May 2014 Issue | Leroy Hood, MD, PhD Institute for Systems Biology

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Welcome to *Functional Medicine Update* for May 2014. This month, as you know, is part of this series that we are putting together starting with Dr. James Fries in the month of April of 2014 on what I call the origins of the functional medicine model, and how the functional medicine model derives its basic formalism from that of systems biology, the advancing frontier of understanding how systems are interconnected to give rise to whole-organism activity.

This might seem like an old concept because it really goes back to traditional Chinese or to even Greek and Egyptian medicine of old. Certainly it is also embedded within Ayurvedic medicine, so it has thousands of years of fundamental understanding at an empirical level. But it is only really within the last, say, 25 years, as we've gotten the ability to integrate and collect huge amounts of data, where we start to understand, at a mechanistic, cellular, and tissue, organ, organ system level, the nature of systems biology in health and disease.

We had a very remarkable introduction to this concept talking to Dr. James Fries in our last issue in April, in which he introduced the aging/compression of morbidity/natural death concept. He really was a pioneer in 1980, in the *New England Journal of Medicine*, of a new concept for what I would call personalized or individualized health care. You're going to be very pleased that we're going to continue this theme with another extraordinary leader, visionary, innovator in this field, Dr. Leroy Hood, the co-founder and president of the Institute for Systems Biology in Seattle, WA, but—as you will learn—far more than that. He is a Renaissance man, a person who has spanned tremendous domain as it relates to innovation and creation, a medical doctor and PhD who has created environments within genomic science that has catapulted us forward in understanding what personalization really means at the individual, cellular, and organismic and systems biology level. Through this lens of Dr. Hood we're going to, I think, take the model of Dr. Fries to the next level of understanding of what the nature of 21st century medicine might look like as we start to not only have access to these technologies, but apply these technologies successfully in patient management and promotion of a personalized approach towards health care, based on the genes and environment of every individual patient.

So with that in mind, let's turn to our discussion with Dr. Leroy Hood.

INTERVIEW TRANSCRIPT

Clinician/Researcher of the Month

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Over the 32 years of my doing Functional Medicine Update I've had extraordinary privilege in dealing with a number of luminaries in the field, internationally—many Nobel Prize winners, many pioneers of medicine and health. But I'd have to say today is an epic moment for me. I'm going to have the chance—and you will have the chance as well, vicariously—to meet one of my heroes. As you know, I had the wonderful couple of years with Linus Pauling back in the early 80s and worked with Bruce Ames for a while, but certainly Dr. Lee Hood has been on my list of amazing figures in the transformation of health care.

The Genomic Era of Today Made Possible By Early Biotech Equipment Development

For those of you that may not be entirely familiar with Dr. Hood's background, his range of impact on science and medicine is extraordinary. He has been involved with molecular immunology, biotechnology, genomics. Although he's an MD/PhD and I have always wondered how an MD could have such far-ranging expertise, he is credited—and I think appropriately so—with he and his colleagues at Caltech developing the DNA gene sequencer and synthesizer and the protein synthesizer and sequencer—four pieces of equipment that really pioneered and heralded the age the genomic era in which we live today, and the whole deciphering of the human genome.

He's been really a pillar in biotechnology and played a role in founding more than 14 biotechnology companies—some names that you are probably familiar with, like Amgen, Rosetta Inpharmatics, Integrated Diagnostics, and the Accelerator. He has co-authored numerous textbooks, and really a book that for me was very pivotal called The Code of Codes, obviously about the Human Genome Project.[1] He's a recipient of virtually every major scientific award and honor that you can get, from the Lasker Award for studies of human diversity, to the Kyoto Prize in advanced technology, the Delores Russ Prize, and most recently—and probably most prestigiously—the National Medal of Science. He has in excess of 890 publications. A pretty formidable bibliography, and it ranges across so many fields that it would take us several days to do adequacy in describing it.

Dr. Hood, such a privilege to have you as a guest for Functional Medicine Update. I guess the place I'd like to start is we had the privilege last month of interviewing one of your former medical school colleagues, Dr. James Fries, who obviously spoke very highly of you. How did you and Dr. Fries connect, and how did your paths end up going such interesting and different ways, with you moving into this whole area of molecular biology with your background? It's really an interesting kind of historic question.

LH: Well, you know, I think that had to do completely with Johns Hopkins as a medical school and the flexibility it gave its students. When I was an undergraduate at Caltech I had really a terrific technical background. I decided there I'd like to do human biology and medicine and disease. So I decided to go to medical school, and Hopkins had this accelerated program, where if you had an unusual career path in mind, you could go through the summers and get done in two-in-a-half to three years. So when I went to Hopkins I did the accelerated program because my intent was to learn human biology and pathology, and then to go back and get a PhD and continue my fundamental research rather than getting into the clinical side of things.

Jim was a classmate there at Hopkins, and I think all of us who went to Hopkins experienced this enormous encouragement to think ahead and take unusual paths and unusual kinds of opportunities. They no longer have that program. I think it's a real shame. Hopkins, at that time, really had some exceptional people, and I'm still good friends with a number of them that have again reached out. One of them is head of the National Cancer Institute's Surgical Branch at NIH, and Steve Rosenberg has been a pioneer in immunotherapy and all sorts of things, and on and on. So it was just a marvelous place to go to medical school and it encouraged interesting career paths.

JB: That broad thinking obviously is symbolic of all the contributions you've made over the years. Let's now segue over to Caltech and how you happened on with your engineering mind, with your group, into the development of pieces of equipment that people really thought were going to be impossible to develop. I recall early in my career in the 60s doing DNA analysis one nucleotide at a time. How did you come about these extraordinary discoveries?

If You Want to Change a Field, Invent a New Technology

LH: You know, that's really an interesting question, Jeff. When I went to Caltech as a young assistant professor in 1970, I determined that my laboratory would have two major thrusts. One was to develop technology, and that came about as a consequence of having a PhD mentor, Bill Dreyer, at Caltech. One of his fundamental theses was if you really wanted to change a field, invent a new technology that opens up new dimensions of data space. And the second area was molecular immunology. What was really interesting, as I got deeper and deeper into molecular immunology I really became convinced that the challenge for both biology and medicine (the study of disease) was biological complexity. Darwinian evolution operates by a random and somewhat chaotic process, and as a consequence, it builds solutions to biological problems that are Rube Goldberg-like in complexity, and that meant we had to have much better tools and strategies for dealing with complexity, both in biology and then in medicine than we had early in the mid-1970s, and that's really when I first started realizing that we had to think about disease, we had to think about biology, in a systems way. That is, we had to take a global and comprehensive view of it and not just look at a narrow slice of it. The challenge was in the mid-1970s there weren't the tools, nor was there the conceptual framework for dealing with complexity—for being able to look at systems in a global and holistic way.

Interestingly enough, that analysis of biological complexity then pushed me into a series of interesting paradigm changes that I think position us very uniquely with systems medicine and P4 medicine, which we'll talk about later today. One was the paradigm of change of bringing engineering to biology. We actually ended up developing five instruments that did several important things. One is they generated new kinds of data rapidly, and hence high-throughput biology, and hence they really ushered in the whole

realm of big data, and that was an important element.

One of the instruments led me into the second paradigm change, namely the automated DNA sequencer got me invited to the first-ever meeting for the Human Genome Project. Twelve of us were invited and we were asked to comment on the validity, the technical feasibility, of this approach. What we concluded was, one, it was feasible (although in 1985, technically difficult), but, two, we were split six to six, for and against, and the six against it were really against it and that was when I first realized how conservative most scientists are. Now, when you make arguments about new ideas, people tend to map whatever you say into what their preconceived notions are, and so it took us five years to finally push the genome project through. What that did from the point of view of my story was it gave us a parts list of all the genes and hence all the proteins, and that parts list is really a key component of this thing we'll call systems biology.

Bill Gates Funded First Cross-Disciplinary Department of Molecular Biotechnology

The third paradigm change was the realization, in developing the automated sequencer, that we had to bring together an engineer, a chemist, a computer scientist, and a molecular biologist to really solve the problem, and it made me realize that biology departments in the future had to have embedded in them a cross-disciplinary series of talents that allow you to take leading edge biology and use that to drive the development of new technologies, and in turn use those data to create new analytic tools. So I proposed at the end of the 80s at Caltech that I do such a department there and the biologists absolutely opposed it, so Bill Gates made it possible for me to move in '92 to the University of Washington and I created there the first cross-disciplinary department of molecular biotechnology, and it was really spectacularly successful. It created the first key technologies for the field of proteomics, the study of complex protein mixtures. It developed the software that was utterly essential for the Human Genome Project. We developed my fifth instrument there—an instrument called the inkjet synthesizer, which allowed us to synthesize rapidly DNA and hence DNA arrays. And we developed a multi-speed, multi-parameter cell sorter that was a revolutionary new principle, and on and on.

Institute for Systems Biology Established in 2000

What happened at the university was a bureaucracy that wouldn't let me take the next step I wanted to take and that was to create an Institute for Systems Biology. The reason for that is bureaucracies are evolved from the past, and they are honed to deal with the present, but they really have difficulty dealing with the future. We just needed so many things to make systems biology work that I resigned in 2000 and created the first Institute for Systems Biology that has spent the last 14 years very successfully pioneering systems science—this holistic and global approach to studying biological problems, and very soon to studying medical problems, and of course that led to this thing we call systems medicine that is a systems biology approach to disease, and the realization that systems medicine had two central features that begin to let it deal with the complexity of biology. One was that the image that in the future every individual patient will have a virtual cloud of billions of data points of many different types of data (molecular, and cellular, and genetic, and organ, and higher level phenotypic data, and even social network data of individuals). These were all needed to be seamlessly integrated together and dimensionality reduced to be able to create models that allowed us to optimize wellness and minimize disease for the individual.

And the second feature was the realization that in disease, the reflections of the disease are embedded in

what we call the network of networks. That is, there are networks that operate at the genetic level, at the molecular level, at the cellular level, at the organ level, at the individual level, and these networks, in an integrated manner, handle the information of life. Disease causes networks to become disease perturbed. That alters the information that they can display, and if you can capture those changes in disease-perturbed networks, you gain deep insights into disease mechanisms and have new strategies for doing both diagnostic and therapeutic approaches to the disease.

The Tipping Point: DNA Sequencing Will Soon Be Third Generation

That kind of approach—this systems medicine—I would argue has reached a real tipping point in that it has pioneered a whole series of new technologies and fundamental strategies for doing things. I'll give you just a couple at a very high level. We're pushing the idea that DNA sequencing will be soon third-generation. We'll look at individual molecules and put them through nanopores and analyze the signals electronically. What that means is you can get very long reads of DNA very, very rapidly and we envision a time in five to eight years where we'll have a hundred dollar genome that can be done in 15 minutes and that is going to make the genome the equivalent of a simple medical test. Yet the genome is one of the two foundational types of biological information that lead to both normal and disease phenotypes—the second, of course, being how the environment impinges on the organism and modifies the genome readout.

Some of the things we've done, then, is we've looked at diseases dynamically, studying them in animal models, being able to look at them at their origin when we induce the disease and follow the progression of the disease all the way through, and understand multiple biological networks become disease perturbed and they describe beautifully the phenotype and the deep mechanistic nature of a variety of diseases. We've looked at neurodegenerative diseases, we've looked at cancer, and we've looked at liver toxicity in this way.

A second thing we've done with systems medicine is to show that sequencing the genomes of families gives you a really powerful new approach to identifying disease genes. We've now looked at almost 2000 complete human genomes, 14 or 15 different diseases, and in all cases we've had deep and fundamental new insights into what's happening into diseases that have at least a partial genetic basis and so forth.

New Discovery: A Systems Approach to Blood Diagnostics

Maybe the most spectacular thing we've done is we've worked out a systems approach to blood diagnostics, which deals with the horrendous signal-to-noise issues you see when you look at normal bloods and diseased bloods and there are lots of differences, and 99 percent of the differences are noise; they are not reflective of the disease. We've used these systems approaches recently to create a panel of 13 blood proteins that give us the ability to distinguish benign lung nodules from their neoplastic counterpart. And that simple identification will end up saving the healthcare system north of 3.5 billion dollars a year, and the reason for that is so many people with benign nodules undergo expensive surgical procedures and that can be prevented by saying, "No, this nodule is benign. You don't have to take a guess and try and do the surgical procedure." We've taken a similar approach to post-traumatic stress disorder from looking at soldiers that are back from Afghanistan, and again, for the first time, we have a quantitative panel of biomarkers that distinguishes, at the 95 percent level, PTSD soldiers from their normal counterparts, so this means it's the first time ever a neuropsychological disease has had a

quantitative assay, and it means a big revolution not only in diagnosis, but especially in therapy because for the first time big pharma will have concrete markers that it can use to assess the effectiveness of drugs.

I could go on. We have computational methods for identifying new kinds of drug targets and we can make drug discovery more efficient, infinitely cheaper, and on and on. But the bottom line is that there is a convergence of systems medicine of big data and its analytics, and of patient-activated social networks, that go together to give this thing we describe as P4 medicine (namely, predictive, preventive, personalized, and participatory). And I just want to say a word about the patient-activated social networks. They are really going to be important because I think they will be the driving force for catalyzing the transformation that is to come in our healthcare system, in a move toward this P4 medicine, and I'll describe how I think we can carry that out in just a few moments.

Six Ways P4 Medicine Differs From Traditional Medicine

What I would emphasize is P4 medicine differs from traditional evidence-based medicine in six really important ways. One, it's proactive. Number two, it's focused on the individual. Number three, it's really focused on wellness. Number four, It's focused on, for each individual, generating this virtual data cloud of billions of data points so you can carry out the analytic assessment of what's needed to optimize wellness and minimize disease. And five, and I think this is one of the most important of the revolutions, it acknowledges that the system we use currently for clinical trials and drugs is utterly broken and is not working at all. The approach is to take thirty thousand patients that you're testing a lung cancer drug in, give them either the drug or a placebo, and to abstract from that set of patients the responses and the curves, and from those curves to make predictions: (A) about how the population of patients will respond, or (B) about how effective the drug is. The reason that is utterly the wrong way to go about it is each of those thirty thousand patients is unique genetically and each is unique environmentally and you can't conglomerate all of those responses together. What P4 medicine does is it analyzes each individual uniquely, and then it aggregates these individuals based on what characteristics you're interested in, and I would say only in that manner can you get sepsis patients that are going to respond effectively to a given drug, or you know won't respond to other kinds of drugs. And then the sixth thing is this patient-activated social network and its real importance.

So the question, which I think is really interesting, is how then do we impose this heretical, radical new vision of medicine into the healthcare system? The approach that we've come up with is to create a large pilot project which is going to involve a longitudinal Framingham-like study of a hundred thousand well patients, and to be able to make many, many measurements across time over a period of up to 20 or 30 years, and from that set of patients we'll see the individuals dividing into two categories: there will be a set of patients that remain well and perhaps get even healthier, and there will be another set of patients that will over time transition from wellness into disease. And the idea, then, is for the first time we'll be able to study: (A) the entire longitudinal development or progression of the disease, but (B) we'll be able to look at the very origins of the disease and come to understand mechanisms that are operating and new diagnostics for very early detection of disease. If we can, then, change that trajectory very early on from a disease trajectory back to a wellness trajectory, you're going to save the healthcare system billions upon billions of dollars. And the only way to do these early wellness-to-disease transition studies is through longitudinal studies of normal individuals in exactly the way we've talked about.

So the idea, then, would be to look at six or seven different types of data—genome data, clinical chemistries, quanti-self data (heart rate, sleep quality, all of those kinds of things). We'll look at the gut microbiome and how it changes. We'll look at fingerprints in the blood for brain, heart, and liver that can distinguish wellness-to-disease transitions very, very early, and so forth. It means we will soon have this virtual cloud of billions of data points that we can analyze, and what we hope in this case to come out with are for each patient a list of actionable opportunities that will uniquely give them the opportunity to improve their health. And we think a lot of these actionable opportunities will revolve around the area of nutrition and optimizing nutritional deficiencies that arise because of genetic variance in the genome, and we know lots of these already.

I have a friend, for example, from Microsoft, who started getting early-onset osteoporosis in his mid-30s. He had a genetic analysis done and discovered a calcium transporter that was defective and he took, for a year and a half, twenty times the normal amount of calcium and he brought his bone structure back to normal, and now 12 years later he's a perfectly normal healthy male individual. So a deficiency led to a calcium defect that he can cure by dealing with increasing the concentration of intake of calcium.

We feel that for every single individual there are going to be multiple actionable opportunities. So this kind of study will do three things. One, it will let us create a data cloud for each of the individuals, which, when analyzed, will optimize wellness and minimize disease. Two, we can take the data from those individuals that remain well and mine it for metrics of wellness, which we've never had before. I mean, wellness now is a fuzzy, soft, psychological definition, and it frankly is just exactly what PTSD was prior to our development of this quantitative blood assay. And number three, we're going to see transitions from wellness to disease in the hundred thousand for virtually all major diseases, and we'll be able to look at these early disease mechanisms at early diagnosis and try to begin attempting early diversion back to a wellness trajectory.

Wellness 100K: Ambitious Study Will Follow One Hundred Thousand Individuals

How are we going to scale up? We're going to start with a hundred individuals, then in a year a thousand, then in another year ten thousand, and finally go to a hundred thousand. In fact, for the first 100, which we call the Pioneer 100, we're starting with 108 individuals that have been recruited. It's under IRB. We have coaches that will transmit these actionable opportunities to the individuals. We have a panel of experienced physicians that will oversee this whole process to make sure that we don't run into the kind of difficulties with the FDA that 23andMe did. And of course in the long run, what we really hope to be able to do with the 100K Well Person Project is to discover the new kinds of technologies we need to measure immunity, inflammation, a whole variety of things we don't measure very well now. What we plan to do at the end of this next year is spin off a company that will be the vehicle for scaling this kind of approach eventually up to billions of people. It is what we see as reaching across the world and beginning this democratization of health care that was inconceivable even a few years ago. But the important point is, if you think about it, this hundred thousand longitudinal wellness person study has every one of the six fundamental features of P4 medicine that I described, and I think it will be the opening wedge into the transformation of medicine from this traditional evidence-based approach to a P4-based approach. We're looking forward in a really exciting way to the next 10 or 20 years as we see this revolution playing out.

A long answer, Jeff, but at least you have a quick synopsis of how I see medicine being transformed.

JB: Well, Lee, to say that was a tour de force would be one of the great understatements that I've ever made in the 32 years of Functional Medicine Update. That was absolutely brilliant and what an extraordinary landscape you took us across. I mean, no one who is listening to this could be without goosebumps. That was a transformative discussion that you provided for us. As you were talking, I reflected back on a conversation I had two weeks ago with Bob Langer at MIT and Denny Ausiello, who you probably know, who is the head of medicine at Harvard and Mass General.

LH: I do know Bob really well. What a wonderful person and scientist.

JB: In this conversation I was having with the two of them I asked them about you. I just said, "You know, Lee Hood has made such incredible contributions and now at the Institute for Systems Biology his group is doing just pioneering work." Both of them almost simultaneously said the same thing to me. They said that Lee Hood is one of the few people that has crossed all boundaries to consolidate information and make it clinically relevant and social changing, and that is a very unique feature that characterizes your brilliance in terms of the impact of your work. I thought that was probably one of the most complimentary things that a person could receive. I wanted to pass it on to you.

LH: It is an enormous compliment coming from people like that, that's for sure.

JB: What was it in your life that…I'm not going to say gave you permission because I'm sure you've never asked for permission, but let's say gave you the sense that you could cross these boundaries that often are kind of defined by disciplinary myopia. I had the same conversation with Dr. Pauling 25 or 30 years ago and asked him how he did this because it comes at some professional peril. How did you do this?

LH: I would say that it really all starts with my upbringing in Montana. My father was an engineer and he embedded engineering in me and that's how I've always viewed biology. My mother was an interesting only child that grew up with what she felt an inappropriate dependency on her parents, and she was determined to have her kids be free and unfettered of constraints. She encouraged us from our very earliest years to go out and climb mountains, to explore new possibilities to do whatever really turned us on. And I would say a third thing that was really transformational for me was that in high school I had three of the best teachers I had in my entire career: a chemist, an historian, and a mathematician. All three of them were really terrific at saying, "You know, what do you really want to do? Have you really thought about what your potential is? Do you want to go to a state school?" And one of them—my chemistry teacher—had gone to Caltech during World War II and he decided any good student he ever got he would send there. He started pounding on me at the beginning of my third year, so I ended up applying to Caltech. I went there as an undergraduate, and it gave me this deep fundamental mathematical/chemical/physical background that was just wonderful for doing science. Had I gone to one of the classic liberal art schools I was thinking about I suspect I would have never gotten that background. I think these things end up being the serendipity of your early life and that they frame, in a very powerful way, the potential you have for the future.

JB: Obviously that speaks so highly to the importance of education and the education n-of-1 experience—almost like we're talking about the medicine of n-of-1, we have this educational epigenetic events n-of-1 with our mentors. How do we get this kind of excitement, vibrancy, fearlessness, courageousness to cross barriers down to bright women and men, girls and boys, that are being educated

today? How do we do this?

The Institute for Systems Biology Offers K-12 Science Education

LH: You know, ISB actually has a group of eight full-time people that are working on K-12 science education, and we've created a cadre of strategies that starts bringing powerful, inquiry-based science thinking as early as elementary school, it goes through middle school, and then into high school, and we really encourage independence and free thinking. I think the key is to train the teachers as to how they have to deal with their students to give them this sense of unboundedness, to give them this sense of opportunity and their own potential. I think we've done really a good job in transforming education—K-12 science education—in the Seattle school district. We've worked with the Renton school district more recently, and in all cases we see significant improvement in student scores, and what's interesting is the biggest improvements we see are in the students from disadvantaged families. They're the ones that come the farthest when given these kinds of opportunities.

You are so right. Education, K-12, I think really sets the boundaries as to will we go into a technical field, will we become a scientist or an engineer, and even the important point of how do we think about the problems of society? Do we have emotional, irrational senses of what's right and evolution is evil, or can we think about things analytically and try and dissect pros and cons of global warming and all the other kinds of things? I think education is key, and I think, frankly, the education we do on our own kids is where you really want to start because you can put them in a frame of mind where you give them the sense that being unbounded. Both of our kids, I think, very much came away with that and they've been really successful. One's an environmental scientist at the University of Alaska in Juneau and one is a discrimination lawyer just setting up her own firm in Los Angeles now. We have the power to transform our kids if we have the energy and the knowledge of how to do it.

JB: Yes, I think this is very, very proactive for our listeners. Certainly I, as now a grandparent of five grandchildren, am reminded every time I'm with them and I'll be reminded by this conversation that the models that we're setting up for their inquiry process in life will stick with them and become part of them as they move into adulthood.

LH: You know, what I did with both my children and now I'm doing with my grandchildren, actually, was to tell stories about a mythical science fiction character who gets into all sorts of difficulties, and I have the kids problem solve about how to get him out of the difficulties. My son and daughter both have off-scale analytic skills, and I'm convinced that it was because I spent four or five years telling these stories and having them problem solve all sorts of different kinds of things. You can do marvelous things with your kids.

JB: That's fantastic. Let me ask one last question. I don't mean to put you on the spot but I think everybody listening probably has this in the back of their mind, and that is with all this extraordinary optimism that you shared with us—in a sense, for vitality of the future—there is the reality of today and how medicine is practiced. Docs are down in the trenches and they're caught up with these reimbursement codes and uninvited third-party reimbursement people that are in their offices (called the insurance companies) that they didn't really invite but they are there to oversee and proctor how they are doing standards of practice. As a participant in your Pioneer 100 Wellness Project, which I'm very excited to be one of those 100 people, I recognize I'm going to be experiencing something very different,

probably, than the average patient that goes into their offices. What's your view as to how we are going to transform the kind of daily grind of medicine? Is it going to be a long process, do you think, or do you feel like we will have a shifting paradigm that's like Thomas Kuhn's paradigm-shift mechanism/tipping point?

Insurance Companies Will Come to Understand the Cost Savings of P4 Medicine

LH: Well, I think it will be a shifting paradigm, but I think it's definitely going to take some time, and I see the origins as arising in some of the most progressive healthcare systems. Geisinger is a really progressive healthcare system. Inova in Virginia; we're collaborating with them on interesting ways to do similar kinds of things to what I've talked about here. I think what we'll see is some of the most progressive healthcare systems will adopt this and what will happen is the savings will be so enormous that people will be forced to respond in kind even if they are skeptical. It's going to take a while to begin moving things around, but I think it is going to happen. I will say when we announced this Pioneer 100 program that is very much focused in Seattle, I've had three physicians, now, from the community come to me and say, "I'd like to move my practice over to focus in increasing ways on wellness and to become involved with this program so that I understand it in depth." I think it is going to be a paradigm change, but it's going to be incremental in the sense that good functional units will use it and see its power, and then it will become increasingly important. I think as the insurance companies, as the payers, come to understand, "Look, you can use systems medicine and save 3.5 billion on lung cancer patients," those are compelling arguments quite apart from the fact you've improved healthcare quality as well. You know, it isn't going to happen overnight, but I think over a ten-year period we'll see an enormous transformation.

JB: Well, Lee, I can't tell you how much I appreciate you giving all of us this infusion of energy, optimism, excitement, and commitment to excellence about where the future of healthcare is going. I'm so excited that we're going to be able—thanks to your graciousness—do a collaborative program with the Personalized Lifestyle Medicine Institute at ISB in October of 2014, and the chance to be a participant in the Pioneer 100 program will get me more engaged in P4. I think what you've described as an unbounded opportunity for reducing human suffering and improving quality of life of hopefully billions of people in the years to come. There's probably no better way to spend a life than focusing on that objective.

LH: I couldn't agree with you more, and we're looking forward to our interactions with you and the meeting this October as well, so maybe we'll see some of your listeners there.

JB: I think you will definitely do so. Thanks a million. We really appreciate it.

LH: Thank you.

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