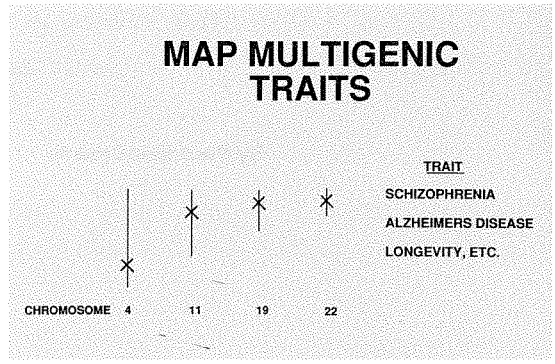
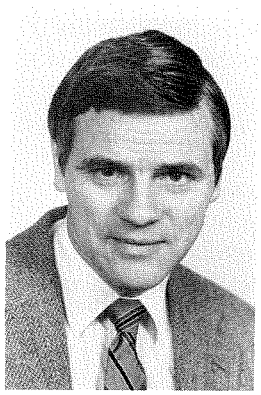
Speculations About Future Humans

by Leroy Hood





There are three forces that may fundamentally change human physiology and/or behavior. One is culture. A second is medicine, which in the future is going to profoundly change how we deal with disease and, possibly, how we view ourselves. The third, and perhaps the most intriguing force, is evolution—either natural or engineered. I will discuss the impact of medicine and evolution on future humans.

As we move into the 21st century, the Human Genome Program will profoundly alter how medicine is practiced. This program plans to decipher the units of human heredity—the 23 pairs of chromosomes present in each and every human cell. Chromosomes are made up of DNA, linear strings with four different letters in an alphabet. Thus the language of DNA uses its four letters to generate the information necessary for making humans. These chromosomes, collectively known as the human genome, direct the complex process of human development, in which we all start as a single cell, the fertilized egg, and go through a successive series of cell divisions and development to generate the 10^{14} highly specialized cells of an adult human. Our genome contains approximately 100,000 units of information, or genes, which are differentially expressed to make each type of cell distinct—for example, a hair cell different from a brain cell. Each gene specifies a protein molecule, a linear string composed of 20 different types of subunits. The order of these subunits dictates how each protein folds to become a three-dimensional molecular machine. (Proteins give our body shape and form, and catalyze the chemistry of life.) Hence, the Human Genome Program will provide valuable information for understanding how humans function in health and disease.

For each human chromosome, we are defining a genetic map that will permit us to identify the genes that determine certain human traits such as blue eyes or brown hair. We are also creating a second type of map—the so-called sequence map—that will enable us to specify the order of every gene's subunits, so that we can identify and decipher each of the 100,000 or so genes that exist in the human organism. We are hoping these maps will allow us to identify the genes responsible for such simple traits as skin color or blood types, as well as those responsible for diseases such as Alzheimer's or cancer. The important point is that once we have detailed genetic and sequence maps, it will be very easy to find the unknown genes that control additional important human traits, such as schizophrenia, longevity, and heart disease. Every one of these genes has the potential to serve as a diagnostic or therapeutic agent in medicine of the future.

We will certainly be able to use this genetic mapping approach to understand and eventually treat disorders caused by defects in a single gene—diseases such as sickle-cell disease, cystic fibrosis, and Huntington's disease. Even more important, we will be able to look at traits and diseases that are caused by a multiplicity of genes and to develop both diagnostic and therapeutic approaches to dealing with them. Here, we will have thousands of new opportunities to use genes as therapeutic agents for a variety of different diseases.

It is clear that in the future we will be able to engineer three-dimensional biological shapes such as proteins, and that this will give us the capacity to custom-design biomedically useful molecules. For example, we might be able to design a cancer-specific protein that is able to recognize a particular type of tumor cell and to which we can attach functions that can specifically destroy those cells. We'll be able to carry out genetic-engineering therapy in which we will substitute "good" genes for "bad" genes. Currently, there are significant technical problems in genetic therapy, but in 25 years, we will be able to manipulate genes with complete facility, put them specifically into particular types of tissues, and have them function in a fully normal way.

Detailed genetic and sequence maps such as the example at left will allow identification of numerous human diseases and traits.

The techniques of genetic and cellular engineering will offer new and powerful insights that will profoundly change our approach to many of the diseases we worry about today. I fully expect that the 21st century will be the century of preventive medicine. We will take DNA from each child as he or she is born and examine the perhaps 100 genes that predispose humans to common diseases, such as cancer, heart disease, and autoimmune disorders. We will then know which diseases each person will be susceptible to. We will be able to circumvent the limitations of any bad genes a person might have, either through chemical therapeutics or through appropriate genetic engineering.

Let me talk about one category of especially perplexing diseases—mental disorders. The brain is a marvelous instrument with 10^{11} different cells (neurons) that communicate with one another via chemicals transmitted over the sites, or junctions, at which they touch one another. We now know that there are perhaps 80 of these little chemical messengers, or neurotransmitters, and that they almost certainly play a critical role in how we think, behave, and feel. As we come to learn more about these messengers, we will be able to deal with many types of mental diseases. For example, *l-dopamine* has played an incredible role in alleviating, even reversing, Parkinson's disease for some patients. In the future, we will understand the types of neurotransmitters that are necessary to bring about permanent kinds of changes in a wide variety of brain-related disorders, such as schizophrenia and manic-depressive disorders.

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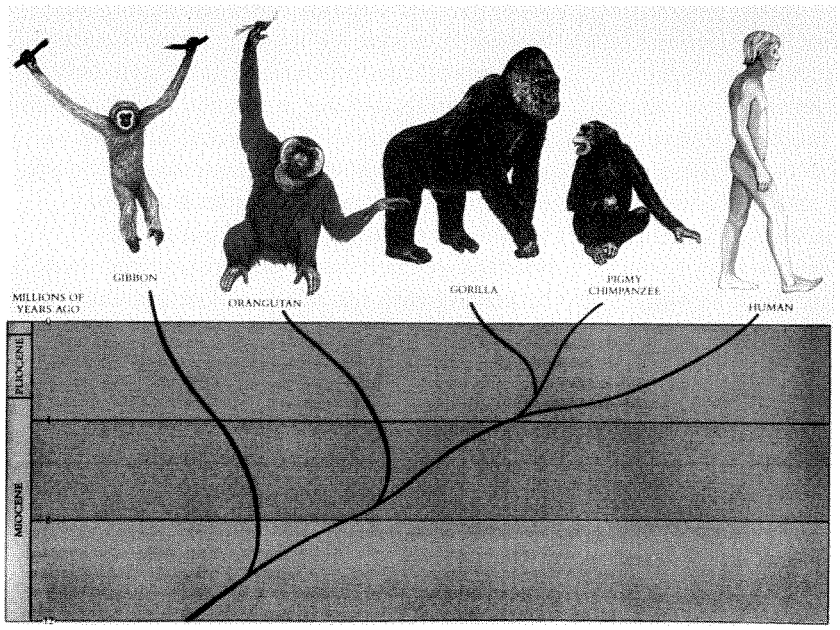
As we come to understand the brain, it seems to me that two questions will be of remarkable interest. The first is, how much unexploited potential is present in the brain, and can we learn to exploit that potential? We all know that children are extraordinarily adept at learning languages, not only their own native language, but any language. What other kinds of permanent knowledge-imprinting can be done early in life, at midlife, or later in life, and how can these imprinting processes be effective? I believe we will have powerful opportunities for enormously enhancing the capacities that we have. The second and equally intriguing question is whether we can enhance our existing potential by playing with the balances of neurotransmitters that exist in the brain or by making other kinds of modifications in these molecules. I think there will be real opportunities to develop the essential properties of the mind in the future.

The aging process is another area in which I think we can expect to make great advances. Here again, there are two central questions—will it be possible for us to live longer, and, even more important, can we extend the duration of a high-quality life? In the future, will we have 80-year-olds with the vitality of 20-year-olds? My own belief is that genetic mapping will make it possible to identify genes that play a key role in longevity; and that we will ultimately come to understand a great deal about the physiology of aging. Perhaps we will live longer; even more important is my conviction that the quality of life will be significantly extended for most of us.

But here I need to make a critical distinction. The kinds of changes I have been discussing up to this point have had to do with genetic engineering of somatic, or body, cells as opposed to sex cells. In other words, these are changes that do not alter the genetic instructions that are passed on to the next generation. The changes are specific to the individual, and they die with the individual. In contrast, modification of the germ line, which alters the genetic material in the sex cells—the sperm and egg—*adds these changes to the gene pool*. Once this is achieved, it becomes possible for humans to pass these changes on to their children and thus change the course of their own evolution.

I noted earlier that of the three forces—cultural, medical, and evolutionary—that have the potential to fundamentally alter human behavior and/or physiology, evolution was the most intriguing in that it is potentially the most far-reaching. Up to now, evolutionary change has proceeded with agonizing slowness. Earth was created 4.5 billion years ago. The first cell that had a nucleus arose about 1.4 billion years ago, and the creation of multicelled organisms occurred just 600 or 700 million years ago. Humans are, of course, a much more recent evolutionary invention. Our hominid ancestors branched off from the chimp and gorilla evolu-



tionary line about 4 or 5 million years ago, and Homo sapiens, our own particular species, emerged perhaps half a million years ago. One of the incredibly interesting questions is, are we the final product of primate evolution, or will there be another branch that will perhaps end up viewing contemporary humans as we now view the chimpanzee? That is a deep question, with some extremely interesting implications. If further human evolution is to proceed, then it must operate by virtue of the two major mechanisms of evolutionary change, namely, mutation and natural selection. Mutations are occurring all the time in human populations, so that is no problem. However, natural selection does not operate effectively in human populations, in part because of modern medicine. Hence, it appears that humans cannot evolve further without directed efforts. Humanity today comprises one large, interbreeding gene pool. It offers very few opportunities for the isolation of small communities that appears to be a necessary precondition for the emergence of new species, unless we were to undertake a deliberate program of germ-line genetic alteration.

In the not-too-distant future the genetic engineers will be able to engineer themselves.

There are two logical possibilities. One is selective breeding, which has been carried out successfully with dogs for centuries. You only need to look at a Chihuahua and an Irish wolfhound side by side to realize what an incredible divergence in phenotype has been generated by selectively breeding dogs over the last 5,000 years. There are also dramatic differences in humans. These include not only considerable differences in physical traits, but in mental abilities as well. By selective breeding, we could effect significant physical and/or mental changes in humans. But while humans *could* do this, I think it is unlikely. Not only would it take a directed and committed effort over many generations to bring about these changes, but one would also have to keep these selectively breeding individuals isolated from the larger human gene pool. Even slight interbreeding would dilute and cancel the desired genetic changes you would need to create the kind of evolutionarily superior "post-human" species I alluded to earlier. Indeed, enormous ethical concerns would arise from any such attempts, and certainly it would be difficult if not impossible to reach agreement on the so-called "desired" traits. So it appears unlikely that humankind will change through selective breeding.

There is a second option, germ-line engineering. It is certainly going to be possible to discover anti-aging and anti-cancer genes, and perhaps to permanently enhance qualities such as intelligence and memory. We will have the capacity to choose whether or not to genetically engineer beneficial changes in humans that would then be passed on to their descendants. Would germ-line engineering benefit humans? Should it be seriously considered? Obviously this possibility, distant though it is, raises a host of serious social, ethical, and legal issues. I would argue that scientists have an important obligation to raise these questions for debate in society, outlining the opportunities and the dilemmas they raise. We must communicate to the public the benefits and challenges raised by future genetic-engineering possibilities. We also have to make a serious commitment to improve education, particularly from kindergarten through grade 12, so that we have a public capable of understanding the alternative choices that are before us. In the future, scientists will have to become more involved in the process by which society makes decisions, for some, perhaps directly, as politicians, rather than indirectly as advisors. In the not-too-distant future the genetic engineers will be able to engineer themselves. The fascinating question is, to what extent will they engineer themselves and for what purpose? □

Leroy Hood, BS '60, PhD '68, the Ethel Wilson Bowles and Robert Bowles Professor of Biology and director of the NSF Science and Technology Center for Molecular Biotechnology, has been a pioneer in developing the instrumentation for sequencing and synthesizing proteins and DNA.