

Whitman College

Commencement Address by Dr. Leroy Hood

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“The Book of Life”

A new book provided by the Human Genome Project has recently been published, the Book of Life. This book offers deep insights into the nature of humanity and our relationships to the world of which we are a part. And it offers deep insights into our futures.

What exactly is the genome? It is nothing more than the set of instructions that specify human development; that is, how each of us started as a single cell (a fertilized egg) and how each of us has progressed to an adult human composed of a hundred trillion cells of thousands of different types (e.g., muscle cells, brain cells, etc.).

The language of the genome is DNA. DNA has a very short alphabet, just four different letters, G, C, A, and T, but the genome contains a remarkable amount of information—three billion letters of the DNA language. The Human Genome Project has translated these 3 billion letters into the Book of Life. It contains 500 volumes, each volume consisting of 1,000 pages, and each page averaging 1,000 six-letter words—a staggering large instruction set for human development and physiological responses to the environment.

Operationally, the human genome is composed of one long sentence of 3 billion letters that have been cut into 24 different pieces, ranging in size from 45 million letters to 280 million letters. These pieces are called chromosomes, and collectively they are termed the **human genome**. Each of the 10^{14} cells in a human contains this Book of Life—the genome.

In a book, the information, in part, is contained in words. The language of DNA has words, and those words are called genes. Here is where the analogy with a book breaks down because what the genes do is encode proteins. Proteins are the molecular machines of life, which carry out all the functions of life. If you look at another individual, virtually everything you see is composed of proteins.

In a book, there are higher levels of information organization. In a book, the words are collected into sentences and the sentences into paragraphs and the paragraphs into chapters. Each of these gives a higher level of meaning to the content of the book. So it is with the human genome; the genes and proteins are gathered into the biological systems that execute the essential functions of life. The heart is a biological system that pumps blood to our tissues and provides them with oxygen and nutrients. The brain is a biological system that allows us to think, remember, and learn.

It was in February of 2001 that the first draft of the human genome was published. That draft really was quite remarkable. It gave us four new fundamental insights into what we are as humans. First, there was a surprise. We appear to have in our Book of Life only 30,000-35,000 different words, or genes. This was surprising to many of us because the genome of a small worm (hundreds of these worms could be placed on your fingernail) had been sequenced earlier and it contained about 20,000 genes. It is quite

remarkable to think humans require only one-third more genes than the simple worm. How we do that is still an unanswered puzzle.

A second observation was also quite striking. If we rifle through the Book of Life for the different races—Caucasian, Black, Mongoloid—what we find, surprisingly enough, is that there are essentially no race-specific words. Indeed, the Book of Life for two Black people may differ more than those for a Caucasian person and a Black person. The concept of race is cultural, not genetic. That is a point we will return to later.

A third observation that came from the human Book of Life is remarkably gratifying. If we again rifled through the Book of Life for a human, a fish, a fly, and a yeast (a small, single-celled organism that makes beer), what was absolutely amazing was the large number of shared words (although the spellings were somewhat different). Even more important, many fundamental biological systems composed of those genes and proteins were remarkably similar. This underscores the enormous unity that exists in all life. We all descended from a single common ancestor at the beginning of life and subsequently diverged (changed) in very different directions. However, all life is intimately interconnected by this common heritage.

The fourth observation from the Book of Life was in many ways the most surprising. It reemphasized the connectedness of all life. If we rifled through the Book of Life in humans, we see, interestingly enough, 200 or more genes derived from other organisms. These 200 genes may have come from bacteria at some point in our evolution. Of course this observation runs counter to the classic view of evolution: the view that all of your genes came only from your parents. We thought evolution proceeded in this vertical manner — from grandparents to parents to children. But it seems that there is a much broader possible context of evolution, one in which any living creature can actually incorporate information from surrounding organisms. Of course, this again stresses the interconnectedness of all living organisms.

The Book of Life has given us four remarkable insights into humanity. It has also catalyzed two striking paradigm changes in science, one relating to biology, and the second relating to medicine.

The paradigm change relating to biology is that biology, in the future, will focus on systems approaches to studying biological complexity. For the first time, we have all the genes and proteins so we can study a system in the context of how all of its components interact rather than in the context of one gene or one protein at a time — which is how biologists have studied biology for the past 30 years. Indeed, the Institute for Systems Biology, which I co-founded two years ago, is dedicated to the creation, application, and dissemination of systems biology. It is my conviction that systems approaches to biology and medicine will dominate the 21st century.

The paradigm change in medicine will be even more remarkable. This paradigm change will be realized in the next 10 to 15 years. It will drive us from our current reactive medicine — you come in when you get sick and the physician attempts to make you well — to a predictive and a preventive medicine, and ultimately a personalized medicine.

If we look through the Book of Life of myself and Whitman President, Tom Cronin, we would be amazed to find that the books are essentially identical except that maybe one in a thousand letters is different. Most of those letter differences have no effect on who we are, but a very few of them may actually cause gene defects that predispose to various diseases.

For example, if you are a woman and you have a single bad copy of the breast cancer 1 gene, you have a 70 percent chance of getting breast cancer by the time you are 60 years of age. Why only a 70 percent chance? If it is a defective gene, why doesn't it always cause breast cancer? There are two possible explanations. One is that in some cases, defective genes require certain environmental signals for their activation. Another more likely explanation is that you generally do not get diseases from single defective genes; you need a number of defective genes that act in concert.

The important point is that within the next 10 to 15 years we will have identified hundreds of genes that predispose to virtually all of the common, late-onset diseases such as cancer, cardiovascular disease, neurological diseases, a variety of metabolic diseases, and the like. What we will be able to do is take from each of you a blood sample, interrogate the possibility of defects in hundreds of genes, and write out a probabilistic health history of what is likely to happen to you. This is the predictive approach to medicine we will see over the next 10-15 years.

Prediction without cure is an anathema to medicine. Because of the systems approaches to medicine discussed earlier, physicians (and biologists) will be able to study the defective genes and interrogate them in the context of the biological systems within which they operate and learn how to circumvent the limitations your defective genes impose.

What this means is that once we have your predicted health history, we can say, "Here is a course of action which, if you follow, will delay, if not prevent, the onset of the predicted disease and extend your life span.

What are the preventive medicines of the future? They could be changes in environment; they could be certain specially designed drugs; they could be gene engineering; or a critical potential preventive therapy for the future is embryonic stem cells. These possibilities, accordingly, couple the predictive and preventive medicine of the future. Indeed, this future medicine is highly personalized because each human will be treated uniquely.

It is quite clear predictive and preventive medicine is going to propel us into a different world. My

prediction is that the world of predictive and preventive medicine will extend the life span for each of us by 10-30 years and that we will be productive, if not creative, during these extended years—probably well into our 90s. This is the world of predictive, preventive, and personalized medicine.

This paradigm change in medicine obviously presents enormous opportunities for mankind. However, it does raise fascinating ethical, social, and legal issues that are certainly perplexing. Let me mention a few examples.

One, if we can extend the productive, creative life-span of the average individual out into the 90s or even beyond, society is going to have to readjust how we think about our senior citizens. Society does not treat them very well. How can we capture this enormous potential creativity and productivity? That will constitute a major challenge for society.

Second is the question of who gets to look through each of our Books of Life? Who gets to know what our predictive health histories might be? Is it our family? Is it our insurance companies? Is it our employers? These questions concerning genetic privacy are deep and complex. There are a number of genetic privacy laws — some reasonable, and others absolutely irresponsible, now being considered in Congress. We can only hope that wisdom will prevail.

Third is the nature of the preventive therapies that will be required to realize the full potential of preventive medicine. The use of stem cells is one of the most powerful potential preventive therapies, yet it is shrouded inappropriately in issues of religion raised by a highly vocal minority. There are two types of stem cells: embryonic stem cells, and adult stem cells. There are those who believe, based on religious convictions, that it is okay to use adult stem cells but not embryonic stem cells. Unfortunately, adult stem cells have inevitably lost many of their options for development. Hence, it is only embryonic stem cells that hold the diverse potential required for the myriad of preventive therapies that will be necessary for medicine of the future. We really have little choice but to explore the enormous potential of embryonic stem cells. I find it very alarming when doctrinaire and narrow views of religion block our ability to lift the yolk of disease from tens of millions of our human colleagues.

This Book of Life, as you can see, is really quite remarkable. It has given us some deep insights into who we are and how we are connected to the rest of the world. So, what are the lessons that you graduates, and even the rest of us, might take from these insights?

There are basically three lessons. One is the idea that humans are one race. The differences we see between races are fundamentally cultural. The causes of these differences have to do with poverty, lack of education, and inappropriate health care rather than differences in genes. For example, the root cause of Middle Eastern terrorism is poverty—and we delude ourselves if we think the fundamental solution to terrorism is military action.

What is the take-home lesson for the graduates? The lesson is that each of us has a responsibility to make certain our colleagues of the human race have equal opportunities for education, health, and employment. These are global and international problems. If, however, each of us responds to these challenges in our local communities, we can make a real difference. And local achievements sum eventually to more global solutions.

The second take-home lesson relates to the interconnectedness of all life and the unique responsibility humans have as sentient organisms to maintain a balance and connectedness among all living organisms. It is critical that we leave our children and our grandchildren with an environment in which they would like to live. It is critical that we deal with the issue of a sustainable environment. Once again, we can make an enormous difference if each of us is committed to doing that in our local communities, to changing the balance between economic exploitation of the environment and a sustainable environment—to know and understand this critical cost/benefit calculation.

The final point is that we all, graduates and the rest of us, have an enormous obligation to continue learning about the ongoing advances in science and technology because they present us with opportunity as well as challenge. We have to use the opportunities for the betterment of humankind and we have to deal thoughtfully and rationally with the challenges. We have to be able to make wise decisions. We have to be able to determine what are the appropriate regulations and rules and what are the appropriate levels of support. All of this requires education and the application of rational analyses.

We have yet a further obligation and that is the obligation to educate those in our communities who may have been less fortunate, whether children or adults. We have an obligation to help our fellow citizens become informed so they too can deal with and take advantage of the opportunities and come to rational, reasonable decisions about how to deal with the challenges.

In summary, I would say that the Book of Life has given us a wonderful view of how broad and interconnected humanity is—to one another and to the world of living organisms. We have the insights and tools to move humanity ahead to the next level. The question is whether we have the will and leadership to move ahead. You graduates have a unique opportunity to make the world a better place for all of us.