbiome out of our scientific work, and it shows really interesting things, like that your microbiome, if you stay healthy, gets increasingly unique as you get older, and there are signatures associated with that, or you can predict a lot about your microbiome from the things that secrete into the blood.

0:43:03 But, one of the big issues is that a lot of people won't do a microbiome test. Why? Basically, when you're doing this as a research study, or someone wants to go do a microbiome, what do they have to do? Well, you've got to poop in a bucket or on a piece of paper. You've got to take a little shovel, you've got to scoop that up. You've got to put it into a vial, all that stuff, and people don't like that as much, so one of the things that we got into at Thorne then was, well, can we come up with a better way to get a fecal sample? One of the things that came out of that was the invention of something that we call the Microbiome Wipe. It's exactly what it sounds like; it's a special polymer, you use it just like toilet paper. You can then put it into a vial, close it, you shake it, and in 10 seconds it will dissolve away in a solution that preserves the DNA for sequencing, which then we showed that it worked in this paper in *Frontiers in Immunology*.

0:43:57 The cool thing about that is that that makes it as easy as basically your normal daily behavior to get a microbiome sample. A great anecdote that came out of that: Sara Gottfried is a real well known physician; she was on a podcast, and she talked about how she's working with this NBA team, and the NBA players would never do a microbiome sample even though they knew it was maybe useful, but they couldn't get over the ick-factor, but we sent her out the wipe, and they all did it. Anyway, she shared that on the podcast that it was no problem, so it's kind of lowering these barriers in order to be able to do that. We actually got Number Five Most Innovative Company in Wellness from *Fast Company* a couple weeks ago, and that was what they cited, actually, was the wipe. Another thing: a painless, at-home blood-measurement device called the OneDraw, and this now lets us mail to somebody's house—who can do this in a research study or something—but basically, you can capture enough blood to do

thousands of metabolites and develop wellness tests off that, or proteins, or any of that stuff.

0:45:04 So, there starts being a lot of a focus around, how do we deliver information in ways that are simple? We can deliver solutions. Understanding that you don't just want testing, but also solutions, Thorne is the largest natural—I think might be the largest—and was just rated as the highest quality natural-product maker in the United States, and we have a 700—we're just building it out, just doubling it in size—but a 700,000 square foot manufacturing facility in South Carolina. So, there's just all these pieces that have to come together in the industry side, and it is a little slower moving, sometimes seeming, because in academia, you come up with your idea, you write the paper, you send it in. Then you do the new idea, the next paper, the new idea, the next—and you're just, you're learning and you're churning, and in industry, you're still learning a lot, but then it's like, "Okay, I got to sit here for a year and turn this into a product that gets out there."

0:45:58 Then the scale of it, once you get those things locked in, can be really tremendous, but it is a little bit of a different game, but very interesting in trying to drive that forward. What we're hoping is for lots of synergies between some of the kind of stuff we're doing and what Lee's doing with the million-person project and so forth, so we can accelerate the whole vision for scientific wellness that much faster.

Rich Bendis: I have a million more questions I'd like to ask you about Thorne, but we don't have time today; it might be a follow up podcast. I think you're the first scientist who has basically said that academia is faster than industry in getting things done. [laughs]

Dr. Nathan Price: We're spinning through ideas faster, not actually implementing it.

Rich Bendis: Intellectual advancement is faster in academia than it would be an industry. Dr. Hood, we don't really have the time to go into all of that, but I really want to talk about your inspiration of actually going from pure science into entrepreneurialism with all the startups that you've been involved with. Talk just briefly about that. Then also, more importantly, what do you consider some of your greatest entrepreneurial and

commercial successes?

0:47:04 I would say, from my point of view, entrepreneurialism has two important elements. One is the element of: What's the vision? What's the idea? What's the creation that you're going to implement in terms of spinning off as a company? I remember when I went in 1979 to the president of Caltech, my lab had invented four instruments for synthesizing and sequencing DNA and proteins, and I argued to him that I'd like to get Caltech's help in commercializing this. Then he gave me a long lecture on, "The role of academia is education and scholarship. It isn't commercialization." And I said, "No, the role should be to transfer knowledge to society that's useful since they pay for everything we do." And he said, "Well, you have your own opinion. Go do it yourself."

0:48:06 Then I went off, and the result of that was the first major company that I did, Applied Biosystems, which commercialized these instruments and was very successful. But I will say, in each case, when I went to the University of Washington and created a cross-disciplinary department, that engendered an enormous amount of intellectual activity, both license-type things and spin-off companies. When I went to ISB and created yet a second new entity with a brand-new vision, I've had seven or eight companies that I've spun out of that. I would say the most recent is a non-profit company called Phenome Health which is actually pioneering the million-person phenome project.

0:49:00 I think in the end that if we're successful, it could be the most important of all the companies I've ever done. I will say I did Applied Biosystems and Amgen, both of which were enormous financial successes. I did Arivale, which was a pioneering, paradigm-shifting view of what health is, and I think with Phenome Health, if we succeed with the million-person project, I guarantee you it'll be the biggest revolution in healthcare ever.

Rich Bendis: Congratulations, and I'm glad you're still inspired to do big things. We need people who think big in order to accomplish big things. We're coming close to a close, and I have a few other things I want to talk about, and I'll throw it to whomever wants to cover them. One is really one of the themes of the book, is that healthspans are more important than lifespans.

0:50:00 Who would like to take the difference between the healthspan which we've been talking about for a long time, and lifespans, and really the relationship between the two? And why is one more important than the other?

Dr. Leroy Hood: Nathan, go ahead.

Dr. Nathan Price: Healthspan basically just refers the time over the course of your life that you will remain healthy. When you do these studies, especially in animals when you're looking at longevity and you're looking compared to healthspan, there are certain interventions that might eke you out, and you'd stay alive for a long period of time, but you're frail. If you ask people what they want, they don't want that. No one is really that engaged with, "I want to stay alive as long as possible on whatever device." In fact, Atul Gawande's book, *Being Mortal*, is a beautiful example of how different the end of life is than we want it to be. So rather, what we really are interested is the extension of healthspan. That is: How long can you stay healthy and vibrant, and are there fundamental limits to how long healthspan can be?

0:51:04 There's a lot of debate in the scientific community about that, but that is the focus. The idea is: Can we create, through scientific wellness, ways that you can live into your 90s and feel as good as you did in your 30s and 40s? Can we break beyond these barriers over time, such that you can live to your 200s, or your 300s, or whatever? And we don't really know the answer to that yet, other than we are about to enter—especially with the birth of AI, which we also have a chapter on that, we didn't get into that as a topic—but as we start seeing this acceleration and this interplay that's happening now between the capabilities that are now about to just massively accelerate on the AI side, coupled with what we already have on this massive acceleration on the biological-data side, we're almost certainly entering into the greatest period of biological-knowledge expansion ever.

0:51:57 The center of that, then, is: Can we accelerate that through what we would call this vision of scientific wellness, in such a way that we reap the benefits of a majorly expanded healthspan that we would get to enjoy? That's really the crux of the pieces are there, but we've got to be able to

pull them together and implement it and pull it off in reality, which is always tough and will be a good ride and a good experience to figure out.

Dr. Leroy Hood: And the point is, wouldn't it be great to go into your 90s and 100s, be mentally agile, physically active, still being creative, productive, happy, interactive—that's what we all aspire to.

Rich Bendis: I think I aspire to it, and since you and I are closer to that than Nathan is, we can relate to it a little more than Nathan can at this point in time. [laughs] What I understand also is that you're still very active, Dr. Hood, and you basically, if you don't mind my saying, you're in your mid 80s at this particular point in time, but really feel like you're more like in your 60s or 70s at this point. Is that correct?

0:53:05

Dr. Leroy Hood: My biological age is 15 years younger than my chronological age, and I hope I'm behaving like I did in my 60s. [Rich laughs] That's what I'll say.

Rich Bendis: I've heard that about me as well, but for different reasons than you, probably. I'm going to close on the scientific side because I think there's something that's personal that you're very interested in as well, and that's really the research in Alzheimer's, which is one of the most debilitating diseases we have in front of all of us, and it's impacting more and more people as we have a more aging population. Would you like to talk a little bit about why you got involved in Alzheimer's research, where you are with that today, and what caused you to focus some of your attention in that area?

0:53:51

Dr. Leroy Hood: My wife was diagnosed with Alzheimer's in 2005, and as many of you know, Alzheimer's is a disease that has a gradual but irrevocable decline, and she exhibited this in absolutely a classic fashion. She's actually, amazingly enough, still alive today and responsive to things, like, we used to love music, so I play the recorder and take it in and play with her, and she can respond to that in a very nice fashion. But to cut to the chase, her diagnosis got me interested in Alzheimer's, and I met a number of really remarkable people who pushed toward the idea that Alzheimer's is a very

complicated, multi-dimensional disease, and correspondingly, its treatment has to be multi-dimensional, and really pushed the idea that behavior and environment, and even to a certain extent, genetics, were all critical.

0:55:02 So, what systems biology is a master at is the integration of these different types of approaches, and both Nathan and I have really pioneered thinking in a multi-dimensional way about Alzheimer's. To give you an example, we have created, together with a colleague, a model of Alzheimer's that I think has been very much driven by a data-driven process, and it's allowed us to make predictions, and make projections, and see insights into where things are going, and we can see that the future clearly will be very different from the past. I predict there will be a time within five years or so where we'll have the markers that say, "You're very likely in the next 10 to 15 years to get Alzheimer's, and here are five things you can do to ensure you never do it."

0:56:05 That's the kind of commitment both Nathan and I have toward Alzheimer's. We could be much more specific, but I just want to be very positive; if I knew in 2005 what I know today, I think my wife would be in a very different position than she is today.

Rich Bendis: I'd like to encourage both of you to keep that research going, because it's something that, just like cancer, impacts almost every one of our families today. Alzheimer's and dementia is also basically impacting families in a similar way, so, sorry to hear about your wife. Both of you keep up your good work because it's something that the whole world needs, is to look for some answers for Alzheimer's.

We're going to close now, and I could go on for a couple more hours. Potentially after the book's released, we can do a follow up and talk about your next book that you'll be going together because I know there will be more of those.

0:56:58 Is there anything that we haven't covered that you would like the listeners to know? I'm talking to Dr. Leroy Hood and Dr. Nathan Price who are the coauthors of *The Age of Scientific Wellness*, which is going to be released next week but is available now on Amazon. Anything, Nathan or

Dr. Hood, that you'd like the listeners to know that we haven't covered?

Dr. Leroy Hood: I'd like to make just one point. Data-driven health is all about a commitment on the part of each individual to be their navigator into the adventure of data-driven health, to submit to the analysis, and to carry out the actionable possibilities they generated for ensuring you're going to be functional, active, and emergent in your 90s and 100s.

Rich Bendis: I will endorse that. I believe that is something I would subscribe to. Nathan, anything you'd like to add?

0:57:56

Dr. Nathan Price: Just to invite people who are listening to join us in this journey for scientific wellness. It's a tremendous time of discovery. There are so many possibilities now for improving your health, understanding your life's trajectory, being able to understand from genomics and more of these measures, and being able to navigate through and give yourself the best chance you can for an extended healthspan. I just think that it's very exciting. It's one of the reasons we wrote the book, is that we hope people will be enthused about this, and we need that if we're going to really make a big shift in the way that medicine is done. We don't see that revolution coming top-down because there are too many entrenched economic interests. It has to come from the people who will benefit the most, and that's all of us, so we hope that people will be enthusiastic about that.

Rich Bendis: I want to thank both of you for including *BioTalk* on your book tour, and even though it's virtual, I know you're actually going to meet some people in person as you continue your tour.

0:58:58 We've had the privilege of talking to Dr. Leroy Hood, who's the cofounder of the Institute for Systems Biology and many things; and Dr. Nathan Price, who's a Chief Scientific Officer of Thorne HealthTech, and also one of Dr. Hood's research partners. They're releasing their new book, *The Age of Scientific Wellness: Why the Future of Medicine Is Personalized, Predictive, Data-rich and In Your Hands*, and it's available on Amazon today, so go out and buy it, because it talks a little bit about what we can do to control our own health in the future so that we can all live to be

100. Dr. Hood, Dr. Price, thank you very much for being on *BioTalk*.

Dr. Leroy Hood: It's been a pleasure.

Dr. Nathan Price: Yeah, thanks, Rich.

Narrator: Thanks for listening to *BioTalk* with Rich Bendis.

End of recording.