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Dr. Francis Collins

The Genome Era: What It Means To You

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Hi. I'm Francis Collins, Director of the National Human Genome Research Institute at the National Institutes of Health and welcome to DNA Day. I want to talk to you about the genome.

What the heck is a genome anyway? That's a funny word and some people have gotten it mixed up with a gnome, but it's not really the same thing. In fact, the genome is all of the DNA inside each cell of your body. And whatever living organism you happen to be, you have a genome.

It's made up of these wonderful base pairs arranged in a ladder, in a double helix. And those base pairs are either A pairing with T or G pairing with C. And it's the order of those letters that determines the information that are carried by that DNA strand.

The human genome has three billion of those base pairs. That's our genome. That's a lot of information. So for instance, if you were to take the DNA inside just one cell of your body and you were to stretch it out, end to end, how long would it be? Well, it would be about that long, about six feet in fact, all packed in there inside each cell of your body, but with the order of those letters being just right.

Well, that's pretty exciting but until recently it was pretty theoretical, because we didn't have the tools to be able to actually read those letters. But the Human Genome Project came along and it made it possible to read out those three billion letters and in April of 2003, we did that.

Now if you printed those out onto the pages of telephone books and you stacked them on top of each other, it would actually take 142 Manhattan phone books to represent all that information. And yet the Genome Project determined that in the space of about 13 years, two years less than expected and it's all now available for anybody who's interested in trying to sort out how it works.

In fact, you could put in on a CD-ROM. On this very CD-ROM is the entire sequence of the human genome. You could stick it in your computer and start reading those A's, C's, G's, and T's. But of course that's not the easiest way to work with it.

The way that most scientists work with the information is by going to the internet and on your screen is the URL that every, is used hundreds of thousands of times a day by scientists who are studying the human genome, trying to figure out how it provides the instructions for life, and how misspellings in that genome can cause the risk of disease. So medical research has been profoundly influenced by this development.

Well, what have we learned so far from reading this sequence? I can mention a few cool things that we have discovered, but only a few because of the time. First of all, we've been saying for the longest time that we had a hundred thousand genes. A gene being a packet of information that carries out a particular instruction.

Well, guess what? Now that we have the information accurately in front of us, the number is actually a lot smaller. It's probably about 24 thousand. And that makes our gene count not that much different than a lot of other simpler worms and flies and plants, that we used to think that we were very superior to. Well, we've still are pretty fancy organisms, but apparently are gene count is not the only reason.

Another thing we've learned is that when you look at the part of the genome that seems to be most functionally important, we thought that would be pretty much the parts that code for protein, you know DNA makes RNA makes proteins. So that part would be the most important. But it turns out two-thirds of the most important part of the genome is not that at all. And falls in places that we didn't recognize as being all that interesting. So we have a whole new area of research that's come out of this discovery.

Thirdly, we've looked at lots of people now and we can say that in fact the similarity between your genome and mine is very high. In fact, we are 99.9 percent the same. And that would be true regardless of where your ancestors came from or where mine did. The human species is one, big recently developed family. And so our genome sequences reflect that. And that's pretty interesting and in that regard, we're a lot more like each other than many other species on this planet.

Well, you might ask okay, the Genome Project finished all of its goals in 2003, what's next? Where do we go from here?

Well, a lot of interesting things are under way because we have the information. Beginning with the study of how certain diseases come about and what we might do about them, because that was the point after all.

So, consider the story of Sam. Sam is a seven-year-old boy with progeria, a very dramatic form of premature aging. Sam looked just like any other baby at birth but by the time he was four or five years old, he took on the appearance of a little old man. And this is progressing rapidly and we need to find an answer in order to do something for Sam and the other kids like him.

Until very recently we had no idea what the problem was. But using the tools of the Human Genome Project and working with his parents, who started a foundation to support research on this, my own laboratory was able to find a single letter that is misspelled in the genome of kids with progeria.

One place out of those three billion where there ought to be a C and instead there's a T. That's all it seems to take in that vulnerable spot. But the good news is that now it allows us to understand what this disease is all about and we're already now on the pathway towards developing a treatment. I can't tell you how soon it will be, but we've got a really good idea and we didn't have that before.

Well, is this only about rare diseases? What about more common conditions? Well, it's about them too, because we understand that virtually all diseases have some hereditary contribution whether you're talking about diabetes or Alzheimer's disease, asthma, high blood pressure, heart attack. Those all tend to run in families although not in an easily understood way.

The Genome Project and its latest new child called the Haplotype Map Project is enabling us to go and find those subtle sequence differences, those spelling changes that may place one person at risk for diabetes and another for heart disease. And in the example of diabetes, again in my own lab using these tools of the Genome Project, we've been able to identify subtle changes in a gene that has a very complicated name HNF4 alpha, that play a role in increasing the risk of diabetes by 30 percent. And people have a particular spelling of that gene and that spelling is very common. Many of you listening to this have that and are presently unaware that it puts you at some risk.

Well, is that a good thing to know? Yes, absolutely because it tells us something about the disease and already it's leading us in the direction of figuring out new ideas about treatment. And here's a disease that's terribly common and getting more common all the time. We know a lot of the reasons for that relate to diet and lack of exercise, but we know hereditary is in there too. And we're on the pathway to figuring out how that all works. And that's got to be a good thing.

Now, okay, that's fine, but that sounds like research that somebody's doing in a laboratory somewhere. Will any of this actually affect your life? What will the impact be? Well, I'm going to predict boldly that this is going to have a strong effect on the lives of all of us in the next 10 or 20 years, particularly in terms of your health care. But in other ways as well.

And so as we think about this on DNA Day, I refer you to a quote from Wayne Gretzky, the hockey star, who said when somebody asked him how he was so good at the sport that he played. He says, "I skate where the puck is going to be. Not where it is. But where it's going to be." Well, where's the puck going to be for medical research and medical care and how is genomics going to play a role in that?

Well, first let me say, that for us to achieve the kind of outcome that I think we're all excited about, we're going to need a lot of you to help. So there are careers waiting for you to jump in on, that will be very exciting in the next 10 or 20 years. Some of those careers, a lab researcher, who works hard to understand how the genome works and how sometimes it doesn't using the tools of the bench researcher, studying things in test tubes, and working with cells growing in culture.

We'll need clinical researchers who interact with patients, trying to understand their disorders, and do something to treat those. We'll need computational biologists. People who are equally at home with biology and with computer science because after all DNA is this wonderful digital code. It's the kind of thing a computer loves to work with, but we need smart people to program those computers to get all that information and make sense out of it.

We'll need people to study the ethical, legal, and social issues that arise out of this because there are going to be plenty of them as well.

In the delivery of medical care based on understanding the genome, we'll need genetic counselors to explain this complicated information to people; and in fact all health care professionals, doctors, nurses, social workers are going to need to be familiar with genetics and genomics so that they can incorporate this into the mainstream of medicine. And we'll need teachers to explain this information to people in school and people not in school.

We'll need legal experts, policy experts to be sure that this plays out in a fashion that benefits people. And frankly we'll need all of you. Everyone in our society is going to need to be an informed citizen because there are many decisions that will need to be made and they will require some familiarity with the things we're talking about here on DNA Day.

Well, what are some of the concrete consequences that are already with us. One you may be familiar with is the use of DNA in criminal justice. DNA is a unique signature. Except for identical twins, each of us has a completely different DNA sequence than anybody else on the planet, which means you can use it in a way that's actually more powerful than an old fashion fingerprint to identify whodunit in a particular case.

Let me tell you about Kirk. Kirk is a former Marine who was accused of a brutal murder in 1985. He maintained his innocence and yet he was convicted and sentenced to death by a judge and jury. It turned out after he had been on death row for ten years, that DNA testing came along and made it possible to assess whether in fact he was the criminal and he was not. The DNA test shows it wasn't him and he was set free.

And in fact, a few years later the same DNA test was used to convict the actual criminal who had escaped detection and had been walking around for the previous 15 years and is now behind bars.

DNA testing in just the last few years has led to the release of 157 people who had been convicted of violent crimes that they didn't do. And now DNA testing has allowed that to become known.

What else can we do with this information about DNA? Well, I mentioned the way in which it's going to affect medicine. It's going to affect medicine in a way that becomes personalized. So you're all familiar with this iPod of course which is a way of storing a lot of information. Doctors will use perhaps instruments like this to store your genome and lots of others as well because these gadgets can store, oh 60 gigabytes or more of information, and that's the kind of personalized information about the genome that's going to very much be beneficial in medical care in the future.

Personalized medicine means not asking everybody to do the same thing, but actually having a program of staying healthy that's personalized just for you based on understanding your DNA. It'll also be an opportunity to develop better treatments. Treatments that are based upon specific understanding of what's wrong in the disease as opposed to just trying to guess what might work.

The genome will allow that. It will also allow the ability to predict who's going to respond positively to a particular drug and who really shouldn't have that drug because it's not going to work for them or maybe even make them worse. The field of pharmacogenomics is a very exciting part of where we're going.

And none of this is science fiction. These are all things that are happening today on a small scale and will be happening on a rather large scale in the course of the next 10 to 20 years. So you can expect that in the next 10 or 20 years, if you want to practice better prevention, keep yourself healthy, the genetics will be a significant part of that. And if you fall ill anyway, the treatments that are waiting for you will be based on an understanding of the genome and will be much more precise and much more based on rational understanding of disease than many of the things we currently have today. And that's good.

If you want to start down this pathway, then be sure you have the information already collected that might be important for this. I'd encourage you to go to the URL you see on your screen now and download this software tool that allows you to collect information about your own family, in terms of what medical conditions they have encountered, because that will continue to be an important part of understanding how individuals ought to practice better medicine for themselves. And this tool will allow you to collect that information, print out a pedigree, and then take it to your physician at sometime where you might want to then assess what you should be doing to stay healthy. Family history will continue to be an important part of that.

Well, we also do need to be thoughtful. With all of these advances and all their promise for medicine, there's also the potential for the information to be misused. And so the Human Genome Project from the beginning has had a component of the effort focused on the ethical, legal, and social issues that arise from these advances in science.

Thomas Jefferson said our laws and institutions must go hand in hand with the advances of the human mind. Well indeed and that's what we're trying to do with this program.

There are many challenges to face. I believe they're all addressable but there're going to take energy and thoughtfulness and the participation of a lot of people. We need to be sure for instance, the genetic information which has so much potential to help people doesn't get used against them. We all have glitches in our DNA. I'm sorry if that's bad news for you but it's the case. We all have misspellings in dozens of genes and if that's enough information to cause you to lose your health insurance, we're all at risk. The best solution to that is a legislative one and we're fairly close to seeing that happen in the U.S., which is a very good thing.

There are several other issues to worry about as well. One that people bring up fairly often is whether in fact the study of variation, this sort of point one percent of the genome will be used in ways to practice discrimination or prejudice against people.

Again, there are reflections in that point one percent of somebody's DNA about where their ancestors came from, what part of the world. But the bottom line is we are all so much more alike than we are different and the more we study the genome, the more we know that. So I would argue as a scientist in this circumstance, that the study of the genome ought to be a great way to reduce prejudice not to increase it.

And finally some people are worried about whether we would use this information to try to create perfect children at some future time. The movie *Gattaca* portrays a society where genetics is used in that fashion.

[Excerpt from film played.]

Frankly, most of this is just wrong scientifically 'cause DNA does not really determine characteristics like personal behavior or musical talent. It's playing a role but the environment and learning experiences, the decisions that you make, are at least as important if not more so. So I think most of those scenarios don't make a lot of sense.

Just the same, we do need an informed group of citizens, all of us, to participate in those discussions and make sure that as science goes forward, that it's done in a way that we all believe is benefitting people to the maximum possible way.

And that is why on DNA Day, I think we all ought to reflect on the remarkable moment we have here in history. We've crossed the threshold. For all of human history, we didn't know our own instruction book. Now, we know it. It's up to all of us and that includes everyone of you to be sure that we use that information wisely.

But this is a great opportunity. I hope that some of you will decide to join in on this genomic research adventure that we're starting into and will help us understand by studying this instruction book, how life works and how we can apply that information to diagnose, prevent, and treat disease, because the opportunities to do that are greater than they have ever been.

So, thank you for listening. Thank you for being part of DNA Day.

May all your bases be paired.

Thank you.

