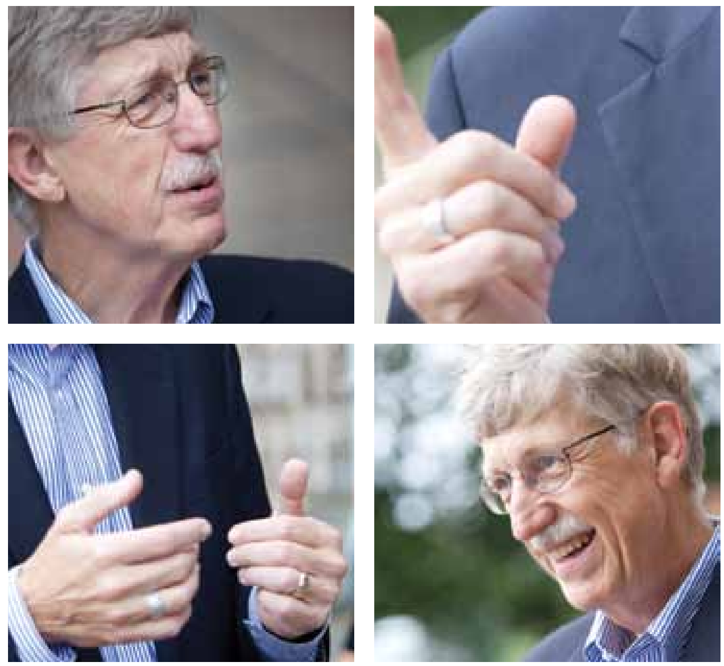
A Conversation with Francis Collins, MD, PhD
Director, National Institutes of Health

Advances in biomedical research seek to enhance health and length of life and reduce the burdens of illness and disability. The National Institutes of Health (NIH) plays a central role in making this happen. Its basic research and translational advances have prompted a revolution in the diagnosis, treatment, and prevention of diseases. As a result, U.S. life expectancy has increased dramatically over the past century and still continues to improve. Not only are people living longer, they are living healthier lives. However, science is not a 100-yard dash. It's a marathon; a marathon run by a relay team that includes researchers, patients, industry experts, lawmakers, and the public.

This is a remarkable time of discovery and the opportunities in science and medicine are at once exciting and urgent. How has basic research prompted a revolution in the diagnosis, treatment, and prevention of diseases? What is NIH doing to advance biomedical research? How does the investment in such research increase the country's global competitiveness? Dr. Francis Collins, Director of the National Institutes of Health, joined me on The Business of Government Hour *to explore these questions and more. Here are some insights from our discussion. – Michael J. Keegan*



On the Mission of NIH

We are celebrating our 125th anniversary. As part of the U.S. Department of Health and Human Services, NIH is the world's largest supporter of medical research, trying to identify new ways to diagnose, prevent, treat disease, and increase the likelihood that all of us will live long and healthy lives—not shortened or diminished by chronic disease. Historically, our contribution to the improvement of human health in America has really been quite dramatic.

There are about 17,000 full-time employees plus contractors with a wide variety of skill sets that work for NIH. Many of them are distinguished scientists with doctoral degrees. Our overall budget this year is about $31 billion, so it's a very substantial amount of taxpayers' money for which we are grateful and feel very responsible.

About 11 percent of the budget is devoted to research in what we call our intramural program. This includes both basic and clinical studies done in our facilities including the main one here in Bethesda, MD, which includes the largest research hospital in the world—the Clinical Center of NIH, 240 beds all utilized for clinical protocols. Patients come here from all over the world to be part of the clinical research studies we perform.

The remainder of our budget primarily goes out in grants to our nation's finest institutions and some outside the country as well. Investigators send us their best ideas. They are reviewed in a two-level peer review system which is very rigorous, and the ones that are judged most meritorious then get supported. Eighty-five percent of our budget goes out in grant awards to research investigators.

On Challenges Facing NIH

Seizing scientific opportunities
The first and most important question is: where are the scientific opportunities? Science is moving very fast right now. We're able to do things that I wouldn't have dreamed 10 years ago would be possible in my lifetime; working with DNA sequencing, working with stem cells, coming up with ways to do imaging of the brain in people who are alive, watching what happens when they do various tasks. These are just amazing opportunities; it is very much a part of my job to be sure that we're pushing the envelope as hard as we can.

Best and the brightest
Connected to that is the need to be sure that we are training and retaining the best and brightest—our most important resource, the scientific researchers. We need to make sure that we're identifying pathways so that young scientists can get the training they need and become highly productive, successful, creative, and have careers that are both inspiring to us and them.

Resources
Without resources nothing can happen; we need the resources to support our efforts. At a time when anything that the government is supporting has come into question because of our nation's fiscal challenges, I spend my time explaining why a dollar invested in biomedical research is an extremely good use of taxpayers' dollars in terms of what it can do for human health and how it stimulates our economy.

On Leading NIH

It's an amazing job; no day is like any other. I am responsible for standing at the helm of this remarkable ship of discovery, steering it in the direction that's going to have the greatest benefit to the public. That means I oversee the actions of 27 institutes and centers which make up NIH, each of which is led by a distinguished scientist who acts as its director. I'm particularly responsible for identifying opportunities for collaboration across institutes and outside of NIH. If there is a problem, say, in obesity research, I seek to get all the institutes to work together on that as well as pursue opportunities to collaborate with other government agencies like the Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), or the Centers for Disease Control and Prevention (CDC), and with other foundations or with industry. I spend my time trying to make sure, especially in this tight budget climate, that we're making the most of those collaborations.

On Shaping NIH's Strategic Vision

When I was asked to come and lead this effort, I spent time thinking hard and talked to a lot of other scientists whose opinions I value and came up with five key themes.

1. **Taking advantage of advances in high-throughput technologies**. Perhaps in the past, biologists tended to think of technology as a secondary area of emphasis. These days, it drives so much of what we can do that it deserves its own kind of push. We are taking advantage of advances in high-throughput technologies to understand the fundamentals of biology and how specific diseases are activated.

2. **Emphasizing the translation of research into medicine.** Secondly, we wanted to be sure that opportunities to take basic science and bring it into clinical applications could be speeded up, emphasized, nurtured, and encouraged in new ways. This is what you call translational science; we are emphasizing the translation of research into medicine.

3. **Putting science to work for the benefit of health care reform.** When I first came to NIH we were in the midst of a national discussion about how we're going to reform our own approach to health care. NIH, while we're not part of the health care delivery system, is responsible for generating the evidence about what works and what doesn't work. We want to provide that rigorous research that would enable patients and physicians to know what kind of interventions are going to be available and what's going to help them.

4. **Placing a greater focus on global health**. My fourth theme, which may have surprised some people, is global health. I think we no longer live in a world where we can afford to think about the health of the United States in isolation from what's going on elsewhere. All those infectious diseases that pay no attention to country borders are just one example of that. It's more than that now with all of the things that are happening in terms of trends in chronic diseases, which cross boundaries as well.

5. **Empowering the biomedical research community.** Finally, and the most critical theme, is to support the researchers that are going to be doing the work; we need to be sure we have set up a system that recruits the best and the brightest to come and join us, providing them with a career trajectory that they can feel is worth investing their time and energy. If we don't have that talent, none of the rest of this will happen.

On the Importance of Basic Research

NIH spends about 53 percent of its budget on basic research, which is defined as research on some aspect of biological processes that does not have an immediate implication or application to a disease. You have to understand how life works at the most fundamental level before you can really understand a disease. This research is the foundation of everything we do. Over decades, the basic science research, which has led to no less than 137 Nobel Prizes for NIH-funded grantees, has been a pathway to the next level of understanding about a biological process that, in turn, has led to insights about diseases that are now making a difference clinically.

For instance, basic science is trying to understand at a fundamental level, what are the causes of various rare diseases? Collectively, rare diseases affect about 26 million Americans; there are about 7,000 of these rare diseases. In the last 10

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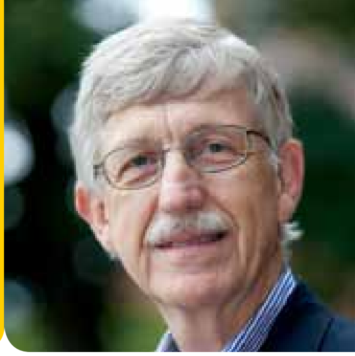


years, using basic science strategies, we’ve uncovered the molecular bases of about 4,700 of these rare diseases. It’s breathtaking the rate at which these insights have been coming. Of course, this research is useful in terms of getting a grasp on what the diseases are all about, but what we really want is to translate that into a clinical intervention. Only about 250 of those rare diseases currently have treatments.

I’d like to share an example from my own research at NIH. In the lab I run, we’re studying the rarest form of premature aging, a condition called progeria. It affects children who age at about seven times the normal rate; sadly, their life expectancy is around age 12 or 13, dying usually from heart attacks or strokes. Nine years ago, basic science led us to discover the cause of it. Following up on that, additional basic science has helped us understand why a single DNA letter out of three billion that was misspelled was capable of causing this multisystem disease; it also suggested something we could do about it. There are now 28 kids with progeria, who have been in a clinical trial for four years with a drug that we believe has all the right properties to help them. This drug was not actually developed for progeria but for cancer; it turns out it has the right properties to affect the pathway that needs tweaking for kids with this disease. Our study of progeria is also teaching us interesting aspects of the normal aging process we all experience; it’s a great example of how research from basic to clinical, then back to basic, can have exponential benefits. It’s a virtuous circle: when you make an observation at the basic level that leads to clinical insights, sometimes when you try it clinically you learn something about the basics as well. You go around that virtuous circle to your benefit over and over again.

On Establishing the National Center for Advancing Translational Sciences (NCATS)

Officially established in fiscal year 2012, the Center strives to develop innovations to reduce, remove, or bypass costly and time-consuming bottlenecks in the translational research pipeline in an effort to speed the delivery of new drugs, diagnostics, and medical devices to patients. We want to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.

Having made basic discoveries, we’re poised to be able to translate them into action and that is in fact a major focus of the National Center for Advancing Translational Sciences. There are a number of steps that you want to follow once you understand the molecular bases of a disease. They’re complicated. They’re failure-prone. They’re risky. We know increasingly how to do that and that’s a great example of how at the present time the basic science informs the translation.

The average time it takes to go from a good idea about a new treatment to getting that drug approved is 14 years. The failure rate is well over 99 percent. Now an engineer looking at a pipeline like that would say there must be something better you could do here to improve success and shorten the time. NCATS was very much founded on the need to try to identify those systematic bottlenecks that caused this process to be so challenging. Where are the bottlenecks? At what point in the process do we lose momentum? Why are failure rates high? Could we take some of the new science that’s coming forward in the last few years and really reengineer that pipeline? We are focusing on the following:

- Use science advances to overcome translational pipeline barriers
- Test pipeline innovations with promising research projects
- Cultivate strong partnerships
- Increase collaboration with the U.S. Food and Drug Administration
- Support an innovative and collaborative training program

On Forging the NIH/FDA Joint Leadership Council

Shortly after Margaret Hamburg and I were appointed to our respective roles at FDA and NIH, we formed the council and agreed that we would personally cochair it. The idea involves getting safe and effective treatments in the hands of patients more quickly—building on the science that's now possible. We're working with FDA on a new approach. When you have a promising drug that you think might be the next big thing for cancer or diabetes we are looking to find the best, most efficacious way to get it to patients fast and safe. The key question: How do you know whether it's going to be safe? There comes that moment where you have to decide whether or not that drug can be given to the first human patient. Right now, the way we test that is to give that same drug to some small animals or large animals at increasing doses. We look to see if there is any evidence of toxicity. It's a system that's slow, expensive, and not very reliable. Animals just aren't the same as humans.

The new approach we're working on with both FDA and the Defense Advanced Research Project Agency (DARPA) is to load human cells representing various organ types onto a biochip and wire them up with readouts that will tell us whether the cells are happy or not when a compound is shown to them. This will allow us to look at a human liver, heart, kidney, or the human brain on a biochip; it should lead to a closer approximation predicting whether a drug is going to be safe. It should also be much faster and cheaper to use once the chip is developed. We're bringing together the engineering perspective of DARPA, NIH's biological expertise, and FDA's intense interest in the regulatory aspects of science. In the end, we might be able to completely reengineer this aspect of the drug pipeline.

On Leveraging mHealth Technologies

Given that cell phones are so ubiquitous, the opportunities to use them to prevent illness or monitor chronic disease are compelling. The use of mobile and wireless technologies to support the achievement of health objectives has the potential to transform the face of health service delivery.

I volunteered for a clinical trial where my iPhone was connected to a gadget that would send my EKG in real time across the country to a cardiologist in Los Angeles; that cardiologist could then tell when I was excited because my heart rate would go up. Fortunately, I didn't have any scary rhythms to report. This is an amazing advance for those who may have a significant cardiac problem; it reduces the reliance on clunky ways of doing ambulatory monitoring.

With the advent of these technologies, we can do this continuously in real time. I'm very excited about the promise of mHealth technologies. Another very exciting application is for diabetes monitoring. I've seen a pilot of a small chip that's embedded under the skin at the wrist that is capable of continuously monitoring blood glucose without having to stick your finger every few hours. It transmits the results to a gadget which you wear like a watch. That in turn transmits this continuous tracing of your glucose to your care provider. If you want to get really good management of diabetes and know exactly where you are, this is where you'd like to have the technology take you.

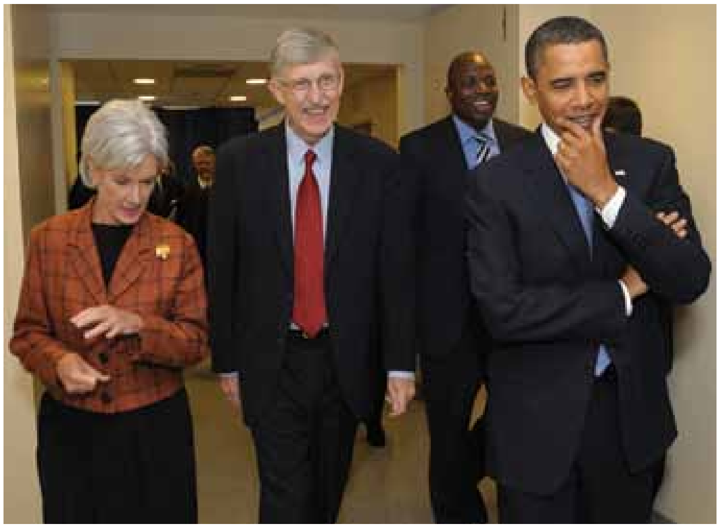
I think we have to be sure we're not just carried away by the gee-whiz aspects of these new gadgets. They have to lead to real-world results and better health outcomes. Otherwise, we're just fooling ourselves. This is where NIH has a really important role to play with so-called mHealth to be sure that as these exciting new technologies emerge, they get put to the test to make sure they really benefit people's overall health status.

On the Future

A big part of focusing on the future involves how we set priorities. How do we decide when resources are limited? Where should those dollars go? There are areas of science that look promising but don't pan out and you want to be sure you don't keep throwing money after an idea that turned out not to be as rewarding as you thought.

My concern is that right now, with considerable stress on everything in the discretionary budget, that many scientists are feeling that pinch and are therefore a little uneasy about taking risks. I would hope that as we get through this national debate about where to place our bets that medical research will emerge as one of those most valuable kinds of investments; I want to be able to say to a young scientist who is just starting: "Yes, this a career path that you can be confident is going to be well supported. You can chase those ideas that are creative and expect that even if they don't always work out, it's going to be very worthwhile." We need that assurance that this is a valued activity. With that we will see an exponential growth in our ability to understand why disease happens and what to do about it. We need to create that environment where incredibly talented scientists have a chance to pursue risky ideas, some of which are going to crash and burn, but some of which are going to transform our understanding of biology and medicine.

It's very clear when looking at the economic data that medical research has been a major driver of American competitiveness, particularly over the last 20 or 30 years. It's also clear that American leadership in biomedical research, which was unquestioned in the 1980s, is now being seriously challenged by accomplishments in other countries. We should celebrate those accomplishments. However, if we're serious about having our own economy flourish, medical research is probably one of the best things to put a bet on given our history—a dollar spent on medical research is a pretty wise investment.



On Public Service

There has never been a better time than right now to come and join our enterprise. We are unraveling mysteries that have puzzled us for all of human history. We are poised to take new discoveries and information to the next level to prevent and treat disease. We have the chance to bring the basic and clinical aspects of research together in a very tight connection in a virtuous circle. This would be the moment to get involved in a great detective story that has great answers—come and join the biomedical research team. We have lots of cool things for you to do. ■

To learn more about the National Institutes of Health, go to www.nih.gov.

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