A new phase of the Cancer Moonshot to end cancer as we know it

Improved screening, novel therapies and a focus on health equity can reduce cancer mortality by 50% in the next 25 years, but these must be underpinned by an investment in basic, translational and clinical research, along with open data.

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In 2016, the Obama Administration in the United States launched the Cancer Moonshot to accelerate progress against cancer. The United States Congress signed into law the 21st Century Cures Act that same year, authorizing US$1.8 billion in funding for the Cancer Moonshot over seven years starting in 2017. Since then, the National Cancer Institute has invested those funds in more than 240 research projects and 70 programs in the cancer research priority areas recommended by an expert advisory Blue Ribbon Panel. Moonshot-supported research has significantly advanced the understanding of cancer and has improved the lives of patients, caregivers, survivors, families and communities afflicted by cancer. Research conducted since 2017 has advanced the field by contributing to the initial Moonshot goals: improving the understanding of cancer; fostering collaboration, data sharing and open access to publications; and addressing cancer disparities.

On 2 February 2022, President Joe Biden announced new efforts to extend the Cancer Moonshot[1] to address bold but achievable new goals: to reduce cancer mortality by at least 50% in the next 25 years and improve the experience of people and their families living with and surviving cancer.

The Biden–Harris Administration described the opportunities for cancer research in seven areas (Box 1).

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Disparities in cancer screening

During the COVID-19 pandemic, millions of people missed recommended cancer screenings. Even in the absence of a pandemic, cancer is often diagnosed too late, and many people lack access to existing, proven, effective ways to screen for cancer as the result of a complex constellation of variables at different levels from the individual to society. To successfully achieve a return to pre-pandemic levels of screening will require a multifaceted approach to reach people for whom earlier diagnosis could mean a dramatically improved quality of life.

There are large differences in access to cancer screening and prevention based on gender, race and ethnicity, region and socioeconomic status. Meaningful progress against cancer for all will mean addressing these disparities and the underlying factors that contribute to them. Several ongoing Cancer Moonshot studies are evaluating approaches to improve the uptake of proven cancer screening modalities where they are underutilized, including telehealth and direct community engagement.

Research to improve screening includes the American Indian Colorectal Cancer Screening Consortium, which has implemented a patient navigation program using community, clinician and patient input[2]; the Accelerated Control of Cervical Cancer program, where a deep learning algorithm was employed to analyze cervix images captured using smartphones, providing a low-cost, practical way to screen for cervical cancer, especially in low-resource settings[3]; and a trial assessing single-dose efficacy of the HPV vaccine to prevent cervical cancer[4].

Lack of health insurance is a known barrier to cancer screening that Moonshot researchers are addressing through technological solutions. Under the Implementation Science Centers in Cancer Control Program (ICS3), researchers developed an insurance support tool integrated into electronic health records to help community health center staff guide patients in enrolling for health insurance. Findings suggested that the tool can help increase cancer screenings and preventive care[5]. In another study, researchers found that implementing a rideshare transportation intervention after colonoscopy may improve colonoscopy completion rates[6]. The model,

Box 1 | Seven priorities for the Cancer Moonshot

- Diagnose cancer sooner
- Prevent cancer
- Address inequities
- Target the right treatments to the right patients
- Speed progress against the most deadly and rare cancers
- Support patients, caregivers and survivors
- Learn from all patients

if successful, could be applied broadly to improve colorectal cancer screening rates in safety-net health systems (where care and resources are provided to uninsured, Medicaid and other vulnerable patients) and settings where procedural sedation is administered.

Screening is especially important for people known to be at greater risk for cancer because of inherited syndromes. As part of the Moonshot, researchers are developing a strategy for detecting hereditary breast and ovarian cancer and Lynch syndromes in broader populations. Those found to have these syndromes will be included in the study, and their relatives will be enrolled in cascade screening. Findings will have important implications for determining how best to screen and monitor these patients over time.

Refractory cancers

Progress against different types of cancer has been made at different rates. There has been much progress in lung cancer, melanoma and childhood leukemias, but much less for the most refractory cancers, such as pancreatic cancer and solid tumors in children. Cancer Moonshot programs have led to progress in some of the deadliest and rarest cancers, including childhood cancers.

The Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium, a diverse group of experts in cancer biology, proteomics, genomics, computational biology and pharmacology, discovered a previously unknown function in the EWS/FLI fusion protein that drives Ewing sarcoma, a rare cancer that occurs in bones or soft tissue around the bones, that may lead to novel therapies[7]. Another group identified TRIM8 as a regulator of EWS/FLI stability, which may provide new therapeutic targets[8]. A new genetic model of Ewing sarcoma in zebrafish helped define the role of the extracellular matrix in the growth of these tumors, which could also lead to novel therapies[9].

Pancreatic cancer comprises only 3.2% of all new cancer cases each year in the United States, but is the third most common cause of cancer-related mortality. With Moonshot funding, the Pancreatic Cancer Microenvironment Network (PaCMEN) conducted translational studies toward improving therapeutic outcomes for patients with this highly lethal disease. Several of these studies have been translated into new clinical trials. In an immunotherapy trial, researchers showed how a personalized cancer vaccine works in combination with various drugs in treating post-surgical stage I–III pancreatic cancer.

For patients with cancers that are not responsive to existing therapies, understanding tumor resistance is especially important. Researchers in the Drug Resistance and Sensitivity Network (DRSN) studied mechanisms of resistance to the FLT3 inhibitor sorafenib, to which one in four patients with acute myeloid leukemia (AML) are insensitive. This work identified several negative regulators of the mTOR and MAPK signaling pathways — which were not previously associated with AML — as modulators of sensitivity to sorafenib. The study showed that aberrations in these pathways are important mechanisms of resistance to FLT3 inhibitors in AML, suggesting that the combination of FLT3 inhibitors and MEK inhibitors could be useful where AML is resistant to FLT3 inhibitors[10].

Another team found that the combination of mitogen-activated protein kinase (MEK) inhibition and autophagy inhibition leads to transient tumor responses in some patients with pancreatic ductal adenocarcinoma—a significant advance in therapy development for a cancer that is almost always fatal[11].

Advancing immuno-oncology

Immunotherapies are effective treatments for certain types of cancer but not others and may even work dramatically differently in two patients with the same type of cancer. As part of the Immuno-Oncology Translational Network (IOTN), researchers are developing effective therapy regimens for 'immunologically cold' cancers that do not respond to such treatments. One group found that a triple combination of local radiation therapy, bempegaldesleukin (a PEGylated interleukin-2) and immune-checkpoint blockade cured mice of advanced, immunologically cold tumors and distant metastasis[12].

Pediatric Immunotherapy Discovery and Development Network (PI-DDN) researchers discovered that in B-lymphoblastic leukemia (B-ALL), the mRNA that encodes the immunotherapy target CD22, is aberrantly spliced, resulting in downregulation of CD22 protein expression on the surface of B cells, which is associated with post-immunotherapy relapses in patients with B-ALL[13]. These promising findings demonstrate that this aberrant splicing of CD22 RNA is an important driver and biomarker of immunotherapy resistance.

Cancer survivorship

As the overall cancer death rate has declined substantially in the past three decades, the number of cancer survivors in the United States has increased to 17 million, and it is projected to increase to 22.2 million by 2030[14]. Cancer survivors need support to navigate cancer diagnosis, treatment and survivorship.

The Blue Ribbon Panel highlighted the importance of routine monitoring and management of patient-reported symptoms in order to minimize debilitating side effects of cancer and its treatment. For patients transitioning to primary care, managing non-cancer-related comorbidities is critical. The ONE TEAM study is looking at delivery of survivorship care through coordinating care with primary care physicians and encouraging patients' adherence to non-cancer medications[15]. Another group is testing a telehealth self-management intervention that provides coaching for patients on follow-up care after treatments for lung and colorectal cancer, which can improve knowledge and confidence, communication with cancer care and primary care doctors, and quality of life.

Among cancer survivors, almost two-thirds are 65 years or older[14]. Older patients have specific nutritional needs, which are often overlooked. One Moonshot study has developed recommendations for clinicians and care teams caring for older adults with cancer, which include formally screening for nutritional impairments; establishing relationships with a registered dietitian or nutritionist; and providing specific guidance for survivors to meet their nutritional needs and overcome barriers to healthy eating[16].

Open data

Many powerful datasets are not being fully utilized due to challenges in data storage, accessibility and processing. These data are critical as means to identify how molecular information affects clinical outcomes.

The NCI's cloud-based Cancer Research Data Commons (CRDC) is making data

sharing more harmonious, by connecting diverse datasets with analytical tools. Similarly, the Cancer Moonshot's new Biobank[17] allows patients with advanced cancers to donate their blood and tissue samples during their treatment. The Biobank will comprise a longitudinal collection of biospecimens and clinical data that will support research on treatment resistance and sensitivity. Patients and providers can access biomarker reports, signed consent forms and other resources on a public-facing website, which integrates with the Oncology Patient Enrollment Network (OPEN) and clinical laboratories. Researchers from anywhere in the world can request access to this growing dataset. Sharing data and knowledge are essential, and so we ensure that all Moonshot publications are open access.

Supporting basic science

Advances in translational and clinical research build on fundamental cancer biology and basic research. Researchers in the Human Tumor Atlas Network (HTAN) have constructed three-dimensional maps of human cancers and created a new, powerful imaging technique that can visualize the cell type and spatial arrangements at the single-cell and tissue levels[18].

The PDX Development and Trial Centers Research Network have determined the genomic landscapes of over 500 patient-derived xenograft cancer models across 25 cancers, which have validated drug target results for different cancers[19]. This group is now creating patient-derived xenograft models from racially and ethnically diverse populations, which are often under-represented in preclinical studies.

A collaboration between the NCI and the Department of Energy, the Joint Design of Advanced Computing Solutions for Cancer (JDACS4C) program, uses artificial intelligence and machine learning to develop simulations of RAS-RAF protein biology and signaling, an approach that has already led to the development of a small molecule that specifically targets mutant Ras and may be suitable for clinical trials.

The past five years has seen remarkable progress in achieving the original goals of the Cancer Moonshot, but the impact of that progress on the detection, prevention and treatment of cancer are likely to become more evident in the coming years. Key discoveries and insights have been made that will translate into improved outcomes for people with cancer, along with an infrastructure to support rapid data sharing and a collaborative culture, which is now embedded within the cancer research community.

However, the critical importance of continued basic cancer research should not be overlooked. Much of cancer's fundamental biology remains unknown, and it is this basic biological research that is necessary for translational and clinical advances in cancer. ❐

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Competing interests

The author declares no competing interests.