DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

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The Honorable Tom Coburn
United States Senate
Washington, DC 20510

Dear ~~Senator~~ Tom Coburn:

Thank you for your September 17 letter requesting that I address four questions about how disease-specific legislation affects the ability of the National Institutes of Health (NIH) to plan and perform research.

First you asked if the NIH already has the ability to create strategic plans and working groups without a legislative mandate to do so. The Secretary of Health and Human Services and leaders of the Institutes and Centers of the NIH have the authorities needed to constitute standing advisory committees, create working groups, and develop plans for research programs; as a result, they do not need legislative mandates to take such actions. The NIH Institutes and Centers have senior advisory councils that oversee the research portfolio of each component. Individually or in collaboration, the NIH Institutes and Centers frequently form other advisory groups charged with planning research on Institute-specific or trans-NIH subjects.[1] These many activities, in conjunction with our peer review panels, are part of our ongoing effort to evaluate the current scientific landscape and to protect and advance our investments in research for public benefit.

Let me provide a recent example of how these planning processes work. The National Institute of Allergy and Infectious Diseases (NIAID) has used working groups to identify scientific opportunities in areas where there are pressing public health needs. One example is influenza—both seasonal influenza, which kills up to 49,000 Americans each year, as well as pandemic influenza such as the recent 2009 H1N1 pandemic. In early 2006 NIAID convened a Blue Ribbon Panel on Influenza Research to help identify areas in which progress was needed. This panel recommended eight areas in which there were opportunities for scientific advancement, including research on improved influenza vaccines.[2] To continue and build upon these efforts, NIAID released *NIAID Influenza Research: 2009 Progress Report*, which identified the development of "universal" influenza vaccines as an expanding area of scientific opportunity.[3]

Currently, the NIAID's extramural researchers are pursuing multiple vaccine strategies for the development of a universal influenza vaccine. In addition, researchers at the

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[1] IC, NIH wide, topical, and interagency strategic plans are available at http://report.nih.gov/strategicplans/index.aspx

[2] *Report of the Blue Ribbon Panel on Influenza* posted June 2007 at http://www.niaid.nih.gov/topics/Flu/Documents/influenzablueribbonpanel2006.pdf

[3] NIAID. *NIAID Influenza Research: 2009 Progress Report* http://www.niaid.nih.gov/topics/Flu/Documents/fluresearch09.pdf

NIAID Vaccine Research Center are making significant progress towards the development of such a vaccine. They have tested in animals a two-step, prime-boost vaccine that generates neutralizing antibodies against many strains of influenza virus.[4] Animal studies of this technique have proven promising, and researchers will soon study the approach in human clinical trials. This past summer, NIAID sponsored, with the Food and Drug Administration, a scientific meeting to revisit progress and challenges with regard to the development of universal influenza vaccines. This comprehensive NIAID effort is just one example of how the NIH constantly examines scientific opportunities and conducts research evaluation and planning activities within its current statutory authority.

You next asked me to address the NIH's ability to foster groundbreaking discoveries without legislation that directs it to address a specific disease or group of diseases. While we seek always to be responsive to the concerns of the public, often expressed through "report language" in appropriations bills, the NIH has considerable statutory authority to plan and oversee the research that leads to important discoveries. Because our science often produces new and unexpected findings and because medicine is often confronted with altered or unyielding threats to public health, the NIH Institutes and Centers must constantly assess their research plans and portfolios. For example, the National Cancer Institute recently organized a group to perform a "horizon scan" of pancreatic ductal adenocarcinoma (PDAC) research, building on previous planning exercises in 2001 and 2008.[5] This new group will examine current research efforts, benchmark our scientific understanding, and identify promising and possibly underexplored areas for future research in hopes of improving the still dire outcome of this dreaded disease.

You further asked me to address the impact of disease-specific legislation on the NIH's ability to allocate resources freely and to study basic biology and mechanisms. When providing technical assistance to the Congress on possible legislation, the NIH generally suggests that Congress provide the maximum flexibility for our mission. Basic research that may lack any overt connection to specific diseases is the foundation for disease-specific translational and clinical research, and it must be preserved to ensure the discoveries that later drive applied work on individual diseases. If Congress is too proscriptive when it directs the NIH to focus on specific diseases, the agency loses its valued flexibility to allocate resources in a manner that optimizes the likelihood that the scientists we support will discover the underlying disease mechanisms that must be understood to achieve our goal of improving the health of our nation.

Let me provide an example of basic research that addresses several specific types of cancer. As early as the 1980s, cancer researchers observed mutations in a certain critical gene, the *KRAS* gene, in a variety of human cancers, including about a third of lung

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[4] C-H Wei *et al.* Elicitation of broadly neutralizing influenza antibodies in animals with previous influenza exposure. *Science Translational Medicine* (2012).

[5] NCI. *Pancreatic Cancer: A Summary of NCI's FY2010 and FY2011 Portfolio and Selected Research Advances*. June 2012. http://www.cancer.gov/researchandfunding/reports/pancreatic-research-progress-2012.pdf

cancers, about half of colon cancers, and as many as 95 percent of PDACs. Basic research on a wide variety of cell types, from yeast to human, has taught us that the *KRAS* gene encodes an unusual signaling protein that acts in conjunction with other proteins as a molecular "on/off" switch for signals promoting cellular growth. Mutations in this gene leave the switch "on", resulting in persistent cell growth and division. Despite what we know about *KRAS* mutations, and despite extensive efforts in both industrial and academic research sectors, we have not yet been able to counter these mutations therapeutically. In order to treat PDAC and many other cancers exhibiting *KRAS* mutations, we must focus on research that increases our understanding of how such mutations drive the biological effects that cause these devastating diseases. Given what we have learned about molecular mechanisms, it would be counterproductive to limit that effort to a specific cell type. In other words, if Congress directs the NIH to study specific diseases without flexibility, it can limit our ability to follow the best leads in science and to pursue discoveries that move an entire research field forward in a way that produces maximum benefit to the public.

Finally, you asked me to address how genomics has revolutionized the study of underlying mechanisms of disease. Recent advances in genomics are transforming the way science is conducted. Our understanding of basic mechanisms has increased exponentially with the widespread adoption of high-throughput screening, genome sequencing, and advances in bioinformatics. This transformation of the biosciences is profoundly affecting the practice of medicine. Advances in the biological sciences have changed the way we view disease. We now recognize that dysfunction of specific biochemical pathways that govern cell behavior may be similar in superficially disparate diseases or quite different in patients with the same category of diagnosis.

When you and I were in medical school, all patients with cancers of a given organ were treated with the same combination of chemotherapy, radiation therapy, or surgery. With today's application of high-throughput screening and genomics, we are now shifting to treating an individual's cancer with a kind of "precision medicine" that is based upon the patient's genome and the genome of his or her individual tumor. As an industry scientist recently told the *New York Times*, "[t]he old way of doing clinical trials where patients are only tied together by the organ where their cancer originated, those days are passing."[6] This is just one more reason why directing research resources toward a particular disease without flexibility, as defined in the pre-genomic era, can run counter to scientific opportunity.

[6] Kolata, Gina. "Cancer Study Points to Tighter Pairings of Drugs and Patients," *New York Times*, September 9, 2012.

In closing, let me be clear that the NIH is not permitted to take a position on the recalcitrant cancer legislation being considered by the Congress. Such statements can only be issued by the Office of Management and Budget as a Statement of Administration Policy.

Thank you for your continued support of the NIH.

Sincerely yours, with best personal regards

Francis S. Collins, M.D., Ph.D.
Director