BIOMEDICAL RESEARCH

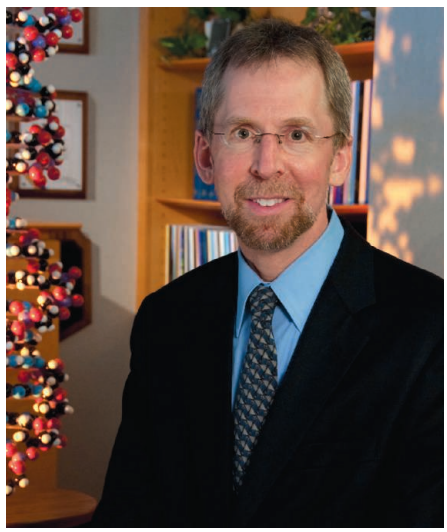
The Genome Project: What Will It Do as a Teenager?

The 10th anniversary of the completion of the draft human genome sequence has been a time for celebration—and also for sober stock-taking. Early successes in DNA research, some critics have said, led to hype about early payoffs for human health. It hasn't worked out that way; clinical applications have been slow to arrive. The need to pick up the pace of translating research into medicine informs the latest strategic plan from the U.S. National Human Genome Research Institute (NHGRI), which published its 10-year map this week in *Nature*.

Unlike NHGRI's last plan in 2003, this one puts the emphasis squarely on clinical objectives. But the institute's leaders avoid overpromising: The impact on health care will begin to build only after 2020, they predict. To get there, researchers need to complete various DNA catalogs, from indexes of genes underlying rare and common diseases, to the genomes of microbes in the human body, to a systematic tally of mutations in tumors. The plan sets new goals, such as making it routine for a physician to order a patient's complete genomic profile. In addition, NHGRI says, researchers must find ways to integrate genomics into electronic medical records and teach clinicians how to use the information.

The plan describes a vision for the entire field in general terms. But specifics can be seen in changes the $516 million NHGRI is making in its portfolio. Three huge centers now dominate the institute's sequencing program, with $115 million in annual funding, but grant competitions now under way will spread the wealth to some smaller projects. These include finding genes behind rare Mendelian disorders, testing ways to use clinical sequencing for patient care, and developing bioinformatics tools tailored for smaller labs.

Eric Green, who succeeded Francis Collins (now head of the National Institutes of Health) as NHGRI director, discussed the plan with *Science* in an interview excerpted here. **–JOCELYN KAISER**



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Q: What has changed in the past 8 years that shaped this new plan?

E.G.: Probably the most striking thing is the technological advances. Eight years ago we did not expect sequencing costs to plummet the way they've plummeted. Understanding the genomic basis of disease is incredibly more clear in terms of opportunities. I feel like the ball is really teed up and now we can really, really hit it hard.

Q: Why did you set 2020 for when genomics will begin affecting health care? Why is it going to take so long?

E.G.: When we talk to people who have a historic view of medical advances, they have pointed out that truly changing medical care takes a substantial amount of time. Often decades. And I've grown sensitive to the criticisms of genomics by some who believe that since 2003, when the genome project ended, we haven't sufficiently improved human health 7 years later. So part of the reason is just to be a little bit more realistic and a little more cautious.

Q: Do you think what happened in 2003 is that researchers really did believe that we'd be there by now, or are you suggesting that the public misinterpreted what they said?

E.G.: Maybe people did sort of imply that. There was huge amounts of exuberance and enthusiasm. We didn't really know we were going to finish the genome project successfully 2 years ahead of time. Maybe some things were said that, while we should in the next 5 or 10 years completely change the face of medicine, that was probably overstating it.

And maybe part of it is we know a lot more. Did we really know there was going to be all this important biological information in noncoding DNA? Did we really know there was going to be as much complexity associated with structural changes in the genome playing a role in disease? The more we look, the more complicated it gets.

Q: So the big sequencing centers are being recompeted with some changes? The budgets would go down?

E.G.: Budgets are tight and we're putting out a more broad set of activities we want in our sequencing program. But we also are going to get more data for that same amount of money because the cost of sequencing continues to drop.

Q: When will the time come that we don't need the big sequencing centers anymore because people can sequence a whole genome in their lab?

E.G.: One might imagine that will be part of the questions asked by review panels [looking at grant applications]. If we don't hear enthusiasm about programs that are being proposed in any of these areas, we wouldn't put all the money into that area.

Q: Where are you hoping we will be by 2020?

E.G.: I'm hoping that by 2020 we will have this incredible mountain of information about how genetic variants play a role in disease, that it will just provide an entirely new venue for really thinking about how to both predict disease, maybe prevent disease, and certainly treat disease.

And one of the key things about this strategic vision is the view that this is not just the genome institute. Every [NIH institute] is doing this now. And I think 10 years from now it's going to be even more the case.

Q: That raises the question, why do you need a genome institute?

E.G.: Ten years from now, somebody should ask [that question]. But we came out with an audacious idea in 2003. If it wasn't for our institute putting out a technology development program called the $1000 genome, I would question whether we would be where we are now. Virtually every hot new technology that you're now seeing, there's fingerprints associated with some of the grants that we put out and continue to put out.

So I think we've proven why we're useful at enabling many others. Even though others might invest even heavier in their disease-specific ways, it still justifies how we're showing leadership globally in genomics.

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