A conversation with Francis Collins

We are joined by Francis Collins, a scientist who needs little introduction to the *JCI* audience. After getting his PhD in Physical Chemistry at Yale University and his medical degree at the University of North Carolina, Collins (Figure 1) zeroed in on genetics as his area of concentration and is noted for his landmark discoveries of disease genes, and later his leadership of the Human Genome Project, which culminated in April 2003 with the completion of a finished sequence of the human genome. Since August 2009, Collins has served as the director of the NIH, the largest supporter of biomedical research in the world. The full interview can be seen on the *JCI* website, http://www.jci.org/kiosk/cgm.

JCI: Could you tell us a little bit about your path to medical school?

Collins: My own path was nonlinear. I never really imagined, as a kid growing up on a small farm in the Shenandoah Valley of Virginia, that medical school was something I would want to do. My parents were in the arts — theater and music — but when I got to tenth grade chemistry, I had this revelation that science was actually really exciting. I hadn't necessarily expected that calling. I went off and received my college degree in chemistry and then completed a PhD in quantum mechanics at Yale. But somewhere along the line, I felt this urge to expand my horizons and discovered that biochemistry and genetics were truly exciting fields. I decided to go to medical school to focus on the science of biology, particularly as it applied to humans. After medical school, I did a fellowship in human genetics at Yale; those first few months in Sherman Weissman's lab were very stressful. I didn't know how to use a Pipetman, and an autoclave — what's that? Remember, my research was in quantum mechanics and most of it was highly theoretical.

So, I had a rapid learning curve with a lot of bumps along the way, but ultimately I started to get my legs under me. One day Sherm and I were talking about how you determine where a disease gene is located on a chromosome, because the whole idea of using linkage analysis was emerging. It was clear we needed to cross large distances in human DNA, and that's where the idea of chromosome jumping emerged. That idea became a big part of my early efforts as a senior postdoc and then as an assistant professor at the University of Michigan.

JCI: In Michigan, you really started to find more of the disease genes.

Collins: I got to Michigan during a wonderful moment when Bill Kelley, the Chairman of Medicine, had recruited people like Jeff Leiden, Craig Thompson, Gary Nabel, Jim Wilson, John Lowe, and Dave Ginsburg. What an amazing environment that was! It really encouraged me to think creatively. I wanted to tackle some significant problems and, based on my own clinical experiences, cystic fibrosis had always been an appealing target and one that desperately needed answers. So, chromosome jumping seemed like an appropriate way to go, and then, after that, we used it to address Huntington's disease and neurofibromatosis. It was probably a little overambitious to take on three major disease gene hunts at the same time in a very small lab, but when you're young and enthusiastic, you think you can do these things.

JCI: In 1993, you succeeded James Watson as the head of The National Human Genome Research Institute and embarked on what some might call the most ambitious biomedical project in history: decoding of the human genome.

Collins: That's quite a saga. I had started a Genome Center at the University of Michigan. I was a Hughes investigator and happy with my life as a researcher, taking care of patients, and teaching medical students. All of a sudden the phone rings and somebody says, "We want you to apply to be the next director." And I said, "That's crazy! A federal employee? You've got to be kidding. The one thing my mother told me never to do is work for the government." So I actually ran away from it for a while. But ultimately, the opportunity to stand at the helm of what history may regard as the most significant scientific effort undertaken in the last many centuries, how could I turn that down?

We got started and by 1998 we were all beginning to believe that this might actually succeed; although, getting the sequence of the human genome done in a 15-year timetable still seemed like it was going to be a heck of a stretch. Then arriving on the scene was a challenge from a private entity [J. Craig Venter and Celera Genomics] running a parallel sequencing project. That was an interesting juncture, particularly because it brought the Human Genome Project, which had mostly been under the public's radar, out into a much more public space. Not all of that was good, as there was too much focus on this being a "race for the human genome" and too much focus on personalities, in terms of who had a yacht — that was him; who had a motorcycle — that was me. I mean, who cares? Let's just get the science done.

I was also deeply engaged in the ethical, legal, and social issues related to genomics. This was a new experiment where a government-sponsored, scientific project took responsibility for investigating ethical, legal, and social issues before they became crises. As individuals increasingly got more information about their genomes, there was the potential for this information to be used against them in terms of health insurance and in the workplace. In 1996, the first bill was introduced to try to address these concerns; and after 12 years, it was a great day indeed to be in the Oval Office as President George W. Bush signed the Genetic Information Nondiscrimination Act. I have a copy of the act that he signed personally to me on my wall. That was a wonderful partnership between scientists, the government, advocates, public policy experts, and people who worried about civil rights — because in many ways, this *is* a civil right. You don't get to choose your DNA; therefore, it shouldn't be used against you.

The project certainly helped me learn a lot about team science, about how you can try to get the best out of every brain that's involved in order to make this project something that's better than any of us could have done alone. And the success of that model, attempted for the first time in biology, has now spun off many others. Whether it's the 1000 Genomes, the Human Microbiome Project, the Cancer Genome Atlas, or the ENCODE Project, all have produced this amazing deluge of information about how the genome functions. All build upon the success of the Human Genome Project, which gives us confidence that this is a model that works.

JCI: With regard to team science, what do you say to those who have inferred that the NIH is funding more team science rather than more investigator-initiated, R01-type projects?

Figure 1
Ushma Neill interviews Francis Collins on September 21, 2012, in New York City. Image credit: Semyon Maltsev.

Collins: I don't think that's an NIH decision. I don't think people should be anxious that there's somehow a top-down plot here, or a conspiracy to force scientists into team efforts that they don't want to be part of.

There's a quote from Harry Truman, "It's amazing what you can get done if you don't care too much about who gets the credit." That has certainly been true of many of these large team efforts. I talk a lot to investigators who've been part of these teams at the junior Assistant Professor level and have asked them, "Did this hurt you? Did you somehow get lost in the shuffle because of a large project with many participants? Have you been injured?" I've never heard anybody say, "Yes." I've heard a lot a people say, "This has helped me hugely. I've made all of these connections. I gained access to the kind of science I could never have done myself. I built collaborations on future projects. This was great."

JCI: You speak frequently with politicians, congress people, and even Presidents.

Collins: A big part of the NIH director's job is to be immediately responsive to any request from Congress for information. Over the course of the last 18 months, I have visited one-on-one with close to 200 members of Congress in the House and the Senate, answering their questions and trying to make the case for why medical research has arrived at such an important and exciting juncture in terms of its implication for advances in health. And also, why it's such a great investment in our own economy. Every single one of those conversations has gone well because our case is so strong. The evidence that we provide to undergird what NIH has done to advance the cause of human health in the last few decades is overwhelming. The evidence that the NIH has also been a major source of economic growth for our country is also overwhelming. But funding support for biomedical research in the US has been under considerable stress. We had that wonderful doubling of the NIH budget between 1998 and 2003, but since then, funding support for biomedical research has gone flat and inflation has eroded it further — we now actually have about 20% less in terms of resources to put into medical research than we did 10 years ago. That is extremely frustrating when you see the potential for breakthroughs that we are trying to pursue and that could be achieved so much faster.

If Congress takes no action between now and January 2, 2013, then sequestration will kick in — that would mean an 8.2% cut in NIH support, which would be about $2.5 billion disappearing. This could be an extremely dark year for researchers coming in for the first time trying to get funding support because, while it might be an 8% cut in terms of the overall NIH budget, it would be more like a 30% cut in the new and competing grant pool. That would drop success rates to historic lows. It's a matter of great concern.

JCI: When I told my PhD mentor that I was going to get a chance to talk to you, he wrote me in an e-mail, "Tell Francis I said hello and to do something about the paylines."

Collins: I would say he's exactly right; we need to do something about the paylines. But there is no magic dial that we can turn to make that one in six chance of receiving an NIH grant go back to one in three without having the overall base of support heading in the right direction. That's not just a job for me, although I do everything I can to make that case, it's a job for all of us. The whole biomedical research community needs to recognize and articulate that NIH funding is actually a wonderful investment that the public makes.

All of us need to take some part of our time, in a way that doesn't misrepresent the facts, to explain to the public and to our elected representatives why NIH funding is such an important investment for the US, and what the damage would be if we allow this continued deterioration. We could lose important fractions of the newest generation of young scientists, who may simply decide it isn't worth it to keep banging their head against this wall. This is a very serious circumstance, and no one out there who cares about this can assume that somebody else is going to send that message. We have to do this together.

JCI: What would you have done if you were not an MD and scientist?

Collins: I was on a path to become an academic professor of chemistry, and I might very well have followed that track. But I'm really honored and delighted by the doors that have opened since then. I could never have imagined this path as a kid growing up on a dirt farm with no plumbing in the Shenandoah Valley.

I have a message for anybody who's listening to this, particularly who's in an early phase of their own career: if you feel like you haven't quite got it straight yet in terms of what your path should be, don't worry. If you do have it all figured out, you're probably wrong! Be available to opportunities you didn't expect, doors that open that you didn't know were there. Be flexible — if a door that you thought you were about to walk through seems to be closing, that's a chance to be creative about other options. Science offers you so many opportunities to do fascinating things. Nobody should imagine that you can just plan a linear pathway for your career and have it turn out that way — because it won't. We have a chance to have a scientific life that is truly broad, truly remarkable, truly rewarding, and the chance to work with lots of other interesting people and do things for humanity that are happening at a dramatic pace. What a great time to be working in this field.

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