



U.S. Senate Committee on Appropriations

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Contact: Tom Gavin, 202-224-3904

U.S. Senate Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies Testimony of Brent Iverson

WASHINGTON, D.C. – The U.S. Senate Appropriations Labor, Health and Human Services, Education, and Related Agencies Subcommittee on Monday held a hearing to examine the proposed Fiscal 2008 budget for the National Institutes of Health. As part of that hearing, the subcommittee heard testimony from Dr. Brent Iverson, Distinguished Teaching Professor and the Raymer Professor of Chemistry and Biochemistry at the University of Texas at Austin. His testimony is below.

My name is Dr. Brent Iverson. I am a Distinguished Teaching Professor and the Raymer Professor of Chemistry and Biochemistry at the University of Texas at Austin. I am here representing NIH funded scientists at research universities, both public and private. I was an undergraduate business major at Stanford University until I worked in Professor Jim Collins's chemistry research laboratory. My undergraduate research experience in that NIH-funded lab charted the course that directly led to my scientific career.

Today, I want to tell you about NIH funding from my individual perspective, to help put a face on the budget numbers. My research spans the interface of organic chemistry and molecular biology, on the basic science end of the medical research spectrum. I have well over 100 publications, many in the most prestigious scientific journals. I hold 20 current or pending patents, most of which are licensed and are being used by companies across the country.

I would like to make three points concerning the importance of growing the NIH budget. The first point concerns being able to take full advantage of what the budget doubling allowed us to start. In my own lab, the increased funding provided by the doubling allowed the development of a powerful new method we call APEX that allows us to engineer better antibodies.

Antibodies are the hottest segment of the pharmaceutical industry today, with over 20 now approved for the treatment of diseases such as cancer (ex. Avastin and Herceptin, for treating colon and breast cancer, respectively) and rheumatoid arthritis (ex. Humira). Antibodies are even being pursued as a new approach to treating infectious diseases. Antibody drugs represent the new generation of so-called targeted therapies, because

they are capable of seeking out and attacking only their intended disease targets with remarkable precision. The result is a much more concentrated therapy, one that avoids many of the serious side-effects of more traditional approaches such as the standard chemotherapeutic agents used to fight cancer.

Our APEx method allows us to take existing antibodies and make them more powerful by factors of 10 or even 100 or more. This can often make the difference between an effective or ineffective antibody treatment. For example, we started with an antibody against anthrax that could delay but not prevent death in animals exposed to live anthrax spores. After making the original anthrax antibody about 20 times better, our engineered antibody prevented illness and even cured animals treated with the same dose of live anthrax spores. That antibody is being pursued commercially and may soon become a stockpiled countermeasure.

With APEx developed, we need continued strong funding to take full advantage of it. We are ready to start working on engineered antibodies that attack a variety of disorders such as allergies, inflammatory diseases, and cancer. I am very worried that in the current funding climate, our ability to pursue these diseases is going to be severely limited. You can only imagine my frustration at working so hard to develop the means of making a difference, then having limited support to apply it broadly.

I would like to make a second important point, this one concerning basic science breakthroughs. Tight funding as we currently have now has the effect of making grant funding decisions overly conservative. I have been on many NIH funding panels and have seen this phenomenon in action. Right now, only about 10% of the grants in my research area receive money, so the panels must choose the ~~and~~ miss, sure things+ that represent the obvious next steps of research. It is not that the panels are overly conservative, it is just that no panel can reject these proposals because they will almost certainly lead to advances based on the strong scientific foundation upon which they are built. But what about new ideas that are not proven yet? In other words, the ideas that come out of nowhere, establish new paradigms and change the way we think. With such a limited number of grants supported, there is no money in the system for us to work on more speculative projects, ones closer to the leading edge of knowledge. There is also not enough money to fund those scientists who have not yet had the opportunity to generate extensive preliminary results, namely new faculty members.

Scientific breakthroughs rarely come from a research effort aimed at the ~~and~~ miss obvious next step+. In my experience, our breakthroughs have come when we least expected it while we were exploring beyond the boundary of what we understood well. For example, I want to draw your attention to the cover of the brochure you have been given today. There is an outline of a complicated molecule in the green panel. It is actually a molecule from my laboratory that binds to a large, specific sequence of DNA using an entirely new type of interaction we have named threading polyintercalation. Our molecule is the first reported to bind to the DNA double helix with a topology that can be described as being similar to how a snake might climb a ladder.

This new approach came from a highly speculative project in my lab intended to make an artificial protein, but once we started analyzing the behavior of our molecules, we realized that what we were doing was also applicable to targeting DNA. Although not yet ready for commercial application, imagine a new class of drugs of the future that target the DNA sequences of viruses, bacteria, or cancer cells directly. Talk about getting to the heart of the matter!

Without increased funding, our ability to explore boundaries such as these and make startling breakthroughs is going to be severely limited. True breakthroughs that move science in new directions often take years to turn into a practical new therapy and only occur when scientists are given the freedom to take scientific risks. I am deeply concerned that a lack of money today to explore beyond conservative boundaries will have a crippling effect on medical breakthroughs that will be felt for decades.

As a corollary to this, I am also concerned that the current lack of funding support will take a heavy toll on young scientists in two ways. The most direct is that they will not receive enough funding to launch their careers because there is only enough for the established scientists. As a more indirect effect, I am worried that the bleak funding picture will dissuade the best and brightest from even pursuing a career in academic scientific research.

I would like to finish by describing my concern about science education. I hope all of you understand that the product of NIH research funding to University researchers is not only the research itself, but additionally, the training of students. It is a very simple equation. Limited funding for research now means fewer trained scientists for the future and consequently fewer research breakthroughs for years to come. As a result, I am very concerned that our place as the world leader in medical research is not secure.

I generally accept 3-4 new PhD students in my laboratory every year. My former students now work in academics as professors/researchers or in many companies around the country. With a significantly reduced chance of getting a grant funded, I am forced to take proportionately fewer graduate students. In fact, I am not accepting a single new graduate student this current year in the antibody engineering lab. The bottom line is that limited funding means we are also limiting the number of students being trained, and I believe our country needs more, not fewer, highly trained scientists to maintain a healthy technology-based economy.

Finally, being on the campus of one of the largest undergraduate institutions in the country, I am acutely aware that NIH research funding has a tremendous impact on large numbers of undergraduates. I have had over 100 undergraduates work in my lab. Across our campus, around 1000 undergraduates will take part in state-of-the-art scientific research, most of it in state-of-the-art labs with NIH funding. The positive impact of this is almost incalculable. Most of these individuals will not go on to become scientists like I did, but they will be able to articulate to the rest of society what science is, and what research means for our country. With every study pointing to the frightening inadequacy of scientific education across our population, a rare piece of

good news is undergraduate research. We need leaders in all segments of society who understand science and can make appropriate choices as we chart the increasingly technological future of our country and our world. Again, it is a simple equation. Not enough money for the labs means proportionally fewer undergraduate as well as graduate student research opportunities across the country.

As a University researcher in the prime of my career, I need to see enough money in the NIH budget so that I can take full advantage of what the doubling allowed me to create. There needs to be enough money in the system to help provide an environment that allows risk taking, thus making scientific breakthroughs more likely and allowing young scientists the opportunity to launch their careers. We also need budget growth to continue the essential scientific training of students ranging from undergraduates to PhDs. All of this is essential if the United States is to remain the world leader in both academic and commercial medical research.

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