

## BIOMEDICINE

# A U.S. “Cancer Moonshot” to accelerate cancer research

Patient engagement and data sharing must improve

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In January 2016 President Obama announced a “Cancer Moonshot” to “accelerate our understanding of cancer and its prevention, early detection, treatment, and cure” (1). A Blue Ribbon Panel (BRP) of scientific experts was convened to make recommendations to the National Cancer Advisory Board (NCAB), the adviser to the National Cancer Institute (NCI), on research opportunities uniquely poised for acceleration. These recommendations were presented on 7 September 2016 (2). As co-chairs of the BRP, we describe our approach, what it produced, and our expectations.

The BRP chose to focus on areas well positioned to benefit from additional coordination and support promised by the Cancer Moonshot. The BRP established working groups to focus on research areas that were not already well advanced. Each working group was charged with developing two to three recommendations for research already begun. What sets these recommendations apart from previous efforts and ongoing investigator-initiated research is the opportunity to establish coordinated, multidisciplinary collaborative projects with the impetus of the Cancer Moonshot.

More than 150 people—including scientists, clinicians, patient advocates, and industry representatives—participated in the working groups. To supplement the working

groups, NCI led a campaign to collect input from the wider research community and the public. This included a website where more than 1600 ideas and comments were submitted (3), all of which were reviewed by the BRP cochairs and the relevant working groups. The majority of the ideas submitted aligned with those discussed by the BRP; all had been considered. Thus, the recommendations of the BRP reflect what the broader community sees as ripe for progress.

## RECOMMENDATIONS AND EMPHASIS

Ten recommendations were generated by the BRP emphasizing the importance of direct patient engagement in cancer research, a deeper understanding of why some therapies work and others do not, the dynamics of tumor evolution, and the need for mechanisms of data sharing, access, and analysis.

One recommendation calls for **development of a patient engagement network**. The vast majority of Americans do not have easy access to genetic and other molecular testing methods at the core of precision cancer medicine; thus, a broad segment of the cancer patient population is not evaluated for newly approved medicines or is excluded from clinical trials. A national program would allow large numbers of patients to have their tumors profiled and to directly contribute the data (including tumor genomics and information about immune cells and microenvironment) plus information on their clinical status and outcomes to a nationally federated and shared database. This would inform research on therapeutic agents and help identify new, clinically relevant cancer groupings. Such a database could collect and integrate patient-reported

Immunotherapy—a Blue Ribbon Panel focus.  
[Cytotoxic T cells (red) killing a cancer cell.]

symptom and side-effect data, which could lead to improved symptom control.

Only about 5% of all cancer patients are enrolled in clinical trials. One contributing factor is lack of awareness of eligibility for trials. The network would help by providing a database of eligible patients for clinical trials and “preregistering” them. This effort will link and expand existing efforts and could fundamentally change how patients access and interact with clinical trials. Conducting such an effort at the proposed national scale and scope can be done only with the support of the Cancer Moonshot.

Patient (and public) engagement is also key to the recommendation to implement evidence-based approaches to prevention. The need to extend colorectal screening—which can save many lives—and make it more accessible to a wider population was highlighted. Most individuals with cancer-predisposing inherited mutations or alleles are unaware of it and so are not monitored for early detection of cancer. One recommendation is a pilot project in which all patients with newly diagnosed colorectal or endometrial cancer would be screened for DNA mismatch-repair deficiency; those with such defects would then have targeted genome sequencing for mutations in DNA mismatch-repair genes associated with Lynch syndrome (a hereditary dominant predisposition to a number of cancer types). When such mutations are identified, first-degree relatives of the patient would be offered the opportunity to be screened. Identification of affected individuals would allow early detection and thus reduce morbidity and mortality.

Another cross-cutting theme is **the value of cataloging molecular and cellular changes that occur in the course of tumor development—in the tumor but also in the tumor microenvironment and the immune cell milieu**. Although researchers know an increasing amount about the state of human tumors at diagnosis, knowledge is needed to be able to predict which cancers will respond to specific therapies, how they become resistant to those therapies, which will **develop metastases, and which will recur**. Thus, **one recommendation calls for development of a “Tumor Atlas” that, like The Cancer Genome Atlas (TCGA), would contain detailed cellular, molecular, and genomic (and other omics) information on the cancer cells in a tumor, linked to patient demographic and clinical data**. It would also characterize the noncancerous surrounding cells, including immune components. Unlike TCGA, this atlas would include information representing all stages of tumor evolution, from precancerous lesions to primary can-

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cers, to development of treatment resistance, through metastasis—from the same patient, where possible. Such an atlas would enable development of computational models that could predict progression and treatment response and help reveal new therapeutic targets and biomarkers. Even more than TCGA, a tumor atlas of this complexity requires a coordinated, collaborative national effort.

Another recommendation calls for **analysis of samples already available from patients who have received the standard of care**. Many thousands of patients have been treated with similar standard-of-care regimens. Some have had outstanding responses with substantial prolongation of life, some responded but eventually relapsed, and others did not respond at all. The underlying molecular, genetic, and cellular mechanisms that may distinguish these groups of patients—even if they initially fall within the same disease classification—remain poorly understood. A detailed genomic analysis of acquired biopsies, as recommended, would lead to better understanding of how to identify patients who are or are not likely to benefit from existing therapies. A catalog of potential immune targets (on the tumor and in the tumor microenvironment) would identify targets for vaccines and other immunotherapies.

A need to better understand unique features of childhood cancers is integral to many of the BRP's recommendations. One recommendation is to **enhance understanding of how fusion oncoproteins, which result from recurrent chromosomal translocations and are a hallmark of many childhood cancers, drive cancer development**. Because few models of these cancers exist, new experimental models are needed to study the mechanism of action and key vulnerabilities of these oncoproteins, as well as to develop therapies and preventive approaches for childhood cancers. The ability to speed this basic research and to carry it out at the needed scale will require a network of investigators with unique expertise—the kind of collaborative effort that the Cancer Moonshot seeks to foster.

One recommendation proposes a **cancer immunotherapy clinical trials network**. Despite recent successes in immunotherapy, patients with many types of cancer—including pediatric cancers—do not show long-term responses to these treatments. Differences in the mutational burden between pediatric and adult cancers may result in less susceptibility of pediatric cancers versus adult cancers to immunotherapies, such as checkpoint inhibitors. This network would help define the cell surface landscape of high-risk pediatric cancers to identify key targets (i.e., those that are uniformly and specifically expressed on tumor cells and are required for cell viability) against which to develop specific im-

munotherapies. This recommendation calls for defining the essential elements that help tumors in children evade immune attack.

The recommendation to improve symptom management through accelerated systematic efforts to gather information on patient-reported outcomes is of critical importance to survivors of childhood cancer, many of whom experience disabling long-term side effects.

Several of the recommendations address cancer health disparities. Part of the goal of enabling direct patient engagement is to broaden the spectrum of patients involved in clinical research. Much of the data on the association between genomic changes and clinical outcomes represents patients coming from “privileged” hospitals, and it is essential to have the wider population represented. Similarly, outreach to a more diverse group of patients is essential for the recommendation to increase implementation of evidence-based approaches to prevention.

Finally, an important theme across many

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### **“... research [based on] BRP's recommendations will depend on ... funding ... approved by Congress.”**

recommendations is **the need for infrastructure to connect existing and future data repositories, analytical tools, and knowledge bases**. The BRP recommends the establishment of a Cancer Data Ecosystem, which would consist of research platforms accessible to researchers, clinicians, and patients; they would serve as research resources and provide information that patients and clinicians could use to plan treatment and predict outcomes. Development of this system will be a major undertaking and will require extensive development with the NCI and the extramural community, both the academic and private sectors. New funding models and cooperative efforts anticipated by the Cancer Moonshot Initiative will be key to success.

#### **WHAT HAPPENS NEXT?**

NCI intends to begin to implement the recommendations, with the goal of funding some initiatives in summer 2017. Given the novelty and scope of the recommendations, NCI is considering nontraditional funding mechanisms and research structures, such as those used by the Common Fund and the Precision Medicine Initiative, to complement traditional funding approaches.

The ability to conduct research stemming from the BRP's recommendations will de-

pend on whether, and how much, funding is approved by Congress. Because the BRP focused on research that could be accelerated, in most cases, they could proceed in a limited fashion without new funds. However, they would advance more quickly if funded to a higher level. Many recommendations build on collaborative efforts that leverage the work and funding of multiple partners.

Some approaches or ideas are advanced enough that new research can proceed quickly; others will take longer. For certain recommendations, it will be necessary to first address policy issues, such as medical coverage and reimbursement, patient privacy and consent, and barriers to data sharing. For example, patients identified as genetically at high risk for particular cancers, along with their relatives, may need to receive screening and preventive care that are not covered by insurance. Another example is establishing a national standard for biospecimen collection and storage. Some of these policy issues are already the focus of discussions by the Cancer Moonshot Task Force directed by Vice President Joe Biden. Other recommendations will require additional technology development before they can be fully realized.

**Potential for progress will depend on collaborations between NCI, other federal agencies, and the private sector, including those on data sharing, strategic computing, and public-private partnerships around drug development.** Although NCI and other government agencies will lead the implementation of many of these recommendations, nobody “owns” them; thus, many may be carried forward by foundations, pharmaceutical companies, advocacy organizations, or other groups.

Although the BRP recommendations clarify what efforts might lead to transformative changes with new funding, these will not come at the expense of traditional funding expectations. Many ideas the BRP received are being and will continue to be pursued through the NCI's standard research funding process. Excitement about the Cancer Moonshot process is balanced by a commitment to the value of basic research, population studies, technology development, and traditional approaches all of which are essential if we are to continue making progress. ■

#### **REFERENCES**

1. White House, Memorandum—White House Cancer Moonshot Task Force, 28 January 2016; <http://bit.ly/WhiteHouseMemoMoonshot>.
2. Cancer Moonshot Blue Ribbon Panel (NCI, 2016); [www.cancer.gov/brp](http://www.cancer.gov/brp).
3. Clinical Trials Ideas (NCI, 2016); <https://cancerresearch-ideas.cancer.gov/a/index>.

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