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Introduction

Mr. Chairman and members of the Committee, thank you so much for inviting me to testify today at this very important hearing. I am Ed Miller, Dean of the Medical Faculty and CEO of Johns Hopkins Medicine. Johns Hopkins Medicine is the organization that represents the Johns Hopkins University School of Medicine and Johns Hopkins Health System.

I am pleased to be here to give you my perspective on the findings of the report: "A Broken Pipeline? Flat Funding of the NIH Puts a Generation of Science at Risk." The report highlights, in a very personal way, the impact of the current funding environment on the careers of some of our country's most promising young scientists. As the person charged with the privilege and responsibility for the operation of one of the many institutions across this country whose mission is to train future physicians and researchers, as well as provide patient care, I can tell you that my counterparts at other universities and I struggle everyday to help all our investigators navigate the current funding climate.

I believe we may lose a generation of enthusiastic, inquisitive scientists if they conclude NIH grants are out of reach. The statistics are very discouraging. Today only 1 out of every 4 grants is ever funded – 8 years ago it was 1 in 3. Only 12 percent are funded after the first submission. For first- time applicants these odds seem insurmountable and they are discouraged. They spend many weeks and countless hours preparing their proposals only to be told their score was not high enough and they should rewrite and resubmit. Or worse yet, they are not scored at all. No wonder they are discouraged. I also believe that in the quest to obtain funding, all of our scientists, both young and more senior, are becoming risk-averse, and curtailing their proposals and the most cutting edge science may remain undone because in an environment of scarce resources only the safe-bets are funded.

First, I commend you and your colleagues in Congress for their historical commitment to biomedical research and National Institutes of Health (NIH) and the support this provides to our nation's research universities. What many Americans may not realize is that 85 percent of the funding that Congress provides to NIH actually comes back to their local communities. Many of the startling advances in identifying early indicators and causes of diseases are the result of those well-spent federal research dollars. I am convinced we are on the cusp of a dramatic transformation in health science discovery and cures. Unfortunately since 2004 the levels of funding for the NIH have not kept pace with inflation and NIH has lost upwards of 13 percent of its purchasing power. Not only have we lost ground to inflation, but at Johns Hopkins we have seen an actual decrease in our total awards from our peak level in FY 2005. This is having an impact across our entire institution but has had a particularly insidious effect upon our young investigators.

Going forward, NIH needs at a minimum, funding increases at least equal to the biomedical research inflation index (BRDPI). Anything less, is a real cut to science, threatens the careers of our young faculty and will weaken the nation's role as a worldwide leader in the biomedical field. The current projection for BRDPI for FY 2008 through 2013 is 3.5 percent. But if past is prologue (in FY 2007 it was 3.9 percent and FY 2006 was 4.6 percent) one might expect actual BRDPI levels to exceed current projections. The biomedical research community is seeking an increase of $1.9 billion which represents BRDPI plus 3 percent. This infusion of $1.9 billion will allow research labs to keep pace with rising costs and provide resources for new and innovative projects.

We in academia are cognizant of the overall fiscal situation that members of Congress and this and future Administrations face. We are also aware that there many compelling demands upon the discretionary funds available to appropriators. Nonetheless as a community, we feel it is critical that we come before you to reiterate how important it is to support biomedical research not only for ourselves but future generations. The plight of our young investigators exemplifies perfectly both the current and future risk of allowing our international leadership in this area to erode.

Funding climate hinders high impact research

I hear from my faculty that NIH study sections, with the limited funding available to them, tend to favor safer bets. Study sections look for increasingly more preliminary data in grant applications. In essence they are seeking so much preliminary experimental information that many applicants say most of the proposed project would have to be already done before they get funding. They are funding incremental steps, not bold initiatives. This modus operandi clearly discourages creativity and cutting edge ideas.

I also hear that because the chance of being funded is much lower, all investigators - especially the younger ones - are spending more of their time in grant writing instead of doing the creative research. I fear that their goal then is not to do creative research but to survive by going for more sure bet type of research for the sake of securing continuous funding.

We also hear that many highly accomplished investigators are also suffering with limited funding. The upshot is that the government has invested tremendously in the past into our intellectual capital, and now we may not reap the benefits.

Let me share an example that clearly demonstrates the tremendous value of supporting our young investigators and the nature of cutting edge research. In September of 2006, Carol Greider, PhD (Professor and Director of Department of Molecular Biology and Genetics, Johns Hopkins University School of Medicine), Elizabeth Blackburn, PhD (Professor of Biology and Physiology in the Department of Biochemistry and Biophysics, University of California, San Francisco) and Jack Szostak PhD (Professor Department of Genetics, Harvard Medical School) Harvard were awarded the most prestigious prize in American medicine - the Lasker Award. They shared the award for their work in telomerase: an enzyme that helps maintain the ends of chromosomes. The award is based on findings the three made with respect to cell function and genetics, twenty-two years ago, and is considered today to be one the most advanced areas of biomedical research. At the time Dr. Greider was in her early 20's. Her more senior colleagues Szostak and Blackburn were in their early and mid- 30's respectively. These three were well below today's average age of 43 for obtaining the coveted first R01 grant. Subsequent research has revealed that telomerase is elevated in more than 85 percent of all human cancers. It enables cancerous cells to divide indefinitely, making them virtually immortal. Several biotech companies are now devising anti-cancer drugs to block telomerase. If Doctors Greider, Blackburn and Szostak were seeking funding for this same body of work today, would current success rates provide them funding?

I can not help but worry that groundbreaking work such as this is being delayed or left completely undone today. A case in point is that of Joel L. Pomerantz, PhD an Assistant Professor in the Department of Biological Chemistry and the Institute for Cell Engineering at Johns Hopkins University School of Medicine. He wants to use new technologies that are the keys to ground-breaking biomedical discoveries. These new technologies or high-throughput methods provide an opportunity to examine entire biological systems, which are large networks of interacting molecules. The high-throughput technologies have provided young investigators new "microscopes," with which to observe thousands of genes in complex biological systems and generate new hypotheses, producing ground-breaking ideas.

His laboratory has developed ways for using such methodology to screen for genes involved in the normal immune response (lymphocyte activation), and also for genes that function in signaling pathways that are dysregulated in different forms of human cancer and in autoimmune disease. Thus, his screens promise to yield genes that could advance our knowledge of basic immunology and cell biology but might also emerge as targets for the development of novel therapies for cancer, autoimmunity and other diseases of aberrant cell growth and function. It is important to note that it has only recently been possible to do such research. This has been made possible by: the sequencing of human, mouse and other genomes, and the emergence of RNAi technology and the ability to generate genome-wide RNAi libraries that can interrogate the function of most, if not all, known or predicted human or mouse genes.

We now find that study sections are slow to embrace this more novel, creative and unbiased global approach, preferring the traditional hypotheses that link one event to another in a linear way; yielding a potential biased view of a complex system. Dr. Pomerantz and others tell us, given that these technologies cannot guarantee a specific outcome, their use to screen for genes involved in specific pathways or disease status in an unbiased way has been met with resistance. As such, the more traditional, simple hypotheses are proposed rather than the more creative, unbiased way to discover critical biological and disease pathways. This situation is particularly heightened because of the limited NIH funding -- leading to a regression rather than progression in the way we do science.

Fortunately for Dr. Pomerantz and the members of his lab, Johns Hopkins has been able to provide some institutional support and private foundations have funded his research on a small scale, and they have already made interesting insights in only a few years. But the conventional wisdom is that the NIH will not support such ventures in an R01 application, unless the applicant is already well-established, well-funded, and one of the very, very few lucky recipients of a Pioneer or Innovator award.

Dr. Pomerantz is 40 years old, has tremendous credentials (degrees from Brandeis and the Massachusetts Institute of Technology and has trained with 2 Nobel Prize winners: Philip Sharp and David Baltimore), and a very promising career before him. He recently submitted an R01 application which was scored on the first round, but failed to meet the 12% payline. He now has 2 more chances to resubmit. Without NIH funding, the fate of Dr. Pomerantz's proposal is uncertain.

Let me share the story of one more of our faculty whose experiences also parallel what you see in the "Broken Pipeline" report released today: Ben Ho Park M.D., PhD. Dr. Park is an Assistant Professor of Oncology with a joint appointment at the Johns Hopkins Whiting School of Engineering, Department of Chemical and Biomolecular Engineering who has some novel ideas about treating breast cancer. Using powerful molecular genetic techniques, his lab is attempting to identify genes involved with clinical drug resistance. It has been previously demonstrated that loss of tumor-suppressor genes and/or their downstream effectors can confer resistance against certain chemotherapies. The lab hypothesizes that there are other genes where inactivation in a recessive manner can also lead to clinically relevant drug resistance. This problem is of extreme importance to clinical oncology, as the emergence of drug-resistant cancers is what limits the effectiveness of current therapies.

The lab is also trying to understand pathogenic mechanisms of growth/hormone receptor signaling. The continuous exposure of breast tissue to estrogens and other growth factors likely plays a role in the carcinogenic process that transforms a normal breast epithelial cell into a cancer. The lab is trying to elucidate the molecular mechanisms of aberrant receptor signaling that contributes to this process.

Instead of thinking about breast cancer research, Park says he is spending 90 percent of his time chasing grants. He even has his trainees applying for their own grants to make up for the lab's drop in NCI dollars. He reports that 9 out of 10 applications do not get funded and for those that do, R01 awards are then reduced 29 percent. So his $218,000 grant is now only $155,000.

Park says he has not had to let people go from his lab, but "I can't think about science any more. I have to focus on getting grants" from foundations and philanthropists. Even those grant applications from his trainees have to be reviewed and rewritten by Park to give them the best chance of getting approved. It means time away for all from their research into developing novel means for treating breast cancer.

Dr. Park reports that unfortunately his story is not unique and he worries that if the current funding environment is not reversed soon, we are going to lose a lot of very talented people in science. In a letter to the editor that appeared in the *Baltimore Sun* last spring Dr. Park and a fellow cancer researcher at the University of Maryland wrote:

> *The tragedy stems from our inability to continue to do bold new research that can ultimately affect the prevention, diagnosis and treatment of a myriad of diseases such as cancer. Working in academics is a privilege because it affords scientists the ability to strike out on new creative and innovative projects that would not be allowed in most biotech or pharmaceutical companies.* **…** *Thus, the ultimate repercussion of decreased federal funding is not loss of academic scientists, but rather the millions of lives that biomedical research could have otherwise saved.*

Conclusion

Federal support for biomedical research has helped to transform our ability to detect disease, treat patients, and deliver healthcare with greater effectiveness and affordability. At the same time, the return on investment for the American taxpayer has been high, as research has fostered discoveries that have led to new patents and products, and to the creation of new companies and job opportunities.

The recent enactment of the America COMPETES Act as well as the NIH reauthorization legislation enacted at the end of the last Congress, demonstrates that the President and Congress have embraced the notion that funding for basic research is essential to strengthening America's competitive standing in the world. However, the funding levels envisioned in neither bill have been realized – particularly with respect to NIH. The reauthorization bill called for appropriations of $30.3 billion for FY 2007, NIH only received $29.1 billion. $32.8 billion was authorized for the current FY 2008, NIH received only $29.5 billion. For the upcoming FY 2009 the bill authorized "such sums as are necessary." The President has proposed a freeze at the 2008 level and I understand that the budget resolution currently before the Senate calls for an increase to $30 billion. The fact is: federal investments in biomedicine and basic science across the disciplines have taken the U.S. to the leading edge of innovation. The question we now face is whether as a country we are willing to pay the price to remain in the lead.

Returning to our focus today, the young investigator, I believe it is critical to point out that most ideas that turn into Nobel Prizes come from investigators before they reach the age of 40. While we can not pinpoint today, whose work will ultimately be recognized in this way, it exemplifies why support for their work must continue and why we must support “out of the box” thinkers during the early stages of their careers. Who knows, perhaps the work all these scientists are conducting - or would hope to conduct if funding were more readily available - could be as critical to future breakthroughs in healthcare as that of past Nobel and Lasker award winners. It would be a shame to never know.