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CANCER RESEARCH: FUNDING INNOVATIVE RESEARCH

HEARING

BEFORE A

SUBCOMMITTEE OF THE

COMMITTEE ON APPROPRIATIONS

UNITED STATES SENATE

ONE HUNDRED ELEVENTH CONGRESS

FIRST SESSION

SPECIAL HEARING

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CANCER RESEARCH: FUNDING INNOVATIVE RESEARCH

MONDAY, JULY 6, 2009

U.S. SENATE,
SUBCOMMITTEE ON LABOR, HEALTH AND HUMAN SERVICES, AND EDUCATION, AND RELATED AGENCIES,
COMMITTEE ON APPROPRIATIONS,
Philadelphia, PA.

The subcommittee met at 9:30 a.m., in the Kirby Auditorium, National Constitution Center, 6th and Arch Streets, Philadelphia, Pennsylvania, Hon. Arlen Specter, presiding.

Present: Senator Specter.

OPENING STATEMENT OF SENATOR ARLEN SPECTER

Senator SPECTER. Good morning. Ladies and gentlemen, the time of 9:30 a.m. having arrived, the Subcommittee on Labor, Health and Human Services, and Education, and related agencies will now proceed.

I'll begin by thanking Chairman Inouye of the full committee and Senator Harkin, chairman of the subcommittee, for authorizing this hearing.

The purpose is to explore the standards used by the National Institutes of Health (NIH) for awarding grants.

NIH has been described as the crown jewel of the Federal Government and some say it is the only jewel of the Federal Government.

NIH has produced some remarkable scientific advances. Really, with the research techniques available and the availability now of stem cells; especially embryonic stem cells, which can replace disease cells, it's practically the Fountain of Youth.

The funding for NIH has increased dramatically in the course of the past two decades.

When I chaired the subcommittee for a decade with the concurrence of Senator Harkin, who was then ranking minority member, the funding was increased from $12 to $30 million; on the stimulus package enacted earlier this year, on my amendment, an additional $10 billion was added to the funding.

In sub-years during the 1990's, and the early part of the 2000 decade, funding increased as much as $3 to $3.5 million and there was a great upsurge in the allocated grants.

That had slowed, with the budget crunch, and across the board, and failure to have cost-of-living adjustments, which had met a decline in recent years of some $5 billion.

The $10 billion allocation from the stimulus package has created a wave of excitement with the availability of 15,000 grants. It's a real job producer; 70,000 high-paying jobs in a 2-year period.

The administration's proposal, this year, is to have an increase in NIH funding of $443 million, which is totally insufficient. Doesn't even keep up with the cost-of-living increase and some of that minimal funding has been attributed to the stimulus package, but the stimulus package was not designed to substitute for annual funding.

Today's hearing is partially in response to an article in the New York Times, 1 week ago, yesterday; which raises very significant questions about the grants which were allocated, whether they are on-target. Comments which were made by a distinguished oncologist, Dr. Robert Young, the Chancellor at the Fox Chase Cancer Center in Philadelphia, pointed out that the grants are very conservative, only likely to produce incremental progress, and with this kind of an approach, there may be a major difference in cancer prevention and treatment when transformational kind of grants are crowded out.

The comments go on to illustrate quite a number of situations where grants with really great potential for innovation have been rejected, because they are uncertain.

The point is made that if they could be proved and established you wouldn't have to have the grants.

One of the applicants is a distinguished research scientist from Fox Chase, Dr. Ellen Jaffe, who has published research; a respected established researcher, but when she had some ideas for a very dramatic kind of research they were rejected out of the conservative approach of the National Institutes of Health.

We have a very, very distinguished panel today; experts from major cancer institutes in this area.

You couldn't find a better place to hold a hearing of this sort then in Philadelphia with the pre-eminent scientists and oncologists in the field.

One of our witnesses today is Dr. Craig Thompson from the hospital of the University of Pennsylvania. Dr. Thompson is the Director of the University of Pennsylvania's Abramson Cancer Center and he is the John H. Glick Professor of Medicine and Biology.

These Chairs are named for renowned people and just a personal comment about Dr. Glick; he's my doctor.

As is known, I've had a couple of bouts with Hodgkin's, and have had a couple of responses with chemotherapy. A pretty tough regimen and Dr. Glick has been my doctor. So, it's interesting to see a Chair named after your doctor. I think that would be done some time in the distant future when he was no longer on the scene, but Dr. Glick has moved upstairs, and still treats a great many patients. Has a very remarkable practice.

One attribute, that I shall mention, is the way he answers the phone. He carries his cell phone with him. Something I could never manage to do and on the first ring, John Glick. I make a fair number of calls. I've never heard such prompt responses. It isn't average. It isn't 5 out of 6 or 19 out of 20. He seldom misses.

I had a very deep concern about NIH long before I had my own personal problems, but as you might have imagined, they have been intensified when it is personal.

We now turn to our first witness, Dr. Lawrence Tabak. He is the Acting Principal Deputy Director at NIH, as well as the Director of the NIH Institute of Dental Research. He has an undergraduate degree from the City College of New York, a Doctor of Dental Science degree from Columbia, and a Ph.D. from the State University of New York.

We appreciate you coming from Washington today, Dr. Tabak.

In accordance with the subcommittee rules, we ask that your testimony be limited to 5 minutes.

Please proceed.

STATEMENT OF DR. LAWRENCE A. TABAK, D.D.S, Ph.D., ACTING PRINCIPAL DEPUTY DIRECTOR, NATIONAL INSTITUTES OF HEALTH, BETHESDA, MARYLAND

Dr. TABAK. Good morning Mr. Chairman. It's my pleasure to testify before you today on NIH's efforts to fund additional innovative research.

I've submitted my testimony for the record and I'll use this allotted time to just summarize key points.

Senator SPECTER. Thank you.

Dr. TABAK. Innovation, transformation, and impact are notoriously more difficult to recognize prospectively, then retrospectively. Still these challenges do not reduce our responsibility to aggressively engage the issue of supporting research that has the greatest potential impact. With this in mind, I'd like to highlight several areas that NIH is engaged in to strengthen our support for a more innovative and high-impact research.

In 2007, NIH launched a comprehensive effort to enhance our peer-review system and make it more sensitive to both the impact and the innovation of the proposed work. After receiving extensive national input, we worked to implement cost strategies that emerged and, in fact, reviewers for the applications of the recent Challenge Grant and Grant Opportunity Programs, to be funded by the American Recovery and Reinvestment Act, have used a new review process that emerged with a scoring system that emphasizes the potential impact and risk of the proposed projects.

Another effort to support innovation comes from the NIH Road Map for Medical Research and the Common Fund. It supports transformative high-impact research that expands beyond the traditional boundaries and holds significant promise for improving the public's health. Road Map acts as an incubator space for these new ideas and approaches and though it is still relatively new, it has produced initial results so promising that the Congress provided a legal foundation for an NIH Common Fund supporting these efforts through the passage of the 2006 Reform Act.

Though the Common Fund has many facets, let me focus on three programs designed, specifically, to support innovation and its researchers and projects.

The first are the NIH Director's Pioneer Award Program. This is a high-risk research initiative that supports individual scientists of exceptional creativity, who propose pioneering and possibly, transforming work.

Second, The New Innovator Award Program, which targets similarly creative investigators, but are at an earlier stage in their career, and then third, and complimenting these programs is the Transformative RO1 Research Program, the so-called "T-RO1," which will support transformative projects proposed by individual scientists or collaborative teams.

Given your particular interest in cancer research, let me highlight a couple of the many highly innovative programs supported by the National Cancer Institute (NCI).

Forthcoming, are new physical science oncology centers where physicists, chemists, mathematicians, and biologists will work collaboratively to form new perspectives on the physical forces involved in cancer.

Twenty years ago, many questioned the decision to make so vast an investment in the Human Genome Project, an effort that could not guarantee that its knowledge would lead to immediate medical applications; however, recent Genome Wide Association Studies are helping to reveal the genetic roots of a rapidly expanding of array of diseases, such as cancer.

The NIH has examined and strengthened its support for innovation amongst scientists across all career stages and for scientific projects from laboratory to clinic to community. We have sought ways to remove the roadblocks that have hindered into disciplinary cooperation and the exploration of unconventional leads.

From the Common Fund in its program through initiative taken by NIH institutes and centers, and from our enhanced approach to peer review, we are already discovering unexpected connections between and among disciplines, diseases, and biological processes.

PREPARED STATEMENT

To conclude, in our support for innovation, we must not lose sight of the importance of what Thomas Kuhn, who popularized the concept of "paradigm shifts," termed "normal" science. He emphasized that both normal or evolutionary research and revolutionary research are essential to improve our efforts to improve human health.

This concludes my testimony, Mr. Chairman, and I would be pleased to answer any questions you may have.

Senator SPECTER. Well, Doctor, your full statement will be made a part of the record.

[The statement follows:]

PREPARED STATEMENT OF LAWRENCE A. TABAK

Good morning, Mr. Chairman. I am Dr. Lawrence Tabak, Acting Deputy Director of the National Institutes of Health (NIH), and Director of NIH's National Institute of Dental and Craniofacial Research. It is my pleasure to testify before you today on the NIH's efforts to fund innovative research, in biomedicine generally and in cancer research particularly.

Shortly after WWII, the cornerstones of NIH—its peer-review process and its scientific and public advisory structure—were set in place. Our current grants program, refined through an ongoing iterative process that reflects the changing demands of science and society, continues to rest on this foundation. Much admired and often imitated throughout the world, the NIH peer-review process has produced impressive results. These results have been widely documented, most recently by Kenneth Manton and his colleagues in their study of the longitudinal correlation of investment in NIH research with a significant decline in mortality in four major

chronic diseases. The NIH's grant process has allowed the Agency to fulfill its mission of seeking scientific knowledge to improve the public's health.

Given the rapidity of scientific progress and the remarkable technology that we have available, we know that we must continue to enhance our support for potentially innovative, high-impact research. There is a tension inherent in our grant-making process. Given finite resources, how do we balance support for projects that promise more certain results with those that are riskier, but hold the possibility of greater reward? "Innovation", "transformation", and "impact" are notoriously more difficult to recognize prospectively than retrospectively. These challenges do not reduce our responsibility to aggressively engage the issue of supporting the research that has the greatest potential impact.

CURRENT NIH SUPPORT FOR INNOVATIVE RESEARCH

Let me highlight several areas that NIH is engaged in to strengthen our support for more innovative and high impact research. In June 2007, NIH launched a comprehensive effort to enhance our peer-review system and make it more sensitive to both the impact and innovation of the proposed work. Extensive input was sought and received from a wide range of stakeholders across the country, which led to a comprehensive report released in February 2008 detailing the challenges facing our current system, and proposals for improvement. Four interrelated core strategies emerged to enhance our system of peer review: (1) engage the best reviewers; (2) improve the quality and transparency of reviews with a greater focus on scientific impact; (3) provide for fair reviews across career stages and scientific fields with a greater focus on early stage investigators and transformative research; and (4) develop a permanent process for continuous review of peer review.

A new review process and a new scoring system has been implemented and was employed for the recent Challenge Grant and Grand Opportunity ARRA programs. Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of five core review criteria: significance, investigator(s), innovation, approach, and environment. Under the approach criterion, specific consideration is given to the level of risk. The scoring system will be changed completely to modify previous patterns of review.

The NIH Roadmap for Medical Research was introduced by former NIH Director, Dr. Elias Zerhouni in 2003. The intent of the Roadmap was to support transformative, high-impact research that expands beyond the boundaries of any single NIH Institute or Center and holds significant promise for improving the public's health. Congress provided a legal authority for an NIH Common Fund, which institutionalized the Roadmap concept within the NIH Reform Act of 2006 (Public Law 109–482). The Common Fund acts as an incubator space in which new ideas and approaches can be tested, developed, and, ultimately, moved out of the Common Fund and into the larger biomedical research community.

Though the Common Fund has many facets, I will focus on three of its programs that specifically support innovative researchers and projects. The NIH Director's Pioneer Award Program, first announced in 2004, is a high-risk research initiative designed to support individual scientists of exceptional creativity who propose pioneering—and possibly transforming—approaches to major challenges in biomedical and behavioral research. To date, there have been 47 awardees; and already, their work is producing impressive, potentially transformative, results. For example, in what has turned out to be quite timely research, a Pioneer awardee is employing antigenic cartography to map differences in seasonal influenza strains worldwide. This knowledge should significantly improve our ability to track the influenza virus and select proper strains for vaccine preparation. The New Innovator Award Program is targeted to highly creative investigators who are earlier in their careers and who have the potential to produce solutions for broad, important problems in biomedical and behavioral research.

Complementing the Pioneer and New Innovator Programs is the Transformative R01 Research Projects Program (T-R01), which will provide support for transformative projects that individual scientists or collaborative investigative teams propose. The program is specifically designed to support exceptionally innovative, high risk, original and/or unconventional research with the potential to create new or challenge existing scientific paradigms. Applications for this new program were recently reviewed with a two-stage process. About 100 of 700 of the applications received met the threshold for transformation potential to be considered further for support. Applications making this initial cut where then carefully reviewed by a very experienced panel of scientific notables and final funding decisions are to be made during this fiscal year.

CANCER INITIATIVES

Given your particular interest in cancer research, I will highlight several of many highly innovative programs supported by the National Cancer Institute (NCI). Forthcoming are new Physical Science-Oncology Centers where physicists, chemists, mathematicians and biologists will work collaboratively to develop new perspectives on the physical forces involved in cancer. Initial competing awards will be funded with fiscal year 2009 appropriated funds; the plan is to fund administrative supplements to the parent grant with ARRA dollars. Remarkably, 7 Nobel laureates either applied for or participated in the review of this exciting new program, together with 24 members of the National Academy of Sciences and 9 National Academy of Engineering members who were included among the groups that applied for this opportunity. This is clearly not business as usual.

Many questioned the decision to invest so many international resources in the human genome project—an effort that could not guarantee that its knowledge would lead to immediate medical applications. Recently, however, Genome Wide Association Studies are helping to reveal the genetic roots of a rapidly expanding array of diseases. NCI's Cancer Genome Atlas Project recently announced (September 2008) the first results of its large-scale, comprehensive study of the most common form of brain cancer, glioblastoma. The team discovered new genetic mutations and other types of DNA alterations with potential implications for the diagnosis and treatment of glioblastoma.

NCI also has invested in innovative research into biomarkers—molecules found in the body that can signal an abnormal process or disease, and can be meaningful in understanding the presence of disease or response to treatment. In 2006, NCI, the U.S. Food and Drug Administration (FDA), and the Centers for Medicare and Medicaid Services collaborated to form the Oncology Biomarkers Qualification Initiative (OBQI). OBQI was designed to qualify biomarkers for use in clinical trials and, ultimately, to speed better agents to cancer patients. For example, researchers are assessing the use of positron emission tomography (PET) to detect fluorodeoxyglucose (FDG), a potential biomarker in nonsmall cell lung cancer and non-Hodgkin's lymphoma clinical trials. FDG–PET is an imaging test that uses a radioactive sugar molecule to produce images that show the metabolic activity of tissues. In FDG–PET scanning, the high consumption of the sugar by cancer cells—as compared to the lower consumption by normal surrounding tissues—identifies these cells as cancer. FDG's presence can be detected by PET imaging in tumors as small as one centimeter. FDG–PET clinical trials could have significant impact on patient management by validating a tool that can identify response to treatment and help facilitate new drug development.

CONCLUSION

Thomas Kuhn, the pioneering American intellectual who popularized the concept of "paradigm shifts," underscored the importance of what he called "normal" science in determining the consequences of revolutionary discoveries. Both revolutionary and evolutionary research is essential in our efforts to improve human health. Not long ago, vaccines against cancer seemed an unlikely development. Then, scientists at the NCI developed a virus-like particle technology that formed the basis for new commercial vaccines that target specific cancers. In June 2006, the U.S. Food and Drug Administration approved the vaccine Gardasil, which is highly effective in preventing infections from the four types of human papilloma virus that cause the majority of cervical cancers in women. The vaccine, made by Merck & Co., Inc., is based on laboratory research and technology developed at the NCI. NCI played a pivotal role in what holds promise to be a major public health success story. Worldwide use of this vaccine could save the lives of 200,000 women each year.

NIH has examined, and strengthened, its support for innovation: among scientists across all career stages; and for scientific research projects from laboratory to clinic to community. We have sought out ways to remove the roadblocks that have hindered interdisciplinary cooperation and the exploration of unconventional leads. Through the Common Fund and its programs; through initiatives undertaken by NIH Institutes and Centers; and, as early studies suggest, from our enhanced approach to peer review, we are already discovering unexpected connections between disciplines, diseases, and biological processes.

NIH continues to enhance its ability to identify and support innovative and high-impact research through the creation of experimental spaces for testing new ideas; the introduction of novel programs; and the invention of new approaches to assess results. Supporting innovative research and pioneering researchers is a top NIH priority. If NIH is to continue along this path, NIH's stakeholders—the whole of the Nation, and researchers around the world—must themselves embrace a new para-

digm. If we agree to accept more risk, we must also accept more risk of failure. To do otherwise is to hinder innovation. As Elias Zerhouni often noted, "The best way to ensure failure in science is to try to ensure success." Therefore, we must identify the amount of risk that is acceptable and in that context balance NIH's research portfolio to support an optimal balance of innovative and evolutionary research.

This concludes my statement, Mr. Chairman. I will be happy to answer any questions you may have.

Senator SPECTER. You talk about undertaking high-risk projects. The information in the New York Times article pointed out that on the category of Pioneer Awards only 3 to 5 percent of the applicants get funded. The fund set aside for Transformative R01 Grants was only $25 million. Are those figures accurate?

Dr. TABAK. The success rate of Pioneer Awards is low by design. Only the most transformative projects meet the high bar that is required.

Senator SPECTER. When you say that "Only the most transformative projects," what do you mean by that?

Dr. TABAK. These are projects that have the potential of changing existing paradigm within science. These are not projects that will add to a previously existing paradigm. These are projects that will take us into an entirely new direction.

Senator SPECTER. Is it true that only $25 million has been allocated for the RO1 item?

Dr. TABAK. In fiscal year 2009, the transformative RO1's were allocated through the Common Fund of up to $35 million.

In fiscal year 2010, this is scheduled to double. This is up to, again, depending upon the quality of the applications received.

Senator SPECTER. What percentage is that of $30 billion?

Dr. TABAK. Well, obviously, a very small percentage, Senator.

Senator SPECTER. Well, isn't that really unreasonably low when you are looking for innovative approaches?

Dr. TABAK. In any application to the NIH there are, as you know, sir, three components. There is the application itself submitted by the applicant. There is the peer-review process that the application must go through, and finally, there is staff considerations taking into account and inform by the peer-review process. So, all three of these parts would be required to come to agreement that, in fact, something is transformative or innovative in nature.

Senator SPECTER. Well, Dr. Tabak, aside from the criteria, if you only have $35 million, that doesn't go very far when you're looking at allocation by the Congress of $30 billion, plus $10 billion more.

Dr. Richard Klausner, a very distinguished former director of the National Cancer Institute said this, "There is no conversation that I have ever had about the grant system that doesn't have an incredible sense of consensus that it is not working. That is a terrible wasted opportunity of scientists, patients, and nations and the world."

Do you disagree with that?

Dr. TABAK. Sir, we do not have a set amount of research that we intend to fund that comes under the Innovative or Transformative heading. Investigators are surely encouraged to submit their most innovative and creative proposals. I think that part of the understanding that came with the review of the peer-review process is that elements of it demonstrated a conservative aspect, if you will. This is why in the changes that we have proposed and have begun

implementing in the peer-review process, we think that we will be able to ensure that a higher emphasis is placed on things like impact, rather than the fine methodological detail that, perhaps, dominated the review process in the past.

Senator SPECTER. Dr. Tabak, that sounds great, but isn't it really a matter of how many dollars are allocated to these high risk transformative processes?

This is what Dr. Robert Young, Chancellor at Fox Chase said. "The grants that are made are only likely to produce incremental progress, the ones which are crowded out or applications that could make a major difference in cancer prevention and treatment."

Do you disagree with that?

Dr. TABAK. The process that we use, sir, which, you well know, is peer review and so if in the judgment of the peers a particular work is or is not transformative, this plays a major role in determining whether or not NIH will support an application.

Senator SPECTER. But what are the standards used by the peers?

Dr. TABAK. So in the past, as you know, sir, there was a series of criterion which, unfortunately, did not in our view, and in the view of many that we spoke to around the country, appropriately emphasize things like the overall potential impact of the proposed work. This is why we have enhanced the peer-review system to include this very important principle. What we have found in past programs such as the Pioneer Award and, subsequently, with the New Innovator Award are upon release of these new types of programs. It takes a bit of time for the community; that is, both applicants and reviewers alike, to re-equilibrate to a new standard of excellence.

Senator SPECTER. Well, is there an effort made to a new standard?

Dr. TABAK. Indeed, and so this is why you will see that the number of Pioneer Awards have increased each year since the inception of the program. That's why we hope that we will be able to increase significantly the number of Transformative RO1's, because as the community, both applicants and reviewers alike, adjust to what is expected it allows for us to support applications of this type.

Senator SPECTER. Dr. Tabak, there is a view that the Congress had not become involved in the decisions made by the National Institutes of Health on a scientific basis. There is a concern about politicizing the process. Members of the House and Senate are really not equipped to do that, and we're about to hear from very distinguished research scientists on this subject. The reality is that you are on the spot a little bit in responding to the New York Times article and you're a volunteer, and you're not responsible for setting this policy. But I know you will listen closely to what the witnesses will say and it's my request on behalf of the Appropriations Committee for you to go back and take a look at what you will hear today, because I think you are going to find some very strong criticism of the NIH policy.

We are searching for cures. My own instinct is that most of the maladies of the world can be cured if we put sufficient resources into the National Institutes of Health and that it is scandalous that more has not been done since war was declared on cancer in 1970.

The subcommittee has asked NIH for a projection for what it would cost to cure cancer. When I say, "cure cancer," I'm going to ask you what the realty is considering the many strains of cancer. Be able to figure, $335 billion over 15 years and at a time when we're considering comprehensive health reform, this is a front-burner subject, which is the reason why we moved as fast as we did to have this hearing.

We expect to take up comprehensive health review this week and for the balance of the month. So, it is very timely to make an evaluation as to what we're dealing with here.

When a comment is made about curing cancer, is that realistic Dr. Tabak?

Dr. TABAK. I can't predict when all cancers can be cured, sir. As you surely know, cancer is not a single-disease entity, but in fact, many disease entities. I would really not be able to make that type of prediction.

Senator SPECTER. Well, how about a prediction on Hodgkin's?

Dr. TABAK. Sir, again——

Senator SPECTER. Too personal?

Dr. TABAK. Again, sir, part of the reason that it is so difficult to predict is as we learn more and more about human biology, we never know where the next breakthrough comes. It sometimes comes from places that we never would have anticipated.

Senator SPECTER. Do you think there is the capacity with our research ingenuity to pretty much eradicate the radical maladies of the world, with sufficient dollars for research?

Dr. TABAK. I think with appropriate time, yes, sir, because we have already enjoyed so much success in eradicating a subset of diseases and conditions.

Senator SPECTER. Well, let me ask you to undertake the very difficult question of a judgment on how much time and how much money it would take? Because at a time when we are looking at comprehensive health reform, you couldn't find a better time to come to the Congress and say, this is what we might do on cancer, what we might do on heart disease, on autism, on Parkinson's, on juvenile diabetes, on Alzheimer's.

Dr. Tabak, I would appreciate it if you would stay for our panel because we may have some follow-up questions as a result of what they testify to.

Dr. TABAK. My pleasure, sir.

Senator SPECTER. Thank you again for coming from Washington.

We will now call our panel of Dr. Pestell, Dr. Jaffe, Dr. Thompson, Dr. Curran, Dr. Kaufman, and Dr. Seiden.

Thank you all for joining us.

I have some reluctance to see cancer treatment slowed up by the presence of you six distinguished scientists here this morning, so I will try not to keep you too long. But I do think it is very important to hear your views and try to give us some guidance as to what we ought to be doing.

We appreciate what you have done and Congress is very anxious to support you and make the most generous allocations that we can to the National Institutes of Health, and to the extent that we can realistically, hold out the prospect of curing these maladies. There is a lot of interest in doing so.

Our first witness is going to be Dr. Richard Pestell, Director of the Kimmel Center at Jefferson. He is the principal investigator of the Institute and designated cancer center, M.D. and Ph.D. from the University of Melbourne in Australia.

Thank you for joining us Dr. Pestell and the floor is yours.

STATEMENT OF DR. RICHARD G. PESTELL, M.D., PH.D., DIRECTOR, KIMMEL CANCER CENTER, THOMAS JEFFERSON UNIVERSITY, PHILADELPHIA, PENNSYLVANIA

Dr. PESTELL. Good morning Senator Specter and again it is a privilege to be here to provide testimony, and I'm very grateful for the opportunity.

Senator SPECTER. You didn't have to put in your curriculum vitae that you were from Australia, we could have told that right away.

Dr. PESTELL. Being Australian all the way through, is that okay?

Senator SPECTER. Yep.

Dr. PESTELL. If I may, I thought I'd start with a couple of personal comments and then read——

Senator SPECTER. Pull the microphone a little closer. Those television cameras will reach a great many more people then the number who are present in the audience.

Dr. PESTELL. Is that louder now? Okay. If I may, I'd like to start with a couple of personal comments and then read part of my testimony, and then summarize a couple of thoughts of action steps moving forward.

Senator SPECTER. All of the written statements will be made a part of the permanent record.

Dr. PESTELL. In brief, I came to the country almost 20 years ago because I thought this was the place where many different types of cancer would be cured.

I absolutely believe that cancer is understandable, it's treatable and it's beatable. I believe that the combination of the process of funding this type of destination will inevitably lead to a continuing number of cancers that are cured and that will happen in this country. Again, I believe it's very much a part of a team effort that will make that possible. I'll read part of my testimony now, if I may, in the response to the concern that innovative ideas and projects were said to often struggle to secure the necessary financial backing to proceed, which was the key questions raised by the editorial. I do believe it warrants further analysis.

I'm a long-term cancer researcher and the current director of the Kimmel Cancer Center at Thomas Jefferson University, and I suggest an alternative view and suggest an approach to examining further these conclusions using more quantitative metrics.

I think extraordinary progress has been made in the understanding and treatment of many different types of cancers and through NCI-supported research tremendous progress has been made.

I think highlights include the revolution in thinking based on the discovery of oncogenes, the use of molecular genetics to determine therapy and disease outcome, and that has certainly improved the quality of care for our patients.

NCI-supported research has lead to a continuing revolution in the way that cancer, its diagnosis and its treatment are ap-

proached. I think of considerable importance is that NCI has supported a very cost-effective biomedical research infrastructure, which are these NCI-designated cancer centers, because the fundamental discoveries that are required to cure the various diseases that are cancer requires sustain, support and in a constant environment.

The Kimmel Cancer Center was established in 1991 as an NCI-designated cancer center and it conducts basic clinical research and has an education mission.

There has been a substantial rise in the number of scientific publications that have occurred in the last 3 or 4 years, since I have had the privilege of taking over the cancer center, and I wanted to give a couple of examples of major discoveries that have been supported by NIH, and that have, importantly, impacted the quality of care and cure of several diseases.

Recent fundamental discoveries of transformation content include the discovery that colon cancer is maintained by a paracrine mechanism involving a secreted factor. This really changes the way of thinking about colon cancer.

Both of my parents died of colon cancer and we have been very focused and interested in changing the paradigm of how we treat these diseases, which affect so many individuals.

If we think differently about the way that cancers are caused and these secreted factors and we can develop antibodies to those secreted factors, we can intervene in a very real way.

The second discovery, which has taken place at the Kimmel Cancer Center, is the discovery of a "commandeering tumor suppressor model." This changes, completely, the paradigm of thinking. Its research has been supported by the NIH and it changes the paradigm from the idea that tumor suppressor's work within a cell, to the idea that tumor suppressors commandeer the local tissue environment and that there are many factors within the local area of the tumor, and these maintain and sustain the tumor. This change in thinking has lead to the development of a new treatment which involves an antibody, and we have shown in mice, using this new understanding that we can completely block breast cancer metastasis in mouse models. So, again, a complete paradigm shift and this research have been supported by NIH.

The third paradigm shifting, NIH funded research, that I would like to mention today is some work done on a gene called Caveolin1 and this research has changed the fundamental thinking on breast cancer, and has led to a new classification or proposed new classification of this disease. Looking at the fibroblasts within the tumor, rather than the epithelial cell, this subtle but very important change, has led to a completely different marker for prognosis in patients who are treated with breast cancer.

So, I would like to suggest a couple of practical thoughts moving forward, if I may. These are to enable us to determine, quantitatively, the outcome of some of the research. How do we know this research is innovative? How do we know it will succeed? It's obviously an important balance between these two questions.

So, I think it is important for us to develop surrogate measures of the impact of the researcher's work. There are a number of surrogate measures that exist. One of them is the citations of an indi-

vidual investigator's work over a certain period of time. The second is the H-index, which is predictor of an individual investigator's scientific impact; the number of times there work is quoted.

The third is the G-index, which looks at—if you like stocks on the rise, the relative effectiveness of——

Senator SPECTER. Dr. Pestell, about how much more time will you require?

Dr. PESTELL. About 35 seconds.

Senator SPECTER. Okay.

Dr. PESTELL. All right.

Another idea, of course, is to look at the number of publications that appear from team research in an organization.

PREPARED STATEMENT

So, if I could in closing, just recommend that this is an opportunity to look for better surrogate measures for determining the innovative impact. We can subtlty turn the direction of the NIH criterion to include the emphasis on innovation.

I know that a new scoring has been developed which emphasizes innovation within NIH funded Arrow One Grants. I think it's important for us to develop new metrics to determine the potential of innovative research and, finally, I think it is important to set aside a larger pool of funds to support, specifically, high-risk innovative grants, and the identification of that subset of new funding warrants further attention.

[The statement follows:]

PREPARED STATEMENT OF RICHARD PESTELL

I have been asked to respond to a recent New York Times article. This article highlighted that the National Cancer Institute (NCI), which awards billions in Federal funding for research grants, "tends to choose projects that are not likely to result in groundbreaking discoveries related to treating and curing cancer". Innovative ideas and projects were said to "often struggle to secure the necessary financial backing to proceed". The questions raised by this editorial warrant further analysis.

As a long-term cancer researcher and the current Director of the Kimmel Cancer Center at Thomas Jefferson University, I would suggest an alternative view and suggest an approach to further examining these conclusions using more quantitative metrics. Extraordinary progress has been made in the understanding and treatment of cancer, through NCI-supported research. Highlights include the revolution in thinking based on the discovery of oncogenes, and the use of molecular genetics to determine therapy and disease outcome. NCI-supported research has lead to a continuing revolution in the way that cancer, its diagnosis and its treatment are approached. Of considerable importance the NCI has supported a cost-effective biomedical research infrastructure required to conduct collaborative team-based groundbreaking discoveries, in particular through the support of NCI-designated Cancer Centers.

The Kimmel Cancer Center, established in 1991, is an NCI-designated center conducting basic and clinical research and an education mission. The Kimmel Cancer Center currently has several hundred active members in both the clinical and basic sciences. The Cancer Center is funded by $19.7 million per year of NCI peer-reviewed funding and $46.8 million in peer-reviewed cancer funding. The NCI peer-reviewed funding has increased since 2005 from $11.4 million to $19.7 million and peer-reviewed cancer funding has increased from $31.8 million to $46.8 million. As indicated below, the research supported by this funding has led to a dramatic increase in the number of scientific publications per year by basic and clinical scientists in the Cancer Center. I will herein use an NCI-designated Cancer Center to illustrate their importance.

The Kimmel Cancer Center has a long track record of fundamental transformational research discovery supported by NCI grant funding. These basic molecular genetic studies have been translated into clinical research and clinical care.

These discoveries include the identification and characterization of the genes encoding the mismatch repair enzymes involved in repairing the damaged DNA which contributes to colon cancer onset and progression.

Recent fundamental discoveries of transformational content include:

—The discovery that colon cancer is maintained by a paracrine mechanism via a secreted factor GCC (guanylyl cyclase c). These studies provide a potential alternative model for colon cancer treatment—envisaging the disease as a disease of hormonal imbalance. These studies are paradigm shifting as they provide a secreted factor as a tractable target for intervention.

—The discovery of the "commandeering tumor suppressor model". In this model one gene commands the local tissue microenvironment, and very importantly cancer stem cells, to affect the different cell types that conspire in the progression of cancer. The first evidence was the discovery that a cell fate determination factor, Dachshund, blocks breast cancer metastasis in vivo and the identification of the mechanism promoting metastasis via a secreted factor. Further, these studies demonstrated antibodies to this secreted factor abrogated the breast cancer metastasis to the lungs in animals. The demonstration of a similar situation in humans could lead to treatments to limit the spread of breast cancer cells in patients and thereby reduce the lethality of breast cancer.

—Very recent studies by the Kimmel Cancer Center have shown that breast cancer disease outcome is predicted by levels of a specific protein called Caveolin1 in the breast fibroblasts. These discoveries have lead to a new prognostic indicator for therapeutic response and provide a fundamental new mechanism by which breast cancer onset and progression occurs. Further, these studies provide the basis for a proposed new classification of breast cancer. It is anticipated that these discoveries will have a major impact in increasing the targeted efficacy of breast cancer treatment in the coming years, focusing particular treatment regimes to those who would be responsive and sparing others from difficult treatment to which they would not respond.

The key questions raised by the New York Times article are whether the established NCI/NIH funding mechanisms limit the funding of truly transformative research and how can we determine the relative effectiveness and impact or medical research conducted by NCI-funded investigators? Several surrogate measures are currently used at this Cancer Center to determine the impact of an investigator's research on the biomedical community:

—The number of citations for the individual investigators work.

—The H-index which is based on the set of the scientist's most cited papers and the number of citations they have received in other people's publications. A value of 45 or higher is frequently associated with membership in the highly prestigious and selective United States National Academy of Sciences; and a value of 18 is frequently associated with promotion to a full professorship.

—The third index, the G-index, is used for quantifying scientific productivity of physicists and scientists based on publication record. It is often difficult to predict the impact or transformational nature of specific research. However, we believe these surrogate measures represent useful quantitative aspects. For example, approximately 15 percent of the Kimmel Cancer Center members, supported by our major National Cancer Institute funding mechanism have an H-index of over 30, and approximately 10 percent have an H-index over 45. Such data strongly indicate that the NCI support for research by our Cancer Center members translates into research of high impact on the biomedical community.

—Another reflection of the significant activity of the researchers in the Kimmel Cancer Center is the number of publications by Cancer Center members in scientific journals, and the increase in publications per year by clinical and basic scientists in the Cancer Center. For example, over the past 3 years, the number of publications per year by Cancer Center members in scientific journals has increased by more than 40 percent, reaching a level of almost 400 publications per year in the past year.

—An additional important surrogate measure of the effectiveness of NCI in supporting translational and transformational research include patents submitted and/or issued and what companies developed from those new scientific discoveries, in other words how do laboratory discoveries get translated into the realm of public availability. The Kimmel Cancer Center, has been issued 80 patents and has 61 patents pending.

Several important questions remain to be formally addressed:

—What are the superior quantitative measures of the impact of new research supported by NCI? Ambitious goals of the clinical translational science awards include improving the health of regions and or populations. NCI-designated Cancer Centers have developed metrics to improve equitable access to cancer pa-

tients. Metrics related to the quality of life of patients with cancer, in addition to mortality, represent important priorities related to treating cancer.

—Are there additional surrogate measures of the research vitality in the United States reflected by NCI investment. One possibility includes the influx of qualified researchers for positions in the United States, which may reflect a perceived unique opportunity to conduct high impact medical research by the global academic community. A formal comparison of scientific impact by NCI-funded research with other cancer funding agencies may be warranted and would be required to formally establish.

—How can the current research culture promote "groundbreaking discoveries related to treating and curing cancer". Promoting transdisciplinary research (biology/nanotechnology/physics/material sciences/stem cells) with an RFA intention of groundbreaking discoveries may be helpful. Emphasis by broad think tank input on areas of research that are most likely to provide groundbreaking results, such as stem cell research. Emphasis within journal publications, promotion and tenure committees, coupled to the surrogate measures above may enhance the focus on all important transformational discoveries. Collectively this report emphasizes that this is an excellent time to evaluate researchers funded by NCI or other cancer agencies for their impact using the currently available surrogate measures.

Senator SPECTER. Thank you very much Dr. Pestell.

We now turn to Dr. Michael V. Seiden, President and CEO of Fox Chase Cancer Center; principal investigator of the Fox Chase University of Pennsylvania, NCI Grant, undergraduate degree at Oberlin, M.D. and Ph.D. at Washington University Medical School.

Thank you for joining us Dr. Seiden and we look forward to your testimony.

STATEMENT OF DR. MICHAEL V. SEIDEN, PRESIDENT AND CEO, FOX CHASE CANCER CENTER, PHILADELPHIA, PENNSYLVANIA

Dr. SEIDEN. Thank you Senator.

The critique of federally funded cancer research in the New York Times recently was, in my opinion, largely on target. While the current review process for proposals does a good job of ruling out bad research, we do have difficulty identifying and perhaps, more importantly, funding the kind of truly innovative research that might lead to dramatic paradigm shifts and fundamentally change the management of the cancer patient and the cancer problem.

Having said that, I don't want to insinuate that the current funding strategies don't work, they do work. We've made significant progress in cancer in recent years.

Cancer statistics are improving slowly. I also applaud the NIH effort of introspection on its peer-review process, and I do believe that new changes require careful review, since they do offer the potential to change the way we refund research. However, the peer-review process, as currently structured, does have some important blind spots. For perfectly understandable reasons the process tends to support the status quo and encourage a systematic cautiousness that has the unintended consequence of discarding the highest risk, most innovative, and in some cases, what might ultimately prove to be the most promising research proposals.

I'll suggest three specific strategies to continue to challenge NCI and all scientists to shift toward more innovative research.

First suggestion is focused on supporting theme based as compared to what I might call specific aim-based science.

At Fox Chase Cancer Center, for example, we launched an initiative we called the Keystone Programs of Collaborative Research,

designed to bring the power of team-based science to bear on some of the most important cancer problems.

The scientific theme for each Keystone Program was conceived by a self-organized group of scientists and clinicians, and aimed to integrate and focus their joint expertise on a significant cancer problem. Beginning with more than a dozen proposals we conducted competitive external peer reviews of the team, their core competencies, prior accomplishments and long-term goals. Importantly, the applications did not include any specific aims or any specific details about scientific approach. The Center eventually awarded four Keystone Programs; $5 million in support from philanthropy and other internal sources. I want to emphasize that the Keystones articulated important themes, but not specific aims or experiments, given the investigators dramatic latitude to pursue ideas they found exciting and potentially at high risk.

So, on this first example, the NCI might place a much larger portion of its budget into funding high-quality, multi-functional teams that have a theme. I would encourage these applications to be designed in a way that emphasize specific gains and scientific approaches. The support should be structured with maximal flexibility so the teams could go where the science leads them.

The funding period for these grants might be as long as 7 to 10 years to give the scientist time to explore high-risk avenues of investigation without the pressure to switch focus or tactics to ensure incremental advances to prove to the NCI that they were being productive and hence, deserve refunding.

Midterm reviews could be considered, but the metric for success should be evidence of creativity, not evidence of productivity. The initial peer review and the midterm review would clearly require a major shift from the current review process that typically looks for the number of publications and follow on grants, instead of really big discoveries. Indeed, the current grant process often rewards the proof of something you've already suspected or had already partially proven.

A second strategy to boost creative science would be to invest in grant programs that relied less on preliminary findings in the review process, but instead focused on big, new ideas.

A third strategy might be to build review teams that would not be—consciously not be laden with content experts, because these individuals, almost by definition, are the same people who have defined the current field and hence, might be least likely to embrace applications that espouse whole new paradigms or theories around an area of science.

Importantly, I do not mean to suggest that we discard our current grant programs and that they are proven to produce real results. However, we should build new granting mechanisms that strongly encourage higher-risk science.

PREPARED STATEMENT

In closing, it is likely apparent, but nevertheless should be emphasized, that building new programs will threaten the solvency of the existing programs, unless there is ongoing increases in the NCI budget.

The cancer community greatly appreciates your efforts, Senator, in building a stronger NCI and wishes you continued success in expanding funds to this important institution.

Thank you for your time.

[The statement follows:]

PREPARED STATEMENT OF MICHAEL V. SEIDEN

I want to begin by thanking you for the opportunity you've given this group today to share its thoughts about how we can make cancer research smarter and more productive in countering this terrible disease. The city of Philadelphia was, in many ways, the birthplace of American medicine more than two centuries ago, and the caliber of the stellar institutions represented by the leaders present here today suggests that this great city will also help define the future of medicine—particularly cancer medicine.

The critique of federally funded cancer research in The New York Times recently was largely on target. While the current review process for proposals does a good job of ruling out bad research, we do have difficulty identifying and funding the kind of truly innovative research that might fundamentally change our view on the cancer problem.

Having said that, we should stop short of a flat statement that current funding strategies don't work—they do work. Significant progress has been made against cancer in recent years. More people are surviving longer than ever before, and the number of new drugs on the market and in clinical testing—many in entirely new categories of action—is climbing every year. And like our peers at other research organizations, including those represented here today, Fox Chase scientists have been generally well funded to pursue vital investigations that are making a difference against cancer.

The peer-review process as currently structured does have important blind spots, however. For some perfectly understandable reasons, the process tends to support the status quo and encourage a systemic cautiousness that has the untended consequence of discarding some of the most promising research proposals being offered up by some of our most creative scientists.

So the question before us today is this: What can be done to change this unfortunate reality? What can be done to intelligently identify and support potentially game-changing new ideas in the fight against cancer?

One thing we might do is look to the National Cancer Institute (NCI) cancer centers to see what local solutions some of them have come up with to spur and develop the most innovative ideas from their own research faculties. Might some of these offer models for change at the Federal level?

At Fox Chase Cancer Center, for example, we last year launched an initiative we call the Keystone Programs for Collaborative Research, designed to bring the power of team-based science to bear on some of the most important cancer problems today. The scientific theme for each Keystone program was conceived by a self-organized group of scientists, clinicians, and other research professionals at Fox Chase seeking to integrate and focus their joint expertise on a significant cancer question identified by the group. There are currently five of these research programs at Fox Chase. Beginning with more than a dozen proposals, we conducted a competitive external peer-review, eventually awarding each Keystone program at least $5 million in support from philanthropy and other internal sources over 5 years. These efforts articulated themes but not specific aims or experiments that would be conducted by the group. Early indicators suggest that these programs are bringing people together in entirely new collaborative combinations that are bridging disciplines and silos across Fox Chase and encouraging a new level of creativity among our already terrific scientists.

So one solution to the problem at hand might be for the NCI to place a much larger portion of its budget into funding high-quality, multi-functional teams that have a theme but not necessarily specific aims. This support should be structured with maximum flexibility so that the teams could go where the science leads them. The funding period for these grants should be long—7 to 10 years—to give the scientist time to explore high-risk avenues of investigation without the pressure to switch focus to making more sure incremental advances to prove to the NCI that they are being productive and hence deserving of refunding. Mid-term reviews should be considered, but the metric for success should be evidence of creativity not evidence of productivity. This would clearly be a major shift in the review process, which typically looks for the number of publications and follow-on grants instead of really big discoveries. Indeed, the current grant process often rewards the proof of something

one already suspected or had already partially proven prior to submitting the grant. Ideally, these teams should be required to include junior faculty, who will also receive sustained funding.

In parallel with the availability of this new funding, the research universities would need to enter into a more robust dialogue about rewarding biomedical scientists for this kind of team play as opposed to encouraging primarily the pursuit of individual grants.

Another move the NCI could make to boost the most creative science would be to invest in grant programs that eliminated the use of preliminary findings in the review process, substituting instead an assessment of prior accomplishments by the investigator. Currently, even for grants where preliminary data is called optional, there is a bias to fund those grants with the largest amount of this not-so-optional preliminary data.

Another strategy that would help identify the most innovative cancer research for funding would be to build multi-disciplinary and perhaps multi-agency review teams. These review teams would consciously not be laden with content experts, because these individuals, almost by definition, are the same people who have defined the current field and hence might be least likely to see whole new paradigms.

These are only a few of the approaches that might be taken at the Federal level to do a better job of identifying and supporting truly groundbreaking research into cancer. And we must act. The need, as everyone in this room understands, is compelling. The NCI cancer centers were not designed to be grant-getting machines. They were created as a way to focus our energies and talents as a nation on eliminating cancer for our patients. If we can refocus the research process to adopt some of the ideas put forth here today, I know we can do even more to find needed answers for the patients we serve every day.

Thank you very much for your kind attention.

Senator SPECTER. Thank you very much Dr. Seiden.

We will now turn to Dr. Craig Thompson, director of the University of Pennsylvania, Abramson Cancer Center, which is a NCI-designated cancer center. Dr. Thompson is a Dartmouth grad and has a medical degree from the University of Pennsylvania.

Before your clock starts to run, Dr. Thompson, how does somebody get a Chair name for him while he's still on the faculty, like Dr. Glick has?

Dr. THOMPSON. It's possible only when one has an inspirational leader such as Dr. Glick, who you mentioned earlier, Senator. We were able to create a Chair in his name because of the dramatic benefit he has provided to the patients here in the Delaware Valley in cancer, and as a result, Dr. Glick has gone back, as you said, to patient care, and I have taken over his duties in administration with the support of his Chair.

Senator SPECTER. Is it common to have a Chair named during a person's lifetime——

Dr. THOMPSON. It is——

Senator SPECTER [continuing]. And still well practice?

Dr. THOMPSON [continuing]. Possible, but extraordinarily rare.

Senator SPECTER. So how do your feet feel in those big shoes?

Dr. THOMPSON. They're very big shoes and I'm still trying to fit them, sir.

Senator SPECTER. All right, on to the subject matter.

STATEMENT OF DR. CRAIG B. THOMPSON, M.D., DIRECTOR, ABRAMSON CANCER CENTER, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PENNSYLVANIA

Dr. THOMPSON. Well, I'm pleased to comment on the recent concerns about the progress in cancer research and treatments. I think it's important for us to remember what really has been accomplished in the last two decades.

Over this decade cancer death rates have declined progressively for both men and women. Since 1990, the death rate from cancer has declined 10 percent in women and 19 percent in men. That's a dramatic improvement over what had occurred previously.

The doubling of the NIH budget from 1998 to 2004 brought forward a Bolis of new approaches for the treatment of cancer. These will provide benefits to cancer patients for the next several decades.

Over the last 5 years, however, support for innovative research has declined in cancer as the national priorities in other areas have arisen. Funding has actually declined 12 percent in terms of cancer research support. This has raised concerns by the community that innovative new ideas are not being funded. Only 1 in 10 new applications to the NIH are funded and research has increasingly shifted; as research into cancer is a complex disease, requires additional expertise to team-based science.

The NIH is responding in the way that Dr. Tabak addressed to try and stimulate in this new era of team-based science, new innovative approaches and award new types of grants. But, in addition, this is a national effort.

What you see here before you are the directors of the cancer centers that are supported in part by the National Institutes of Health, here in the Philadelphia area. All of us have responded to this challenge in our own ways to help support and maintain innovative research.

The comprehensive cancer centers, like the Abramson Cancer Center receive funds from the NIH and other sources that we pull together to support pilot grants for new, young investigators, and developmental grants for senior investigators who have new ideas.

Team-based science awards that come out of the NIH have, as a component, the training of our youngest and brightest new scientists as part of that team.

I just want to provide two examples of what's happened at the Abramson Cancer Center recently.

As part of our core grant support from the National Institutes of Health, we receive funding for developmental projects and we awarded one to a young cancer researcher who came up with the innovative, but unproven idea that one of the complications of aggressive treatment for cancer; such as, you yourself experience Senator Specter, is that it causes a risk of instability to the patients DNA or chromosomes. We know because of the National Genome Sequencing efforts, that these instabilities arise as a complication of cancer therapy, and she realized that the use of drugs that have been developed for the treatment of HIV might actually benefit cancer patients by preventing those instabilities of the chromosomes as cancer patients are treated; therefore, decreasing the rate of cancer in secondary cases of patients that have been treated with cancer. She was able to receive developmental funds directly from the Abramson Cancer Center to support that idea, obtain preliminary evidence to support that idea in animals, and now for the first time is a fully funded researcher from the National Institutes of Health funded with that opportunity.

In one of our innovative program project grants, team-based science, lead by Celeste Simon, a senior, female investigator, she

was able to fund a young junior investigator to use a new approach to cancer treatment using anti-malarial drugs. Drugs that were first developed to prevent malaria in patients that visit areas where malaria is endemic for the treatment of metastasis in cancer and prevent the most dreaded complications of cancer; metastasis, that young investigator, after 4 years of funding within the program project, now has received his own funding from the National Institutes of Health.

So, what we are doing in the Nation's effort is to spur that innovation locally, so that it can receive recognition as more proof of principle is obtained for those researchers.

PREPARED STATEMENT

Finally, I think though, we are all here today because there is no doubt that only 1 in 10 grants being funded means that there are new ideas that are not being supported; the excitement of the air, our stimulus funds and what they provide in terms of opportunities to fund new, innovative approaches in research and development in cancer care that will hopefully reverse this trend.

It is no doubt that these funds will stir new scientific discovery and innovation. Just look at the number of grants that have been recognized as having been submitted in response to the stimulus packages. But what is needed is additional long-term support for cancer research of this complex disease, if America is to continue to lead the world's war on cancer as it has for the last three decades.

Thank you Senator.

[The statement follows:]

PREPARED STATEMENT OF CRAIG B. THOMPSON

Good morning Senator Specter and thank you for inviting me to present testimony today. I am the Director of the Abramson Cancer Center, the Associate Vice President for Cancer Services at the University of Pennsylvania Health System, and the John H. Glick Professor of Medicine and Cancer Biology at the University of Pennsylvania School of Medicine here in Philadelphia. I have been an (National Institutes of Health) NIH-funded investigator for more than 20 years and before that served as a medical officer in the U.S. Navy for 8 years. My current research focuses on studying how alterations in the control of cell metabolism contributes to cancer cell development and survival. Previously, my research has contributed to the development of new treatments for autoimmune diseases and leukemia.

At Penn Medicine we are dedicated to our joint missions of medical education, biomedical research and excellence in patient care. Each year we teach over 700 students, train 1,300 residents and provide care associated with 80,000 inpatient stays and over 1.4 million outpatient visits. In 2008, we received over $390 million in funding from the NIH for discoveries to improve human health. Of this total, investigators in our National Cancer Institute (NCI) designated Comprehensive Cancer Center received more than $140 million in NIH funding. NIH grant support received by Penn Medicine has enabled innovative, cutting edge, and potentially revolutionary research into cancer and related diseases. This observation applies to bench research as well as more mature research involving patients. Consequently, I like others was puzzled by a recent New York Times article suggesting that the NIH funds only projects that are based on conservative science and are "unlikely to take significant steps towards curing cancer or other diseases".

For example, at the Abramson Family Cancer Research Institute, the NIH has provided funding for research into developing techniques to genetically modify immune cells so they selectively attack the patient's ovarian cancer, an exciting, but unproven technique to improve immunotherapy.

In addition, investigators from the Abramson Cancer Center received grants to determine if the genes a patient inherits predispose him or her to neuroblastoma or testicular cancer, cancers that disproportionately affect children and young adults.

These studies have led to dramatic breakthroughs in our understanding of the causes of such tumors, and challenging the dogma that these diseases result from mutations that arise during development.

Penn Medicine researchers recently received funding for team science approaches to: (1) Develop new imaging modalities to improve cancer diagnosis using techniques that have not previously been used in medicine, and (2) study whether metabolic alterations exhibited by cancer cells can be exploited therapeutically. These areas of investigation were previously believed to be impossible to exploit by the cancer community.

Finally, the NIH has continued to fund our brightest and most innovative junior scientists. One junior investigator received funding last year to develop an entirely new approach to cancer treatment through inhibiting a process known as autophagy, which is largely unexplored in cancer biology. Another junior investigator received funding to explore the use of anti-HIV drugs as cancer therapies.

We, like all institutions engaged in biomedical research, have been greatly concerned that NIH funding has remained flat in recent years. From fiscal year 2003 through fiscal year 2008, we estimate that the purchasing power of the funds allocated to NIH actually decreased by 12.3 percent. Consequently, we would agree that potentially worthwhile avenues of investigation may not have received adequate funding due to financial constraints. Still, the projects described above were funded by the NIH. Although some may view these projects as "risky", such studies have the potential to revolutionize cancer care. The strongest of such applications and those most likely to be translated into direct patient benefit have continued to be funded, and we heartily welcome the additional research support made available through the $10 billion awarded NIH through the American Recovery and Reinvestment Act.

In closing I want to be clear that, while we support Ms. Kolata and the New York Times' goal of ensuring funding for research is granted to projects that show the most potential to produce results that further the goal of curing cancer, I dispute the allegations that the NIH and NCI have failed in this task. These agencies are continuously exploring the funding of new research ideas that have the potential to be paradigm-shifting and thus have high potential for leading to fundamental improvements in cancer prevention, diagnosis, and treatment. I again thank Senator Specter and the rest of the subcommittee for having me here today, and for their attention to this important matter.

Thank you.

Senator SPECTER. Thank you very much, Dr. Thompson.

Our next witness is Dr. Eileen Jaffe, Professor and Senior Member at Fox Chase Cancer Center, where her research is in the field of enzymology, undergrad degree from State University of New York and a Ph.D. in biochemistry from the University of Pennsylvania.

Thank you for joining us this morning, Dr. Jaffe, and we look forward to your testimony.

STATEMENT OF DR. EILEEN K. JAFFE, ADJUNCT PROFESSOR, UNIVERSITY OF PENNSYLVANIA, FOX CHASE CANCER CENTER, PHILADELPHIA, PENNSYLVANIA

Dr. JAFFE. Thank you, Senator Specter,, for the opportunity to speak to you today and particularly for your concern about how we might spur scientific research.

The peer-review process that's used by the NIH struggles to support innovative research. This problem is inherent to peer review and it's not specific to the cancer problem, and I've been a researcher, for more than 25 years, at the Fox Chase Cancer Center since 1991.

I've served on multiple peer-review panels including study sections of the NIH. I have submitted proposals for review and I have been funded continuously by the NIH since the early 1980's.

So, from my perspective, peer review works. It works to identify the best and strongest science within the current paradigms.

However, as Gina Kolata's article pointed out, peer review fails to support the sort of innovation that will move science forward rapidly. Instead peer review supports safe, incremental advances. This is primarily a result of human nature. It's exacerbated by the current level of funding. While the pool of money available to research grants is much larger than it was a few decades ago, the pool of applicants is also considerably larger.

The intense competition that results from this makes reviewers very cautious in their selection and, as a result, there is an inherent bias against bolder, challenging ideas. The problem is rooted in human nature. True innovation is seen as different, and the human response to different is suspicion. This is often interpreted with responses like, I don't like this. There must be something wrong with this. I must find fault with this. Right now, the review process is such that two reviewers are asked to write a detailed review and often there is a third or fourth reviewer who gets to comment, read the proposal. If two of the assigned reviewers rate a proposal as outstanding, which is the highest score that you can get, but a third senses that human discomfort that comes from being presented with something different, that's enough to dismiss the proposal.

Allow me to use my own research as an example.

About 6 years ago, we discovered that proteins could move in a way that hadn't been previously recognized. This went counter to what was in the textbooks. We saw that this knowledge could be used for antibiotic development and could be applied to diseases such as cancer. In some ways, these new ideas could be considered "revolutionary," and many grant reviewers appreciated this extraordinary potential, but for others, the newness of the ideas was uncomfortable and they found a variety of faults.

Of course, at first, I too was insistent upon verification of our unexpected discovery, but further testing proved our conclusions.

Now, with the last one, we started to present our work at conferences; people would come up to me and say, but proteins don't do that.

I made several different grant applications, and I use as an example, the most recent NIH application concerning antibiotic development. In this case, we had substantial preliminary data and the application was rated as outstanding in all categories by two reviewers. However, the third met the proposal with skepticism. So, despite the two outstanding marks, the grant proposal was placed well outside the funding range. This is an example of a split score.

The split-score phenomenon has been a common theme for all of the proposals that I have submitted related to the application of this discovery to drug development. I suggest that this split score might be used to identify grant applications that might deserve a second look. The discrepancy in scores, particularly if the negative score reflects a level of disbelief, may be an indication that something truly innovative is in the works.

We, as a society, can ill-afford to let these opportunities pass and a second look at these grants might be warranted.

I propose that an independent peer-review process could be put in place to further evaluate split scores; particularly, where the primary and secondary reviewers both score the grant as outstanding.

Of course, this independent review should be appropriately rigorous. But these reviewers, perhaps as part of what's called a special emphasis panel, would be directed to re-evaluate selected split scores. They would be what you might consider emotionally mature. They would be empowered to actively seek out the bold, the beautiful, potentially frightening and truly transformative ideas that might accelerate scientific progress.

The NIH does have policies in place for supporting innovative research. The problem is not with NIH policy; rather, it is in peer review.

For truly innovative research where there is this potential discomfort or fear factor and where only one reviewer needs to experience an emotional response to the unfamiliar, the peer-review system fails.

PREPARED STATEMENT

In summary, because scientists, like all human beings, tend to choose the familiar as prudent, new ideas are not being funded. Support for innovative new ideas is essential for scientists to make the kinds of leaps that we could be making and that our patients need and deserve.

Whether it's through the mechanism that I've proposed today or through a combination of tactics, this need should be addressed. Of course, increased funding will help ease the problem, but increased funding without a change in the process may simply fuel biomedical growth, rather than biomedical innovation.

Again, I thank you for your commitment to the NIH and for the opportunity to speak with you today.

[The statement follows:]

PREPARED STATEMENT OF EILEEN K. JAFFE

Thank you for the opportunity to speak to you today and for your concern with how research is funded, and how we might speed scientific progress by funding innovative research. Today, I am sure you will hear from my assembled colleagues a few ideas on how to spur innovation, and I intend to offer one as well that could easily be integrated into the existing system.

I have been a researcher in cancer and basic science for more than 25 years. I have served on peer-review panels and study sections for the National Institutes of Health (NIH) and I have submitted proposals for review and have been funded.

From my perspective, peer review is probably the best approach to selecting solid scientific ideas for support. Peer review is also probably the best approach to weeding out the truly silly applications, or those without scientific foundation.

In other words, the system works. In fact, the ability of our Government to fund scientific research, particularly through the NIH, is the envy of the world.

The science of cancer medicine is just one example. While we still have some way to go in the field, more people are living longer with cancer, more people are surviving cancer and more treatment options are becoming available.

However, as Gina Kolata pointed out in her June 28 New York Times article, there is one critical flaw. The system does not encourage the sort of innovation that moves science forward rapidly and, instead, encourages slow, incremental advances.

This is a result of both human nature and the current level of funding. While the pool of money available for research grants may be larger than it was a few decades ago, the pool of eligible applicants is also much larger. Currently, only about 10 percent of grant applications succeed, which makes the reviewers responsible for reviewing grants very, very cautious in their selection. As a result, there is an inherent bias against bold or challenging ideas.

The problem is rooted in human nature. True innovation is seen as different, and the human response to "different" is generally a feeling of discomfort, often interpreted as "I don't like this" or "something is wrong with this."

Right now, the review process is such that two peer reviewers are asked to write a detailed review of a proposal, one as lead and one as secondary. Often, there is a third, and sometimes a fourth reviewer who is assigned as a "reader." This person usually writes a very brief statement. If two of the assigned reviewers rate a proposal as "outstanding," but a third senses that human discomfort that comes from being presented with something different, that is enough to dismiss the proposal.

Allow me to use my own research as an example.

About 6 years ago we discovered that proteins could move in a way that was not previously realized. We saw that this knowledge could be applied to antibiotic development and to other diseases such as cancer. In some ways these new ideas could be considered "revolutionary", and many grant reviewers appreciated this extraordinary potential. But, for others, the newness of the ideas was uncomfortable and they found a variety of faults:

". . . it's too difficult, she must be misinterpreting her data . . ."
". . . she hasn't proven that these drugs will actually work in humans . . ."

And trust me when I tell you that at first my results surprised me too. However, I had the data to back up my conclusions. I also have a solid scientific reputation, built on a long track record of funded grants and quality scientific publications in top tier journals.

I made several different grant applications. One to NIH without preliminary results, which addressed cancer targets, was dismissed without a full review. One to the National Science Foundation about finding drug targets, some related to cancer, received a mixed score—ranging from outstanding, excellent, and good to just Fair. Two attempts at the NIH Pioneer Award program failed. However, the most recent NIH grant application concerning antibiotic development, for which we had substantial preliminary data was rated as "outstanding" by two reviewers, while the third met the proposal with skepticism.

So, despite the two outstanding marks, this grant proposal was placed well outside that about 10 percent region that leads to funding.

This "split score," as it is known, should be a red flag signaling that the grant application may deserve a second look. The discrepancy in scores might be an anomaly, or it might be a good indication that something truly innovative is in the works. We, as a society, can ill-afford to let these opportunities pass.

I propose that, in each granting agency, an independent peer review process ought to be put into place for these split scores, however rare they may be, particularly where the primary and secondary reviewers both score the grant as outstanding. Of course, this independent review system should be conducted with all the due skepticism and intellectual rigor that forms the basis of scientific thinking. However, they should also be empowered to judge scientific merits based on the reputation of researchers and the quality of their work. In fact, this independent peer-review board ought to actively seek out the bold, beautiful, truly transformative ideas that might accelerate scientific progress. It ought to identify chances worth taking.

I also want to point out that this discussion is pertinent to all scientific research and not just cancer. The public generally does not understand that supporting basic science can lead to important therapies for a myriad of diseases, including cancer. Basic science deserves as much attention and support as cancer research. In NIH, basic science is supported by many of the individual Institutes, but most often by NIGMS.

Fox Chase's history bears this out. In 1927, Dr. Stanley Reimann led with the novel belief that the key to understanding cancer lay in the study of normal cell growth and not only in the studies of tumor tissues.

In the mid-1960s, Baruch Blumberg came to Fox Chase to continue work he began at NIH in understanding genetic variations among different populations. It was, by his own admission, a fishing expedition: basic science with no particular goal in mind. Yet, through a combination of keen insight, chance and technical prowess, Blumberg and his team discovered Hepatitis B, and were instrumental in creating a vaccine for the disease, which is often linked to the formation of liver cancer. Millions of people have received this vaccine, preventing an untold number of deaths from liver cancer. For this work, he was awarded the Nobel Prize in 1976.

Then, in the late 1970s, researcher Irwin Rose along with Avram Hershko and Aaron Ciechanover discovered the process of how proteins are broken down and recycled within cells. Their discoveries established a new paradigm in biology that formed the basis of Velcade, a drug approved for multiple myeloma, and they won the Nobel Prize in 2004.

These are just two local examples to demonstrate that innovation can come from smart people performing basic science, often without a specific clinical goal in mind.

In today's climate, it is unclear that either Blumberg or Rose would receive funding for their work.

In summary, the peer review process exercised by the NIH has made good incremental progress toward the development of therapies for disease treatment and prevention. But because scientists, like all human beings, tend to choose the familiar in their quest to be prudent, new approaches are not being funded as they should in order for scientists to make the kind of leaps that we could be making, and that our patients need and deserve.

Whether it is through the mechanism I have proposed today, or through a combination of tactics, this need must be addressed. Of course, increased funding will help ease the problem. But increased funding, without a change in the process, may simply fuel biomedical growth, rather than biomedical innovation.

Again, thank you for your commitment and for the opportunity to speak with you today.

Senator SPECTER. Thank you very much, Dr. Jaffe.

We now turn to Dr. Thomas Curran, Deputy Scientific Director of The Children's Hospital. Dr. Curran received his Ph.D. from the Imperial Cancer Research Fund Laboratories in University College in London.

Thank you for joining us, Dr. Curran, and we look forward to your testimony.

STATEMENT OF DR. THOMAS CURRAN, Ph.D., DEPUTY SCIENTIFIC DIRECTOR, STOKES RESEARCH INSTITUTE, CHILDREN'S HOSPITAL OF PHILADELPHIA, PHIALDELPHIA, PENNSYLVANIA

Dr. CURRAN. Thank you very much, Senator, and I really appreciate this opportunity to come here and testify in front of you.

Yes, I have an accent as well. Mine comes from Scotland, though, not Australia.

I came to this country to pursue a career designed to come up with cures for cancer. It's a long-term strategy. It's a very hard task and the NIH made my progress possible.

I am representing Children's Hospital of Philadelphia (CHOP), the Nation's leading medical research environment for children. We have approximately $100 million in NIH grant funding annually out of the total $200 million budget. We really want to thank you, Senator, for making our successes possible because your activity as an advocate, and as a leading light in supporting biomedical research, is what has sustained the current funding climate that makes our work actually happen.

The best science makes the best medicine. We feel that science and medicine should be tightly integrated in the research environment.

Winston Churchill once said that "Democracy is the worst form of government, with the exception of all the other forms."

The NIH peer-review system could be described as the worst form of funding science except for everything else. We really are the envy of the world, but we can improve the system. We can change it and we have to, in order to stay at the very top. The system works best when approximately 1 in 3 grants are funded.

You've heard that right now we're funding about 10 percent of applications. Reviewers can pretty much spot the top 10 percent; that doesn't require any deep thought. It's the next level of grants that are very hard to spot. We can predict breakthroughs in hindsight and it's just hard to do it before they happen.

I think the solution is to ensure that competitive grants have the opportunity to be funded at a rate of about 1 in 3 in the different categories that you've heard about.

Let me give you one example.

In 2003, I proposed a new approach for the treatment of children's brain tumors, of medulloblastoma;the grant was turned down. The reviewers thought it wouldn't work. So, I revised the grant. I answered the comments, came back in and the grant was funded. It was very successful for the next 5 years and then I submitted a renewal recently. It was turned down again. I revised the grant and persistence paid off. It was funded. That's the way the NIH system works. You actually can benefit from the comments received in peer review to modify an application and make it even stronger.

I'm pleased to say that that study has led to a clinical trial that just opened in January of this year.

CHOP has a major focus on the childhood cancer, neuroblastoma, which kills 15 percent of children with cancer. It's a devastating disease. CHOP has invested significant effort in building genomic capabilities to apply the very latest technologies to understanding the causes and predicting potential treatments for neuroblastoma.

Recently, several studies have come out from the laboratory of Dr. Maris, which have underscored the success of this kind of approach. In fact, in one case, he identified a gene mutation that predicted a potential therapy and that therapy was already in existence for treating adult disease, and so a clinical trial was initiated approximately 1 year after the initial discovery. So, these technologies can indeed accelerate the application of science to medicine. But, indeed, sometimes the ideas are risky.

One way to leverage those resources is to utilize foundation support. Foundations that usually give small, starter grants that can allow you to test the feasibility of off-the-wall or innovative ideas.

One example of this is Alex's lemonade stand. Alex Scott was a young neuroblastoma patient. She lived for 4 years with neuroblastoma; took on all sorts of different experimental therapies. She died at the age of 8, but she lived a very full life. She launched her own foundation, which has now raised $25 million for cancer research, based on selling lemonade in lemonade stands. She's inspiring to all of us.

PREPARED STATEMENT

The peer-review system, as I said, is the best that exists in the world in terms of funding science. We can modify it. The changes that have been suggested, which include shortening the application, the emphasis on ideas, the attention paid to the track record of investigators, can all help find tune the system. But the real success will come from increasing the amount of funds dedicated to supporting the best and the brightest ideas through activities like your own, in providing this $10 billion fund from the stimulus package.

Thank you very much, Senator, and I encourage you to continue the fight.

[The statement follows:]

PREPARED STATEMENT OF DR. THOMAS CURRAN

Good morning Senator Specter. My name is Dr. Tom Curran, I am the Deputy Scientific Director of The Children's Hospital of Philadelphia (CHOP) Research Institute, the Nation's second largest recipient of pediatric research funding from the National Institutes of Health (NIH). From 1922, when our research was conducted in a single basement room until the present day, when we just opened the state-of-the-art Colket Center for Translational Research, we have grown into an world-renowned institution conducting groundbreaking research on diabetes, neonatal seizures, childhood cancer, hemophilia, pediatric heart disease, cystic fibrosis, nutrition disorders, and numerous other diseases and disorders that affect children. This work is supported by more than $100 million in Federal grant awards out of a total annual budget of more than $200 million. At CHOP, we pioneer new therapies, integrate novel technologies, and tackle the toughest healthcare issues that face our patients and their families.

We appreciate this opportunity to testify this morning because our success is achieved in large part with support from the NIH. You, Senator, have been a leading light, and a much needed, advocate for the NIH and this hearing provides us all with an important forum to affirm the pivotal role it has played in advancing the scientific discoveries that lead to cures.

While work is underway to reform our Nation's healthcare delivery system, we must continue to make medical research a national priority. This will not only save money, it will also save lives. I am confident that with your leadership, the NIH will continue to thrive and contribute even more to the health and wellbeing of current and future generations of Americans.

Winston Churchill once said "Democracy is the worst form of government except all those other forms that have been tried". The same could be said for the NIH peer-review system. It is the envy of the world (it even handles reviews for other countries), but of course it is not perfect and it can be improved.

The system works best when approximately 1 in 3 of all applications are funded. Your successful efforts to add an additional $10 billion in funding from the American Recovery and Reinvestment Act will help ensure there is room for projects that have a high risk of failure or that seem to have flaws. However, at present, it is my understanding that only 1 in 10 applications are funded—and all of these are likely to be excellent and meritorious. Unfortunately, because it is so competitive, some very good projects may not be funded at the first attempt due to resource limitations even with this tremendous spike. For example, in 2003, my proposal to develop a new treatment for children's brain tumors, the most common solid tumors in children, was initially rejected because the NIH reviewers didn't think it would work. After addressing their concerns, I revised the application and it was accepted on my second attempt.

Five years later after we demonstrated that our approach worked incredibly well in mice, the renewal of the grant was turned down. Once again persistence paid off, and a revised grant is now funded. I am pleased to say that this work has led to a clinical trial of a novel therapy for medulloblastoma that opened early this year. Medulloblastoma is the most common malignant primary brain tumor, comprising nearly 15–20 percent of newly diagnosed cases in children.

It is important to note that sometimes ideas are so risky that it is best to devote modest resources to test them out until feasibility has been demonstrated. In this way, NIH funding synergizes with funding from other sources such as foundations. For example, recent work at CHOP identified new genes and possible treatments for neuroblastoma, which causes 15 percent of all childhood cancer deaths. After just 2 years and 2 studies, we went from having little information on what causes neuroblastoma to now having information on why some children develop it and others don't. Using CHOP's highly automated gene-analyzing technology at our Center for Applied Genomics, we were able to discover that variants in the gene BARD1 increase a child's susceptibility to a high-risk form of neuroblastoma.

As gene studies continue to better define the genetic landscape of cancer, pediatric oncologists can develop more precise, targeted treatments to improve survival and quality of life for children with this complex disease. That work is being done at The Cancer Center at Children's Hospital, which has one of the Nation's largest research and clinical programs in pediatric oncology.

The research that leads to these innovative findings was supported by NIH grants, but ultimately it was the result of decades of work—some supported by CHOP and some supported by organizations such as the Alex's Lemonade Stand Foundation, created by young Alex Scott, a 4-year-old neuroblastoma patient who sought to raise money to help "her doctors" find a cure for kids with cancer. She passed away at the age of 8, but her legacy lives on as we get closer to a cure

through the help of thousands of lemonade stands and other fundraising events held across the country by children, schools, businesses, and organizations—having raised more than $25 million for childhood cancer research. Other sources have helped fund our neuroblastoma research, including the Evan Dunbar Foundation, the Rally Foundation, the Andrew's Army Foundation, the Abramson Family Cancer Research Institute and the Giulio D'Angio Endowed Chair. I cite this example because NIH funding can be leveraged by contributions from other sources to further accelerate important work.

We are all good at spotting breakthroughs in retrospect; however, it is pretty hard to predict them before they happen. Maintaining a high level of multi-year funding for innovative ideas is key to the translation of basic science discoveries into medical advances.

Since we do not know with certainty where the next breakthrough in cancer research will come from, it is important to keep an open mind and to make space for high-risk/high-impact studies. The recently adopted modifications of the NIH peer-review system are designed to do exactly that.

By placing emphasis on novelty of ideas, reducing the length of grant applications, and by factoring in investigator's track record, I believe we will increase the likelihood of supporting the best research.

Again, we recognize you for working tirelessly to increase the NIH budget so that good ideas do not languish untested. This has resulted in a tremendous increase in knowledge and better treatments for cancer patients, as evidenced in the two examples I cited. Essentially, every major innovation in the understanding and treatment of cancer has resulted directly from NIH support.

In closing, it is my opinion that the best way to ensure the United States continues to lead the world in cancer research and in the translation of discoveries into better treatments is to continue the critical investments made in the NIH to ensure it can provide long-term continuous support for the top third of grant applications it receives.

Senator SPECTER. Thank you, Dr. Curran.

Our final witness is Dr. Russel Kaufman, President and CEO of the Wistar Institute, a nonprofit biomedical research center in Philadelphia. It is a NCI-designated cancer center.

Dr. Kaufman received his M.D. and undergrad degrees both from Ohio State University.

Thank you for being with us, Dr. Kaufman, and the floor is yours.

STATEMENT OF DR. RUSSEL E. KAUFMAN, PRESIDENT AND CEO, THE WISTAR INSTITUTE, PHILADELPHIA, PENNSYLVANIA

Dr. KAUFMAN. Thank you Senator Specter and once again, like all of us here, we appreciate the support that you have given to science.

I think that what we can provide is perspective. We can do that sometimes through specific examples and that's what I'm going to attempt to do. I'm not going to repeat what many people have said because I agree with most of what has been said here today.

I've been taking care of cancer patients for over 30 years. During that time, I've seen a number of advances. Cures for acute leukemia, major advances in lymphoma and you raised the issue of Hodgkin's disease; I think it's a good example of the challenges that we have in cancer therapy, because for many years our approach to Hodgkin's disease has been based on giving a kind of broad-based chemotherapy that's very toxic, but not targeted. Advances in science have now led to a number of targeted therapies. But they've yet to crack the critical nut that affects cancer. With Hodgkin's, only in the last few years have we even identified what the malignant cell is in Hodgkin's. So, I would say that for most of my career, we didn't know what the malignant cell was. We

couldn't even target that cell. We now know that we can direct therapies towards that cell.

So, to further my perspective, I've served on a number of review panels and for the last 2 years, I chaired the counsel that reviews all of the peer-reviewed grants at the American Cancer Society. I can tell you that the scientists take peer review very seriously. We've got a modest honorarium for doing all of this and most of us participate in this process. However, I think it is important for everyone to realize that there are two levels of review; there's the primary review and these reviews go to a counsel, which sets the final funding. This is not based on—we don't call it a quality score, we call it a priority score. The priority integrates a lot of different factors in that, so innovation, creativity, impact, all of those and I would say that, at least, on the last 2 years that I have served at the ACS Counsel, we funded many highly innovative grants, and in my time at NIH reviewing, we also fund many innovative grants.

There are some though, as Dr. Curran has said, that are sent back to the reviewer and said please deal with these issues. By persistence, many highly innovative grants can be funded.

The issue you raised about the amount of money that goes towards that is based on the funding organization that determines that priority. So, as reviewers we don't.

I feel that the review process works well in terms of determining the amount of money, that's an agency decision, and certainly not our decision.

Now, the other important point is that highly innovative science can be funded by our institutions. So, at The Wistar Institute, we are a small place. We don't have much money, but we've committed about $30 million to supporting research over the last 7 years. Some of that is recruiting the most highly innovative scientists and funding their work directly.

On the average, it takes about a million or a million-and-a-half to fund a new investigator and the ones we recruit are the most highly innovative, and the most creative.

We don't hire people who we think are going to do middle of the road work. So, our own institutions and funding agency's such as foundations can also support high-innovation, high-risk research.

Now, let me talk about the research process just for a minute. Some of the delays are because cancer is a very complex disease and we don't have what the crucial nut is that we can crack to solve this problem. But it's our belief that we need persistent and adequate funding. If we don't have adequate funding for research, we have all kinds of problems.

The peer-review committees will retreat to a very conservative position and as Dr. Curran has said, we believe that somewhere between 25 and 30 percent of all grants should be funded, and that will improve things. It will also provide predictability and allow scientists to sustain their programs.

Team-based science is very important. We have to have new methods for how we're going to select teams and how we're going to support this work. So, I fully support this and at Wistar and that's why we're putting together teams. Many times these teams

are across all of our institutions. So, the team members belong to all of our institutions. So, this creates problems.

As you know, baseball teams, it's hard to keep a team together. So, these are some of the challenges that we have with team-based research.

I would like to give you—if I may, have another 30 seconds to give you one example, though, of where we think it is important to fund basic research and to understand what the basic problem is.

For many years, an enzyme called telomerase has been known to be an essential enzyme for cancer cells to divide. Telomerase heals the ends of chromosomes so that they don't get too short and the cells don't divide. We recruited a young scientist; Emmanuel Scordolakis, 3 years ago and he took a novel approach to determine the structure of telomerase, and also submitted a grant to NIH. Now, we funded that work because we believed in it. Because our scientist felt it was important. He has now solved the structure of telomerase and having solved the structure of it, we now know where the binding pocket is that can inhibit that enzyme. This, we think, may be a critical step because telomerase is essential in all cancers. It's this kind of work that has to be funded, which is funding basic research, so that we're not just doing large clinical trials using drugs that aren't effective.

PREPARED STATEMENT

So, we believe that this is the fundamental approach. The peer-review process is not broken, but can be improved and NIH has taken those steps to do that.

Thank you Senator.

[The statement follows:]

PREPARED STATEMENT OF DR. RUSSEL E. KAUFMAN

The Wistar Institute is an international leader in biomedical research with special expertise in cancer research and vaccine development. Founded in 1892 as the first independent, nonprofit, biomedical research institute in the country, Wistar has long held the Cancer Center designation from the National Cancer Institute (NCI). The Wistar Institute works actively to ensure that research advances move from the laboratory to the clinic as quickly as possible.

The Wistar Institute is pleased to have the opportunity to address the subcommittee.

The Nation has made great progress in fighting cancer since President Richard M. Nixon declared a war on the disease in 1971. Due to advances in biomedical research, a diagnosis of cancer is no longer a certain death sentence. Survival rates for breast, prostate, and colon cancers have increased dramatically for patients whose disease is detected and treated early. We have cured childhood leukemia and testicular cancer, and we have sound strategies for preventing cervical cancer and melanoma. More than 40 million Americans count themselves as cancer survivors because of progress in cancer research.

In recent years, however, some have argued that the pace of discovery has been too slow and our ability to translate new knowledge into effective therapies for cancer patients has been compromised in part by the very institution charged with managing the country's investment in cancer research—the NCI. Critics contend the NCI's peer review system is flawed, that reviewers are too conservative in their decision-making, choosing to fund research proposals likely to deliver minor advances in our understanding of the disease rather than innovative, out-of-the-box ideas that could yield the next major breakthrough or cure.

Speaking as a cancer researcher, as chief executive officer of a basic biomedical research institute and director of its NCI-designated Cancer Center, and as one who has served on several NCI study sections and was recently appointed to serve on

the NCI committee that reviews Cancer Centers, I must disagree. Overall, the NCI has stewarded Federal cancer research funding wisely and effectively. It has fostered broad involvement of the academic research community in funding decisions, establishing a peer-review system that is highly regarded as a model across the globe. By its nature, peer review ensures that individuals who truly understand the science select the most meritorious projects for funding. While many of us believe the peer review process must be refined as research priorities change, the fundamental tenets of this system remain sound.

The nature of biomedical research has undergone a monumental shift over the past decade. Multi-disciplinary team science is evolving as the research community begins to tease apart and analyze the wealth of information about human biology revealed by the first complete sequencing of the human genome in 2003. At The Wistar Institute and other research institutions, scientists who specialize in diverse disciplines come together in collaborative teams to study human biology at the molecular level. The fundamental discoveries they make are the necessary first steps to developing better treatments and cures for disease.

The nexus of this paradigm shift to team science is the NCI's Cancer Centers Program. Across the Nation, 63 NCI-designated Cancer Centers are actively engaged in transdisciplinary research to reduce the cancer burden. Since 1972, The Wistar Institute has maintained its designation as one of 7 of the 63 Cancer Centers dedicated to basic science. The Cancer Centers are the jewels in the NCI's crown: they organize the Nation's cancer-focused science into a major, collaborative, impactful effort. They are defined by their significant institutional investments in shared services and technologies, and their culture of collaboration—both within and among cancer centers—whereby scientists working in teams actively pursue innovative, leading-edge research with the common goal of eradicating cancer. The Cancer Centers actually increase the return on the Nation's investment in cancer research by leveraging their Cancer Center Site Grants and other NIH funding with their own institutional funding and philanthropy to support research critical to advancing the field. Cancer Center directors also have specific developmental funds for new, highly innovative research areas.

In this age of scientific revolution, our governing systems must evolve in stride. Recognizing that the increasing complexity and interdisciplinary nature of modern medical research presents new challenges to its peer-review system, the National Institutes of Health (NIH) last year undertook a thorough, formal review of its grant-making structure and developed a plan for making improvements. Among the key elements are new criteria for evaluating grant proposals which give weight to creativity and innovation, and allocation of more funding to young investigators. In addition, the plan seeks to engage the most broad-thinking and creative reviewers and avoid bias toward more conservative and proven approaches at the expense of innovation and originality. With these new guidelines, which are being implemented in the current grant review cycle, the NCI has strengthened its commitment to funding the best science, by the best scientists, with the least amount of administrative burden.

We have achieved significant progress in cancer research, but there are essential facts about human biology that we must learn in order to be able to cure cancer. A fundamental problem remains: the prevalent cause of death is metastasis, the spread of cancer. Most cancers are highly treatable, even curable if they are caught before they spread. With recent advances in basic cancer research we now understand why cancer cells metastasize, we know the features of cells and the cellular environment that make them likely to spread. But we still don't have cures for metastatic cancer. It is critical that we continue to explore the basic features of cancer cells that have spread, in order to develop effective therapies.

A recent discovery from a Wistar Institute lab illustrates this point. Last year, a young investigator determined the structure of an enzyme, telomerase—a discovery which is transforming the field of cancer research. This investigator deciphered the active region of this enzyme, which is essential to our growth and aging, and which plays a major role in the development of almost every type of cancer. Researchers have tried for more than a decade to find drugs to deactivate telomerase, but they have been hampered by a lack of knowledge of its structure. With this new information, we can begin to search for other molecules that "fit" the structure of telomerase and deactivate it, literally stopping cancer in its tracks.

While exploration of these fundamental questions of biology might seem like incremental or inconsequential advances to some, they are the critical foundation from which we will solve the cancer problem. Under the stewardship of the NCI, we have seen great returns on our Nation's investment in the cancer research enterprise, and we are poised to realize the promise of discovery.

Thank you.

Senator SPECTER. Thank you Dr. Kaufman.

I would like to ask everybody on the panel to comment about Dr. Klausner's statement; former Director of NCI, National Cancer Institute.

He said, "There is no conversation that I've ever had about the grant system that doesn't have an incredible sense of consensus that it is not working."

Would you agree or disagree with that Dr. Seiden; Dr. Seiden, yes, no?

Dr. SEIDEN. The peer-review process is imperfect and is frustrating. I have to say that there has been a dialogue to attempt to improve it and I think that process is still under evolution, but it is challenging to get it right.

Senator SPECTER. I take that to be a qualified yes.

Dr. KAUFMAN. I disagree with his point. I think Dr. Klausner's a brilliant scientist, a member of the National Academy of Science, but hasn't really ever participated in the peer-review process. You know, he started his work at NIH, stayed there and was the Director of NCI. He's a brilliant scientist, but I think that the peer-review process is not fundamentally broken.

I believe that all of us who participate in that, we give it the most honest effort possible and we believe that we are recommending the funding of the best research.

Senator SPECTER. Well, Dr. Kaufman, would you disagree with Dr. Young's statement that the current system at NIH is likely to produce only "incremental progress," and it does not undertake research projects, which would "make a major difference in cancer prevention and treatment that are all too often crowded out?"

Dr. KAUFMAN. Well, I believe that the current process does create incremental progress, but incremental progress is essential. But we don't know where the solution lies and so what groups of people are going to decide where we're going to take the big risks?

Senator SPECTER. Well, of course, you need incremental progress, but do you think that a focus there crowds out a more transformative opportunity?

Dr. KAUFMAN. Right. So the point that I made earlier was that we need incremental progress and we need to be stable and consistent, and we need to have a big enough research enterprise to accomplish that.

I agree with Dr. Curran that we should be funding 25 to 30 percent of grants that are funded, because in my perspective, those are the ones that are high quality. However, the funding agencies should set aside an adequate amount of funds to fund those that the review committees think really are innovative.

I think that $35 million may not be enough money for that.

Senator SPECTER. Dr. Curran, funding 1 in 3 would be ideal. You identified now that there is a funding in 1 in 10, what would it cost to fund 1 in 3?

Dr. CURRAN. I can certainly provide you with those numbers once I calculate them. I can't give you the numbers off the top of my head right now.

Senator SPECTER. Well, let's see. If you have 10 percent and——

Dr. CURRAN. Right.

Senator SPECTER [continuing]. You want to have 35 percent; that's three and one-half times $30 billion.

Dr. CURRAN. Right. One other complication——

Senator SPECTER. Could you do the math, Dr. Curran?

Dr. CURRAN. Absolutely not.

Senator SPECTER. It's more than a hundred million.

Dr. CURRAN. When you change the goalpost, you also change the number of grants coming in. So, it's a complicated analysis. You can certainly say well, okay, it's just going to cost three times more.

Senator SPECTER. Change the goalpost?

Dr. CURRAN. Yes.

Senator SPECTER. So if you put up more money, you get more applications?

Dr. CURRAN. You get more applications.

Senator SPECTER. So funding one 1 in 3 wouldn't be limited to just $100 million?

Dr. CURRAN. It's a moving target and so you have to work——

Senator SPECTER. You're moving very fast Dr. Curran.

Dr. CURRAN. Very fast. You start with exactly the number you said.

Senator SPECTER. Dr. Thompson, do you think that the current NIH standards are too cautious?

Dr. THOMPSON. I think Tom Curran actually said it earlier. Tom and I talk about this a lot, since the Children's Hospital of Philadelphia and the Hospital of the University of Pennsylvania are the two entities spanned by the Abramson Cancer Center. We spend a lot of time talking about how you would improve research.

I think the NIH system of peer review is the best in the world and I think that it continues to foster innovation——

Senator SPECTER. The best in the world, but is it good enough?

Dr. THOMPSON [continuing]. But I think half of that innovation comes from the American public itself, which is that if you take our best and brightest students and you put them into funding that exists through the channels that we've all discussed, they will question the discrepancies. They will come up with the innovative new ideas. It's that system, the constant challenging of new investigators brought into the system, against the existing principles that have given us and led America to be the innovation leader in research of all aspects, particularly in medical research over the last three decades.

I think the system needs to be tweaked. We've talked about various ways to understand better the track record of individuals so that the senior scientists that can best train and foster people get better funding. We can talk shorter grant applications so more time is spent on innovative ideas, but in the end, the peer-review process is working and it works with the American young that are coming up, and with new ideas, and challenging existing paradigms. That's how we're going to get better cancer treatments and cures, Senator.

Senator SPECTER. Dr. Jaffe, I'll be very specific in your situation. I'm going to read you part of the New York Times article, which praises you and points out some of the problems that you've had.

It says:

"For 25 years, Dr. Eileen K. Jaffe received Federal grants to run her lab. As a senior scientist at the Fox Chase Cancer Center, with a long list of published papers in prestigious journals, she is a respected, established researcher.

"Then Dr. Jaffe stumbled upon results that went against textbook explanations, suggesting that it might be possible to find an entirely new class of drugs that could disable proteins that fuel cancer cells. Now, she wants to find chemicals that might be developed into such drugs.

"But her grant proposal was rejected out of hand by the Institutes of Health, not even discussed by a review panel. She had no preliminary data showing that the idea was likely to work, something reviewers always want to see, and the idea was just too unprecedented.

"Dr. Jaffe epitomizes the scientist who realizes that if she was single-mindedly pursuing her own unorthodox career, her 'career may be ruined in the process,' in the words of Dr. Brawley of the American Cancer Society."

Do you think the NIH approach ought to give more latitude to the kind of innovative application you made?

Dr. JAFFE. Well, we're talking about—I used as an example a grant that was revised, actually. It went in several times and the one that I talked about earlier this morning, and this is another application that Gina Kolata was talking about, which was dismissed out-of-hand for lack of preliminary data.

These are two very different kinds of applications. To some extent, the work that was dismissed out-of-hand for lack of preliminary data, falls in that category of grants that doesn't require preliminary data. As opposed to the more routine RO1-type support that I've had for the last 20, 30 years. As I said, the process works for funding established paradigms. The process fails when one sees a truly new direction that challenges old ideas.

I would tell you that when we first stumbled upon our discovery it was disturbing. It suggested that we had to go back and look at the results of our laboratory for the last 25 years, results that were published in prestigious journals, and potentially re-evaluate that data. Nobody wants to do that.

Senator SPECTER. Thank you Dr. Jaffe.

Dr. Pestell, let me shift gears just a little. There has been identified as a so-called "Valley of Death," between the bench of the laboratory and the bedside, in terms of clinical application of the great research achievements of the National Institutes of Health scientists.

At the suggestion of one of my former chiefs of staff, a young man named Craig Snyder, I've introduced legislation which is called, "Cures Accelerated Network," which seeks to establish a separate but affiliated entity to NIH with additional funding to try and supplement clinical application.

What do you think of that idea?

Dr. PESTELL. I think that there has never been a time in history where we've known so much about cancer. We have a large number of drugs that are available to be tested, and I think that streamlining that process is absolutely critical, and it's no doubt, the most cost-effective way of making immediate impact on the lives of patients with cancer.

There is a second process, which I think, is complimentary to it and that's the construction of clinical translational sides institutes, in which the ability to increase the efficiency of us of clinical infrastructure that already exists, which can be deployed regionally will, I think, advantage that initiative. The time from discovery to plac-

ing drugs in patients is way too long. There are all sorts of inefficiencies which exist within the current infrastructure of clinical trials, deployment. We have a responsibility to ensure appropriate regulatory oversight, but it can be dramatically enhanced in the efficiency of moving these fundamental discoveries to the bedside.

Senator SPECTER. Dr. Tabak, would you come sit next to me? I want to bring you back to the panel for just a minute or two.

Dr. Seiden, in seeking to have a separate agency for cures acceleration to approach the "Valley of Death," it's a very tough job to get a new entity. Did you think that there was any appropriate role for NIH to make grants to cover the so-called "Valley of Death," to find that the practical application to assist here in regulating the research achievements to the bedside?

Dr. SEIDEN. The "Valley of Death," I think is very real and getting wider. I think that funds particularly targeted to crossing ideas into the area where they can help the public are incredibly important.

Whether this Agency should be part or separate from the NIH, I think is, at least in my mind, a little more complicated. One of the challenges for it to be effective it has to be relatively nimble and it has to figure out how to work with industry in a way that sometimes has been a little challenging for the NIH; that said, it would be important if we built a new government agency to do this, that it not replicate some of the challenges that the current Government agencies have with working with industry. I see that as one of the really big challenges.

Senator SPECTER. Well, if NIH were to undertake that, the object is to promote health and if all of the eggs are in the research basket, you have the "Valley of Death," and there's not a practical application.

One of the factors on my mind is that NIH doesn't like to divert any of its funds from research and I don't blame NIH. NIH would like to have more money and I would like NIH to have more money.

I think Dr. Curran and Dr. Kaufman are modest in just wanting three and one-half-times the $30 billion. I think the yield would be greater.

What do you think Dr. Kaufman? Would it be realistic to ask NIH to do some of this work in the clinical application?

Dr. KAUFMAN. Sir, I have a little bit of experience in this area. I'm Chair of BioAdvance, which is the Greenhouse of Pennsylvania, for southeastern Pennsylvania of which you're probably familiar with. This funds early stage biotechnology and there is this "Valley of Death" between what we do as academic researchers, and to get to that point, there is a great need for proof of concept funds.

The SBIR process is a little bit beyond the proof of concept funds, so there is a gap there. But there is an entirely different mindset for people who fund that kind of research; typically, it's under economic development rather than NIH.

So, in Pennsylvania, the Greenhouse, the BioAdvance, is under the Department of Economic Development, not under the Department of Health, because the ideas that need to go into that have to be people from the biotech industry looking back, and commer-

cialization interest looking back, as much as it is science looking forward.

Senator SPECTER. Dr. Thompson, the University of the Pennsylvania hospital has the benefactors of Leonard and Madeline Abramson, who have done so very much on supporting cancer research.

Do funds from a source like that enable you to take more research on the innovative projects as opposed to looking to NIH for the peer review, which may be somewhat more restrictive?

Dr. THOMPSON. It certainly is true that funds that have benefited the Abramson Cancer Center from the Abramson family and have allowed us to undertake innovative research that couldn't be funded on the scale that we do for translation. Because translation really requires a scale of funding that exceeds what we can get from standard grants as the others have said.

One thing that the Abramson Institute, which is funded by the Abramson Family Foundation, has allowed us to do is to explore new ways to harness the immune system to fight cancer and to do real innovative clinical trials at the level of cost that those trials invoke, and that's been a transformative principle for us in the Abramson Cancer Center. So, yes, sir, those funds really do allow us for innovation and some way of receiving that kind of funds in a public-private partnership would greatly facilitate traversing this "Valley of Death," as you described it.

Senator SPECTER. Dr. Pestell, Jefferson has the benefactor of Kimmel, Sydney Kimmel, and a very generous allocation of personal funds.

Does that help you more with an innovative branch, as opposed to being limited by what NIH will approve on grants?

Dr. PESTELL. Yes, although relatively modest by standards, the endowment from the gifts of Sydney Kimmel has allowed us to provide funds for pilot projects, which are characteristically out-of-the-box transformational ideas. We followed up those studies and many of those have led to subsequent peer-review funding by NIH; so, absolutely, sir.

Senator SPECTER. Dr. Kaufman, you commented about $30 million you have, is that from private funding so that you don't have to go through the peer-review process on that?

Dr. KAUFMAN. That's right.

Senator SPECTER. It's the Kaufman review process?

Dr. KAUFMAN. It's the Kaufman and close associates. So, it's basically the program leaders within our cancer center that make those decisions of how we allocate those funds. But we can fund highly innovative research, but that money comes from gifts and it also comes from what we bring in from tech transfer, from our technology transfer; in other words, royalties that we get from our work. We put all of that back in to fund—we try to fund the most highly innovative research.

Senator SPECTER. To what extent, Dr. Kaufman, do those royalties—how big a factor are the royalties?

Dr. KAUFMAN. Well, for us they are very big. We don't have grateful patients, we have very ungrateful mice who don't want to donate anything and we don't have eventual graduates, so we're not a teaching institution. So, we only get our money from two

sources. We either get it from royalties or we get it in discretionary dollars. We get it from royalties or we get it from gifts, but NIH, consistently, is the biggest source of funding for our research.

Senator SPECTER. Dr. Seiden, how does Fox Chase do on Dr. Seiden: We generate a couple of million dollars a year in royalties, but most of our discretionary research dollars come from philanthropy and/or monies we make on the clinical portion of the business.

Senator SPECTER. How about at the Hospital of the University of Pennsylvania, Dr. Thompson, on the royalty line?

Dr. THOMPSON. I think that we, like the other institutions, receive royalties for a number of innovations. We receive royalties for the drug discovery that was described in the New York Times article, Herceptin, because the first antibody was actually made by investigators who are now on faculty at the University of Pennsylvania. But we also rely, equally, on funding from philanthropy and from grateful patients.

Senator SPECTER. And Children's Hospital, Dr. Curran?

Dr. CURRAN. Yes. We actually sold a royal to rights to the Rodatech, rotavirus vaccine for $180 million. If I may clarify my previous comment, I was not arguing for tripling the NIH budget, only the portion devoted to the competitive grant-review process, which is a much smaller percentage than $30 billion.

Senator SPECTER. Well, Dr. Tabak, you have a fair amount of gris to the mill here.

There have been some courageous statements made by a group of research scientists who have to come to the National Institutes of Health. There might be some motivation not to be too critical, but I think the experts here have been candid, somewhat critical.

What do you have to take back to Washington on the 12 o'clock or——

Dr. TABAK. Thank you Senator Specter.

First, I want to thank you for this hearing and for the opportunity to listen to your colleagues.

Much of what I heard reinforces views that were expressed during the peer-review process, which we held regionally around the country and I think, in some instances, reinforces the view that we are on the right track on some things. But as you have pointed out, sir, there is more work to be done.

I will take back the comments made by the panelists to discuss with my colleagues so that together, this is a partnership, we continue to refine things to the very best possible end result.

Senator SPECTER. Well, thank you all.

My own sense is having been in the field and having the experts from the National Institutes of Health, it is an enormously impressive hearing. A big U-shape 25, approximately, directors of the NIH come in.

The question which I would like to pose is how long would it take and how much would it cost to cure Parkinson's or to cure juvenile diabetes? I know in asking those questions there is no finite answer, but when you deal with the Congress, you need to be if not specific, at least, speculative.

Your judgments are very valuable. You know, obviously, a lot more about it then anybody else does and that's why we pushed to

try to get answers as concrete as possible. We aren't really likely to fund 1 in 3 on the current standards.

My proposal and I'm trying to get in the comprehensive reform, is to take the $30 billion, which we've moved only to slowly, it was stagnated at that point. If we add the $10 billion more—I've talked to the chairman of the two relative committees, Senator Dodd on the Health Committee and Senator Baucus, on the Finance Committee. They have the work; it's not the Appropriations Committee to try to fix the new floor of NIH at $40 billion. You have to have realistic annual appropriations, but if you start from 1 in 10 at $30 billion and you want 35 percent, that is 3.5 of 10 percent. We're really not going to get there.

So, it would be my hope, Dr. Tabak, that you would take back an underlying message, if not a dominant theme, that you need to give more attention to doctors like Dr. Jaffe, who are more on the transformative side, and that incremental progress is important. But there has to be a way to move beyond that in a more dramatic fashion. You take that message back and when I see my 99 colleagues on the Senate floor this afternoon; we're voting at 5:30 p.m., I'll tell them there was one unanimous view today, more funding.

CONCLUSION OF HEARING

Thank you all very much.

[Whereupon, at 11:30 a.m., Monday, July 6, the hearing was concluded, and the subcommittee was recessed, to reconvene subject to the call of the Chair.]

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