What is the importance of understanding the human genome?

Understanding the way the genome functions will dramatically change the way we think about health and disease. Imagine a device like a TV set that is not working. The average person would bang on the side hoping to set it straight. He or she, however, probably would have no idea what really was going on inside that box. If the set were brought to a repair shop, the technician would have two things that the average person would not: an understanding of how the TV works and a wiring diagram of what is inside the box. With that knowledge, they can often replace or fix a part that isn’t working.

Although we’ve seen great advances in medicine during the past century or two, we are still for the most part ignorant about how the body works. To a remarkable degree, medicine is empirical — like banging on the side of the set hoping to make it work. But you could think of the genome as the code that will help us to understand the body’s wiring diagram. For the first time, medicine will be able to approach medical problems by being able to understand precisely what is wrong and determine if it is fixable. This won’t guarantee that every illness or condition will be cured, but it will provide us with a new set of tools for making diagnoses and developing treatments based on a much more thorough understanding of the basic causes of disease.

Will understanding the genome enable us to predict and prevent disease?

If you knew that you were at risk for something like Alzheimer disease, though, and there was nothing you could do about it, perhaps it would be better not to know.

Our use of the human genome to prevent disease will never be an exact science because diseases are not solely determined by genes. Except in a few well-understood diseases such as sickle cell anemia or cystic fibrosis, the presence or absence of a particular gene is not the whole answer. Combinations of genes and their interaction with the environment in which we live are equally important. I think we have to remain very critical of genetic testing as a prevention model.

This issue has received a great deal of attention and also raises many ethical concerns, such as the ability of a person found to be at risk to get insurance or deal with the concept of living under a “death sentence.”
Will this help my doctor figure out what’s wrong with me?

I think we’re going to see major advances in our ability to diagnose certain conditions or diseases. Although genes by themselves don’t (in most cases) cause disease, they probably do contribute to a substantial degree. We already have genetic tests that allow us to be much more precise in identifying disease and in determining the correct treatment option. This is where this concept of the wiring diagram comes in. Once we understand who all the players are in the disease pathway, we’ll be able to develop new drugs that can be aimed at a whole new set of targets. If you understand this pathway you can begin to identify targets for treatment and for diagnosis.

Will the genome map allow physicians in the future to design a custom-made treatment for each individual?

I think that’s where we’re heading. Currently, if you are diagnosed with high blood pressure, your physician may recommend a drug to try. If it works, great. If not, you move on to try another. Your doctor really has no way of knowing why you have high blood pressure.

But if we understood the genetic contribution to high blood pressure, we could perhaps develop a test that could determine which of several genetic risk factors for high blood pressure you might possess. This in turn might suggest that a specific drug will work best for you.

Another patient might have genetic risk factors that indicate his or her high blood pressure would more likely respond to a drug in a different class. This would guide physicians to use the most appropriate drug first — with the anticipation that positive results would be achieved quickly, with less trial and error and less likelihood of side-effects.

What will a doctor’s visit be like in the future?

Let’s say you come in with a particular symptom. The physician is going to be able to test for genetic alterations to help diagnose your condition. Based on your unique genetic profile, the physician can determine which drug or class of drug is most likely to be effective in treating that condition. To take it a step further, such a test might also reveal how you, as an individual, metabolize a drug differently than others do. With that information, a physician can tailor a dosage or watch for side effects that you might uniquely be susceptible to.

Most of this entire testing process is going to take place in a genetic testing lab, invisible to the patient. This is what most people describe as individualized medicine — an attempt to customize treatments.
What about gene therapy?

A: In basic terms, gene therapy is used to replace or repair a missing or defective gene or to deliver a gene product to a highly targeted site. The gene-therapy field has enjoyed a few successes and some setbacks in recent years. It is a field that is in its infancy and has a tremendous promise for the future. But many challenges must be overcome before it is going to be a mainstream approach to treatment.

As those challenges are overcome, disorders that are determined by a change in just a single gene — such as Tay Sachs disease or certain forms of cystic fibrosis — may be treated or even cured by gene therapy. Other conditions like cancer, in which multiple genes and other environmental effects contribute, will be much more difficult to address.

There are a lot of promising approaches. Therapy is going to be affected by genomics and genetics at three different levels. First, specific testing will lead to better diagnosis and recognition of the most appropriate treatment. Second, better understanding of disease mechanisms offers the possibility of developing better drugs treatments. Finally, we are learning to manipulate gene function — the ability to turn on genes that you want turned on or turn off genes that you want turned off.

Are there risks in moving too fast?

A: Understanding or predicting the weather doesn't actually permit us to change it, though we may be able to manipulate it to some degree. The same holds true in genetics.

Are we doing more harm than good if we start fiddling in something where we don't understand the whole system? The answer is yes, there is a risk. That has been clearly demonstrated in some of the gene therapy trials. We have a lot to learn before we can be in control and there will be aspects that we will never be able to control. Even so, I believe we are going to see dramatic and positive changes in this century.

Is this the end of this stage of research, or the beginning of the next stage?

A: Right now, we have given names to genes, but we are a long way from knowing how they function. It is like somebody handing you a city phone book and hoping you can use it to determine what is going to happen tomorrow in that city.

Well, chances are pretty good that the names of the people who are going to make things happen tomorrow are in the phone book. But that doesn't tell you anything about what they are going to do or why.

But the phone book does tell you who the players are. Without it you wouldn't even know where to start. And as you add more information — where someone lives, who they talk to, what they believe in, what they did yesterday — then you begin to have a better understanding of what might happen in the city tomorrow.

We are not talking about predicting the future, but we might be able to put the present into the correct context, better than we can today.

The Human Genome Project is that first step; the phone book that tells you who the players are.
Q: You came from Harvard to lead UAB’s efforts in genetics research and clinical treatment. What role will UAB play in our understanding of genetics?

A: Our vision in the UAB Department of Genetics is to be a leading force in understanding and connecting genes to the pathways in which they participate. From there we will begin to apply that knowledge to medicine, to translate these discoveries into tests and treatments. Additionally, we are a clinical practice department, and I would like us provide service to the community using the most appropriate, best validated and best developed technological tools available.

Our clinical offices are located in a brand new, $35 million building on UAB’s campus. We’re very proud of this state-of-the-art facility, and can offer a full range of the available genetic tests, including chromosomal analysis, molecular testing and biochemical testing.

One of UAB’s key missions is education — training tomorrow’s physicians, researchers and allied health personnel. We must be able to present what is learned about the human genome to physicians in training and also practicing physicians. Physicians out in practice are going to need to know how to access this information and how to use it.

We also have a responsibility to help educate the general public. If people aren't able to understand the possibilities and limitations of genetic tests and treatments, they won't have confidence that this new knowledge will be used in a responsible way. At the same time, it is important that our policy makers have an understanding of genetics and genomics. It will be their job to ensure that the appropriate protections are in place and that people can be confident that genetic testing is going to be used to help them, not to limit their options.

Bruce R. Korf, M.D., Ph.D., joined UAB Jan. 1 as chairman of UAB’s Department of Genetics. Before joining UAB, he was medical director of the Harvard-Partners Center for Genetics at Harvard Medical School. Korf holds the Wayne and Sara Finley Chair of Human Genetics at UAB and is board-certified in pediatrics, neurology (child neurology), clinical genetics, cytogenetics and clinical molecular genetics.

Q: How does the sequencing of the human genome compare to other monumental medical discoveries, such as the development of antibiotics?

A: Antibiotic discovery was a triumph of technology. It was the culmination of an era that began with the major conceptual breakthrough that infection with microorganisms can cause illness.

Sequencing the human genome is a similar technological achievement that is also the culmination of a conceptual breakthrough, in this case understanding the way information is stored and utilized to direct development and physiology. It can be thought of as a capstone of scientific achievement in the 20th century.

The first human genetic disorders were discovered in the first decade of the past century. The century ended with the announcement of the gene sequence. So you have virtually one century in which science unraveled the codebook that determines how the human body is put together.

FOR MORE INFORMATION on genetic research and treatments at UAB, call Media Relations, (205) 934-3884.