Eileen K. Jaffe, Ph.D.
Professor/Senior Member, Fox Chase Cancer Center
Testimony before
Subcommittee on Labor, Health and Human Services, and
Education, and Related Agencies
Committee on Appropriations
United States Senate
Philadelphia, Pennsylvania
July 6, 2009

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 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 ~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 six 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 ~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 National Institutes of Health 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.

Testimony
Before the
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies
Committee on Appropriations
United States Senate

Providing Support for Innovative Research Projects

Statement of

Lawrence A. Tabak, D.D.S., Ph.D

Acting Deputy Director, National Institutes of Health
and
Director, National Institute of Dental and Craniofacial Research, National Institutes of Health
U.S. Department of Health and Human Services

For Release on Delivery
Expected at 9:30 a.m.
Monday, July 6, 2009
National Constitution Center, Philadelphia, PA

Good morning, Mr. Chairman. I am Dr. Lawrence Tabak, Acting Deputy Director of the National Institutes of Health, 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 4 major chronic diseases. [1] 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

[1] Manton, KG, Gu, Xi-Liang, Lowrimore, Gene, Ullian, Arthur, Tolley, H. Dennis (2009) NIH funding trajectories and their correlations with U.S. health dynamics from 1950 to 2004. *Proc Natl Acad Sci USA* Early Edition, www.pnas.org/cgi/doi/10.1073/pnas.0905104106.

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 (Pub. L. 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. 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 FY 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 non-small 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 National Cancer Institute 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 (HPV) 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 National Cancer Institute. 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 paradigm. 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.

STATEMENT OF CRAIG B. THOMPSON, M.D., DIRECTOR OF THE ABRAMSON CANCER CENTER, PROFESSOR OF MEDICINE AT THE UNIVERSITY OF PENNSYLVANIA SCHOOL OF MEDICINE
JULY 6, 2009

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 NIH-funded investigator for over 20 years and before that served as a medical officer in the US 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 1300 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 NCI-designated Comprehensive Cancer Center received over $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".

Testimony of Thomas Curran, Ph.D., FRS
Deputy Scientific Director
The Children's Hospital of Philadelphia Research Institute
The Children's Hospital of Philadelphia

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-reknowned 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 over $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 one in three 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 over $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.

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%. 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 committee for having me here today, and for their attention to this important matter.

Thank you.

Testimony from The Wistar Institute

Presented to the U.S. Senate Labor, Health & Human Services Committee;
Subcommittee on Appropriations

July 6, 2009

Presented by: Russel E. Kaufman, M.D., President and CEO, The Wistar Institute

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. 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 National Cancer Institute (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 seven 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 National Cancer Institute, 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.