

EXPERT PERSPECTIVES ON GENE-BASED MEDICINE

Ethical dilemmas. “Designer babies.” Probable risks. The new era of personalized, gene-based medicine brings with it a host of controversial issues. Below, see how experts in the field address some of the key controversies. Their perspectives may help clarify your own views.

Francis S. Collins, M.D., Ph.D.

Director of the National Institutes of Health (NIH) and a leader of the Human Genome Project

How straightforward is the path from genetic information to medical treatments?

“The path of going from the discovery of the genetic basis of a disease to actually having a cure is long, torturous, unpredictable, and full of the risks of failure. But the power of genomics puts into our hands the opportunity for rational approaches to diseases that previously were outside our grasp. Rare diseases, common diseases, neglected diseases of the developing world—we know so much more about those now, 10 years after the completion of that draft of the human genome, than anybody could have imagined. The progress in scientific research is breathtaking. The progress in medical applications that you will find when you go to the doctor still mostly lies ahead.”

Is genomic science currently impacting medicine?

Will it transform the practice of medicine?

“There is a long, growing list of ways in which genomic medicine is finding its way into the mainstream. If you're a woman with breast cancer who has a tumor less than two centimeters, and your nodes are negative, you have a very good chance of having access to a test that's going to tell you whether you need chemotherapy or not. We didn't have that until genomics came along. If you are somebody considering a drug for HIV that, unfortunately, causes a very serious hypersensitivity reaction in about 6 percent of people, there's now a test to find out whether you're in that category or not. But it's just really the start of what is going to be a transformation of the practice of medicine. That whole transformational process will play out over a decade, or a decade and a half. It'll happen gradually enough that most people won't quite realize that it's different.”

Does everyone have genetic risk factors?

“None of us like to think that our DNA instruction books have any misspellings. ‘Surely there must be some perfect specimens, and maybe I'm one of them.’ Well, sorry. There aren't any of those. We're all walking around with dozens, maybe hundreds, of glitches that place us at a little bit of risk for something—maybe diabetes, maybe heart disease, maybe Alzheimer's.”

Are direct-to-consumer (DTC) genetic tests of any value?

“Let's be clear. These are the early days for this. We have not discovered an awful lot of the important risk factors for common illnesses that are still waiting to be discovered in the next few years. So what you get right now is an estimate of risks being a little higher or a little lower. But the chance to have a little bit of a prediction about your future, as imperfect as it is right now—and it's very imperfect—could still be a learning opportunity, a teachable moment.”

When you had three different DTC companies analyze your genes, they reached different conclusions about some risk factors. How could that be? Is this kind of testing a settled art?

“New discoveries are coming along every day. So the numbers are changing. The way in which [DTC companies] take the lab data and compute a risk for a person is not at all a settled art. So be aware, this is not the kind of prediction that is all done. This is the sort of thing where you might get a result today, and then you should check back in a year and see, ‘Now what's happened? Has it gone up? Has it gone down? Has it gone away?’”

Ethics of Manipulating Genes (text)

Philosopher Philip Kitcher discusses the moral and ethical implications of molecular medicine.

www.pbs.org/nova/body/ethics-of-manipulating-genes.html

Ronald N. Green, Ph.D.

*The Eunice & Julian Cohen Professor for the Study of Ethics and Human Values, Dartmouth College, and author of *Babies by Design: The Ethics of Genetic Choice**

What are the upsides of having more information about our personal genomes?

"One of the most obvious benefits of expanded genomic sequencing and information is health care—maintenance and the prevention of disease. If, for example, one learns that one has a susceptibility to diabetes, that information can lead to changes in diet and exercise. There's also a significant benefit for all of us as more and more people engage in genetic testing and sequencing. We're going to learn a lot more about the correlations between our genes and health conditions. That's going to make a very big difference in health care generally. That information is going to benefit both research and, finally, clinical interventions and care."

What are the downsides of having more genetic information?

"One of the negative implications of this new genetic knowledge is that we're going to geneticize ourselves. We're going to start thinking of ourselves more in genetic terms than ever before. 'Do I want to date that individual? What's her genetics? What's his genetics? What career should I pursue? What does my genetic readout tell me?' We're going to have a burden of knowledge, an information overload. And some of it is really not very valuable or credible—some of it's going to be merely probabilistic and may mislead us and burden us in new ways. I respect people who are already saying, 'I don't want to know it,' because it's a burden of information."

Is there a danger that we will place too much emphasis on genetics?

"There's always been a tendency to engage in deterministic genetics. Scientists, medical people, and educators must make very clear the limits of that point of view, that so much of our nature is environmental. It's where and how we're raised. The genes are always interacting with the environment, including our internal environment and other genes."

Can we protect an individual's privacy in this age of genomics?

"Genetic privacy can be protected by good legislation, regulations, best practices, and so on. But we are entering an era of total exposure of our genetics. Anybody who wants to get a sample of our DNA can do it in myriad ways. And then the question becomes, How valuable is that information? Will a black market develop? I think it's almost inevitable."

How does genetic testing invariably involve family members and their privacy?

"When we speak about 'my genes,' it's almost always 'our genes.' It's the genes you share with children. It's the genes you share with other members of your family. One of my concerns is the testing of children, even prenatally, for their genetic conditions and situation. That raises many questions, including stigmatization. 'Oh, I'm not going to let Mary play soccer because she's got this cardiac risk that I've learned about.' It may be completely erroneous. So we do have a problem of invasion of privacy."

Will this new era of gene-based medicine be costly?

"The further development of genetic information and knowledge may have the effect, in the short term, of increasing medical care costs. But that knowledge, eventually, leads to new, very inexpensive ways of addressing conditions. If we can go in and biochemically alter those genes that predispose one to breast cancer, then we save a whole course of surgical intervention, chemotherapy, etc., with one preventative intervention. So, I think we're going to see new challenges and economic costs in the short run. But in the long run, I think genetic knowledge will prove very valuable and cost-saving."

How important is the new science of genomics?

"We're entering an unprecedented era in terms of self-knowledge. We're a little bit like Europeans at the start of the 16th century, with a whole continent ahead that's unexplored. We have our inner world, the world of our genome, with all of its correlations with health, our physical form, behavior, and other issues. We are now developing the tools to go forth and explore it. This will be the century of the genome, in my personal view."

Thomas H. Murray, Ph.D.

President and CEO, The Hastings Center, and former director of the Center for Biomedical Ethics at Case Western Reserve University

How much does a person's genetic makeup predict his or her destiny?

"We need to understand that genetic information is not quite as deterministic, powerful, and toxic as a lot of the discussion about it leads people to believe. Your genes help shape your life, but your genes don't write out in detail what your life is going to be like. Your genes are not your destiny."

Direct-to-consumer genetic testing companies are controversial. What is your opinion of them?

"On the whole, these direct-to-consumer genome sequencing companies are doing us a service. They are enlisting early volunteers in the genomic revolution, people who are curious to find out what their genes may or may not tell them about their life possibilities. I suspect that many people are learning that the results tell them less than they thought they would. The promise that this personalized genomic information is going to tell you very significant things about yourself is sometimes greatly exaggerated."

Are you concerned about the use of pre-implantation genetic diagnosis (PGD)?

"As long as people are using PGD only to identify those embryos that are free of horrendous genetic diseases, I think many people will regard it as a blessing. If people begin to use it for reasons that tip over into the frivolous category—some would regard sex selection as having crossed that boundary—there are many other categories most of us would regard as frivolous. If we choose our children based on frivolous attributes, I worry about the very nature of the relationship between the parents and that child."

Why do people who advocate for the rights of the disabled have reservations about PGD?

"The idea that we would use pre-implantation genetic diagnosis to eliminate the birth of people with disabilities is a complex one. Many people with disabilities are leading very, very rich and full lives—including some of the genetic disorders that we most commonly test for, like Down syndrome. People with Down syndrome have a huge range of function. And I know many families who feel that they're actually blessed to have children with Down syndrome. So the idea that we would eliminate all that diversity is not an obviously and completely good thing. We have a mantra at The Hastings Center: 'Good ethics begins with good facts.' So it's very important for prospective parents to know what it actually would mean to raise a child with a particular disorder. It might be full of great joy for many of us."

Why does this new age of genomics bring with it moral dilemmas?

"What new technologies like genome sequencing give us is the power to make decisions and to intervene where before we didn't have that power. When something bad happened to us genetically, it was just fate. But now, if we can know, and if we can act to change that fate, suddenly we have power and choice. And that power necessarily means a moral responsibility for making that choice in a thoughtful and serious manner. Technology gives us the power to intervene, which requires human choices, which confers moral responsibility. That's the basic equation."

Eric S. Lander, Ph.D.

Professor of biology, MIT, director of the Broad Institute, and a leader of the Human Genome Project

Is a person's genome a good predictor of his or her fate, health-wise?

"It's important to understand that the genome is very informative for some things. But it's not a crystal ball with all the answers, where you can run your hand over it and say, in some fashion like the old movie *Gattaca*, 'I can predict that you're going to die of heart disease. I know that you're going to get this autoimmune disease at this age.' Even when you have identical twins, with many autoimmune diseases, one gets it, the other doesn't. They have identical DNA! So that tells us there's a limit to what the genes do. It says environment matters a great deal as well. Random chance matters."

How useful is genome sequencing for most individuals? Would you have your genome sequenced?

"Will everybody run out and get their genome sequenced? I haven't run out to get my genome sequenced, because as much as I love the human genome—and I work on it every single day—I don't think my own personal genome today contains many answers for me. Well, that may change at some point. If I got cancer, I'd get my cancer genome sequenced immediately, because I do think there are things you could learn from that. If I had certain types of genetic diseases in my family, inheritable diseases, I might get it sequenced. But I think we shouldn't create a fetish that our genome sequence is going to be this magic crystal ball that tells all."

What do you think is the greatest importance of genomic information?

"I actually think the deepest impact will not be on precise, personalized predication. I think the deepest impact will be on a biological understanding of the basis of disease. And that's not about individual people's genomes separately. It's about what we learn collectively from genomes by looking at 10,000 people with diabetes, 10,000 without diabetes, 5,000 people with breast cancer, and asking, 'What are the cellular processes that get affected?' That's something you don't learn from single people. You learn it from integrating information across a population."

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DAVID H. KOCH

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