TEARING DOWN THE SILOS:
ADDRESSING SYSTEMATIC BARRIERS IN THE RESEARCH PROCESS

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During the 2008 Presidential campaign, both major party candidates, Barack Obama and John McCain, put forth policy proposals designed to reduce mortality and morbidity of cancer in the United States. Then Senator Obama's plan outlined eleven important goals aimed at reducing the cancer burden in this country. [1] In a speech to the National Academy of Sciences on April 27, 2009, President Obama specifically cited the need to identify and overcome scientific and bureaucratic barriers as key "to rapidly translating scientific breakthroughs into diagnostics and therapeutics that serve patients."[2] Through the passage of the Patient Protection and Affordable Care Act (PL 111-148) in March of 2010, President Obama has begun to implement programs that focus on nine of the proposed goals. [3] The two goals that were not addressed in that law and will require further attention by the current administration or by Congress are to double funding for cancer research and to improve federal coordination of cancer research, treatment, and awareness programs.

With the serious financial situation our country is facing and public and private budgets strained, the goal to fully double funding for cancer research unfortunately may not be a realistic immediate goal. However, it is imperative that funding for life-saving research and treatments, both public and private, not become another victim of the recession.

Although significant progress in cancer research has enabled some reduction of the cancer burden, continued lack of harmonization has created silos within the biomedical research enterprise, creating barriers among those receiving and using funding. The cancer research enterprise is unprecedented, but underutilized across all sectors. The National Cancer Act (PL 92-218) gave the National Cancer Institute (NCI) extraordinary authority to strengthen the nation's efforts against cancer. [4] The NCI embraced this new authority, and through collaboration with the academic sector, there are 65 designated cancer centers that serve as major research hubs leading many research efforts toward new discoveries. But far too often, those discoveries and breakthroughs are stifled, never getting to the patients who need them, due to lack of communication and arduous regulatory and bureaucratic roadblocks.

A COMPREHENSIVE APPROACH IS NEEDED

Research organizations, regulatory agencies, and industry exist within institutional, educational, communicative and scientific silos that need to be jointly addressed and reduced. Additional partnerships are

[1] The Obama-Biden Plan to Combat Cancer. September 2008: http://www.kaisernetwork.org/election2008/Obama-Biden%20Plan%20To%20Combat%20Cancer.pdf Accessed 11/23/10
[2] Obama, B. (2010, April). *Remarks by the President at the National Academy of Sciences Annual Meeting*. Speech presented at the National Academy of Sciences, Washington, DC.
[3] Patient Protection and Affordable Care Act, P.L. 111-148, 124 Stat. 119 (2010).
[4] The National Cancer Act of 1971, P.L. 92-218, (1971).

needed between several areas of research, detection, treatment, prevention, surveillance, product regulation, care delivery and reimbursement of services.

All components of the biomedical research community must identify joint priorities and commit to tearing down the silos that are prohibiting efficient use of limited resources to truly change the way in which they approach treating this disease. **Collaboration is needed to address systematic barriers existing in the research process in order to effectively translate new discoveries to therapies for patients**.

Most government agencies often work insularly and are isolated by policies and bureaucracies among the federal health agencies and their relationships with the private sector. While each agency has a core mandate and functional requirements that needs to be met, they also play pivotal roles in the long-term approach to innovation. Institutional barriers can impede a streamlined approach to new drug development. Focusing solely on the specific day-to-day duties instead of also examining an agency's potential contribution to the larger, common goal of reducing the cancer burden can slow overall progress. Policies and research approaches are needed that can allow federal agencies to support one another and remain focused on the overarching goal of accelerating innovation. An example of an attempt to achieve integration is the Joint NIH-FDA Leadership Council, initiated by the Secretary of HHS in February 2010.[5] The Council aims to oversee activities across the two agencies to find areas of cooperation on issues of safety, quality, and effectiveness, thereby supporting components of the mission of both agencies.

Bureaucracy and policy is not limited to government agencies, as these same problems exist between federal agencies and drug developers as well and directly among manufacturers. While competition is a key economic force, a synergistic approach toward achieving an identified goal is often more effectual than multiple entities working to succeed through the system individually. Such an approach could help spread risks associated with drug development as well as capitalize on diverse areas of expertise. This is particularly true for the future of cancer treatment which will likely depended on the use of multiple targeted products in combination in order to yield the best outcomes based on specific tumor characteristics. This more "personalized" paradigm will bring a new set of challenges to the healthcare system that may require new approaches to researching and regulating novel combinations, the utilization of companion diagnostics to identify subsets of patients, alternative trial designs to evaluate smaller populations of patients, and tailored reimbursement strategies for targeted therapies. The Foundation for the NIH has demonstrated success to convening multiple sectors and developing innovative cancer research strategies. This includes the Biomarker Consortium's projects to examine the use of novel endpoints, as well as the recently initiated I-SPY2 breast cancer trial which utilizes a novel approach to identify candidate drugs.[6]

NEW AND INTERNATIONAL MODELS OF INVESTMENT AND COLLABORATION

Over the past two decades, many non-profit and international models emerged that challenge traditional relationships between government and industry. The increase in philanthropic funding of research has occurred in some cases due to a frustration with the inefficiencies of the current system. An Organization such as the Multiple Myeloma Research Foundation, funded at approximately $115 million to date, has been successful in bringing 4 new treatments to market.[7] The Michael J. Fox Foundation for Parkinson's Research and Stand Up to Cancer each have been equally as proficient in providing funding to research organizations

[5] FDA-NIH News Release, February 24, 2010: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm201706.htm Accessed 11/28/10

[6] The I SPY 2 TRIAL (Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis 2). 2010. http://www.ispy2.org/. Accessed 11/28/10

[7] The Multiple Myeloma Research Foundation. (2009). *Annual Report 2008*. Retrieved from: http://www.themmrf.org/assets/about-the-mmrf/2008_annual_report.pdf

focused on developing new treatments. International models from Israel and Singapore, which approach the cancer enterprise from an economic growth standpoint, can be an influential guiding tool for government agencies to promote cancer research and drug development as an economic driver.[8][9]

MOVING FORWARD

While the aforementioned examples demonstrate how researchers can effectively work together, they must be seen as models for how larger-scale collaborative efforts between research entities and industry could be executed. We must also evaluate the gaps in coordination between federal health agencies and industry and evaluate areas that are wasteful and unnecessarily duplicative

RECOMMENDATIONS:

1) **REEVALUATE THE ACTIVITIES OF HEALTH-RELATED AGENCIES**
2) **DEVELOP MULTIDISCIPLINARY MECHANISMS TO SUPPORT TRANSLATIONAL RESEARCH**
3) **DEVELOP PROCESSES IN HEALTHCARE DELIVERY THAT ENHANCE RESEARCH**

RECOMMENDATION 1: REEVALUATE THE ACTIVITIES OF HEALTH-RELATED AGENCIES

The National Cancer Act created the National Cancer Program to be spearheaded by the NCI Director. The success of the National Cancer Program can not be measured solely as the research accomplishments facilitated by the NCI, but rather by its contribution to the larger goal of reducing the national cancer burden. This can not be achieved by a single agency. It is critical to examine the impact other federal agencies have on NCI-based discoveries to. For example, in 2007 the Food & Drug Administration (FDA) Science Board declared the agency's "mission at risk" due to its eroded scientific foundation.[10] Clearly, without a scientifically rigorous regulatory body, discoveries facilitated by NCI-based research could be inefficiently or inappropriately evaluated, and ultimately not achieve the envisioned improvement to patient's lives.

Even prior to the report that highlighted the need to advance the science of regulation, the FDA acknowledged the need for assembling oncology expertise at the agency through the establishment of the Office of Oncology Drug Products.[11] While this has made several improvements to the regulation of oncology programs, a comprehensive FDA Oncology Program is still needed to facilitate and increase the transparency of intra-agency collaborations, standardize review guidelines, and establish jurisdiction and sufficient interactions between FDA Centers that are frequently involved in the review of increasing complex new product applications. A robust cancer program can also build upon existing collaborations in order to increase the scientific methodologies used by the agency. Programs like the FDA's Advancing Regulatory Science Initiative which is aimed building on the achievements of existing programs to modernize medical product development along with the creation of the Reagan-Udall Foundation which will support the scientific infrastructure of the FDA, present great opportunities moving forward.

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[8] The Office of the Chief Scientist – An Overview. 2010. http://www.moit.gov.il/NR/rdonlyres/CD3AF19B-2619-415B-B2F4-B747101C5202/0/TheIntellectualCapital3550.pdf Accessed 11/24/10

[9] Agency for Science, Technology and Research (A*STAR). The Biomedical Research Initiative. October 2010. http://www.a-star.edu.sg/tabid/108/default.aspx Accessed 11/24/10

[10] Report of the FDA Subcommittee on Science and Technology: FDA Mission at Risk. November, 2007: http://www.fda.gov/ohrms/dockets/AC/07/briefing/2007-4329b_02_01_FDA%20Report%20on%20Science%20and%20Technology.pdf Accessed 11/28/10

[11] FDA News Release, July 16, 2004: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108326.htm Accessed 11/28/10

The President should initiate a review of the activities of all federal health agencies to identify areas within the National Cancer Program that can be strengthened. This should include all agencies involved with research, communication, surveillance, reimbursement and other key functions that impact the oncology drug development enterprise. This should be accomplished with a focus on creating an environment that is more susceptible to both interagency and public-private partnerships.

In order to achieve the goal of improved outcomes for cancer patients, a top-down approach is the most effective avenue for organization of these collaborations. Coordination across Federal health agencies, industry and public-private partnerships will maximize the efficient use of funding, greatly reducing duplicative funding and furthering communication.

The President should create a task force lead by the Secretary of Health and Human Services, in collaboration with agency officials, academic researchers, and patient advocates to comprehensively examine the various cancer-related efforts of federal agencies and the silos that exist amongst and between them. Effective coordination will require all parties to make concrete policy recommendations to eliminate the existing bureaucratic, cultural and communication-related barriers.

RECOMMENDATION 2: DEVELOP MULTIDISCIPLINARY MECHANISMS TO SUPPORT TRANSLATIONAL RESEARCH

The traditional "study section" approach to peer-reviewed grants has long been the gold standard for scientific research funding and is therefore used for most government granting mechanisms. As new programs designed to accelerate translation of new discoveries to available treatments, such as the Cures Acceleration Network (CAN)[12], begin to be implemented **individuals with specific expertise in drug development and commercialization should to have more direct involvement in the grant writing and review processes.** Such experts are able to provide an interdisciplinary perspective and can help identify priorities with the greatest potential for success. New review paradigms could employ models such as those used by the Interagency Council on Biomedical Imaging in Oncology, the Joint NIH-FDA Leadership Council and Interagency Oncology Task Force which, in addition to utilizing academic scientists as reviewers, seeks input from the FDA and industry, in order to create a coordinated development plan.

Under current resource constraints, prioritization of studies will become increasingly important. The Institutes of Medicine (IOM) recently concluded that around 40% of advanced clinical trials funded by the NCI are never completed.[13] While this can be attributed to numerous causes, the methods used, as well as the feasibility to conduct a study, should be evaluated by reviewers that have extensive knowledge of the challenges faced by clinical researchers.

RECOMMENDATION 3: DEVELOP PROCESSES IN HEALTHCARE DELIVERY THAT ENHANCE RESEARCH

Even with significant progress in research and treatment there are still gaps in understanding which individuals will benefit from many of the therapies. The fact that clinical trial participation is low, with only 3-5% of adult oncology patients enrolling in a trial contributes to that problem;[14]and is further exasperated since only about 15% (of the 3-5%) are representative of a minority population.[15] In addition, for FDA

[12] Patient Protection and Affordable Care Act, § 10409, 124 Stat. at 978.
[13] Mendelssohn, J. et al. A National Cancer Clinical Trials System for the 21st Century: Reinvigorating the NCI Cooperative Group Program. National Academy of Science. Released April 15, 2010.
[14] Du W, Mood D, Gadgeel S, Simon MS. An educational video to increase clinical trials enrollment among lung cancer patients. *J Thorac Oncol.* 1, (Jan 3, 2008):23-9.
[15] Cancer Clinical Trials: Participation by Underrepresented Populations. ICC Cancer Fact Sheet: http://iccnetwork.org/cancerfacts/ICC-CFS11.pdf Accessed 11/12/10

approval the trials may have stringent exclusion criteria to minimize potential variables that possibly will impact the ability to directly measure the contribution of the experimental agent. This means that patients often times are excluded from registration trials due to factors such as co-morbid conditions, age, or treatment history. Therefore, clinical trials used for the purpose of product approval, which are the opportunity for gathering the most rigorous information on patients and the experimental drug, are not necessarily reflective of the population a drug may ultimately be used in and exclude a large segment of the U.S. population.

New and better processes and systems are needed to collect and aggregate patient data that is produced as a part of the routine care process. The recent investment in health IT and incentives for adoption of electronic health records (EHRs) in the Affordable Care Act will lay the foundation for new research opportunities. In order to capitalize on this investment it will be important to develop means for the information contained in EHRs to be used in an appropriate capacity for research. Historically, the predominant use of EHRs has been to support administrative processes. **During this time of widespread implementation the federal government should develop policies that enhance data collected within EHRs to optimally contribute to research activities**. As a starting point, collaborative efforts should be encouraged between agencies focusing on developing large-scale, interoperable health data networks to facilitate improved outcomes research and comparative effectiveness research on diverse patients that are treated in a variety of settings.

TEAR DOWN THE SILOS

As outlined in this paper, we must move quickly toward tearing down the silos that exist in the research and development process if we are to accelerate the movement of new discoveries to patients. Beyond providing support for new collaborations and partnerships among all of the public and private entities involved in the cancer research and development process, we must ensure effective policies are in place to prevent current and future obstacles from hindering innovation. The cancer community must be guided by the principle that both outcomes and patient benefits will be greater when achieved through collaborations vs. the efforts of disconnected silos. If we are to truly reduce the burden of cancer at a pace at which the millions of patients afflicted by this disease need and deserve, the entire cancer enterprise must take action to tear down the silos and adopt a philosophy of synergy and collaboration.