What the Next Quarter Century Holds for Science and Medicine

Francis S. Collins
Director
National Institutes of Health

Twenty-five years after the launch of the Human Genome Project, one of the most significant scientific advances of our generation, we talked to Francis Collins, who was at the helm of that effort, about what he has learned and what he's looking forward to.

Q:

The Human Genome Project, a bold effort to sequence all 3 billion base pairs of the human genome, significantly advanced our understanding of disease. Beyond expanding our knowledge, how has this project transformed how we pursue science?

The Human Genome Project was a consortium that brought together more than 2,000 researchers from across the world and across disciplines, all with the shared goal of producing a complete DNA sequence of the human genome. This was the first "big science" project for biology. It could have gone all wrong, with subgroups having different skills and accountable to different funding agencies. But we saw a tremendous willingness of individual researchers to join forces for the collective good, not worrying too much about who got the credit. A new paradigm for releasing data was also implemented: once we started to generate human DNA sequence data, those data were released into the public domain every 24 hours.

Q: In a recent Nature magazine article you penned with James Watson and Eric Green, you wrote that we need to be audacious yet flexible. If you wait for absolute clarity on how to achieve the ultimate goal, you risk missing opportunities that present themselves only after researchers start work. How is this approach shaping existing initiatives today?

We are at a remarkable moment in biomedical research, where we're figuring out the fundamentals—how life works and how disease occurs. Now we need to turn this opportunity into medical advances—health promotion, disease prevention, and treatment of illness when it strikes. But that challenge is daunting. The human body is incredibly complicated. Some of our best ideas seem not to work. But, we are forging ahead to apply some of the most daring principles of innovation. A number of large-scale scientific endeavors have been informed by this growing experience.

In April 2013, President Obama announced the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative, which aims to develop and apply new technologies that can discern how brain circuits work in real time, and may also elucidate the mechanisms of some of the most challenging diseases of the brain and central nervous system.

The Precision Medicine Initiative (PMI), announced by President Obama during the 2015 State of the Union Address, aims ultimately to make it easier to provide each person with the treatment or prevention strategy best suited to his or her specific circumstances. In order to do this, the project requires the study of many, many people. The PMI research cohort has established a target of enrolling 1 million voluntary participants to help researchers better understand the factors that affect a person's health circumstances, whether that be disease prevention or optimal therapeutic options for illness.

Q: The scientific and technological advances that are upon us or within our reach give us great hope for a future where scientific discoveries can be translated into better health faster. What does the next quarter century hold for us?

The breakthrough that we all hope will happen 25 years from today has likely already started somewhere in a laboratory. But those basic science ideas need to develop and go through all of the steps of discovery to be realized. History teaches us that it will take many scientists standing on each other's shoulders to advance these ideas until ultimately the day will come when we have a clinical achievement we can celebrate. If the seeds of our success for 2040 are not already sown, we are in trouble.

We need to be sober about which battles we're going to win in the next quarter century. But I think we'll win quite a few. In the next 25 years, I believe we will:

1 **Know more about what makes us healthy.** We will have information—environmental exposures, genetics, and human behavior—that will be useful for people interested in living long and healthy lives. The million or more people who will be part of the PMI will give us information we've never had before. Now, the opportunity in front of us is to convince people to use that information to live healthy lives, or we will continually be confounded by the fact that even the best information does not always translate into broad public acceptance and behavior change.

2 **Unravel the molecular causes of disease**. We will get to the point of having interventions that, if not curative, can turn a serious condition into one much more manageable. Cancer is leading that revolution right now, and other diseases are not far behind.

3 **Create an AIDS-free generation.** By applying things we already know, we can reduce the incidence by treating HIV/AIDS as soon as it is diagnosed, greatly reducing spread. We can develop a vaccine that can be made available to individuals all over the world who are at risk; that has the potential to prevent new cases of HIV/AIDS altogether. We have the opportunity to celebrate the end of the most frightening epidemic of modern times.

4 **Deal with the threat of emerging infections.** If we're lucky enough to avoid a serious worldwide pandemic of influenza, we could have a vaccine in the next five to ten years that works universally against all influenza strains, saving tens of millions of lives.

5 **Understand the brain better.** The brain is the most complicated biological structure in the known universe, and diseases of the brain have enormous consequences. A better understanding of how those 86 billion neurons function in normal

> The breakthrough that we all hope will happen 25 years from today has likely already started somewhere in a laboratory.

situations and how they are interfered with in conditions like autism, schizophrenia, traumatic brain injury, epilepsy, Alzheimer's, Parkinson's, and many more devastating illnesses will be the basis for developing new prevention and treatment strategies. It is perhaps too bold to think that in 25 years we can fully understand the brain. It will have so many layers that scientists will keep peeling those off for hundreds of years. The BRAIN Initiative provides a strong foundation we can build upon.

6 **Advance single-cell biology and structural biology.** The idea of being able to dive deeper into single-cell biology and understand how individual cells carry out their normal function in their normal environment is going to be powerful. Similarly, advances in structural biology will give us a series of insights into basic biology and provide us with fresh new approaches to drug development.

7 **Manage big data.** Biomedical research, which is already shifting into the mode of being heavily computational, will become even more so. Big data problems will be more challenging, and the way in which we collect and analyze data will require effective strategies to manage them. This includes capturing data that are meaningful and setting up a commons for those data that will be accessible to qualified researchers.

8 **Encourage convergence across disciplines.** The scientific disciplines that we have now—biology, chemistry, physics, computer science, engineering—are all going to blur. New technology, the availability of data, and a stronger foundation of basic scientific knowledge will call for new ways of training the next generation of scientists.

9 **Be more inclusive.** It is critical that in 25 years we must have a truly inclusive biomedical research workforce that reflects the diversity of our country. We must also ensure that clinical trials include racially and ethnically diverse participants and take into consideration culturally appropriate approaches.

10 **Partner with patients.** Patients are more informed and engaged than ever, and this will drive transformation in the way we deliver healthcare and how we pursue research. Research volunteers are our partners in biomedical research—the data provided by participants through biological samples, electronic health records, and participation in clinical trials are the underpinnings of biomedical research.

Q: Many medical breakthroughs from biomedical research are within our reach. How do we ensure that we stay on a trajectory of progress?

The outlook for science has never been brighter—we know more today than ever before about the molecular basis for thousands of diseases that affect millions of patients. For the trend to continue, we need partnerships, we need the talents of investigators willing to try out wacky ideas, and we need resources to sustain our work for generations to come.

Investing in research is an excellent way to bend the cost curve of healthcare. The U.S. has mounting deficits, and we should prioritize the allocation of funds to areas that have the greatest impact—and we know that research delivers human and economic benefits. We've seen that, beyond the scientific impact of the Human Genome Project, it gave us tremendous economic returns. In fact, every $1 invested by the U.S. government in the Human Genome Project generated $178 in economic activity. Yet, unfortunately, the purchasing power of the National Institutes of Health has fallen by almost 25 percent since 2003. We need to reverse that trend.

We must plant the seeds of discovery in order to reap the medical advances we need and deserve. Nobel prizes remind us every year that there's this long arc of discovery that starts with a basic science agenda that may not be connected to any disease at all, but ultimately, over the course of years or decades, will transform our search for cures.