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Senator Stevens, Senator Inoue, and other members of the committee:

I. My Life in Science.

It is my pleasure to appear before you and speculate on the future of science. I admit to having no crystal ball, but I am here to give my predictive powers a workout. First, as requested, I will tell you about my own research.

A. Biological Water Channels—the Aquaporins.

Water is often described as the "solvent of life," since it has long been known to be the major component of the human body. About 70% of our body mass is water, and the same is true of all other life forms. Without water there is no life.

The organized distribution of water within and between body compartments is essential to our well-being. While you are listening to me speak, each of you is bathing the surface of your brains with spinal fluid, secreting tears to protect the surface of the orbits of your eyes that are filled with aqueous humor. You will be releasing water in your exhaled breath, sweat, saliva and digestive juices. Your kidneys will be concentrating urine. At the same time, the trees outside will be absorbing water from the soil and releasing it from their leaves. Despite major advances in molecular biology, the mechanism by which water enters and leaves cells was a long-unanswered problem in biology.

All of these processes involve a simple cellular plumbing system that is conserved throughout nature and is made from a family of proteins referred to as "Aquaporins." These proteins were a serendipitous discovery made in my laboratory 14 years ago while we were pursuing research of an entirely unrelated project. We now have greatly increased understanding of fundamental processes in physiology, and we anticipate that this knowledge will in the future allow us to prevent or treat a host of clinical problems.

B.Clinical and Physical Significance of Aquaporins.

AQP1 is responsible for a blood antigen incompatibility and water permeation through capillaries; defects in AQP0 result in cataracts; AQP2 is responsible for excessive renal concentration which underlies fluid retention in heart failure and pregnancy as well as defective concentration in bedwetting. AQP3 is known to enhance the integrity of our skin and is the focus of anti-aging skin products. AQP4 mediates the deleterious brain edema following strokes and head injuries and appears to prevent or ameliorate epileptic seizures. AQP5 is essential for normal function of our secretory glands protecting us from corneal injury, dental caries, and heat prostration. AQP7 is implicated in obesity and AQP9 is involved in the insulin-deficient and insulin-resistant forms of diabetes as well as the liver damage from arsenic poisoning. Plant aquaporins may be manipulated to increase crop tolerance to drought, and microbial aquaporins may be future targets of antibiotics. While our original discovery was initially a total surprise, we now look eagerly to accomplishing exciting new applications.

C. Future of Science as Predicted from my Experience.

In order to speculate about the future, I will need to revisit my own past. I have to tell you that I think my childhood was a wonderful preparation for a future in science.

1. Early Education.

Not to be underestimated is the importance of the human side of science. As my family and friends could tell you, I am a regular person from an unexceptional background. My parents were the offspring of Norwegian farming families from South Dakota. My mother never went to college, but my Father was able to study at the U of Minnesota and taught chemistry at St. Olaf and Augsburg Colleges—small liberal arts schools in Minnesota. Fortunately for my five siblings and me, our parents read to us every night from the Bible as well as the books of Laura Ingalls Wilder, Lewis Carroll, and Robert Louis Stevenson. I believe this provided the literary background helpful for any career.

My siblings and I attended public schools, and our teachers were highly respected members of the community. Growing up in the late 1950s and early 1960s, I certainly benefited from the post-sputnik emphasis on science in the classroom. Although children often find textbook math and science to be dull, our teachers brought the lessons to life: by doing practical calculations such as our speed in a 100 yard dash; by taking us on nature walks; by performing simple hands-on scientific demonstrations. We loved optics but sometimes used the magnifying glasses for unintended purposes, such as incinerating ants on the sidewalk, We were fascinated by building simple electrical circuits, even though we sometimes used them to shock each other. Our excuse was always "But hey, it's science!"

2. Career Pathway.

I actually did not intend to pursue a career in pure science but studied science because I wanted to become a physician. I was a medical student when I really became excited about science while working on a research project to identify the cause of infectious diarrhea—often referred to as the "la Turistas." In a lab at Johns Hopkins that was entirely funded by US taxpayer support, I worked alongside an exciting and colorful international cohort of scientists—including Israelis and a Palestinian, Chinese and a Filipino, an anti-Francoist Spaniard and a debonair Italian. Despite the different cultures we became the best of friends and have remained colleagues ever since.

Determined to combine clinical care and medical research, I was fortunate to receive an early NIH grant for clinical investigators that allowed me to work in a lab to gain the experience needed to succeed at science. I do not wish to underplay the difficulty though, and my family always encouraged me, even though it meant forgoing a potentially lucrative medical practice, to pursue my dream. I was optimistic despite the financial compromise, the absence of a promised faculty position, and the total lack of certainty that I would ever succeed.

II. Issues related to US Science.

Due to the longstanding generosity of the American Taxpayer and the wisdom of both of our national political parties, the United States has been the world's leading scientific presence for as long as I can remember. Unfortunately, I am not completely optimistic about the future, and I greatly fear that we will be overtaken by other countries.

A. Prominence of US Science.

My laboratory has always had complete freedom to collaborate with the best scientists in the US. Nevertheless, you may be surprised to learn that it was our collaborations with scientists in Europe and Japan that led us quickly in new directions that were not feasible here in the US. For example, our high resolution immuno-electron microscopy studies were undertaken in collaboration with investigators in Denmark and Norway. The atomic structure of the aquaporin protein was solved by membrane crystallographic studies with scientists in Switzerland and Japan. We collaborated overseas simply because these scientists were the best in the world in the highly specialized techniques.

B. US Government Funding of Science.

My own career was entirely supported by research funds from the US taxpayers in the form of NIH grants. In my own case, the research funding provided an opportunity to pursue science by following discoveries—even when they did not conform to the original plan. If I were a scientist in traditional industrial laboratory, I would never have had the flexibility to discover and further explore the aquaporin water channels, because this project did not fit into the company's primary objectives. I worry that US government funding for scientific research may some day come with absolute restrictions that prevent change of focus when unexpected discoveries appear.

I also worry that US government funding for scientific research will be reduced at this time of a huge federal budget deficit. Unfortunately, failure to provide steady research funding will be most severely experienced by the newly trained scientists who are beginning their independent research programs. These young scientists are our richest source of fresh ideas, but they can least afford to wait for funding.

This is particularly true of younger physician scientists who have spent up to 10 years in clinical training before they can become independent scientists. While veteran scientists may survive intervals without funding, younger scientists with families are often forced to choose strictly clinical jobs that will never allow them to make important breakthroughs in biomedical science. When they quit research, they quit forever. This is most unfortunate, since these are the same individuals with insight that will allow basic scientific discoveries to rapidly be applied at the patient's bedside.

C. Dependence on Non-US Scientists and the Mistreatment of Scientists.

Much outstanding research undertaken in US laboratories is performed by scientists that came here from other countries. For reasons including increased restrictions on visas for scientists who wish to work and study in the US, the number of graduate students and scientists coming here is now declining. A rare but highly damaging issue has resulted from the mistreatment of scientists by governments. As Chair of the Committee on Human Rights of the National Academies of Science, I am familiar with cases from around the world including two devastating cases in the US.

Taiwanese-American scientist Wen Ho Lee was publicly referred to as "Spy of the Century" while shackled hand to foot for a year in solitary confinement. Dr. Lee was

threatened repeatedly with execution if he did not confess to being a spy for the Peoples Republic of China. An independent review of the charges eventually brought his release with an apology in September 2000, but our standing with East Asian students has not been restored.
<http://www4.nationalacademies.org/news.nsf/isbn/s08312000?OpenDocument>.

During the hysteria following the 2001 anthrax killings, a dedicated infectious disease specialist, Professor Thomas C. Butler, was arrested and charged with multiple federal felony counts when plague bacillus samples disappeared from his laboratory at Texas Tech University Health Sciences Center. Dr. Butler's work was entirely humanitarian, and no evidence of bioterrorism has ever been uncovered. Highly respected by his peers in the US and admired by his colleagues in developing countries, Dr. Butler was hounded by the US Department of Justice. While cleared of all charges related to bioterrorism, a conviction was obtained on confusing technical charges indirectly related to Butler's research budgets. Butler is now serving a two-year prison sentence while his appeal is pending. <http://www.fas.org/butler/>

D. Visibility of Scientists in US Society.

The disappearance of scientists from public life is a concern. Interestingly, several of our nation's founders included individuals who were leaders in science—Benjamin Rush [chemistry and medical biology], Thomas Jefferson [agricultural science], and Benjamin Franklin [electricity].

During my childhood, we would see scientists on the extremely popular Disney television program. Familiar to us was Wernher von Braun who demonstrated rocketry. Nobel Laureate Glenn Seaborg demonstrated the concept of a chemical chain reaction with mouse traps and ping-pong balls during a truly unforgettable program. At that time, Nobel Laureate Linus Pauling was widely recognized for his public efforts that launched the Limited Test Ban Treaty that still protects us from radioactive fallout in the atmosphere. Nobel Laureate Richard Feynman's books were popular reading.

E. Declining Scientific Awareness by US Public.

A final and major concern relates to the decreasing level of scientific understanding by the US public. I challenge the members of this Senate Committee to ask your constituents to name even a single contemporary American scientist. But let me place some of the blame upon myself and my scientific colleagues. Except when challenged for negative reasons, we often consider ourselves too busy to engage in activities that may enlighten the rest of our society.

Widespread scientific ignorance significantly discourages young Americans from pursuing science. In my view, the need to educate our non-scientist citizens is just as important as the need to encourage future scientists. Recent controversies about the teaching evolution in high school biology appears to be a thinly disguised attempt by a minority to establish their particular religious viewpoint in publicly funded education.

Several parameters reflecting a decline in the national level of science understanding b y the American public are apparent. Four hundred years after Galileo, one in five Americans still believes the sun rotates around the earth. Half of all Americans believe dinosaurs and humans coexisted in prehistory—apparently because they saw it on the Flintstones. US school children consistently score below their counterparts in East Asia and often score below children in Eastern Europe. This must have something to do with the failure of more than half of all US adults to read a single book [any book] in a given year.

III. Final Word—Nobel Banquet Speech.

Louis Pasteur said that "Chance favors the prepared mind." Having been raised in the post-sputnik era, I feel fortunate to have benefited from a high quality public school education and subsequently as a researcher funded entirely by the US taxpayer. In closing I will share with you words from my Nobel Banquet Speech from two years ago.

> …in the 21st century, the boundaries separating chemistry, physics, and medicine have become blurred, and as happened during the Renaissance, scientists are following their curiosities even when they run beyond the formal limits of their training.
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> The need for general scientific understanding by the public has never been larger, and the penalty for scientific illiteracy never harsher…Lack of scientific fundamentals causes people to make foolish decisions about issues such as the toxicity of chemicals, the efficacy of medicines, the changes in the global climate. Our single greatest defense against scientific ignorance is education, and early in the life of every scientist, the child's first interest was sparked by a teacher.
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> Ladies and Gentlemen: please join…me in applauding the individuals that foster the scientific competence of our society and are the heroes behind past, present, and future Nobel Prizes - the men and women who teach science to children in our schools.

Thank you.