Testimony Before the Subcommittee on Research and Technology Committee on Science, Space, and Technology United States House of Representatives

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Chairman Bucshon, Mr. Lipinski, and other Committee members:

Thank you for conducting this important hearing that addresses critical issues about the state of the American scientific enterprise.

This is a pivotal moment for our enterprise. On the one hand, the United States continues to lead the world in its investments, both public and private, in most fields of science and technology; and its discoveries and applications of scientific knowledge have enriched the country, improved the world, and expanded opportunities for further discovery and application. But, over the past few years, our financial commitments to the pursuit of science have contracted in most fields, while other countries have quickened the pace of their investments, threatening our reputation as the world's leader in research and development (1).

Under these circumstances, it is important for the nation to evaluate its scientific enterprise---and not just to determine how much we are prepared to invest. We must also understand the operation of our enterprise well enough to know how the basic and applied sciences can most effectively work together to create knowledge and to use that knowledge for the benefit of society through the applied sciences. I take that to be the ultimate goal of this hearing.

Such an evaluation of the scientific landscape is difficult because the terrain is complex and can be viewed in at least four dimensions. First, many approaches to science exist as defined disciplines, and a confluence of disciplines is often required for important discoveries (2); second, within many fields of inquiry, there is a spectrum of activities,

The importance of multiple disciplines to solve problems in medicine

From its earliest days, medical science has been dependent on the disciplines of physics and chemistry. The truth of this assertion is evident from any list of major developments in medicine (4): microscopes (to identify infectious agents and cellular structures), X-ray machines (to reveal the living skeleton and delivery cancer therapy), radioisotopes (to track biological molecules and treat certain cancers), pharmacology (to determine the composition and fate of therapeutic drugs) and the EKG and EEG (to monitor the functional status of the heart and the brain through electrical activity).

More recently, major advances in the study of genes, proteins, and cells---from human beings and many other organisms---have revolutionized the study of normal and diseased human beings. This has been possible only because of crucial discoveries (e.g., crystallography, mass spectroscopy, nuclear magnetic resonance, DNA sequencing methods and machines) that require physics, mathematics, engineering, and chemistry. Furthermore, the massive data sets now available from the use of these methods would neither exist nor be useful without the powerful tools provided by computational science. New devices for characterizing at one time many genes, many proteins or even many individual cells are the products of advances in physics and engineering---such as microfluidics, cryolithography, materials sciences, and nanotechnology.

Similarly, the ambitions of newly launched initiatives, such as the President's BRAIN project or therapeutics based on genetic signatures ("precision medicine"), will depend on principles of electrical circuitry, optogenetics, computation, mathematical modeling, and chemi-luminescence. In other words, the future of medicine, just like the past and present, will depend on the vibrancy of allied fields of science and technology and on the alertness of leaders of those fields to the possibilities for productive interaction.

Basic research is endangered but essential for future discoveries that will be applied to medicine

Most facets of medical research have been transformed over the past decade or two by the unveiling of genetic blueprints and the identification of the specific genetic and biochemical lesions that cause most human diseases. This means that even basic biomedical scientists without direct medical experience can now study human diseases and the means to prevent and treat them more effectively. Because the benefits of such work are immediately obvious and highly valued, the tendency to shift away from fundamental studies to such disease-targeted (or so-called "translational") sciences is

ideas, articulated by Vannevar Bush nearly seventy years ago (3), that have been the basis for the past successes of American science.

Because the boundaries of research are more difficult to define than the extremes, there will inevitably be overlap in the ambitions of the entities that fund research, just as there are in the ambitions of those who perform it. But, when research appears to be tilting towards the applied, it is incumbent on those responsible for basic research---especially the major funders, such as the U.S. government---to rise to its defense. At the same time, those government agencies, along with universities, private funders, and commercial entities, should be seeking ways to collaborate for at least three purposes: to learn where and how scarce resources are being committed; to seek opportunities to engage in collaborative work; and to exchange information that may accelerate progress along the full spectrum of research and development.

NCI uses a variety of mechanisms to promote effective, multi-disciplinary research

Especially in times of fiscal duress, it is essential that the government's science agencies maintain the public's trust by deploying their funds in accord with practices that have been productive in the past. The NCI, a component of the NIH, has benefited historically from a portfolio of funding mechanisms. These include the award of various kinds of grants and contracts to individuals, groups, and institutions to perform studies that range from investigator-initiated to agency-determined; the development of an intramural research program conducted by government scientists in NCI laboratories; and the use of a government-owned, contractor-operated cancer research laboratory in Frederick, Maryland.

We use these mechanisms to support basic, translational, and clinical work on a wide variety of cancer-related problems and to train scientists in several disciplines. Over the past few years, we have taken advantage of the flexible nature of the mechanisms to establish new programs that we believe are suited to the opportunities and stresses of our times. Some of these efforts are especially noteworthy in the context of today's

• The Frederick National Laboratory for Cancer Research (FNLCR), itself modeled in part on the Department of Energy's national laboratories, has developed important core laboratories that serve the nation's efforts in nanotechnology (the Nanotechnology Characterization Laboratory [NCL]), imaging, and other complex multi-disciplinary fields. (The NCL is also part of the National Nanotechnology Initiative, collaborating with other NIH Institutes, DOD, NSF, and DOE.)

• The FNLCR recently initiated a nation-wide project to identify new strategies for attacking cancers driven by one of the three major genes in the RAS family. (Such cancers constitute about a third of all human tumors.) The RAS project has engaged a wide range of scientific expertise---in structural biology, protein chemistry, DOE-derived cell imaging methods, and computation--- and investigators at many institutions.

• Both the intramural and the grant-making programs at the NCI have promoted the engagement of engineers, mathematicians, and physicists in cancer research. The intramural program has developed a partnership with physicists at the University of Maryland for collaborative projects. The extramural program has issued a request for applications to continue or create centers for the use of physical sciences in cancer research, and it issues grants and contracts for mathematicians to model cancerous cell behavior and for computational scientists to build cloud-based systems to store and analyze large data sets.

• To provide greater stability for NCI-funded

questions are advertised by the NCI as topics for individual research projects and many grants have been awarded.

Reprise

Our complex and traditionally successful scientific enterprise now confronts expanded opportunities at a time -4(c)43tucpE10(nt)2(i)(f)-8(ul(v)14(0(t)2s)4(t)14(and)1(f)2(i)6(c)44(t)2()4(c)t)2