THE NATIONAL INSTITUTES OF HEALTH: DECODING OUR FEDERAL INVESTMENT IN GENOMIC RESEARCH

HEARING

BEFORE THE

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COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

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THE NATIONAL INSTITUTES OF HEALTH: DECODING OUR FEDERAL INVESTMENT IN GENOMIC RESEARCH

THURSDAY, MAY 22, 2003

HOUSE OF REPRESENTATIVES,
COMMITTEE ON ENERGY AND COMMERCE,
SUBCOMMITTEE ON HEALTH,
Washington, DC.

The subcommittee met, pursuant to notice, at 10 a.m., in room 2123, Rayburn House Office Building, Hon. Michael Bilirakis (chairman) presiding.

Members present: Representatives Bilirakis, Brown, Eshoo, Green, Strickland, and Capps.

Staff present: Steve Tilton, health policy coordinator; Cheryl Jaeger, majority professional staff; Eugenia Edwards, legislative clerk; John Ford, minority counsel; and Jessica McNiece, minority staff assistant.

Mr. BILIRAKIS. I now call to order this hearing of the Health Subcommittee, and I'd like to start by welcoming our witnesses and thanking them for joining us today, in addition to thanking them for all their great work on this subject over the years.

Your thoughts and recommendations should prove valuable as we consider Congress' role in ensuring that genomic research continues to advance.

In particular, I'd like to take a moment to note that we have two of the brightest minds in this field, and I really shouldn't say this because it looks like I'm belittling the roles of the others, but that's the way my remarks are written. In any case, I'm referring to Doctors Collins and Venter, who are testifying this morning. Your contribution to the development of a comprehensive sequence of the human genome has been invaluable, we wouldn't be where we are today if not for your efforts.

The sequencing of the human genome is one of the most significant scientific achievements of the 20th Century. Of course, the impetus for this promising research can be traced back to one seminal event, James Watson and Francis Crick's Nobel Prize winning description of the DNA double helix 50 years ago, and I know the members of this committee are well aware that we recently approved a resolution recognizing both of these monumental events.

As this research moves forward, I believe it's incumbent upon this committee and on Congress to ensure that the National Institutes of Health, which is truly the crown jewel of our biomedical research enterprise, continues to play an active role, and that's

why it's important for us to learn more about how NIH's organizational structure has fostered both the sequencing of the human genome and the dissemination of this information to the research community.

As we will no doubt discuss today, genomic research at NIH is spread across a number of institutes and centers, each of which receives its own line item congressional appropriation, considering that the Director of NIH is only allowed to transfer 1 percent of each institute and center's budget I am interested in learning how NIH plans to continue development and implementing the comprehensive genomic research plan for the 21st Century.

I'm also looking forward to hearing from our panelists today about the challenges they see facing us in the future in this field. While Congress will certainly have to deal with some of the ethical, legal and social implications this new field of research is presenting, I know we all hope that we will be able to take this information and translate it into new diagnostic and therapeutic products that will greatly improve the health of everyone.

I'd like to again offer a warm welcome to all of our panelists and thank them for their time and effort in appearing before the subcommittee this morning, and now I'm pleased to recognize the ranking member, my friend from Ohio, Mr. Brown, for his opening statement.

Mr. BROWN. Thank you very much, Mr. Chairman, and I welcome all of you all here. Doctor Collins, it's nice to have you again in front of our subcommittee.

Last month, this committee reported out, as the chairman said, H.Con.Res 110, a resolution particularly relevant to our hearing today, it recognized the 50th anniversary, as the chairman said, of discovery of the double helix structured DNA. And now, with genetics and the burgeoning field of genomics we truly moved into a new era. The people in front of us today we should thank for much of that progress.

Doctors will have tools to assess diseases in terms of their causes, not just their symptoms. The human genome of an organism can be known in a matter of weeks or months now, and not years or decades. CDC's efforts in sequencing the corona-virus linked to the recent SARS outbreak provided us a glimpse of what this new era may, in fact, hold. Scientists will begin to know why some people and not others get sick from certain infections or environmental exposures. I can only begin to imagine what this means for healthcare delivery in this country. Clearly being asked by your doctor about your family history will take on a full new meaning.

There are also critical non-medicine applications of genomics. Organisms will begin to play critical roles in solving environmental and energy challenges like cleaning up contaminated waste sites and generating hydrogen for clean energy production. The Federal Government has invested wisely in genomic research, their returns promise to be extraordinary, providing friends and loved ones benefit from what we have learned about genetic links to diabetes, to Parkinson's, to Alzheimer's, to breast and ovarian cancer, to colorectal cancer, to Cystic Fibrosis, to Huntington's disease, to a whole host of illnesses.

I think we can all agree genomics will play a central role in our Nation's biodefense. Within 6 months of the anthrax attacks, genomic tools were used to improve our ability to characterize the lethal Ames strain. We should also not overlook the impact this investment has on the public health infrastructure as a whole. When we invest in research, we are also investing in education.

NIH reports that Ph.D. faculty in U.S. medical schools has increased by double digits, as a result of the Federal investment in research. We talk about Federal involvement, we are talking about investing taxpayer money. Taxpayers pay for this research, the taxpayer are entitled to the fruits of his or her investment.

Thomas Jefferson, a stalwart proponent of a knowledge-based society, recognized, "the illimitable freedom of the human mind," in that each generation must advance the knowledge and well-being of humankind indefinitely. The free and unfettered access to discoveries, free and unfettered access to information, are critical, not only because it's the right thing to do, but because locking it uplocking up information or the use of that information will not only slow progress, but also undermine our intent to improve the lives of everyone, not just those who can afford it.

Information sharing was certainly a component of making international efforts to the Human Genome Project a success, we should ask for nothing less as we move forward.

I'm hoping our witnesses today will provide insight on what we need to think about as policymakers as genomic research translates into every-day application. One issue is intellectual property. Are we spending taxpayers money to create a drug or a therapy only to have them pay again, and again, and again, for access to it? Something we have done far too much in this Congress, in this society, with the FDA, with NIH, with CDC.

Another issue is the importance of strong genetic, non-discrimination policies. My colleague, Ms. Slaughter, from New York, has introduced legislation that would address the particular abuse of genetic information by insurers and by employers. I co-sponsored this legislation and hope this subcommittee will consider taking an active position on this issue, rather than waiting for press reports detailing how health insurance providers provide coverage or employees are fired because of genetic profiling. Genomics offers exciting opportunities to strengthen our public health system, to strengthen our public health infrastructure. We are entering a new era as a result in health and in healthcare.

I'm glad our subcommittee is celebrating the Human Genome Project for the landmark achievement that it is.

I thank the chairman.

Mr. BILIRAKIS. I thank the gentleman.

Mr. Green, for an opening statement.

Mr. GREEN. Thank you, Mr. Chairman, for holding this hearing on what is an exciting field of genomic research. For more than two decades, the science community has worked diligently to map the human genome. This is an undertaking that has broad implications for how we study and treat almost every disease known to man, and we all thrilled to see this program succeed, when just last month on Doctor Collins' birthday I note when it was announced that the genome had essentially been completely sequenced. It is

even more impressive that the mapping of the genome has been completed ahead of schedule and under budget, and I think that's something we don't hear in the halls of Congress very often.

This project is a perfect example of how our investment in biomedical research can yield significant results that will greatly improve the health of all Americans, and while I enjoy hearing about NIH because they give me the opportunity to brag about the work being done in my own hometown, Baylor College of Medicine. The human genome sequencing Center at Baylor has been NIH's partner in the Human Genome Project since its inception, along with the Whitehead Institute, for biomedical research at MIT and Washington University in St. Louis, and the Joint Genome Institute at DOE, and the Sanger Institute in England. Baylor has recently completed its portion of the Human Genome Project, chromosomes 312 and a portion of X, and is nearly completing their rat genome project.

As we know, the laboratory rat is widely used in disease models and research programs directed at understanding and treating and preventing many human diseases. In addition to the work being done on the human rat genome project, the Baylor Center is currently engaged in many other sequencing projects, including the sequencing of the honey bee, the fruit fly and the sea urchin. These projects will help science better understand evolution specification, how genes turn on and off during the development of the animal from the fertilized egg, and genome genetics influences on social behavior. In addition, Baylor will soon be beginning to work on the rhesus macaques, the widely used primate for biomedical research, and the rhesus monkey is particularly important because its response to the SIV and is widely recognized as the best animal model for the human immune deficiency virus, HIV infection.

And again, Mr. Chairman, there are so many things we could all talk about, and I'd like to put the rest of the statement in the record, but I'm glad you are having this hearing today, and I apologize there are not other members, but I guess some of us who have watched this project, and supported it, and encouraged the funding for years, it's a great day to have a hearing and talk about the good things that we can do.

Thank you.

Mr. BILIRAKIS. I thank the gentleman.

Ms. Capps, for an opening statement.

Ms. CAPPS. Thank you, Mr. Chairman, and thank you for holding this hearing and for your commitment to the National Institutes of Health.

You know, some days it doesn't look there's very much to find good about my job, being here in Congress, and on those days and on days when I see a lot of bashing of government, Federal Government particularly, in the media, or get a lot of complaints from my constituents about various of our enterprises here, I stop and think aboutand generally, when I'm looking for something positive to think about with respect to our Federal Government I think about that campus in Bethesda and the National Institutes of Health, a wonderful use, in my opinion, of taxpayer dollars, an international Ambassador of good will and scientific research around the world, and it's a pinnacle to me, and I'm pleased that all of you are here

and that we cannot give recognition to what you do, particularly as we are doing today, to discuss and hear from you about the Human Genome Project, certainly one of the great scientific discoveries of all times.

No measure of pride in myself, but we are alive here to see this, and I think about the charts on my chemistry wall when I was a kid in high school and how those used toit's revolutionary what's been discovered. The example of what can be accomplished in this country when our society, through the Federal Government, comes together behind a goal.

And, I wanted to today at least use part of the time to look at that as an example, and a testament to the benefits that we can derive by properly funding the National Institutes of Health. Hopefully, the results in the Human Genome Project will mean a whole new era of medical advances and treatment, and that's where we wantI wantguidance from you and ways that we should support what you do so that that can be an outcome.

This hearing and your discoveries also raise so many new questions about how we should proceed with research, how new treatments are developed, and who will benefit from them. There are choices to be made all along this path. It is going to undoubtedly lead to many fractious debates and contentious legislative battles for this committee on issues we have not even yet begun to think about, and I know that for some ideology often get in the way, and there, too, I hope we can look to you to assist us in that fine line or that delicate balance that we will be uncovering.

I believe, with all my heart, that the opportunities that this project, the Human Genome Project, have provided us far outweigh any of this fractious debate that's going to ensue. I think it's very worthwhile to pursue along and for us to be partners with you and supporters of what you do. I look forward to seeing what you are able to develop from this project, and I support the resolution that we put forth.

This hearing also is a start of a series of hearings on the structure and effectiveness of NIH, and that is something I salute our leadership, that's a project I wholeheartedly endorse.

I'm proud of the fact that I've been here as we have just completed doubling of the NIH budget, and this committee examined what NIH is doing with the added resources, but even as we examined the structure and the funding I hope that we will not shortchange NIH on future funding. The proposed budget, I believe, asks for far too little increases for the NIH, increases so small that many in the scientific community are concerned that the gains that have been won may now be lost, and I believe this is a poor way for us to handle the investments that we have made in previous funding sources to what you are doing.

So, I want that to be part of our discussion. I look forward to ways that we can capitalize on the investments that have already been made, and I thank the Chair for yielding to me.

Mr. BILIRAKIS. The Chair recognizes the gentlelady from California, Ms. Eshoo, for an opening statement.

Ms. ESHOO. Good morning, Mr. Chairman, and to my colleagues, and to the very, very distinguished panel that's here today. I thank you, Mr. Chairman, for holding this very important hearing.

The Human Genome Project is, I think, the most exciting topic that this committee has had before it in years, and I've been here, this is my, I think, ninth year on the committee. Our witnesses, all of whom I believe took part in this magnificent effort, have changed the course of science and of medicine forever. Your work on the human genome is the key to unlocking many of the mysteries of how our bodies function and why they function the way they do.

Genomics is the future of medicine. It will help doctors and scientists determine why one person gets ALS, why another gets Alzheimer's, and why, perhaps, another lives to the age of 105. It will also help determine how to fix problems in the body that lead to these diseases. It will help biotechnology and pharmaceutical companies tailor medicines to combat one type of breast cancer over another. It will help doctors establish early on, when we're still babies, what we're at risk for and how we can prevent or minimize these diseases we are coded to get.

I think that you have helped to bring us to the threshold where we tiptoe into the mind of the Creator, and this is, I think, the most exciting thing of all. I've always been a supporter of funding for research at NIH, which I call our national institutes of hope, and for basic science research at agencies like the Department of Agency and the National Science Foundation. It's efforts like the Human Genome Project that are crystal clear examples of why Congress has a duty and a role to play in funding basic research.

And, while this Human Genome Project is a key to unlocking many of life's mysteries, it also opens up a whole host of questions, many of which it will be up to Congress to answer and with you as our guides. How to protect, how do we protect against genetic discrimination? How do we ensure that everyone, across all social and economic divides, have access to the miracles that genomics bring? How does our healthcare system bear the costs associated with knowing about disease years in advance? How will Medicare handle the costs of a potentially elongated life span? These are only a sample of the issues that will come up over the next few decades as we work to know more about ourselves and use that knowledge for the overall good of the people of our Nation.

As a Member of Congress who represents a congressional district known for its advancements in science and technology, I look forward to hearing each one of the witnesses in their testimony address and, perhaps, hear their thoughts on some of the questions I've raised. I also look forward to working with each one of you over the years to help harness and guide the extraordinary knowledge that you have given to us. It's absolutely magnificent, and I want to salute you for it, and I look forward to the testimony that you are going to offer today.

Thank you, Mr. Chairman.

Mr. BILIRAKIS. I thank the gentlelady.

[Additional statement submitted for the record follows:]

PREPARED STATEMENT OF HON. W.J. "BILLY" TAUZIN, CHAIRMAN, COMMITTEE ON ENERGY AND COMMERCE

Thank you, Mr. Chairman, for holding this timely hearing today. Last month, the country and the world celebrated two of the greatest scientific achievements of all time: the discovery of the double helix structure of DNA and the completion of the

sequencing of the human genome. Testifying before us today are five of the most renowned scientists in the field of genomics research. It is truly an honor to have all of you before our Committee at the same time.

Both Dr. Collins and Dr. Venter should be commended for their leadership in mapping the human genome and providing all scientists will the tools and technology to really move the field of genomics forward. Dr. Patrinos and Dr. Waterston, I understand you both played pivotal roles in the Human Genome Project. Dr. Patrinos, as you are aware, the Energy and Commerce Committee has broad jurisdiction over the Department of Energy and its programs and management. Our jurisdiction includes national energy policy generally, the exploration, production, storage, supply, marketing, pricing and regulation of energy resources, including all fossil fuels, solar energy, and other unconventional or renewable energy resources. Therefore, we have a keen and continuing interest in the activities of the Office of Science. I know the Department of Energy has allocated funding to its own genomics program. I look forward to learning more about how this program will operate and its potential.

Dr. Waterston, many people do not readily recognize that NIH research is primarily conducted extramurally. I know your testimony will help all of us better understand how NIH partners with the university research community. And finally, Dr. Khoury from the Centers for Disease Control and Prevention, thank you for being here with us today. Without question, whenever we discuss the importance of medical research, someone is always quick to point out that the true potency of medical research is realized when we can translate and apply it to patient care. I know CDC is working on this important issue. I look forward to learning more about your plans.

Just as scientists have decoded the genetic map that defines us as human beings, here today we will try to decipher how well the federal bureaucracy is working to advance this promising area of genomics research. Congress has devoted considerable resources to medical research. At the National Institutes of Health alone, in fiscal year 2003, we appropriated $27.2 billion. Genomics research transcends every institute and center at NIH. It has implications for how we study every disease. But, the current structure of NIH, and funding allocations for that matter, may not adequately recognize its importance.

As the authorizing committee for the National Institutes of Health, it is our responsibility to review how the National Institutes of Health operates and try to determine what inefficiencies exist that slow the progress of medical research. This is a critical activity for our Committee. All of us have been touched by someone inflicted with a terrible disease. In my district, for example, a rare childhood neurodegenerative disorder, Friedreich's ataxia, occurs at a higher frequency in the south Louisiana Cajun population than in the rest of the nation. With the help of NIH, in 1996, scientists identified the genetic mutation that leads to Friedreich's ataxia. Once the gene was identified, scientists were able to study the mutation at the DNA level and identify the disease protein and its function. Just last year, NIH began its first phase of a clinical trial on a drug compound that has shown promise in addressing the most life-threatening symptom of Friedreich's ataxia—the heart condition. Because of the advances in sequencing the Human Genome, and the doubling of the NIH budget over the past five years, more progress has been made in understanding the underlying mechanisms of this disorder than in the previous 133 years. Research advances like this means something real to patients. It's the hope they are looking for when they need all the courage they can muster to fight a debilitating disease like Friedreich's ataxia.

Let's bring hope to all patients suffering from disease. It is our responsibility to ensure that NIH is held accountable on behalf of all patients. It is our responsibility to remove barriers that unnecessarily delay the incredible progress we are making in improving human health. This is one of many hearings our Committee expects to hold to review the research and grant programs of the National Institutes of Health. I appreciate all of your assistance in helping us move forward with this project.

I look forward to the witness testimony.

Mr. BILIRAKIS. Our panel today consists of five pretty special people. Doctor Francis Collins is Director of the National Human Genomic Research Institute. Since 1993, Doctor Collins has served as the Director of Human Genome Research at the National Institutes of Health. As the Director of the National Human Genome Research Institute, Doctor Collins oversees the international Human Genome Project, and serves as its primary leader. He will

discuss the unique role of the National Human Genome Research Institute at NIH, and present an overview of his experience managing the Human Genome Project, and outlining NIH's vision for the future of genomics research.

Doctor Aristides Patrinos is Director of the Office of Biological and Environmental Research with the Department of Energy.

Mr. BROWN. Mr. Chair, are you Greek, you say that so well. That was very impressive.

Mr. BILIRAKIS. I thought I'd impress you a bit.

Mr. BROWN. You did.

Mr. BILIRAKIS. The staff usually with some of these names will try to translate them for me, you know, they didn't even attempt that one. They said, oh, well, you will know how to handle that.

Anyhow, Doctor Patrinos receives research activities within the Department of Energy Office of Science, which includes the DOE's Human and Microbial Genome Programs. He also represents DOE on the International Human Genome Project, he will discuss DOE's involvement in genomic research, including how DOE interacted with NIH, a very significant point to my way of thinking, during the sequencing of the human genome, as well as DOE's current Genomes to Life research program.

Doctor Robert Waterston is Professor, William Gates III Chair, Department of Genome Science, University of Washington. Doctor Waterston was the principal investigator at Washington University in St. Louis, one of the five extramural institutes that worked extensively on the Human Genome Project.

In January of this year, he moved west to the University of Washington. Doctor Waterston will discuss his experience in working with the NIH during the Human Genome Project, and in general how the university community interacts with the NIH.

Doctor J. Craig Venter is President of J. Craig Venter Science Foundation. Doctor Venter led the competing private sector initiative to sequence the human genome. Doctor Venter will discuss broadly his involvement with both NIH and DOE, as a predominantly private sector-based researcher.

And, Doctor Muin Khoury is the Director of the Office of Genomics and Disease Prevention, Centers for Disease Control and Prevention Headquarters. He is the first Director of the Office of Genomics and Disease Prevention at the CDC. The office was formed in 1997, to assess the impact of advancements in human genetics and the Human Genome Project, public health and disease prevention.

Doctor Khoury will discuss how the CDC is translating research information generated by the NIH and integrating genomics into public health research and programs for disease prevention and health promotion, the bottom line of all of this I would suggest.

Gentlemen, your written statements are part of the record, we would hope that your comments will complement and supplement those. I'm going to set the clock at 5 minutes for each of you, but if you are in the middle, if you are on a roll on something I certainly won't shut you off, but, hopefully, somewhere 5 and 10 minutes you might be able to finish up.

Doctor Collins, we will start off with you, sir, please proceed.

STATEMENTS OF FRANCIS S. COLLINS, DIRECTOR, NATIONAL HUMAN GENOME RESEARCH INSTITUTE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES; ARISTIDES PATRINOS, DIRECTOR, OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH, DEPARTMENT OF ENERGY; ROBERT H. WATERSTON, PROFESSOR, WILLIAM GATES III CHAIR, DEPARTMENT OF GENOME SCIENCE, UNIVERSITY OF WASHINGTON; J. CRAIG VENTER, PRESIDENT, J. CRAIG VENTER SCIENCE FOUNDATION; AND MUIN J. KHOURY, DIRECTOR, OFFICE OF GENOMICS AND DISEASE PREVENTION, CENTERS FOR DISEASE CONTROL AND PREVENTION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. COLLINS. Thank you, Mr. Chairman and distinguished members of the Subcommittee on Health.

We gather at a historic moment. I want to thank you up front for the wonderful resolution that you recently passed recognizing the milestones that occurred in April. In fact, this was a rather remarkable month, where three simultaneous events occurred; the 50th anniversary of the double helix, the completion of all of the goals of the Human Genome Project, ahead of schedule and under budget we are happy to say, and a publication of a vision for the future of genome research, a document which you have at your place, published in Nature, also just 3 weeks ago.

You have at your place, in addition to that reprint, I just thought I'd bring to your attention a little square packet here which has two DVDs in it that I thought you'd be interested in. One of those is a series of interviews with some of the legendary figures in the scientific community who have worked hard over the last 50 years to get us where we are, and who talk about that, as well as their speculations about the future. And, the other DVD, simply enough, is the sequence of the human genome. It's rather amazing that I can hold that in my hand, the 3 billion letters of our own instruction book, packaged on to this DVD in a fashion that you can stick it into your computer and begin to help us figure out what it all means, because that's very much the phase that we now move into. We are at the end of the beginning, and we can now move into the really exciting part of genomics, which is to understand how it works and how to apply that beneficially to human health.

In that regard, I also bring to your attention this publication about a vision for the future of genomics research, which you have at your place. If we could have the visuals up on the screen I want to just quickly show a couple of things that you will find in that document.

The first one of these is a time line to put this all into perspective, taking us back to Mendel in 1865, who discovered the principles of genetics, working with pea plants in his garden in Czechoslovakia, and then carries us up through 1953, Watson and Crick's revelation of the double helical structure of DNA, followed shortly thereafter by a number of other major milestones, the discovery of the genetic code, recombinant DNA technology. If you will click the button we will go to the next level here, and then an accelerating pace of technological and biological discoveries leading to the discussion about the possibility of reading out the entire sequence of the human genome, a very controversial discussion I might say,

and one which would not have led to an organized effort without the support of the U.S. Congress. The Congress got behind the genome project while many in the scientific community were still somewhat uncertain about whether this was a risk that they thought could be taken successfully.

The next image will show you the first 6 years of the genome project and some of the milestones that were achieved. Again, there's a common misunderstanding that there was only one goal of this project, to read out those 3 billion letters, in fact, that was one of more than a dozen goals, all of which had specific milestones and deliverables, and included the study, not only of human DNA, but also that of several important model organisms, without which we would still be left puzzling over the letters of the code that we now see in front of us.

Those first 6 years were full of challenges, of the need to scale up and cut costs. The next image shows you what happened more recently in the last 7 years, as we went from pilot efforts to sequence genomes to the full-scale effort, resulting in a publication of the draft of the human genome sequence in early 2001, from the International Human Genome Sequencing Consortium on the one hand, in Nature, and from Celera Genomics in Science.

And then, just a few months ago, we witnessed publication of an advanced draft of the mouse genome, a very valuable property, indeed, in order to be able to interpret the human. If you will click the button the thing that we celebrated just a few weeks ago, and which I'm sure Doctor Waterston may say more about because he was a major leader in this effort, was going beyond the draft to the finished version of the human genome sequence which we will be using for all time.

There are three little words, though, in the middle of this image on the right, "to be continued," and that's what I now want to focus on. We are not done with genomics, we are really just getting started.

The next image shows you our metaphor of where we think genomics can now go. This is a house that we want to build, not a real house, but a metaphorical house. It rests, as you can see, on a foundation, the Human Genome Project. It has three floors, applying genomics to biology, to health, and to society, and it has six vertical crosscutting elements; resources, technology development, computational biology, training, ELSI—which stands for the ethical legal and social issues—and education, and those touch on all three of the floors and hold the building together.

This vision for the future is the output of more than 600 scientists over about 18 months, whom we asked to participate in more than a dozen workshops, focused on what the major priorities could now be, now that we have this foundation in front of us. It is an ambitious, one would even say audacious, blueprint of where we want to go next.

In the genomics to biology arena, we would like to get lots more DNA sequence on lots more organisms, and we'd like to do that ever more cheaply, so that, ultimately, we could sequence your genome or mine for $1,000 or less. That would transform the way we do research. We are about four orders of magnitude away from that right now, so that's a very bold goal, indeed.

We need to understand how the genome works, what are the functions of all the elements. We need to understand the protein products of those genes, which actually do the work of the cell, and to apply the same grand scale approach to proteins that has worked so successfully for DNA.

I'm a physician, the genomics to health floor is, perhaps, the one that I have the greatest excitement about, because after much hard work in building this foundation we can now accelerate our pace toward the applications to prevention and cures of disease.

One major effort that we are in the middle of already on that floor is to understand that .1 percent of our DNA where we differ, because that holds within it the clues of why I might be at risk for diabetes, and you for some other disorder. We have the opportunity now to understand that for virtually all diseases in the course of the next 5 to 7 years if we apply ourselves appropriately with this new opportunity and technology.

In the genomics to society floor, which I will argue is just as important as the scientific and medical applications, because there are many non-medical consequences of knowing our own instruction book. Among those issues are genetic discrimination, intellectual property, concepts of race and what that means, and how science can actually benefit that discussion by applying some reality to the often-confused discussions about what race means anyway.

With regard to the discrimination issue, I was delighted to note that just yesterday the Senate Help Committee passed unanimously a piece of genetic discrimination legislation that covers both health insurance and the workplace. I gather Senator Frist has indicated that this will come to the Senate floor in June. It would be wonderful if, in fact, this particular legislative issue, which has been in the works now for some 6 years, if this were to be the year where we saw the American public given the kind of protections that many of them are asking for. The absence of which those protections is impeding research at the present time.

So, we have a wonderful opportunity here, this future that we want to build. We need to stick to a variety of principles, especially collaboration particularly between institutions, and I want to assure you that I and my colleagues here representing DOE and CDC talk about those things on an extremely regular basis. I would think in the course of this discussion this morning you will get many examples of how our agencies are working in a very collaborative and complementary way. Certainly representing here the NIH, all of the institutes of NIH are deeply interested in the topic of genomics are investing in the kinds of outcomes that I've mentioned here, and have participated in a major way in the construction of this vision document that you see in front of you.

So, I think if we, in fact, can buildupon the foundation that's now in front of us, you can imagine a time, perhaps, 6 or 7 years from now, where each of us will have a chance to learn our individual susceptibility for illness, based upon a genetic analysis, and then be enabled to practice individualized preventive medicine based on what we are at risk for instead of a one-size-fits-all approach. Even more importantly, the understanding of the molecular underpinnings of diseases like diabetes, and mental illness, and

heart disease, will enable us to develop a new generation of therapies that are specifically targeted to the problem, as opposed to treating some downstream consequence.

We have a bright future, and I think the genomics revolution will catalyze much of that. I'd just like to conclude by reading a few sentences, from the wonderful book which I would recommend to those who are trying to learn more about the genome, and this is a book by Matt Ridley, called "Genome: An Autobiography of A Species in 23 Chapters," in the introduction he writes the following words: "In just a few short years we will have moved from knowing almost nothing about our genes to knowing everything. I genuinely believe that we are living through the greatest intellectual moment in history, bar none. Some will protest that the human being is more than his genes, I do not deny it . . .,"—personally I strongly agree with that, we are much more than our genes—". . . but . . .," he writes, ". . . there is much, much more to each of us than a genetic code, but until now human genes were an almost complete mystery. We will be the first generation to penetrate that mystery. We stand on the brink of great new answers, but even more, of great new questions."

Members of the subcommittee, it's a pleasure to have a chance to meet with you this morning and discuss those questions and answers.

Thank you very much.

[The prepared statement of Francis S. Collins follows:]

PREPARED STATEMENT OF FRANCIS S. COLLINS, DIRECTOR, NATIONAL HUMAN GENOME RESEARCH INSTITUTE, NATIONAL INSTITUTES OF HEALTH, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Mr. Chairman and Members of the Committee: It is a pleasure to appear before you at this historic moment when we have just completed all of the goals of the Human Genome Project (HGP). I look forward to discussing with you the future of genomics at the National Institutes of Health (NIH), as well as the rest of the broader scientific community. I will start by giving a brief history of the HGP, highlighting our recent success. I will then discuss the National Human Genome Research Institute's (NHGRI) efforts to coordinate our work with other federal agencies, other governments, and the private sector. I will also describe our new vision for the future of genomics, as well as some new initiatives already under way. I hope to make clear that while we have just sequenced the 3 billion letters of the human DNA code, our work is really just beginning. The successful conclusion of the HGP heralds the true dawning of the genomic era. There is an ongoing vital role for the federal government in enabling the future of genomics, and especially in applying it to benefit human health.

SUMMARY OF THE HUMAN GENOME PROJECT

U.S. National Academy of Science Study on the Human Genome Project

The main goals of the HGP were first articulated in 1988 by a special committee of the U.S. National Academy of Sciences (NAS), and later adopted through a detailed series of five-year plans jointly written by the NIH and the Department of Energy (DOE). In 1988 Dr. James D. Watson, who won the Nobel Prize along with Francis Crick for discovering the structure of DNA, was appointed to head the then Office of Human Genome Research, which has grown into the National Human Genome Research Institute that I now have the privilege of directing. As of April 14, 2003, the principal goals laid out by the NAS have all been achieved more than two years ahead of schedule and $400 million dollars under budget, including the essential completion of a high-quality version of the human sequence. Other goals included the creation of physical and genetic maps of the human genome, which provided a necessary lower resolution view of the genome and have major value to research in their own right. The HGP also accomplished the mapping and sequencing of a set of five model organisms, including the mouse. That information generally

empowers the ability to interpret the human genome, rather like the Rosetta stone allowed the decryption of the ancient languages. The NAS study also recommended that, "access to all sequence and materials generated by these publicly funded projects should and even must be made freely available [to all]." We have adhered to that noble standard throughout the last 13 years.

Congressional and Administrative interest

Neither the NAS study nor the HGP would have occurred without the visionary leadership and determination of the Administration and the Congress. At the outset, many in the scientific community did not think that the HGP could be completed in a timely fashion or for an affordable cost. But the Administration and key members of the Congress felt that it was essential the United State government play a leading role in this project, and they correctly predicted that the project could be completed without taking resources from other important science. With the support of the Administration and the Congress, the recent doubling of the NIH budget allowed a dramatic increase in the pace of the HGP.

Last month, we were able to observe a major anniversary, the fiftieth anniversary of the discovery of the double helix structure of DNA by Drs. Watson and Crick, while simultaneously celebrating the completion of the DNA sequence of the human genome. In June 2000, the NHGRI and its partners in the International Human Genome Sequencing Consortium had already completed a "working draft" of the human genome sequence; at that same time, Celera Genomics, under Dr. Craig Venter's leadership, released its own draft version of the human genome and participated with us in a joint announcement at the White House. Since then the federally funded sequencing centers and our international partners have been working to correct all the remaining spelling errors and fill in the gaps in the draft sequence, leading to the public release of the essentially complete sequence on April 14, 2003. This is the reference sequence we will be using for all time. The availability of the 3 billion letters of the human instruction book could be said to mark the starting point of the genomic era in biology and medicine. There is now much important work to do to deliver on the promise that these advances in genomics offer for human health.

Coordination with Federal Agencies, other Governments, and the private sector

The HGP would have been impossible without an outstanding partnership between federal agencies, international organizations, and the private sector. From the inception of this project, the NIH has worked very closely with the DOE, and especially its Office of Science. In particular, I have had the great privilege of working with Dr. Aristides Patrinos, who has skillfully managed the DOE's efforts in this regard. We have also worked very closely with the governments and genome sequencing centers of five other countries: the United Kingdom, France, Germany, Japan, and China. In the United States the three main sequencing centers funded by the NHGRI are at the Baylor College of Medicine, Washington University in Saint Louis, and the Whitehead Institute of the Massachusetts Institute of Technology. Dr. Robert Waterston will be describing for you in a moment his work as the former Director of the sequencing center at Washington University.

The success of the HGP partnership was cited in a recent PricewaterhouseCoopers report, "Managing 'Big Science': A Case Study of the Human Genome Project," in which the author noted that: "A major implication for the future lies with the partnership model of R&D that HGP's organization revealed. Partnerships across agencies, sectors and nations are likely to be the wave of the future for large-scale public efforts at the frontier of knowledge. As a result of the HGP partnership, the first chapter of the human genome revolution is coming to a successful end, and next steps are underway."

NEW VISION FOR THE FUTURE OF GENOMICS

This April also witnessed the publication in the journal Nature of a bold vision for the future of genomics research, developed by the NHGRI. This vision, the outcome of almost two years of intense discussions with literally hundreds of scientists and members of the public, has three major areas of focus: Genomics to Biology, Genomics to Health, and Genomics to Society. *Genomics to Biology:* The human genome sequence provides foundational information that now will allow development of a comprehensive catalog of all of the genome's components, determination of the function of all human genes, and deciphering of how genes and proteins work together in pathways and networks.

Genomics to Health: Completion of the human genome sequence offers a unique opportunity to understand the role of genetic factors in health and disease, and to apply that understanding rapidly to prevention, diagnosis, and treatment. This op-

portunity will be realized through such genomics-based approaches as identification of genes and pathways and determining how they interact with environmental factors in health and disease, more precise prediction of disease susceptibility and drug response, early detection of illness, and development of entirely new therapeutic approaches.

Genomics to Society: Just as the HGP has spawned new areas of research in basic biology and in health, it has created new opportunities in exploring the ethical, legal, and social implications (ELSI) of such work. These include defining policy options regarding the use of genomic information in both medical and non-medical settings and analysis of the impact of genomics on such concepts as race, ethnicity, kinship, individual and group identity, health, disease, and "normality" for traits and behaviors.

This vision for the future of genomics is not just about the NHGRI. It encompasses the whole field of genomics, including the work of all the other Institutes and Centers at the NIH and of a number of other federal agencies. All of the NIH Institutes are already taking full advantage of the sequence and will apply its data to the better understanding of both rare and common diseases, almost all of which have a genetic component. A recent example of the way that the HGP and the knowledge and new technologies it has spawned are already facilitating science is the extremely rapid sequencing by groups in Canada and at the Centers for Disease Control and Prevention (CDC) in Atlanta of the genome of the virus that causes Severe Acute Respiratory Syndrome (SARS). The sequencing of the SARS virus genome provides insight into this new and deadly disease at a speed never before possible in science. In turn, this should lead to the rapid development of diagnostic tests and, in time, vaccines and effective treatments.

NEW NHGRI INITIATIVES

The NHGRI has already begun several new initiatives, and is planning others, to meet the challenge of realizing this new vision for the future of genomics. Many of these initiatives will be co-funded by other NIH Institutes, other federal and international partners, and the private sector. Some examples of these cutting edge programs include:

The Creation of a Human Haplotype Map

Multiple genetic and environmental factors influence many common diseases, such as diabetes, cancer, stroke, mental illness, heart disease, and arthritis; however, relatively little is known about the details of the genetic basis of such common diseases. Together with international partners, the NHGRI has begun to create a "haplotype map" of the human genome to enable scientists to find the genes that affect common diseases more quickly and efficiently. The power of this map stems from the fact that each DNA variation is not inherited independently; rather, sets of variations tend to be inherited in blocks. The specific pattern of particular genetic variations in a block is called a "haplotype." This new initiative, an international public/private partnership led and managed by NHGRI, will develop a catalog of haplotype blocks, the "HapMap." The HapMap will provide a new tool to identify genetic variations associated with disease risk or response to environmental factors, drugs, or vaccines. It will allow more efficient genomic research and clinical applications, thus making for more economical use of research and health care funds. Ultimately, this powerful tool will lead to more complete understanding of, and improved treatments for, many common diseases.

The ENCODE Project: the ENCyclopedia Of DNA Elements

To utilize fully the information that the human genome sequence contains, a comprehensive encyclopedia of all of its functional elements is needed. The identity and precise location of all transcribed sequences, including both protein-coding and non-protein coding genes, must be determined. The identity of other functional elements encoded in the DNA sequence, including signals that determine whether a gene is "on" or "off", and determinants of chromosome structure and function, also is needed. The NHGRI has developed a public research consortium to carry out a pilot project, focusing on a carefully chosen set of regions of the human genome, to compare existing and new methods for identifying functional genetic elements. This ENCyclopedia Of DNA Elements (ENCODE) consortium, which welcomes all academic, government, and private sector scientists interested in facilitating the comprehensive interpretation of the human genome, will greatly enhance use of the human genome sequence to understand the genetic basis of human health and to stimulate the development of new therapies to prevent and treat disease.

Genome Technology Development

The NHGRI continues to invest in technology development that speeds the applications of genomics. Technical advances have caused the cost of DNA sequencing to decline dramatically, from $10 in 1990 to less than $0.09 per base pair in 2002, but this cost must decline even further for all to benefit from genomic advances. The NHGRI, along with many partners, will actively pursue the development of new technologies to sequence any individual's genome for $1,000 or less. Other areas of technology development are also ripe for expansion, and the NHGRI plans to pursue them vigorously.

VISION OF THE FUTURE OF GENOMIC MEDICINE

While it always is somewhat risky to predict the future, I want to leave you with my view of where I believe genomic medicine is headed. In the next ten years, I expect that predictive genetic tests will exist for many common conditions in which interventions can alleviate inherited risk, so that each of us can learn of our individual risks for future illness and practice more effective health maintenance and disease prevention. By the year 2020, gene-based designer drugs are likely to be available for conditions like diabetes, Alzheimer's disease, hypertension, and many other disorders. Cancer treatment will precisely target the molecular fingerprints of particular tumors, genetic information will be used routinely to give patients more appropriate drug therapy, and the diagnosis and treatment of mental illness will be transformed.

CONCLUSION

This year marks a very exciting transition in the field of genomics, with the full sequencing of the human genome marking the successful achievement of all of the HGP's original goals, and thus the advent of the genomic era. When Congress decided to fund the HGP, it did so with the justifiable belief that this work would lead to improved health for all. Those advances are already occurring all around us, and the ability to accelerate the realization of this vision now lies before us. At the same time, we must be sure that these technological advances can benefit all our citizens in a safe and appropriate manner. It is our sincere belief that the newly created discipline of genomics will make a profound difference to the health and well being of all the people of this world.

While I am very optimistic about the future of genomic medicine, we clearly have a great deal more work to do to realize these lofty goals. The vision for the future of genomic medicine that I have described will require major breakthroughs in technology and scientific knowledge. But I am confident that by supporting our best and brightest scientists to work together with our partners within the government and around the globe, we will meet these challenges. We are profoundly grateful for the support the Congress has given to this endeavor. We would not be where we are today without your vital support. Thank you.

Mr. BILIRAKIS. Thank you very much, Dr. Collins.

Doctor Patrinos, please proceed.

STATEMENT OF ARISTIDES PATRINOS

Mr. PATRINOS. Thank you, Mr. Chairman. I am really honored to be invited to testify before you and the members of the subcommittee on genomics research, and I'm particularly honored also to be testifying in the presence and along with my colleagues and friends, some of the top scientists in genomic research, as you pointed out.

Doctor Francis Collins likes to start his story with Mendel, I usually go back a couple of thousand years with Aristotel who wondered how an acorn turns into an oak tree. That's one small point where we disagree a little bit.

Anyway, DOE has made important contributions to biological research since the early days of the Atomic Energy Commission, including the field of nuclear medicine. The Atomic Energy Commission, of course, is our predecessor agency.

The NIH and the Department Of Energy joined forces in launching the Human Genome Project in 1990. Since then our two agencies have worked very closely in managing this seminal research endeavor. This partnership has been a model of interagency collaboration with each agency contributing its unique strengths and capabilities and creating, indeed, a whole that's greater than the sum of the individual parts.

NIH and the Department of Energy, as you've heard from Doctor Collins, with a strong international involvement, completed the Human Genome Project just last month, and as has also been mentioned, 2 years almost ahead of schedule, 2½ years ahead of schedule, and under budget.

Secretary Abraham has, in fact, said that with all the contributions that DOE has made in the field of science none compares with what the Department of Energy has done in the Human Genome Project, echoing many of the things that I heard this morning from you and the members of the subcommittee.

Indeed, it is true that the Human Genome Project inspired what can be a called a paradigm shift in biological research from a pure hypothesis-driven "small science" approach to more of a resource-driven approach. The Human Genome Project also highlighted the importance of interdisciplinary research, including the physical sciences, automation engineering, and computational science.

Modern biological research, including genomics and the study of proteins, like Doctor Collins has already mentioned, rely on many research tools that are developed, in fact, by the physical sciences, such as the synchrotron radiation sources and nuclear magnetic resonance systems for protein crystallography, determining the structure of the individual proteins as a way to understand their function.

The Department of Energy's Office of Science builds and operates many of the scientific user facilities [such as the X-ray sources] for the benefit of the entire scientific community, and those scientific user facilities are increasingly being used by life scientists in their research, maybe a few percentage points about a decade ago, up to almost 40 percent today. This symbiotic NIH and Department of Energy relationship is expected to continue and even grow.

For us in the Department Of Energy, our follow up to the Human Genome Project is, in fact, described in a copy of Science that you have before you, and the chairman has already mentioned it, the Genomes to Life program or GTL. GTL was developed over the last 3 years by our advisory committee, the Biological and Environmental Research Advisory Committee, with broad input from many folks in the wide scientific community from many disciplines. This program adopts a "systems biology" approach to the study of microbes and microbial communities. GTL does not include any research on human biology.

Genomes to Life is a basic research approach that is aimed at the long-term solution of many of the Department's problems that Mr. Brown has already mentioned. They include the bioremediation of mixed waste at many of the contaminated DOE sites, the witch's brew that we have left from the legacy of cold war; also, the enhanced sequestration of carbon by the terrestrial and marine biosphere in order to reduce the atmospheric concentrations of green-

house gases in the atmosphere; and also, as has already been mentioned, the production of clean fuels such as hydrogen, through the miracles of biotechnology.

We expect that the Genomes to Life program will marry the tools of modern molecular biology with advanced scientific computing. Advanced scientific computing is an integral partner with us in this effort, and we expect highly accurate simulations of microbial systems and their interactions with the environment.

We also are proposing to build four scientific user facilities to enable, for example, the high-throughput research activities, including the production of proteins and protein tags as well as advanced systems that would allow us to view intra cellularly the microbes and their functions.

Looking to the future, we expect continuing close collaborations with our partners in the NIH on the Genomes to Life program and other programs as well. Our programs will involve scientists from the academic community, from our national laboratories and private institutions such as Craig Venter's Institute for Biological Energy Alternatives. Craig Venter is a major principal investigator with us in the Genomes to Life program.

Thank you for the opportunity you gave me and I'm, of course, ready to answer any of your questions.

[The prepared statement of Aristides Patrinos follows:]

PREPARED STATEMENT OF ARISTIDES PATRINOS, DIRECTOR, OFFICE OF BIOLOGICAL AND ENVIRONMENTAL RESEARCH, DEPARTMENT OF ENERGY

Mr. Chairman and Members of the Subcommittee: I am pleased to testify before the Subcommittee about the future of genomic research at DOE. I am also prepared to discuss the Genomes to Life program and our interactions with the National Institutes of Health (NIH).

DOE is proud of the contributions we have made to biological research since the early days of the Atomic Energy Commission and of the role we have played in the Human Genome Project (HGP). The NIH and DOE joined forces in 1990 to launch the HGP and we have worked closely over the years to reach the successful completion of the project last month almost two years ahead of schedule and several hundred million dollars under the original estimate of $3 billion. The partnership with the NIH in the HGP has been a model of interagency cooperation with each agency contributing its unique culture and strengths to create a whole that was truly greater than the sum of the parts. The DOE brought to the HGP its strengths in the managerial arena: an impressive network of national laboratories, each with its own area of scientific expertise. DOE leaders' experience in managing large-scale projects (mostly in the physical sciences) provided critical input to the HGP, starting during the formative years and continuing through today.

With the successful completion of the HGP we are entering an exciting new era of biological research greatly enhanced by the modern tools of molecular biology that have been enabled by genomics. This new era of biological research offers the promise of revolutionary solutions to challenges we face across a remarkable spectrum—from agriculture to carbon sequestration to clean affordable energy to the environment to industrial processes to medicine to national security to name but a few. While technologies and research tools will be developed and shared across disciplines, Federal agencies, academia, industry, and international borders, as they were in the Human Genome Project, the specific research challenges and needs will not be shared.

Strategies that NIH will use for understanding disease processes and for developing improved diagnostics and cures will differ greatly from those needed to develop new ways to sequester excess carbon dioxide from the atmosphere, produce abundant and affordable supplies of clean energy, and clean up contaminated waste sites. Although completion of the HGP will thus lead to somewhat divergent research paths, NIH and DOE will continue to coordinate research efforts and explore opportunities for collaboration and cooperation. Such opportunities will emerge from

both the many NIH-DOE ties as well as through the interagency forums led by the Office of Science and Technology Policy in the Executive Office of the President.

DOE's entry into this new era is the Genomes to Life (GTL) program that has been developed with broad scientific community input and led by the Biological and Environmental Research Advisory Committee (BERAC). The focus of the GTL program is on microbes and microbial communities and seeks to harness their properties and capabilities to address DOE needs in environmental bioremediation, carbon sequestration, and clean energy production such as generating hydrogen.

The research approaches and tools that DOE needs to understand microbes so well that we can use them to help solve DOE challenges will, in many cases, be very different than those used by NIH to study disease-causing microbes. DOE needs to understand the nature and biochemical capabilities of microbes in the oceans and in subsurface environments—sites and microbes not likely to be of significant interest to NIH—since the microbes in those environments are the ones that we need to put to work to help us solve energy and environmental challenges. In addition, most of the microbes that DOE needs to understand, live and "work" as parts of complex communities made up of hundreds or thousands of different microbes—a scientific challenge very different from the challenges faced by NIH's need to understand disease-causing microbes.

We believe that many of the scientific discoveries in this new century will happen at the interfaces of scientific disciplines, including the interfaces between biology and the physical and computational sciences. Modern biological research will increasingly rely on the scientific tools that are developed by the physical sciences. One example is the determination of the structure of biological molecules using the synchrotron radiation sources, neutron sources and nuclear magnetic resonance facilities. Most of these facilities are built and operated by DOE and the number of their users from the life sciences has grown from a few percentage points to approximately forty percent in just the last ten years. Another example is advanced simulation of cellular processes using high performance supercomputers. The new generation of medical imagers will also require significant computational resources for the processing of vast amounts of data.

We envision many significant opportunities for future collaborations between NIH and DOE as scientific research becomes more interdisciplinary and more reliant on cutting-edge scientific tools. Many of these tools will be developed by the DOE research programs for DOE applications and some of these tools will be considered by NIH for applications to human biological research and for medical applications. We expect to continue our regular and productive dialog with our NIH colleagues to identify such opportunities for collaboration and to help make them happen.

Despite its microbial focus the GTL program will enable many collaborations with our NIH colleagues, including those from the National Human Genome Research Institute, the National Institute for General Medical Sciences, and the National Institute for Allergy and Infectious Diseases. Discoveries that may serve the DOE missions in bioremediation, carbon sequestration, and clean energy production may prove relevant to applications in human health and medicine. Similarly, insights derived form the study of human biology may help us properly tweak microbial systems to serve DOE needs.

Many have called this new century the "century of biology" because of its promise in providing new solutions to many of humanity's problems. At DOE we plan to exploit these new biological advances for the benefit of the Nation and we expect that our productive research partnership with the NIH will continue and even expand.

I would be pleased to answer your questions.

Mr. BILIRAKIS. Thank you very much, sir.

Doctor Waterston.

STATEMENT OF ROBERT H. WATERSTON

Mr. WATERSTON. Well, thank you for the opportunity to testify about the many opportunities that lie before us for U.S. biomedical research, but I'd also like to take the opportunity to thank Congress for its continuing and unstinting support of the Human Genome Project throughout the years. It's been critical.

I'd love to talk about all the opportunities in more detail, but I'm going to, in fact, direct my remarks to the role of the NIH and, particularly, the NHGRI in bringing genome to fruition. In my role as

Director of the Center at Washington University, I've been able to witness first hand all of this happening.

Initially, the project demanded just a definition of what the goals were, and Jim Watson, in particular, was highly successful at drawing people into the project, but the traditional, very successful system of investigator-initiated peer review grants operated to draw the many ideas from the community and to sift through them. Successful program were renewed and expanded.

As the project moved into it's production phase, the proposals from individual centers were still subjected to rigorous peer review, but the projects required much more oversight to coordinate the efforts from the various centers. And, NHGRI took on this much less traditional role of organizing the groups. Doctor Collins and his staff kept us focused on the task at hand, while never losing sight of the overall goal of a complete finished human sequence.

One key early decision was that of the group to release immediately all the data generated. No patents were filed, and the rapid unfettered access to this data has worked, speeding discovery of the genes behind many genetic diseases already. More will follow.

With the success of the project, we are now in the position of deciding how best to utilize this information to improve human health and well-being. We know that the genome contains all the genetic information passed on from generation to generation, but we understand that information only dimly. Using that information to move from knowing the genetic basis for a disease to an effective therapy is an even greater challenge.

Doctor Collins and Doctor Patrinos have already mentioned the plans of their institutions for the future, and they developed these after extensive consultation with the community. Centers for Excellence in Genomics and the HapMap project are just two of the already initiated programs.

One activity that I'm particularly interested in is the sequencing additional animal genomes. We learned a tremendous amount by comparing the sequence of the human with the sequence of the mouse. We were, basically, peering into evolution's notebook and looking at the results of 75 million years of tinkering. Additional sequences from other animals such as the cow, dog, chicken and chimpanzee will be invaluable as we try to understand the contents of the human genome.

But, as others have mentioned, the genome is fundamental to all kinds of biomedical research and it impacts research both public and private. The doubling of the NIH budget has come at a most appropriate time, and as the Congresswoman already mentioned, it's important that this support be continued, because the task ahead of us is truly enormous, but the results will be worth it.

And, I believe that for both the NHGRI plan and the NIH as a whole this traditional system of investigator-initiated peer review research should continue to serve us well, as we explore the best ways to go forward. And, at this point I think it's really unclear what the best way to go forward is.

But in addition to these initiatives, the NIH and the NHGRI in particular should continue to seek out big, novel goals that will capture the imagination, and are of obvious medical relevance, and will spur the best science.

One example of such a goal might be the sequencing of a very large cohort of well-characterized individual. We would uncover our evolutionary roots and begin to understand how sequence variation contributes to variability in disease susceptibility and to many other traits.

A project like this would push science and society closer to the goal of using the genome for the benefit of all.

I thank you for the opportunity to appear, and I look forward to your questions.

[The prepared statement of Robert H. Waterston follows:]

PREPARED STATEMENT OF ROBERT H. WATERSTON, PROFESSOR, UNIVERSITY OF WASHINGTON

Mr. Chairman and Members of the Committee: Thank you for the opportunity to appear before you. I welcome the chance to share with you my thoughts about the opportunities in biomedical research made possible by the success of the human genome project, and the role that NIH might play in bringing these opportunities to fruition. Congress led in the initiation of the project at a time when many scientists were skeptical, and generous support by Congress throughout the project was essential. Congress will continue to play a major role in determining the next steps.

I will begin by providing you with some brief background about myself and my role in the Human Genome Project. I'll then describe how the genome project worked from a grantee's perspective. Finally I'll describe where we are today and some of the opportunities that lie ahead for NIH and biomedical research.

BACKGROUND

I am currently Professor and William Gates III Chair of the Department of Genome Sciences at the University of Washington. But until December of last year I was the director of the Genome Sequencing Center at Washington University in St. Louis, where I experienced first hand the emergence of this project. I saw it grow from the ideas of a few visionary scientists to the recent completion of the human sequence under the skillful leadership of Dr. Collins, Dr. Patrinos and others. Over a dozen years, the St. Louis Center grew from a team of just half a dozen staff producing about 10,000 bases of DNA sequence a day to a staff of over 150 producing more than 50 million bases of DNA sequence daily. The St. Louis Center was one of the three large NIH-sponsored centers in the human genome project and produced more than 20% of both the draft and finished human sequence. It also played leadership roles in the completion of the genomes from the baker's yeast, *Saccharomyces cerevisiae,* the round worm, *Caenorhabditis elegans,* and the mustard weed *Arabidopsis thaliana.* Today its efforts are directed at completing the mouse genome sequence, as well as producing draft sequences of both the chimpanzee and chicken genomes.

ORGANIZATION AND FUNDING OF THE HUMAN GENOME PROJECT AND THE GENOME SEQUENCING CENTER

The Genome Sequencing Center received most of its funding from the NIH through what is now the NHGRI. But at critical junctures it has also received funding from Merck and two different consortia of pharmaceutical companies, as well as NSF. In 1990 we were one of several laboratories funded to begin the effort of adapting and improving sequencing methods to the task of sequencing whole genomes. This was an exploratory period, in which the NHGRI set clearly defined overall goals and invited proposals from scientists with their many different ideas about how to realize these goals. James Watson, the first head of the NHGRI, played a critical role in fashioning this as an exciting project that would draw in the top scientists of the day. Many groups responded, and the proposals were rigorously evaluated, following the tradition of investigator-initiated, peer-reviewed research that has made US NIH-sponsored biomedical research the envy of the world.

Out of that process came several pilot projects exploring a variety of ways to sequence DNA at an ever-increasing scale. Some worked while others didn't, and as these grants came up for renewal, winnowing occurred, through rigorous evaluation of results—and costs—by panels of peers. By 1997, the community coalesced around the most effective DNA sequencing technology and reached a broad consensus that the technology was now up to the task of sequencing the human genome. While peer review of proposals continued to be the means of evaluating applications, collabo-

rative discussions among all players—both NIH staff and scientists in the labs—became the instrument for establishing direction and policy in the project as a whole.

As the major partner in the international public project, which included some 20 laboratories from 6 countries, the NHGRI and Dr. Collins in particular played a central role in coordinating the effort. Through weekly conference calls, quarterly meetings and many emails, Dr. Collins and his staff kept the group focused on the task at hand and at the same time never lost sight of the long term goal of complete, highly accurate human sequence.

Of the various decisions made by the group, perhaps none was more important than the decision at one of the first gatherings of the international human sequencing community to release all the sequence data immediately upon generation for all the world to use without constraint. No patents would be filed. The sequence was held to be of fundamental importance, like the atoms of the periodic table, and all recognized the many steps between discovery of a sequence and its application to improving human health. This decision gained the confidence of the wider scientific community, but more importantly it meant that the sequence stimulated research in labs both public and private throughout the world from the day the project was begun.

ACCOMPLISHMENTS AND OPPORTUNITIES

The patience and persistence of Dr. Collins and his staff have paid off. After the joint announcement with our colleagues from Celera Genomics of the draft sequence in June 2000, the public scientists continued to refine the sequence. As a result, we have before us today the effectively complete sequence of a reference human genome. About 99% of the sequence is represented. We have closed more than 99.5% of the gaps that existed in the draft sequence. The error rate has been pushed to below 1 per 100,000 bases. This highly accurate, complete sequence speeds the work of researchers trying to find the genes behind genetic diseases. It enhances the ability of computational biologists to interpret the sequence. And most importantly it provides a solid foundation for scientists to build upon.

But of course the sequence is a beginning, not an end in itself. While we know that the genome contains all the genetic instructions handed down in the form of DNA from one generation to the next, we can only read those instructions poorly. It is likely to take decades to understand this instruction set thoroughly, but the effort will be worth it. As we unravel the complexity and as we learn what happens when some part of the code is disrupted by mutation, we will uncover opportunities for improving human health and well-being.

The plans for the future developed over the past year by the NHGRI and DOE and described by my colleagues Dr. Collins and Dr. Patrinos in their testimony outline some of the important next steps. The HapMap that Dr. Collins described begins to explore human diversity. And the Centers of Excellence in Genome Science program that NHGRI began in 2001 seeks to foster innovative approaches toward understanding and integrating genomic information. The University of Washington was the recipient of two of the first three awards.

One important ongoing activity I'd like to highlight is the sequencing of additional genomes. We have learned an enormous amount by comparing the sequences of the mouse and human. We are reading evolution's notebook, the results of 75 million years of mutation and selection. The functional parts of the genome begin to stand out in these comparisons and to tell us important things about how the human genome came to be and how it works. Additional sequences from animals like the cow, dog, pig and chimpanzee will yield still more insights into our genome, while at the same time bringing the power of genomic approaches to the study of these important animals.

But the impact of the genome sequence extends beyond the purview of the NHGRI and even that of the whole NIH. Virtually all areas of biomedical research, in both the public and private sectors, are deeply affected by its availability. Opportunities abound. The doubling of the NIH budget came at an essential time, as researchers scramble to exploit this new knowledge. The broad approach advocated in the NHGRI plan and likely to be reflected in any road map for the NIH will ensure steady progress in our understanding of disease and in developing novel therapies.

But in addition to these initiatives, the NIH should continue to search for new goals analogous to the Human Genome Project of 15 years ago, goals that catch the imagination, that are of obvious relevance to medicine and that focus research for years to come. One example would be the sequencing of a large cohort of carefully characterized individual humans. We would uncover our evolutionary roots and begin to understand at a profound level how sequence variation leads to variation in the population, variation in susceptibility to disease and variation in many dif-

ferent traits. A project such as this would push science and society closer to the goal of using the genome for the benefit of all.

The Human Genome Project required significant adaptations in the time-tested procedures of the NIH. But the NIH responded by taking on this big, novel effort, initially defining the goals and later assuming the oversight role needed to bring the project to fruition. The peer-review system served us well throughout, allowing many avenues to be explored and providing time for the successful technologies to mature. Building on its success the NIH is well positioned to take on this next complex stage of translating this knowledge for practical benefit.

Mr. BILIRAKIS. Thank you so much, sir.

Doctor Venter, you are on.

STATEMENT OF J. CRAIG VENTER

Mr. VENTER. Thank you, Mr. Chairman, it's, indeed, a pleasure to be here with my distinguished colleagues that have covered so much of the genome field over the last few decades.

I think of this group I have sort of a unique vantage point, in terms of I've been extremely privileged to have close to 30 years of federally supported research in a variety of capacities, first for 10 years as a university researcher, then close to 10 years as an intermural NIH researcher, where the unique type of funding in an intermural NIH program is often misunderstood, but is probably the best type of funding we have in this country. It allows scientists like myself to make breakthroughs without having to go through year-long reviews of ideas that are more than often turned down in the extramural arena.

I left NIH in 1992 to form a new not-for-profit basic research institute that has had just the most enviable Federal funding over the past 11 years. That's expanded now to a group of five 501(c)(3) organizations that I'm representing here today.

That funding has come from almost every part of the U.S. Government, much of which is represented here. The very first funding we got was from the Department of Energy, and many people have not understood the DOE's role in genomics and biology, but I think it's becoming clearer as we move into the energy field of applying what we are learning in microbial genomics to maybe create a new hydrogen economy.

We've also had wonderful funding from the NIH from the Department of Allergy and Infectious Disease, starting back with early collaborations with the CDC in the early '90's we sequenced the smallpox genome in collaboration with the CDC, with Allergy and Infectious Disease funding. That went on recently in collaborations with NIH and the FBI, where Claire Fraser led a team at TIGR Sequencing as Mr. Brown commented on, the anthrax genome, sorting out the difference between the Ames strain and the strains that infected people with the anthrax attack.

In addition, we've used this funding to sequence almost every key human pathogen, including the malaria genome and most recently in a wonderful collaboration that initiated at Celera, included TIGR and included the public funded labs, the mosquito genome.

So, we are at a point where we have the human genome sequence, the malaria pathogen, and the Anopheles mosquito vector that carries it. We have the ability to look at variations in the genetic code of the pathogen of the vector and our own genetic code to find new ways to come up with what is the No. 1 infectious dis-

ease killer of children in the world, over 5 million a year from malaria alone, that genomics is providing wonderful new tools, and there's already new vaccines in development based on this recently published sequence.

The DOE itself is responsible for funding approximately one third of the genomes that have been completed and published to date, but we also have funding from USDA and NSF that have been the key funders of plant genomics work, and we've also been privileged to be recipients of funding from Doctor Collins' institute, and we currently have pending a very large grant with his institute to help with the goals that, in fact, I think Doctor Waterston laid out very nicely. The key to understanding the genetic code at this point probably lies in comparative genomics.

We can't read our genetic code. We know what a fraction of our genes do, and we have very little understanding of what the other 99 percent of the genetic code does. As Doctor Waterston said, by looking at comparative genomics, and we have to have a very large number of species, mouse was wonderful, but we probably need 100 or more different Mamayan and closely related and distantly related genomes, using the history of evolution to tell us what's important and what's not.

I think one of the biggest challenges of this next century will be the interpretation of the genetic code, so I disagree somewhat with Matt Ridley's quote that within a few years we will understand the function of all our genes, I wish that were so. I don't think there's enough funding in the Federal Government or enough scientists to make that happen in the next few years, but we should definitely be working in that direction.

I think the most important issue is what this committee is asking, Mr. Chairman, what are the public health aspects and what do we do next. I agree with Doctor Waterston's suggestion that we don't let the first two human genomes that have been sequenced by the last two human genomes that have been sequenced. In my view, the only way that these wonderful discoveries will benefit the American public is if we get it so each of us can have our genetic code determined and understand the differences in our genetic code and how those will lead to the prevention of disease.

We have a chance to transform medicine from reactionary medicine to preventative, and the economic benefits of that are the only hope we have to dramatically change healthcare costs in this country. So, I think in addition to this wonderful comparative genomics work that's being funded, we would like to see the challenge, and I'm delighted to see it in Mr. Collins' testimony, this goal that we jointly have to get to a $1,000 genome. That's going to take dramatic new technological breakthroughs, but if you look at the pace that things have changed over the last few years it's very likely within a decade, before a baby leaves the hospital they will have the opportunity to have their genetic code on a DVD that will be used to help decide which diseases they might have prevalence toward, and to be able to do something about them in advance.

Doctor Collins and I have been two of the biggest supporters of getting the non-discrimination bill passed, and I'm delighted also to see the progress that took place in the Senate. It's had, I think, what, over 200 to 300 co-sponsors in the House for the last 6 years,

I'm delighted to see Mr. Brown is one of the co-sponsors of the House bill. I think this is the single-most important legislation for affecting the future health benefits from the genomic discoveries that have taken place and will take place. And, I think this panel and this committee could go an awful long way to helping get that passed this year.

I think personalized medicine, not in the way most people have thought about it, one drug for each individual, but understanding the statistics associated with disease will give power to individuals over their health outcomes for the first time in human history.

I look forward to this new era in science. I look forward to a positive collaboration with my colleagues in the Federal Government, Doctor Collins, Doctor Patrinos and Doctor Fauci and others. I think this is the most exciting era in the history of science, and I'm, indeed, privileged to be part of it.

Thank you very much.

[The prepared statement of J. Craig Venter follows:]

PREPARED STATEMENT OF J. CRAIG VENTER, PRESIDENT, J. CRAIG VENTER SCIENCE FOUNDATION

Mr. Chairman and Subcommittee members, I welcome the opportunity to testify today before your Subcommittee to present my observations and recommendations regarding the continuing Federal investment in genomic research. My name is J. Craig Venter, and I am the President of the Venter Science Foundation and Chairman of five affiliated nonprofit organizations in Rockville Maryland, that are devoted to pursuing and supporting genomic research and its impact on the public. They are described in the Appendix to my testimony.

I have been honored to participate in federally-funded research from several distinct vantage points: From more than 10 years as an NIH grant recipient at universities; nine years as an NIH intramural researcher and Laboratory Chief at the National Institute of Neurological Diseases and Stroke; and 11 years as the founder and president or Chairman of The Institute for Genomic Research (TIGR), a nonprofit, 501(c)(3) institution. In addition, for three years out of more than a 30-year career in science, I was the President and Chief Scientific Officer of Celera Genomics, a private sector company. As indicated, I now head a new group of affiliated nonprofit basic research institutions devoted to genomic research and public policy. Each experience has shaped my current views on the role of the Government in supporting the many-faceted science of genomics.

The science and technology of genomics have become the foundation of research in biology in the 21st century. Genomics will play a central role in advances in medicine and public health, as well as agriculture, the environment, energy and the economy. During the past decade, we have made unprecedented strides in genome sequencing—the entryway into the genomic era. From the historic decoding of the first genome of a living species by my team at TIGR only 8 years ago, we now know the genome sequence of more than 100 species, including medically important microbes that cause diseases such as anthrax and tuberculosis, the parasite that causes malaria, and the mosquito that carries it. In 2001, to wide acclaim, two independent teams of researchers, both represented here, announced that each had sequenced the human genetic code.

These are profound accomplishments reflecting the cumulative efforts of numerous scientists around the world working in diverse areas of science, technology and basic and applied research. These advances would not have been possible without funding support from a wide range of public, private and federal institutions that sponsored this revolution in science. Prominent among them the National Institutes of Health, the Department of Energy, the National Science Foundation, the U.S Department of Agriculture, private not-for-profit foundations including The J. Craig Venter Science Foundation and the Wellcome Trust in England; and public and private for-profit commercial organizations including large pharmaceutical companies, Celera Genomics, and technology companies including Applied Biosystems, Beckman and Amersham. It is clear to most that we would not have a sequenced human genome without substantial private sector involvement.

We have learned important lessons from genomic research that has been undertaken to date, and anticipate even greater advances having applications to everything from medicine to energy to Homeland defense.

But we have even more to learn. I have estimated that 99% of the discoveries that will ever take place in biology remain to be made. We are at the earliest stages of beginning to be able to interpret the genetic code. With very few exceptions, we do not yet have enough information to understand which genes in a genome are biologically significant and why. We lack sufficient information to understand how groups of genes function as an "operating system" whose programming sometimes promotes health or longevity and sometimes leads to disease. As we go forward, however, we can draw some lessons from the past about how best to fund genomics in the future, in order to serve the public good as efficiently, imaginatively, and inclusively as possible.

THE FEDERAL INVESTMENT IN GENOMICS

The investment by Federal agencies in genomics research is the focus of the hearing today, and I am privileged to be invited to give my views about how we should proceed.

I think that it would be useful to describe the broad support of the federal government in funding basic genomic research from my vantage point. The not-for-profit basic research institutes that I am representing today have had a broad array of federal funding in the field of genomics for more than a decade now, and this has included funding from the major funding agencies within the United States including DOE, NIH, NSF, and USDA. The DOE was the first to fund basic research at TIGR dating back to its formation in 1992 and this funding included support for the development of the whole genome shot-gun sequencing strategy, particularly as it was applied to the study of microorganisms relevant to bioremediation and the environment. DOE has funded approximately one third of the microbial genomes sequenced and published to date. Most recently, the DOE through its Genomes-to-Life program is funding our research that will apply shotgun sequencing to the study of large, complex environments starting with the Sargasso Sea. The DOE is also funding our energy institute, IBEA, to use genomics in attempt to sequester carbon dioxide and produce hydrogen.

The Institute of Allergy and Infectious Disease (NIAID) within NIH, has also been a key supporter of genomics research at TIGR for more than a decade. Starting with a project at TIGR in 1992 to sequence the genome of the smallpox virus, work that was done as part of an international treaty, NIAID has been a world's leader in the use of genomics approaches to understand and treat infectious disease. As a direct result of NIAID funding to my teams, we have the sequenced of the genomes of most major human pathogens including those that cause tuberculosis, cholera, syphilis, various respiratory infections, malaria, and the Anopheles mosquito vector that carries the malaria parasite, the fourth largest genome sequenced to date. NIAID, working with the FBI and other agencies, has funded TIGR to sequence multiple strains of the anthrax bacterium, with the goal being the development of a microbial forensics database that will hopefully provide new insights into the source of the anthrax attacks that occurred in the fall 2001. NIAID has also funded a multi-million dollar Pathogen Functional Genomics Resource Center at TIGR that is providing genomic reagents, laboratory services, and training to the nation's infectious disease researchers.

NSF has been a major funder of basic research at TIGR in both plant and microbial genomics. Beginning in 1996, TIGR was the recipient of a multi-year award from the NSF to participate in an international consortium to sequence the first plant genome, *Arabidopsis thaliana,* which serves as a model for 250,000 other plant species. This work was completed in 2000, four years ahead of schedule. Because of the continued strong federal investment in plant genome research, TIGR has initiated a number of other NSF-funded, genomics-based research programs on important crop species including rice, potato, tomato, and soybean. In parallel with these studies are related efforts on some of the most important bacterial and fungal plant pathogens that are responsible for millions of dollars in losses each year.

TIGR was one of six centers initially funded by the NHGRI in 1995 to begin work on the sequencing of the human genome. Recently, TIGR and our new state of the art DNA sequencing facility have submitted a $156 million grant to the NHGRI that is pending review to apply our expertise in genomics and our interest in developing novel, more cost-effective technologies to the sequencing of large, complex genomes.

Because genomics is the underpinning of virtually all areas of biological and biomedical research in the 21st century, it is important to every institute within the NIH family as well as to every academic and private institution in the world. And,

because genomics is a uniquely interdisciplinary area of science, its success will require imaginative approaches to funding innovative experiments in which genomics specialists, biologists, physician-scientists, computer scientists, software engineers, and others can work together. Genomics will flourish only if we as a nation develop ways to simultaneously support large-scale science, as well as studies by small groups of innovative researchers working in the more traditional mode.

If the promise of genomics is to be fulfilled, we need to adapt current approaches for peer-review and funding decisions for a new era. We'll have to think boldly, increase the community of scientists who are part of the decision-making process, pay attention to ideas for new technology as well as basic research, and, most important, be willing to take a chance on original ideas that could be wildly successful but that could also fail. We have to take chances.

In this regard I want to say how pleased I am to serve on a new NIH committee, established with foresight by Director Elias Zerhouni, to offer guidance about funding highly innovative, "out-of-the-box" research proposals throughout the institutes. I applaud Dr. Zerhouni's judgment in creating this group and look forward to its success. It is a good start to thinking about innovation across the board at NIH, in its support of intramural science as well as at academic and nonprofit research institutions.

Now I'd like to suggest six objectives that the Government should consider as you contemplate the opportunities and challenges for genomic research today.

1. Large-scale genome sequencing should be funded and managed to extract the best value for the American public, in terms of output, innovation and cost.

This objective is based on the reality that, at the present time, genome sequencing is very expensive and requires special expertise. For example, at present, it still costs tens of millions of dollars to sequence a complete human genome, and hundreds of thousands of dollars to sequence all the human genes from one person. We need genome sequencers that are the equivalent of personal computers, but we are not there yet.

While the actual sequencing of human and other genomes is the backbone of genomic research, the promise of genomics to improve the health of individuals will not be achieved until DNA sequencing becomes much faster and much less expensive. Going forward, it is critical that both the NIH and DOE continue to support innovative projects that constantly encourage technological innovation and drive down the costs of sequencing. This is a complicated proposition, as many of the advances are likely to come from the commercial sector, but the government will help create the market that drives the necessary innovation, as it has in the past, by supporting large scale human sequencing.

In the medical arena, to enjoy the promise of personalized and preventative "genomic" medicine, we must compare the genomes of tens of thousands of people to better understand the genetic causes of complex diseases. And with that understanding, we then might develop strategies to prevent or better treat disease.

My own Foundation has set an ambitious goal: to work toward reducing the cost of human genome sequencing to $1,000 per person. The Federal government should have a similar goal. This is a massive challenge for all of us in technology and bioinformatics, as well in genome analysis—one that I think of as "big science"—science that costs a lot to develop, must be highly accurate to be useful, and must be scaleable in order to serve the public good. It requires a network of centers capable of rapid, mass sequencing, a national resource that can be tapped, but does not need to be replicated at every university. Indeed, this is an area that might benefit from the DOE model of the National Laboratories, modified to the needs of this new science. And achieving this price point may well require as broad and diverse a collaboration as did the sequencing of the human genome itself.

2. Special attention should be given to the needs of individual investigators who do not have easy access to large-scale genome sequencing.

This objective derives from the recognition that "genome sequencing" is a basic tool for research critical to the work of *every* NIH institute. We must find better ways to expand the science of sequencing to apply genomics across scientific disciplines and throughout the NIH. And to encourage innovation for public benefit as well as to put pressure on costs, we must allow researchers the freedom to use these tools in new and expanded capacities.

This objective is also based on the importance of giving all of the NIH (and Public Health Service) institutes access to major sequencing centers. It is becoming clear that we need new strategies to apply genomics to "systems biology," and high-risk studies to understand the associations between genotype and phenotype. Precious Federal resources like the NIH and DOE genomic sequencing programs must be

aware of, and responsive to, the needs and priorities of a very diverse federally funded research community.

3. Rapid, open access to all federally funded genome data so that it can be used freely by scientists throughout the world.

Access to data funded by hundreds of millions of dollars of Federal investment must be available rapidly and openly to the research community. It must be made clear that this research is not being done for the benefit of the heads of the few centers that receive massive federal funding. And, another less obvious, but equally important, benefit of this approach is that the availability of these data will stimulate advances in associated computing and informatics technologies. Users will demand much faster and more stable distributed grid systems. This will move us much faster down the pathway of integration of multiple research centers and private physicians, and ultimately improve the health of the American public.

4. NIH-wide genomics advisory board

As a significant driver of success, we must decentralize decision making about genomic sequencing priorities as much as possible, allowing researchers across disciplines to determine what genomic sequencing support they need rather than be confined to a current model in which a single Institute both develops the relevant tools and determines how they should be used and applied. The various institutes at NIH that support genomic sequencing and "applied" genomic research must jointly address priorities and policies that provide the highest value. In my own view, genomic sequencing has become a commodity item for which the contract mechanism is preferable. I make this observation even though my institutions receive federal grants as well as contracts, and we have recently applied to NHGRI to for a cooperative agreement to become one of a few major sequencing centers. At the least, an NIH-wide genomics advisory committee could usefully discuss which support mechanisms are preferable for various kinds of programs and consider why, for example, NIAID and NHGRI use different funding mechanisms for similar genomic sequencing awards. This advisory committee, taking advantage of NIH's broad and diverse expertise, might take as an initial goal the determination of how best to stimulate competition, innovation and cost reduction. Perhaps shorter term contracts, regional technology development centers, and other models in NIH's funding repertoire should be included in the strategy for funding genomics research going forward.

5. Inter-agency genomics advisory board (NIH-CDC-DOE-NSF-USDA-DHS)

Similar to the foregoing recommendation, a broader inter-agency genomics committee, could apply a more diverse experience base and a higher level perspective to cost-containment, innovation and research priorities.

6. Appropriate and clear position on patents which remain the basis of the free enterprise system and the avenue through which most basic research reaches application.

We learned a number of important lessons during the past several years during the so-called "race" to sequence the human genome. No one can seriously disagree about the important role of competition in developing and utilizing technologies and sequencing techniques in genomics as well as in any other area of biomedical research. It is a plain fact that innovation and investment by both the public and private sector will be necessary in genomics for the public good that we all strive to achieve. Thus, the norm for genomic research going forward must be an open and accepting partnership between the private sector and public sector.

We also learned, however, that competition has its negative side, as was evident from the ill-will that occasionally developed between HGP scientists and their counterparts in the private sector. I, for one, regret that. Competition is a useful thing, particularly when it is marked by good sportsmanship, and that will be essential to the public welfare as we move forward. As one component of that public-private partnership, each sector must understand their respective cultures, funding opportunities and limits, research and product-development time-horizons and other business realities, like return on investment and intellectual property. Patents, for example, do raise issues, including one that the Supreme Court has been asked to review, as to whether the experimental use exemption applies to nonprofits. But the private sector cannot be excluded or disparaged because of its own business norms. Genomic research is simply too expensive and ambitious an undertaking for our nation not to rely on every worthy contributor and potentially useful technique.

Concluding remarks

We are now at a crossroads in genomic research and must think strategically if we are to fulfill the promise of this science. In many ways, sequencing has arrived at the point where it's a commodity—a tool for which all the applications are yet to be discovered. So our challenge, both for government agencies like NIH and DOE and those of us in the private sector—whether nonprofit or for-profit, is to determine how to use scarce research dollars most effectively to fund this technology so that it reaches its ultimate potential.

To rise to this challenge we must acknowledge and accept that while the cultures of industry and academia differ—there is still much to gain from collaboration. We must combine the resources of the federal government with the innovation and technology development of the private sector to advance this science and discover practical applications critical to its success.

We must create an open marketplace for genomics research and its applications, encouraging competition and collaboration to reduce costs, encourage private sector investment and bring new technologies to market.

I look forward to working closely with this Subcommittee and the many teams of accomplished scientists you support. I hope to contribute energetically to this cause and lend my support to a new culture of collaboration in this crucial field.

By working together, we will succeed. And society, as a whole, will reap the benefits. The approaches I've described above need to be integrated across all of NIH and all of biological science, and if it doesn't happen the public will be the loser. But if it does happen, we will truly embark on the golden age of genomics.

APPENDIX

THE VENTER SCIENCE FOUNDATION'S AFFILIATED NONPROFIT ORGANIZATIONS

The Venter Foundation includes five affiliated nonprofit entities, three of which conduct basic, scientific research: The Institute for Genomic Research (TIGR), The Center for the Advancement of Genomics (TCAG), and the Institute for Biological Energy Alternatives (IBEA).

The Institute for Genomic Research was founded in 1992 with venture capital funding and an initial goal to identify as many human genes as possible using Expressed Sequence Tags (ESTs)—a controversial, but rapid, cost-effective method that I developed while doing research in the intramural program at NIH. I left NIH to create TIGR in part because, at the time, NIH was not in a position to conduct a large-scale human gene discovery study within the intramural program. In our first two years, we at TIGR used the EST strategy to identify more than half of the genes in the human genome. Then, using many of the laboratory and computational methods that we developed for the human gene discovery program, we pioneered the whole-genome shotgun sequencing of the first complete genome of a free-living organisms, Haemophilus influenzae, a bacterium that causes ear infections in children. Interestingly, an NIH study section said this couldn't be done with available technology. Ultimately, this approach became widely adopted.

In its first decade, TIGR has become one of the leading genomics institutions in the world, developing research critical to the fields of medicine, energy and environmental science.

With financial support from the National Institute of Allergy and Infectious Diseases (NIAID), the Institute has determined the complete genome sequence for forty microbial species, including important human pathogens that cause tuberculosis, cholera, syphilis, stomach ulcers, anthrax, and malaria.

In addition, TIGR has also sequenced a wide range of important environmental microbes—some of which live in extreme environments but may be critically important to the health of the planet—and that carry out a variety of interesting metabolic reactions, including degradation of cellulose and other organic matter, precipitation of heavy metals such as uranium from solution, and production of methane and hydrogen as potential new sources of fuel. These are areas relevant to the field of bioremediation and are of great interest to DOE.

TIGR has also played a leading role in the sequencing and analysis of many important plant species, including *Arabidopsis thaliana,* a small weed that serves as a model for understanding approximately 250,000 other more complex plants—rice, soybean, potato, and tomato among them. Together, these efforts are helping in the search for genes that control the rate of plant growth, yield, and resistance to diseases and drought.

The Institute for Biological Energy Alternatives will use microbes, microbial genomics, microbial pathways, and plants as potential solutions to carbon sequestration and clean energy production. IBEA will work to produce new fuels with higher

energy output in an environmentally sound manner, thereby reducing the production of carbon dioxide. In addition, IBEA will examine removing carbon dioxide from the atmosphere by using genomics to enhance the ability of terrestrial and oceanic microbial communities to remove carbon from the atmosphere. This work also could have a profound impact on the understanding of microbial biology and life definitions, as well as a better understanding of evolutionary biology.

The Center for the Advancement of Genomics is dedicated to incorporating the results of genomic studies into practical use and government policy through scientific and policy-oriented research, education, and enlightenment of the general public, elected officials and students. A particular focus will be to accelerate the pace with which genomics is incorporated into the practice of medicine. To this end, TCAG is building formal collaborations with academic medical centers to conduct the large-scale research that is the necessary foundation of the first fully-integrated genomic medicine practice. TCAG will also seek to better understand evolutionary issues, as well as broad social, public policy and ethical issues, such as genetic discrimination and the role of biology/genomics in mitigating greenhouse gas concentrations and biological energy production.

Indeed, it is because of the vast scope of genomics that TIGR, TCAG, and IBEA were created as nonprofit institutions that complement one another in their research efforts.

Each of these entities shares a common need for rapid, accurate, and low-cost DNA sequencing. Thus, we established a fourth nonprofit, the *J. Craig Venter Science Foundation Joint Technology Center,* which will provide sequencing and informatics support to the research institutions. The JTC, which functions as both a resource and technology development center, will work collaboratively with a wide variety of technology leaders in the private sector, as well as with academic and federal scientists, in our work to advance the efficiency and lower the cost of genomic sequencing.

The JTC will utilize the latest in automated DNA sequencing, supercomputing, networking, and high performance storage technologies to rapidly and accurately sequence and analyze genomes in a more cost-effective manner. The JTC will have a sequencing capacity of 45 million "reads" per year by late 2003 and an ultimate capacity in excess of 100 million "reads" per year. The JTC will support the DNA sequencing needs of TIGR, TCAG and IBEA. A goal of the JTC is to substantially reduce the cost of genomic sequencing so that everyone can benefit from the great promise that genomics holds.

The fifth organization, the *J. Craig Venter Science Foundation* provides administrative and legal support for, and coordinates policy and research activities between, these organizations. In addition, the Foundation explores new ways to foster science education and scientific innovation.

Mr. BILIRAKIS. Thank you very much, Doctor Venter.

Doctor Khoury, you are on, sir.

STATEMENT OF MUIN J. KHOURY

Mr. KHOURY. Good morning. I am, indeed, honored and privileged to be here with you today, especially with these gentlemen on my right-hand side. I must admit I personally or CDC had nothing to do with the sequencing of the human genome, but I suppose we are here to describe what happens next and how we can begin to integrate advances in genomics into disease prevention and public health.

I'd like to describe to you a little bit of CDC's priorities in genomics that, essentially, complement and try to achieve NIH's vision and put it into reality for the next few years. CDC, as the Nation's prevention agency, is working with NIH very closely and with many partners, including our State and local health, to begin to close this widening gap between gene discovery and our ability to use genetic information to improve the Nation's health and prevent disease.

I think we have a long way to go to help translate gene discoveries and to figuring out what genes mean for health and disease in real communities and real time and, perhaps, more importantly,

how we can use that information and what its value-added is going to be for the factors of disease prevention and to improve the health of our citizens.

CDC has developed three priorities for applied genomics research that I'd like to tell you about briefly, and they directly tie with prevention programs that already exist at the State and local levels.

First, is assessing how genomic factors influence population health. CDC uses epidemiologic studies to examine the impact of genetic variation on health and disease in real communities, and how such variation interacts with environmental causes of disease, such as infectious agents and environmental factors, which are the usual target of public health interventions. Integrating genomics, for example, into the acute public health response, (for example investigation of infectious disease outbreaks, will be a critical challenge. Genomics, undoubtedly, will provide new incites into why some people will get sick, but not others given the same exposures. And, this information will be more and more essential to target interventions to reduce the burden of disease in the populations.

The second priority will be in assessing the public health impact of genetic tests for screening and prevention. CDC is providing a public health assessment of genetic tests with a special focus on screening. The recent direct-to-consumer marketing of genetic tests for breast and ovarian cancer is the first such effort to increase awareness of genetic testing in an entire community. CDC is assessing changes in women and health professionals' knowledge, attitudes and behaviors toward genetic testing. This kind of public health assessment will give timely information on genetic tests that will help guide policy and practice. It will show what information is working and what is not working, as we all try to examine the transition of genomics from research to practice.

The third area of priority is assessing family history as a tool for prevention and public health. Advances in genomics have highlighted family history as one of the most exciting, but under-utilized, areas in public health. All of us have the family history of one or more diseases in our relatives. This family history, for the most part, reflects combined effects of numerous genes, along with many shared environmental factors, such as diets and behaviors. And, the bottom line is, for most diseases we are at increased risk of what runs in our families. Family history then may be useful for stratifying risks and developing early disease prevention messages.

In 2002, CDC, along with NIH and others, initiated a public health effort to develop and evaluate in the community family history tools starting with four common chronic diseases, heart disease and stroke, diabetes and colorectal cancer.

We expect that a fully developed and implemented applied genomics research agenda with these three priority areas will begin to produce practical information that would lead to the integration of genomics into community prevention programs that actually work.

In addition, to develop public health workforce competency, CDC keeps responding to State and local requests for training and technical assistance. For example, we've established three centers for genomics and public health at three schools of public health, to prepare professionals for genomics in the 21st Century.

In closing, public health assessment and research will assess the ability and impact of genetic information in practice in the real world. It will ensure that all segments of the population will benefit from new genetic knowledge.

If I may elaborate a little bit on the wonderful image of the genomics building that Doctor Collins showed us earlier, truly the success and functionality of this building will depend on the foundational infrastructure of what's already happening in health care and public health systems, including the flow of essential utility like gas, power and electricity. With that we can make this building work in real life.

And, it's part of the crucial work that CDC and many partners, including State and local public health, must do in order to get this building up and running on a daily basis. This work is essential to close the widening gap between gene discovery and the ability of genetic information to improve the Nation's health and prevent disease.

Thank you for your attention.

[The prepared statement of Muin J. Khoury follows:]

PREPARED STATEMENT OF MUIN KHOURY, DIRECTOR, OFFICE OF GENOMICS AND DISEASE PREVENTION, CENTERS FOR DISEASE CONTROL AND PREVENTION, DEPARTMENT OF HEALTH AND HUMAN SERVICES

Good morning. I am Muin Khoury, Director of CDC's Office of Genomics and Disease Prevention. I want to thank you for the opportunity to discuss CDC's role in integrating advances in genomics into disease prevention and public health. I will describe CDC's work in translating discoveries in genomics into improvements in public health that complement NIH's genomics research agenda. In this genomics era, we need the entire research continuum, from gene discovery to development of practical tools, for integrating genomics into population-based disease prevention programs. In this context, the applied public health research at CDC will evaluate what genes mean for health and disease in real communities in real time and, as importantly, how genomic information can be used to improve the public's health. (1)

CDC, the nation's prevention agency, is keen on integrating new genomic knowledge into public health strategies through training of public health professionals, education, and information dissemination to the public. CDC activities encompass a large array of topics such as acute communicable diseases investigations and developing prevention programs for common diseases like diabetes and asthma. In anticipation of the impact of genomics on all aspects of health, in 1997, CDC developed a strategic plan and formed the Office of Genomics and Disease Prevention (OGDP) to help integrate genomics into public health research, policy, and practice at the national, state, and local levels. (2) Over the past 6 years, the Office has provided national planning and assistance and has developed partnerships with other federal agencies including NIH, public health organizations, professional groups, and the private sector. CDC has initiated a number of public health research projects to assess the impact of genes on the risks of chronic diseases, birth defects, and infectious, environmental, and occupational diseases to specific populations. On May 5, 2003, CDC held a symposium on Genomics and the Future of Public Health to take stock of the great accomplishments in genomics, and to look at how we can best use these accomplishments to maximize their public health benefit. (3)

Applied public health research in genomics is critical to building disease prevention capacity and programs at the state and local levels. In consultation with our partners, CDC has developed 3 priority areas for applied public health research in genomics that will be essential in the next 3-5 years. (1) As I tell you about each of these priorities, I will also highlight some of the ongoing collaborations with the NIH in these areas.

1. Assessing how genomic factors influence population health

CDC uses epidemiologic studies to examine the impact of genetic, environmental, and behavioral interactions on population health. Integrating genomics into the acute public health response, (for example investigation of infectious disease outbreaks, toxic exposures, or adverse events following vaccination) is a critical chal-

lenge for public health. Genomics can provide new insights into why some people but not others get sick from certain infections, environmental exposures, and behaviors. Knowing who will or how many are more likely than most to get sick is useful to targeting behavioral or pharmaceutical interventions and reducing the population burden of various diseases. Understanding the population prevalence of the thousands of genetic variants in different population groups and geographic locations and their associations with health and disease is crucial for planning screening programs and guiding future research. A CDC-wide team recently identified more than 50 genes of public health importance (e.g. genes involved in metabolism of cancer-causing chemicals, and those involved in nutritional factors like folic acid) and has proposed measuring population variation of these genes from stored DNA samples collected during the third National Health and Nutrition Examination Survey (1988-1994), a national representative sample of the US population. (4) This work is planned in collaboration with NIH. Understanding the prevalence of genetic variability in the population for these genes is crucial for public health program planning and future research.

2. Assessing the public health impact of genetic tests for screening and prevention

CDC is evaluating the use of genetic tests as tools for disease prevention. Population screening, a traditional public health interest, requires special attention in this rapidly evolving scientific, social, and legal context. The recent direct-to-consumer marketing of genetic tests for breast/ovarian cancer is the first of many commercial efforts to increase consumer awareness about the potential value of genetic tests in health care or disease prevention. CDC is exploring collaboration with the industry developing these tests to determine the current level of utilization as well as knowledge, attitudes, and behaviors of consumers and health care providers. A population-based approach in collecting valid clinical and laboratory data will ensure that consumers, practitioners, and policy makers have access to timely and current information on genetic tests in the real world and their impact on the public's health. These efforts will also allow a smoother integration of validated genetic tests into practice. One example of these efforts is a 1997 expert panel workshop jointly held by NIH and CDC to explore issues around population screening for iron overload due to hereditary hemochromatosis, including the cost effectiveness of screening for this condition. (5) This collaboration led to the identification of important gaps in research about this condition, some of which are currently being addressed by NIH-funded research. As new research findings emerge, CDC will continue to translate scientific knowledge into useful and effective public health strategies, such as its physician training program that promotes family-based detection of hemochromatosis.

3. Assessing family history as a tool for disease prevention and public health

Family history of disease can reflect the interactions of multiple genes with many risk factors such as diet and behaviors. Although family history is routinely collected in health care encounters, it is inconsistently used to guide individual health care and disease prevention. In 2002, CDC initiated an interdisciplinary public health research effort to develop and evaluate family history as a public health tool for identifying families at increased risk of common chronic diseases and intervening to prevent disease by effecting positive changes in health behaviors. (6) A large proportion of the population has family histories for one or more of the common chronic diseases where people are at increased risk for these conditions as a result of shared genetic, environmental, and behavioral factors. A multidisciplinary working group from CDC, NIH, academia and professional organizations is developing a prototype family history tool for use in assessing adult risk of several common chronic diseases (including heart disease, diabetes and colorectal cancer). This tool will be tested and refined through a series of pilot studies in a variety of community settings. Ideally, it will be used to reduce the burden of chronic diseases by providing personalized risk reduction messages.

Concluding Remarks

A recent report by the Institute of Medicine identified genomics as one of the eight cross-cutting priorities for the education of all public health professionals in the 21st century.(7) In addition to public health research on genomics, since 1997 CDC has been promoting the integration of genomics across all public health functions including training and workforce development. In collaboration with many partners, CDC developed public health workforce competencies in genomics (8), established 3 Centers for Genomics and Public Health at schools of public health to develop training and provide technical assistance to state and local health departments (9), and is actively engaged in offering training and career development opportunities in genomics and public health (10). As public health programs become

increasingly capable of using genomic information in preventing common diseases, CDC is committed to sustaining research that ensures the integration of genomics and family history into prevention efforts at the state and community levels.

In closing, as we enter the genomics era, CDC realizes the importance of research that answers practical questions about the utility of new science for the public's health. A balanced research portfolio in genomics, from the test tube to public health research in the "real" world, is essential. Public health research allows the nation to have a "reality check" on how genetic information is being used in practice and ensures that all segments of the population will benefit from new genetic knowledge. The translation from basic research to the more directly applied research by CDC allows us all to capitalize on the phenomenal achievements of the Human Genome Project to improve health and prevent disease for citizens of the 21st century.

Thank you for your attention. I will be happy to answer any questions you may have.

Mr. BILIRAKIS. Thank you very much, Doctor Khoury.

Well, I will start the questioning. I can't tell you how pleased I am to at least hear you talk, hopefully, of what reflects the real world and what's happening out there, of the cooperation, the collaboration, to use some of your words, the interaction and what not, that takes place among all of you and, hopefully, that reflects what truly takes place, not only at your level, but at every level of the research community.

Let me ask first that question. Is that true, is that a true assessment on my part? Are there any problems? I mean, isn't there—politics exists everywhere, I always say that probably the least bit of politics is in Washington, DC, because we all kind of know each other, we all have labels and things of that nature, which the politics that takes place in our real world, such as in our churches, in our clubs, in our families and what not is amazing, and sometimes I think it's much, much worse than what takes place up here. We usually get along pretty well.

But, so from a politics standpoint, from a competitive standpoint, are there problems out there, and if there are, is there anything that we can do to help out in that regard? Or, is everything honky dory, as you seem to make it?

Mr. COLLINS. Let me start. I think that in general things are in very good shape, Mr. Chairman, and I think one of the main reasons for that is that the interactions between our respective agencies occur at all levels, and they are primarily based upon scientific opportunity.

In my experience over 10 years, having this incredible privilege of overseeing this international project, to sequence the human genome, the reason it worked is because the scientists at every level, from the principal investigators, to the technicians working at the bench, to the funding agency heads, all believed in this as a goal that was extremely compelling from a scientific perspective and a public health perspective. And, I've often reflected what might have happened, for instance, on the international scene, if the effort to sequence the human genome project had been imposed upon the scientific community by, say, their ministers of health and ministers of science. I'm not sure it would have worked out so well, because it really was a bottom-up, grassroots enterprise, and it was based upon science and a shared sense of the vision. It worked remarkably well.

Now, I won't tell you that there was always pure harmony in our weekly conference calls 11 on Friday mornings, there were often

some jitters and bruised feelings about this or that, but there was never any wavering from the sense that we were in this together, the stakes were very high here, we had to succeed. Failure was not an option, and that came up out of the scientific vision and passion that everybody felt. I think that has characterized the way in which we've interacted with the Department of Energy, my friend Ari Patrinos and I live very close to each other in the same group of townhouses. We have breakfast at the Silver Diner on a regular basis that nobody else gets to go to.

Mr. BILIRAKIS. Owned by a Greek probably.

Mr. COLLINS. But, we do, in fact, I think on a regular personal individual level, make sure that things are on track.

I was just at the CDC a few weeks ago for a wonderful symposium they had on genomics, spoke with Doctor Gerberding about our shared vision of this future for genomics in public health, again, person to person, talking about the science, that works really well.

Mr. BILIRAKIS. Did Doctor Collins reflect, basically, the viewpoint of the rest of you? This is your opportunity to, basically, you know, tell us and tell the world if you've got any problems there or whatever.

Mr. VENTER. I think we'd be remiss not to point out that competition plays a very healthy role in almost every aspect of our society, and the scientific community is certainly not immune in any way from that.

And, I think competition in genomics has probably resulted in us having the genome sequence today instead of at the end of this decade, and so it certainly benefits the public at large. I think a lot has been made in the press about the so-called competition between Doctor Collins and myself, but I certainly applaud Doctor Collins, and particularly our referee, Doctor Patrinos, who with pizza and beer diplomacy led to wonderful cooperation and timed simultaneous publications in this field.

I think competition needs to be encouraged to move things faster, to lower cost, to make sure that Federal programs don't get stagnated, and I think all that needs to happen is to make sure that that competition is truly open and productive. And again, I applaud Doctor Collins for recently opening up the competition on the Federal grant cycle for new genome centers.

So, I think we are very much moving in the right direction. Nothing is ever rosy in any group, but I think competition is probably the most healthy thing we have in this country.

Mr. BILIRAKIS. Yes, Doctor Khoury.

Mr. KHOURY. I'd like to echo what Doctor Collins said earlier. I mentioned earlier that CDC had, essentially, no role in the human genome project thus far.

Mr. BILIRAKIS. Yes.

Mr. KHOURY. But, we alwaysI mean, since the formation of our office in 1997 we've maintained and continued an active dialog with NIH and several other agencies. We held to gather national conferences on genomics and public health, actually, we had three of them so far, and as we embark on the next phase I see that there will be increased cooperation and collaboration and more synergy after the completion of I guess the end of the beginning, or the be-

ginning of the end, whatever you said, Doctor Collins, from here thereon we are going to translate together what it means for real people and real time, and that I expect will occur.

And, as Doctor Collins mentioned, he's had active discussions with our boss recently, and will continue to have those.

Mr. BILIRAKIS. Because all of the great work that they do, and their people do and others like them do, if it isn't used, if it isn't put to real use to help people, you know, what good is it, I suppose is one way of looking at it. Isn't that right, Doctor Khoury?

Mr. KHOURY. Right.

Mr. BILIRAKIS. And so, you feel that you see CDC and other departments, and agencies, and offices and what not, which directly deal with, you know, our people, are able to put these into use. You have great cooperation in that regard.

Mr. KHOURY. Yes, I hope so, I mean that's, to me, the ultimate goal of what we are doing here, is to put into action all that great science, and it really has to be built in on a platform of already existing prevention services and public health approaches in what we do. And, we have to together evaluate the value-added of what it means, and how and when it's going to change the way we do business and the way we promote chronic disease prevention, for example, or investigate infectious disease outbreaks, to name a few.

Mr. BILIRAKIS. I have a couple more things, and I'm just going to defer at this point in time and announce, for those who have been here, Ms. Capps, Mr. Green, Ms. Eshoo, if she returns, we will have a second round if anybody is interested in doing so. But, I would now yield to Mr. Brown.

Mr. BROWN. Thank you, Mr. Chairman.

I want to thank both Doctor Collins and Doctor Venter, without the intervention of referee Patrinos, for your comments on the non-discrimination, the genomic non-discrimination issue. Thank you for your support on that, and I hope the three of us, and many beyond, can work on that together. Thank you for that.

I wanted to talk about something that hasn't been brought up, that I would expect especially Doctor Collins and Doctor Khoury might have thoughts about, with their involvement with NIH and CDC, the issue of antibiotic resistance, the whole antimicrobial resistance, antiparasitic resistance, antiretroviral resistance. There are, obviously, it's a growing problem, obviously, in this country, and domestic health and international health, domestic health especially with staph infections, strep, other diseases that can, ultimately, be life threatening certainly international, probably the biggest problem is what's happened with tuberculosis, as you know, where in the Russian prison system where I visited 10 percent of Russian prisoners have tuberculosis, 25 percent of those have multi-drug resistance tuberculosis. Would the two of you especially, because we have charged CDC and NIH to participate in an interagency task force on antimicrobial resistance, and we have come forward with more ideas about how to deal with this issue, we clearly don't have enough new antibiotics, new powerful antibiotics in the pipeline, where does your work come together? Is there some synergy with those agencies, coupled with what's happening with the Human Genome Project, and can we see, can we expect to see

some synergy there that could help us deal with this more quickly and more optimistically, perhaps, than we are today?

Mr. COLLINS. So, I will start, and, yes, I think that's a very important subject, and one where genomics does have a lot to contribute. I will say at NIH my colleague, Tony Fauci, is the lead in this particular arena, as he directs the National Institute of Allergy and Infectious Disease, and is the major source of funding for sequencing of microbial genomes and the application of that information to try to understand resistance and to develop new antibiotics.

But, I think that, this topic in fact, is a major reason for excitement about the field of genomics as applied to pathogens. Doctor Venter already mentioned the example of malaria, where here we finally have the genomes for the culprits, and we can, therefore, begin to design, in a very intentional molecular way, the strategies for the future.

We have the genome of mycobacterium tuberculosis, the agent of TB. I've worked in Africa as a volunteer physician, and the ravages of that disease in parts of West Africa are truly, truly distressing, and we don't have good drugs in that circumstance that take care of the disease quickly enough, and there's a lot of resistance, as you well know, in that circumstance as well, because of inadequate treatments leading then to the spread of partially resistant strains.

So, I believe between NAIAD and CDC there is a very strong recognition and a determination to do something about it, of this problem. The information provided by understanding the full instruction book of pathogens, from staphylococcus on down the line, provides us with new insights into ways to interfere with their growth and, therefore, design new antibiotics that are totally different than the ones we currently have, many of which, as you point out, are not as useful as they used to be because of the resistance problem, but we have to continue to work very hard to stay ahead of the curve in this rapidly developing, worldwide problem of antibiotic resistance.

I think we have a good set of tools and a good strategy, but it's going to take a lot of work, a lot of hard research, a lot of funding.

Mr. KHOURY. Thank you for the question.

To echo Francis' remarks, the CDC has taken the issue of antibiotic resistance very seriously, and there is the counterpart to the NIAID. We have at least two centers that deal with infectious disease issues.

And so, I think from the perspective of the discussion today and our involvement in developing general tools that could be used for genomics in public health, we have, for the most part, at least the discussion that I mentioned earlier, focused on the human genome and the genetic variation in people, but it's, basically, the bug genomes that have to be dealt with as well.

I mean, you mentioned earlier, Francis, the characterization of the SARS virus very quickly, and those things have to be taken into account together, because eventually it's genome versus genome, and antibiotic resistance may be one of those mechanisms that the genomes are adapting to our genome.

And so anyway, to get to the specifics of what CDC is doing in antibiotic resistance I will have to confer with the leaders of that effort at CDC and get back with you on that.

Mr. VENTER. I think the issue you raised is one of the most important healthcare crises we are facing right now, not only in this country but worldwide.

Our team has decoded most of these pathogen genomes, and in every single one we found a novel mechanism of how they constantly evolve in real time to avoid our immune system and to develop resistance against our antibiotics. So, we have to have a continuing warfare against them.

We made the mistake in this country at the end of the '60's of saying we've won the war against antibiotics, and microbial departments shut down around the country, as did funding. We are now spending more, actually billions of dollars, just for drug resistance staph aureus, that's almost as bad as the pre-antibiotic era. And, in the midst of this crisis we have our major pharmaceutical companies shutting down their antimicrobial groups, laying off their entire teams, because these are short-term, acute products, not the long-term chronic ones they need.

I absolutely applaud what the President is doing with the initiative, with the bioshield initiative, because that's providing at least a unique type of incentive for biotech and pharmaceutical companies to try to develop new vaccines, new antibiotics, new antivirals.

While I'm very discouraged and pessimistic of what I see on that side, the genomic side of what we do see also gives us hope. I think the best example of this is the collaboration that TIGR had with Kyron Corporation to develop a new vaccine against meningitis, within the same time period of less than a year that it took to sequence that genome we, with the Kyron team, found several new self-surface antigens that turned out to be very susceptible for antibody development, and there's now two new vaccines in clinical trials. It's the fastest, from start to clinical trial, vaccine development to date.

And so, genomics can that us in that direction, but somehow our major healthcare companies are abandoning it, in part because of liability issues, in part because they don't see the right profits there, so nobody has incentive to do something about tuberculosis. We have very little incentive in this country to do something against malaria, those are thetuberculosis is the biggest infectious disease killer of adults in the world.

So, genomics can help with the answer, but only if there's the infrastructure to deal with it, and we are losing it very rapidly.

Mr. WATERSTON. Yes, I think of it in this larger context of the long-term struggle that we are in with the microbial world. This is an arms race between us and microbes, and genomics, not only gives us the hope that we can understand the particular susceptibilities of pathogens, but we can also understand our own defense mechanisms against those.

And, by this integrated approach to understanding how we can fight these pathogens, we should be able to come up with much more effective strategies. But, it is a long-term approach, and it's not going to be something that is going to turn around things immediately.

Mr. BILIRAKIS. Mr. Green.

Mr. GREEN. Thank you, Mr. Chairman.

Doctor Khoury, in your testimony many of the illnesses you talked about, for example, that you work on at CDC, are either caused or exacerbated by behavioral factors. For example, we know that tobacco use causes a host of health problems, including cardiovascular, lung and certain cancers, and elevated blood pressure and others. Additionally, we were troubled by the recent article in Health Affairs indicating the cost to treat obesity related to illness now was equal to that of tobacco-related illnesses. All this occurs despite the fact that as Americans we've known for decades that smoking and sedentary lifestyle and poor diets are unhealthy.

I appreciate the knowledge that risk factors may encourage individuals to change their behavior, but certainly with the obesity and overweight problem in our country that doesn't seem to be the case. Certainly, there are genetic influences in these cases, and I know certain individuals are predisposed to certain conditions, but behavior does play a part in these cases.

How can genomics research affect human behavior, and aren't lifestyle factors always going to be a problem, even if we do inherit our genes?

Mr. KHOURY. Thank you for this question.

Actually, this is a very pertinent question, because as I mentioned earlier the traditional public health routes of intervention have been not on the genomic side, except for the bugs, but on the environment side, which means behavioral change, diet, exercise, putting fluoride in the water, et cetera, et cetera. And, I think the genomics era is opening up the possibility to understand the whole domain of gene environment interaction, or gene behavior interaction, or gene infectious disease interactions, in order for us to do better on the environmental side. Let me be a bit more specific.

Our family history initiative, for example, one of the three areas I talked about, essentially, builds on what the existing messages are for disease prevention, physical activity, diet, seek, you know, preventive testing for colorectal cancer early on, and we know as society we have our traditional one-size-fits-all public health messages has only given us partial success so far. Two thirds of the population are still overweight or obese, only 20 percent of people exercise daily, and the statistics are really not in our favor.

So, family history, the way we conceived it, was an additional tool to target and personalize the prevention messages to people who need them. That doesn't mean our traditional public health messages should stop, on the contrary, but for a substantial fraction of the population that is at high risk because of the genes that they have inherited, although we don't know what they are yet, and we probably can't measure them for at least a few years, part of the public health approach we are developing is developing those tools that would be used in community settings to change behaviors and personalize the messages on seeking appropriate early interventions and physical therapy, and it's not going to be easy because behavior modification is very hard to do, and no amount of genomics is going to cure that in a hurry. So, there is a long way ahead of us.

Mr. GREEN. When scientists talk about populations when discussing genetic distinctions within various diseases, what should we be looking for as paradigms we should have in mind in assess-

ing genomic and prototomic advances so that we know whether appropriate distinctions are made, again, dealing with these special populations?

Mr. KHOURY. I'm not sure I understand the question, what do you mean by that?

Mr. GREEN. Is there an effort that's being done with—well, for example, racial or ethnic differences in these special populations?

Mr. KHOURY. Our population approach at the CDC, to understand the distributional genes in the whole population and the various groups, essentially, focuses and treats all the populations in a way that will give us enough statistics and information to generalize the intervention messages to appropriate groups. For example, the M. Haines Project that is in my written testimony, which is a national representative sample of the U.S. population and all the ethnic groups in it, essentially, will lead to information that's generalizeable on the prevalence of important genes that may be relevant to a wide variety of diseases.

So, our approach is, essentially, to understand what's going on in the whole population and then try to deliver the interventions that work for everybody.

Mr. GREEN. Thank you, Mr. Chairman. I know I have brief time left, and I'd like Doctor Venter or Doctor Collins to respond if possible.

Mr. BILIRAKIS. Oh, by all means. I know Doctor Venter has been trying to get your attention, too, so you have the time.

Mr. GREEN. I'd like to have a response from him.

Mr. VENTER. Well, I'd just like to add a little bit to the comments that were made. I think the partial answer to both your questions get down to what we define as personalized medicine. I can give you a case history of one, and I think when we give people sort of very generalized information that you should lose weight, or you should exercise more, we all know that, but people who smoke, for example, look for the exception of the 100-year old three-pack-a-day smoker and say, see, there's really no correlation.

I think understanding our own direct genetic predisposition for some diseases takes it from the general to the specific. In my own case, I knew I had a very strong family history of heart disease, but until I learned from looking at some aspects of my own genetic code that I had genetic changes where I could see a very specific risk factor, did I start to take it much more seriously.

So, I think going from general information that we have down to the specific individuals, it may not be a panacea for everybody, but quite often after somebody has a heart attack they have much more incentive for exercising and eating right, maybe we can move that forward a few steps and get it from looking at the genetic code.

On the race issues, I think this committee, this panel, would certainly probably agree that, both Doctor Collins and I have commented on it extensively, we don't think race is a scientific concept, it's a social concept, and so this attempt with categorization based on census categories to applying that to drug responses we think is a very dangerous trend. And again, as you get down to individual medicine, what we want to know are the group categories that would indicate a response to a drug or a treatment, not some-

body's skin color where we doubt that there will be any correlation whatsoever.

Mr. COLLINS. If I could just expand briefly on that. I agree that we need to be very careful in using racial designations as if they had strong biological context and significance. At the same time I think we are all deeply disturbed about health disparities, for instance why is it that prostate cancer occurs at a higher frequency and with greater lethality in African American males than it does in Japanese males? Why is it that diabetes is so common in the Pima Indians?

One should not assume by that observation that that means it is somehow hard wired into DNA. It could well be that a lot of the health disparities that we observe are related to other things that are in the environment, among which are, of course, diet, cultural practices, socioeconomic status and access to healthcare. They are all in there.

So to point the finger at DNA is probably a mistake at the onset. At the same time, we do know that there are some variations in DNA that tend to occur at a different frequency depending on where your ancestral geographic origins happen to be. And, it may be that some of those variants will account for some part of those health disparities and we need to learn that as soon as possible if we are going to apply this sort of personalized and benevolent medical care to everyone.

But, I think of race as a surrogate, for a surrogate, for a surrogate, in terms of what we really want to know. What we really want to know is what are those individual variants in your genome or mine that place us at risk for illness and that might have an effect on whether we respond well or badly to a drug intervention. That is very poorly reflected by the Census designations of race, very poorly, but it's not a complete disconnect, there may be a weak correlation there which may be why people are making claims of this sort.

We need to, as quickly as possible, move beyond this blurry and potentially stigmatizing and misleading information based upon race to the precise genetic information which is going to be medically more valuable and also much less likely to add to the prejudicial aspects that all too often color the conversations about race and health, or race and anything else.

Mr. GREEN. Thank you, Mr. Chairman. I appreciate, again, representing a district that's predominantly Hispanic and the concern about diabetes and a host of other things in a Hispanic community, it's good to know it may not be genetic based, but, obviously, cultural, environmental, and that's something we can deal with.

Mr. COLLINS. We need to figure that out.

Mr. GREEN. Mr. Chairman, thank you again. I'd also like to join my colleague in thanking Doctor Venter about the most important legislation is the deal with the genetic discrimination issue that's out there, and, hopefully, we'll be able to deal with that this session.

Thank you.

Mr. BILIRAKIS. Ms. Capps.

Ms. CAPPS. Ditto on the genetic discrimination. I'm on the bill as well.

I'm sitting here looking, Doctor Collins, at your structure, and the Human Genome Project at the foundation to me feels, in this discussion, as like the floodgates, and that it kind of is, what's now, and I know it's already, what's next is already happening, and has been happening for a long time.

Maybe I'm going to betray my vitae, but I would like to hear from you, Doctor Collins, well from anyone actually, and maybe all of you, on how the decisionmaking process, in terms of choosing or going the next step after the gate, after coming out of the starting gate, research as kind of ethical decisionmaking, we can't do everything, at least not all at once, and what guides you, both in NIH and then from the public/private sector as well, and from the teaching facilities, perhaps, as well.

I'll give you one example of where I was participating in this body that I work in, in terms of some decisionmaking regarding stem cell research and therapeutic cloning, where I think we just totally went ideological without understanding. And, I guess I bring that example up because I think we need, in this body, a lot of guidance because we are going to be related to your decisionmaking process in terms of how we allocate funding, and I take that really seriously.

With Parkinson's, I hear Shared talked about drug resistance, and, you know, there are ethical decisions that are at the basis of this, and I guess I'd really be interested in how you do and how we should make some decisions in that arena.

Mr. COLLINS. Thanks for the question, Congresswoman Capps. I think you are absolutely on target, that we have to be very explicit and careful about how we set the priorities for the next phase, because saying that now the floodgates have opened up and we have all sorts of opportunities is both an incredible blessing and a historic moment, but it's also a great responsibility.

We knew many months, many years ago, that we would, if all went well, finish the goals of the Human Genome Project, which have directed our efforts since 1990. Not wanting to get to that finish line and sort of look around and say, "oh, gosh, what are we going to do next," we, in fact, have been planning for that for several years in a very formal planning process to lead up to this vision for the future, which is a science-based, priority-setting exercise. It began just about 2 years ago in the summer of 2001.

We convened, over the course of those 2 years, a series of about 14 separate workshops, some of them on specific topics, like what can we do now to understand the variation in the human genome that influences disease risk, that was one of them that was particularly interesting. What could we do now about proteomics? What could we do now to expand and accelerate the rate by which we go from gene discovery to drug treatment development? How can the academic sector participate in that in a more vigorous way?

In the midst of all those specific topic discussions, we also had a large meeting, about a couple hundred people, at the beginning of the process and another near the end, to take the temperature about whether we were getting it right from all of these inputs. All told, some 600 or more scientists, both from the public and the private sector, and both from the U.S. and abroad, dropped everything to come to these meetings, and we rarely got turned down by any-

body who was invited to come and be part of this process, because they were all excited about it and appreciated its importance.

Out of that process we originally prepared a draft of this document. It was presented in a public meeting to a couple hundred scientists back in November. They liked a lot of it, they hated some parts of it, so we tore those parts up and rewrote them. We depended upon our own advisory council, a distinguished group of senior scientists, for input in this, and, ultimately, the final draft then got recirculated to all of the major leadership of the last two or three major gatherings, until they were happy with it, and then it was published in a very visible journal for all the world to see this past month.

So, I think as planning processes go, this one was pretty thorough. It also involved every single one of the other NIH institutes, they all had major participating roles in the definition of what the priorities should be, because we wanted them not to look at this as our document from the Genome Institute, but their document that would guide their priority setting as well, and we had multiple involvement from other agencies as well, from the Department of Energy, from the CDC, from NSF, from USDA, all of whom had a chance to put in their dibs in terms of what they thought the priorities ought to be.

Now, this is not going to be a document that just sits there to guide us for the next 10 years. We will have to revisit this on a very regular basis, because things change so quickly. But I do think from a scientific perspective, a medical perspective, and, yes, even an ethical, legal, social and policy perspective, this document aims to accomplish what we are asking for, and I'm pretty confident that we have captured in that process for human health the areas that we ought to pay the most attention to.

Now, some of our colleagues have their own planning process. Doctor Patrinos has already described to you the Genomes To Life process that they followed with the DOE's enterprise, which is nicely complementary to what NIH is doing. The CDC has had their planning process, which we've been fortunate to be part of, all of us talking, I think rather closely, with each other.

So, I think we could, basically, put this forward as a pretty good model of how to arrive at priorities, recognizing that those priorities will have to be revisited very regularly.

Ms. CAPPS. Mr. Chairman, I would hope that at least I could get a copy, if you think it's appropriate, for our discernment, because I think it would be useful for us to have that information as we make some decisions that affect at least the dollars that you work with.

Mr. COLLINS. A copy of the process that we followed?

Ms. CAPPS. And where you are now.

Mr. COLLINS. Yes, this document is, this captures, basically, in the series of 15 grand challenges——

Ms. CAPPS. Okay.

Mr. COLLINS. [continuing] that you see outlined here, what those 600 people said ought to be our highest priorities.

Mr. BILIRAKIS. Without objection, we'll make that part of the record.

Mr. COLLINS. That would be wonderful.

Ms. CAPPS. So that this could be then our working document as well.

Mr. COLLINS. That would be fabulous.

Ms. CAPPS. Thank you, surely.

Mr. PATRINOS. I'm very pleased to say that we followed, as Doctor Collins said, a very similar process with our Genomes To Life program over the last 2, 2½ years, primarily led by our Biological and Environmental Research Advisory Committee, again, a committee of distinguished scientists from the academic community, from industry, and from our national laboratories, but extending also much beyond to the broader scientific community that participated in similar workshops.

There was an additional dimension for us, because we knew as the end of the Human Genome Project was coming up we would be shifting more and more toward the microbial genomics, which is also an effort that we had started in the early 1990's and, therefore, we saw a significant shift in what we were doing on human genomics to microbial genomics.

And, I'd like to use this opportunity to take issue a bit with my colleague, Bob Waterston, when he declared war against the microbes, and to tell you that only a very, very small percentage of that microbial world is pathogenic.

Ms. CAPPS. Yes.

Mr. PATRINOS. The rest of it is, in fact, the actors that are enabling the whole process of life to happen. So, I rise in their defense.

Thank you.

Mr. WATERSTON. I stand corrected.

Ms. CAPPS. Are there other comments? Go ahead, until I get banged down.

Mr. VENTER. I just wanted to pick up very quickly on your stem cell comment, because I think that's one of the most important issues facing a combination of what Congress does and what the scientists do. The best laid plans can go awry when one of the most important areas in modern biology, probably one of the few means that we have of understanding how we go from 1 cell to 100 trillion cells if we can't undertake adequate research in that field. And so, we go from what appears to be a complex field of science to public slogans that has basically derailed and is taking a very big risk of putting the U.S. much behind the rest of the modern research world in this field.

And so, I would turn the question back to you, how do we get it so we can educate Congress appropriately on these issues, so we don't have this type of disaster again?

Ms. CAPPS. I take that challenge, I think it's one that we really need to be very, very thoughtful and as deliberative as we can, and I would suggest to my colleagues that the process that Doctor Collins described, and I'm sure there was not unanimity all along the way, is one that you were willing to set aside that much time to do. And, I would agree that it's that important that we all also in this body ought to be willing to set aside some differences and really use your process as a way to focus on how we can be supportive and not impede that, and also mindful of ethical roles that we need to play as well.

Yes?

Mr. KHOURY. In addition to the processes that you just heard, I mean CDC has gone——

Mr. BILIRAKIS. Where are we here?

Ms. CAPPS. I was hoping you would keep talking, Mr. Chairman.

Mr. BILIRAKIS. Well, all right, just go ahead and respond. She takes advantage of me every chance she gets.

Mr. KHOURY. In addition to the scientific process for choosing priority, the CDC is primarily driven by the need to develop practical tools that work in real life. And so, we tend to listen a lot to our primary constituents and State health departments and local health departments, and we have been regularly convening and talking with these people from the health officers, the State epidemiologists, each State has chronic disease directors, maternal child health directors, and as a matter of fact last year the chronic disease directors got together and developed their own plan of action, which focuses on 4 or 5 priority diseases, including cancer, heart disease and obesity, and asking CDC to developtake the knowledge from the lab and translate it into meaning that affects their practice and what it means to deliver prevention programs at the State and local level. So, this is another set of constituents that we relate to, and, obviously, it has to be driven by the best science that's available, and that's why the collaboration and dialog across agencies occurs.

Ms. CAPPS. Excuse me, if I could just comment, Mr. Chairman.

Doctor Khoury, in some ways you are like us at CDC, I see, because we have constituents, they are the same ones.

Mr. KHOURY. Right.

Ms. CAPPS. The county doctors and medical personnel in our communities. And, we go home also and get that read from our constituents in that same way.

And so, you are balanced within this panel, I appreciate very much your being here today.

Thank you.

Mr. BILIRAKIS. And, I'm going to probably hitch hike on that in a moment.

Mr. Strickland, to inquire.

Mr. STRICKLAND. Thank you, Mr. Chairman, and I want to thank the witnesses. I think you represent the heroes of our time, and you may not feel that way about yourselves, but my colleague, Ms. Eshoo, and I were sitting here earlier and as you were testifying she was saying, "This is the kind of thing that our government, as representatives of the people, should be supporting and encouraging." And, one of you, I don't know which one, made a comment about a very practical matter, and that was probably the only way we're ever going to effectively lower the cost of health care, is to focus on preventive care, rather than reactive medicine, and I think that's absolutely true, and that's one of the reasons why this research is so, I think, exciting to all of us.

I would just like to return to the matter of the possible interface or the intersection of the work that you are doing with the work that is going on in terms of stem cell Research or therapeutic cloning, because I do think that's something that we can't ignore. And, the threat to progress that some of the actions that we've taken pose, you know, it just seems incredibly unreasonable that

some of us who have almost, you know, the most superficial understanding of what you know would impose restrictions on the potential that this research offers to the American people and to the world.

And so, I'm just wondering if you could say a little more about the ways that these research efforts could or do intersect, and why it's so important to have the ability to pursue this kind of research without artificial restrictions being placed on it.

Mr. COLLINS. So, they do intersect in the sense that the genome is the instruction book that directs human biology, directs the biology of all living organisms. One of the major questions that we now have the opportunity to begin to unravel is how genes turning on or off result in a cell going down a pathway to be a neuron, or a liver cell, or a bone marrow cell, they all have the same instruction book, they all started with the same instruction book, they still have it, but they developed along the way a wonderful cascade of genes turning on or off to allow that cell to take on a variety of a remarkable diversity of phenotypes, of ways in which that cell can behave.

Obviously, the stem cell, as sort of the granddaddy of all of those, is one of great interest. As you know, there are federally approved human stem cell lines that investigators may work with under current guidelines, and we are engaged right now in a very aggressive way in trying to determine what genes are already on in those cells that seem to have the greatest potential to go down all of these different pathways, basically, by looking very explicitly at which genes are making RNA, which is an indication that the gene is on. So, that's a direct example of an intersection.

But, I think from my perspective, as one who oversees the genomics arena, the study of stem cells, in fact, crosses all the institute lines, and NIH is perhaps particularly relevant in some of the institutes that are looking at diabetes, or Parkinson's disease, or at Alzheimer's disease, and as you know those discussions have been complicated because of the intersection, in that case not of genomics and stem cell biology, but of stem cell biology and concepts of when human life begins.

In my current position, I do not want to weigh in particularly on that debate. Perhaps some of my other colleagues would feel inclined to do so, but I do think you are correct, there is an intersection here, but it's one that we need to understand a little more carefully, it's not a direct overlap.

Mr. STRICKLAND. Thank you.

Can I just, I understand your position, I would just like to know from your personal opinions, are you personally concerned that our government may be engaging in actions that could have a detrimental impact upon your research? Just your personal opinions as we go down the line, and then, Doctor Venter, you can speak.

Mr. VENTER. Well, let me start, I think we are crossing potentially dangerous boundaries in terms of, I think what's going on in the government is a reflection of the concern in society of not understanding these complex issues.

We learn from every newspaper headline and Super Bowl ads that there's a direct link between genes and behavior, even though

I doubt anybody on this panel would support that view. So, I'd argue, we think very much in a deterministic way in our society.

So, I think people fear cloning as an issue for much the wrong reasons. I am absolutely against reproductive cloning, it's human experimentation, there's no justification on the planet for doing it, but I think most people are against it for confused and wrong reasons.

When we are dealing with the stem cell activities, the scientific community has to learn to police itself or learn that it will get policed by others.

I don't know of any reputable scientist that wants to push the boundaries, but the headlines are full of headline seekers that are clearly not even doing science, let alone reputable science, that confuse the issues profoundly.

So, it's a philosophical discussion, it's an emotional discussion, but I think it's very dangerous when we start to interfere with basic science.

Mr. BILIRAKIS. The gentleman's time has expired.

Mr. Brown?

Mr. BROWN. I should have asked earlier a procedural question, I'd ask unanimous consent to enter into the record Mr. Dingell's statement and statements of any other members who have submitted them.

Mr. BILIRAKIS. Without objection, that will be the case.

I wanted to, Doctor Venter, is it realistic, getting into the preventative, is it realistic that a newly born, that a road mapto kind of use your term there, a road map will be taken of that child some day and that information, the genomic information, will be made available to the family?

When you talk preventative, you know, preventative care and what not, is that one of the ways, or is that essentially the way that you were thinking?

Mr. VENTER. I think it would be the most important outcome of the technology side, the challenge would be in interpreting that information.

We all like yes/no answers, but our genetic code will very, very rarely give us a yes/no answer, we are going to have to deal with probabilities, what does it mean to have a 30 percent increased risk of colon cancer? People think in absolute determinations you should have this drug and not that drug, it's not going to work, but if you know you have a 30 percent chance of having severe side effects or dying from a certain class of drugs there's no justification for having you take them. That's the type of information we will get from our genetic code.

But, the colon cancer example, I think, is a wonderful one. The statistics are pretty overwhelming that when colon cancer is detected early there's over a 90 percent chance of a 10-year survival, and fairly low cost associated with treatment. If it's detected after symptoms appear, that drops well below 65 percent, in fact, the numbers are pretty staggeringly bad, at a tremendous increased dollar cost.

So, if you know that you have an increased risk of getting colon cancer from the genetic changes in DNA paraenzymes, for example, discovered by us in collaboration with Bert Fogelstein, you can

have more frequent early checkups, and as new advances getso we have a simple blood test for it, it becomes a very cost-effective way, it can be detected early, it can be treated early, we have very effective treatments for colon cancer, it's called surgery. It's wonderfully effective if it's detected before there's any metastasis.

The challenge is, we are at such an early stage in our understanding of our genetic code we don't know most of the implications of how to interpret that data right now.

Mr. BILIRAKIS. So, when we—I'm sorry, go ahead, Doctor Collins.

Mr. COLLINS. Could I just add one small caveat to this notion of giving the genome sequence to the parents when the child is born, I believe technologically we ought to be able to do that. I believe that based upon the momentum that's currently occurring in the Congress we'll be able to do that in a fashion that people won't be afraid of the information, because they will have protections against misuse.

But, there will still be, I think, some who don't wish to know about aspects of their genome that places them at risk for things that we currently can't do anything about. Colon cancer is a great example of where we can, I think most people would want to know that one, but if there's information in there that says you are at risk for Alzheimer's disease, and at the moment there is nothing we can do about that, some will want to know that, some will not.

And, arguments have been made, and I think they are fairly compelling, that that is a decision which the individual ought to make for themselves, and, obviously, a newborn doesn't have the opportunity to do that. So, a slight modification of this future view is that you would reveal the part of the genome that's relevant for childhood health, but you might save the parts that are only relevant to adulthood until that person gets to be 18 and then they can decide whether they want the information or not. That's my one modification.

Mr. BILIRAKIS. Well, but that all falls in the category of the question that I think practically every one of you raised, what do we do next? That's certainly part of all that, isn't it? Fascinating.

Doctor Patrinos, as you know it's been discussed already so much, this committee has substantial interest, of course, in your Genomes To Life program, and as I understand it there's a roadmap for the Genomes To Life program which was published in April 2001.

This roadmap indicated that DOE would use DNA sequences from high organisms, including humans, as starting points for analyzing critical life processes. Isn't that correct?

Mr. PATRINOS. You may be referring, Mr. Chairman, to an earlier draft of the document that underwent subsequently many modifications.

Mr. BILIRAKIS. But, not the April 2001 document?

Mr. PATRINOS. It may be, I don't recall the April 2001 specifically, but the real roadmap or an article describing our project is really in the April 2003 issue, that speaks to the use of only microbes and microbial communities.

Mr. BILIRAKIS. But, not humans?

Mr. PATRINOS. But, not humans.

Mr. BILIRAKIS. All right.

So, was——

Mr. PATRINOS. This document that the counsel just raised is a much earlier version that is now null and void.

Mr. BILIRAKIS. [continuing] should we say then that this determination whether humans should be used was sort of a work in progress, and that, in other words, was there a change in mind and a change in determination, or was it sort of just a part of an overall work in progress?

Mr. PATRINOS. It was very much an early part of the work in progress, one that was excised very, very quickly. But, like Doctor Collins described, our process also took a very long time and input from many members of the scientific community. So, we went through several drafts, I would say a lot of drafts.

Mr. BILIRAKIS. I'm told, and I don't know this, but I'm told that it's on your web sites, so you may want to check that out.

Mr. PATRINOS. It may be the web site that describes some of the earlier documents.

Mr. BILIRAKIS. Yes.

Mr. PATRINOS. We keep a lot of the earlier documents, but if it is in there we probably should remove it, and we will do so.

Mr. BILIRAKIS. All right.

All right, I have, you know, I have really nothing further other than, well, first of all, there will be, as per usual, a number of questions that the committee will be sending to you in writing, and we would appreciate a response back, and additionally, gentlemen, you know, what you do is very fascinating, it's got to be pretty darn self-rewarding, too, we are Congress here, somebody mentioned that we did double NIH funding. That's one of the promises that Congress made quite a while ago and we kept. I realize that we don't always have the best image in that regard, but we kept that one, and we're very proud of it, and it was a bipartisan thing, we all worked together toward that end.

But, are there any other ways that we can at least consider to help your efforts to alleviate your efforts, I mean, other than money obviously, money is always there, please let us know. And, hopefully, I speak for Mr. Brown, too, when I say that, but let us know how we can help in terms of any legislation or anything of that nature.

I've always been concerned about duplication of effort. I've always been a bit concerned when it comes to research in general, and I've been kind of convinced by researchers that there's going to have to be some overlap, some duplication of effort, and a lot of good things come from that. Hopefully, it's, you know, not sort of a wasted duplication of effort, and I get the feeling that it isn't in this particular case.

Yes, sir, Doctor Collins.

Mr. COLLINS. Yeah, with your permission, Mr. Chairman, I certainly would like to take this opportunity to thank the U.S. Congress for the way in which you have supported the work that brings us here this morning. We would not be here without that strong support, tracking back to the late 1980's when the Genome Project was only a glimmer in certain scientists' eyes, and a lot of the scientific community was unconvinced of its possible success. Despite that, the Congress took that risk. Throughout the course

of the 1990's and right up to today you have stood behind that and encouraged us at times when things were not necessarily easy to see through the lens that we were trying to examine the future.

And, I want to thank you also for the way in which Congress, has achieved this doubling of the NIH, that has made it possible to expand the opportunities into a host of areas that would otherwise still be waiting for attention.

We are all very excited, as you can tell, about what we can now do, and I promise you we will be back telling you about all of the excitement that we can accomplish and, again, appreciating your strong support, both financially and in terms of legislative initiatives to make that happen.

We are very much in your debt, in terms of a specific thing which this Congress could now do, I guess you've heard from several others this morning that if we could in this year of 2003, the year of the completion of the genome, the 50th anniversary year of the double helix, also give the American public a present, a freedom from fear about knowing your own genome, by this effective piece of Federal legislation, by the House taking up what the Senate has already now brought through its committee, that would be a wonderful accomplishment, a bipartisan accomplishment, one which the administration strongly supports, and that would certainly be first on my wish list.

Mr. BILIRAKIS. Sir, that's pretty fundamental, isn't it, to your continued work?

Mr. COLLINS. Absolutely.

Mr. BILIRAKIS. There's no question about it.

Doctor Patrinos?

Mr. PATRINOS. How can I not use this opportunity to also urge you, Mr. Chairman and members of the subcommittee, to also support the science budgets of other agencies, like the Office of Science in the Department of Energy. I think the strength of the American scientific establishment, just like the strength of America, is really the diversity of its people, and the strength of the scientific establishment also depends very much on the diversity of funding sources.

We are unique in the world in that respect, and we need to nurture and enable that diversity of the funding sources. There should not be a one-stop shopping when it comes to scientific research.

Thank you.

Mr. BILIRAKIS. Thank you so much, gentlemen, we appreciate you very much, and we are indebted to you.

[Whereupon, at 12:02 p.m., the subcommittee was adjourned.]

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