Cancer Moonshot Accomplishments and New Opportunities

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Director, National Cancer Institute
June 8, 2023
126th Meeting of the Advisory Committee to the Director (ACD), NIH
About the Cancer Moonshot

• Initial launch in 2016 to:
  o Accelerate cancer research
  o Foster greater collaboration
  o Enhance data sharing

• Major progress made in implementing recommendations of the Blue Ribbon Panel

• Reignition by President Biden in February 2022

• New goals announced:
  o Reduce the cancer death rate by 50% in the next 25 years (in the U.S.)
  o Improve the experience of people and their families living with and surviving cancer

[cancer.gov/moonshot](cancer.gov/moonshot)  [whitehouse.gov/cancermoonshot](whitehouse.gov/cancermoonshot)
For the lives we can save and for the lives we have lost, let this be a truly American moment that **rallies the country and the world together** and proves that we can still do big things.

Let’s end cancer as we know it and cure some cancers once and for all.

*President Biden*
*February 7, 2023*
President’s NCI Budget for Fiscal Year 2024

$7.8B
TOTAL
President’s budget proposal for NCI for FY 2024

+ $500M
Cancer Moonshot increase (relative to FY 2023 enacted)

+ $216M
Included for “Year 8” of 21st Century Cures Act (to prevent funding gap/“cliff”)

= $716M
As discretionary resources for Cancer Moonshot (no-year funds)

The Biden Administration is proposing a further increase of $1.45 billion in mandatory budget authority for both FY25 and FY26.
Cancer Moonshot Funding Authorized Under the 21st Century Cures Act (dollars in millions)

Learn more: cancer.gov/moonshot
Examples of Progress Made Through the Initial Cancer Moonshot
Initial Cancer Moonshot

Blue Ribbon Panel Recommendations

1. Establish a network for direct patient involvement
2. Create a translational science network devoted exclusively to immunotherapy
3. Develop ways to overcome cancer’s resistance to therapy
4. Build a National Cancer Data Ecosystem
5. Intensify research on the major drivers of childhood cancers
6. Minimize cancer treatment’s debilitating side effects
7. Expand use of proven cancer prevention and early detection strategies
8. Mine past patient data to predict future patient outcomes
9. Develop a 3-D cancer atlas
10. Develop new cancer technologies

In the first four years (2017–2022):

- ~3,000 publications
- 61 clinical trials
- 52 patent filings
The NCI Human Tumor Atlas Network (HTAN)

**Program goal:** Construct dynamic 3D atlases of human cancers

- **Integrate** molecular, cellular, and tumor tissue composition and architecture, including the microenvironment and immune milieu

- Describe **transitions during cancer:** pre-malignant lesions to malignancy, locally invasive to metastatic cancer, response to therapy and development of resistance

- Enable **predictive modeling** to discover biomarkers, understand basic cancer mechanisms, (eventually) refine therapeutic choices for patients

- Represent a **diverse patient population**, including underrepresented and underserved patients

Rozenblatt-Rosen et al., Cell 2020: [https://doi.org/10.1016/j.cell.2020.03.053](https://doi.org/10.1016/j.cell.2020.03.053)
HTAN Atlases as of April 2023

**OHSU**
- **Johnson et al., Cell Rep Med**
  Longitudinal patient atlas constructed over 3.5 years of therapy

**Stanford Duke**
- **Risom et al., Cell**
  Progressive stroma changes associate with transition
- **Strand et al., Cancer Cell**
  DCIS genomic signatures define biology and clinical outcome

**WUSTL**
- **Zhou et al., Nat Gen**
  Transition cell populations and treatment effect

**CHOP**
- **Chen, C et al., Blood**
  KMT2A-rearranged leukemia plasticity, resistance, and stemness

**HMS**
- **Nirmal et al., Cancer Disc**
  Resolution of spatial landscape during progression & immune editing

**MSK**
- **Chan et al., Cancer Cell**
  Discovery of plasticity, metastasis, and immunosuppression signatures

**BU**
- **Krysan et al., Cancer Res**
  Adaptive immune response to neoantigens

**Stanford**
- **Becker et al., Nat Gen**
  Cell state and composition changes in transition of polyps

**Vanderbilt**
- **Chen, B et al., Cell**
  Transition programs & TME chart distinct paths to malignancy

**HMS**
- **Lin et al., Cell**
  Characterization of state transitions and immune interactions

**Broad**
- **Pelka et al., Cell**
  Discovery of myeloid-cell-attracting hub at tumor-luminal boundary

*Manuscript in preparation; figure courtesy of L. Ding, WUSTL HTAN*
Key scientific accomplishments of the HTAN pilot phase

• Discovery of tumor architecture and recurrent cellular neighborhoods as biomarkers of recurrence, progression, and response to therapy.

• Description of the dynamics of stromal and immune organization in precancer.

• Identification of rare cell states that predict tumor metastasis or response to therapy.

• Spatial mapping of tumor and microenvironment co-evolution.

• Development of analysis and visualization tools for HTAN-like data.
HTAN data and resources available for the cancer research community

Human Tumor Atlas Network

HTAN is a National Cancer Institute (NCI)-funded Cancer MoonshotSM initiative to construct 3-dimensional atlases of the dynamic cellular, morphological, and molecular features of human cancers as they evolve from precancerous lesions to advanced disease. (Cell April 2020)

Explore latest Data  Learn more about HTAN

11 Atlases  50 Organs  1311 Cases  3821 Biospecimens

Data Release V3 (Last updated 2023-03-16)

data.humantumoratlas.org
The IOTN is addressing critical steps toward achieving effective anti-tumor immunity

- **Neoantigen Discovery**: Alternative splicing, TCR approaches with IEDB
- **NK Cell Therapy**: Engineering iNKTs
- **B Cell and Antibody Approaches**: Targeting tertiary lymphoid structures
- **Immunosuppression and Responsiveness**: Immune profiling and murine models
- **Novel Therapeutic Targets**: Gly-TR, MUC-1
- **Multimodal Therapies**: Combined immunoRx with other drug therapy, radiotherapy

IOTN White Paper #1, "Cancer Moonshot Immuno-Oncology Translational Network (IOTN): Accelerating the clinical translation of basic discoveries for improving immunotherapy and immunoprevention of cancer," Annapragada et al., JITC 2020
IOTN Key Accomplishments

- **Established a translational science network** collaboratively addressing immunotherapy, immunoprevention, immunoengineering and mitigating immune related adverse events (irAEs) research

- **Created publicly available data and resource sharing catalogs**, including data, pre-clinical mammalian models, software, clinical trials and educational resources

- **Published 410 manuscripts** in high impact journals

- The IOTN Clinical Trials Task Force (CTTF) has collaborated with Accelerating Anticancer Agent Development and Validation (AAADV, [https://aaadv.org/](https://aaadv.org/)) to **bridge the gap in clinical development of immuno-oncology platforms**
Fusion Oncoproteins in Childhood Cancer (FusOnC2) Consortium

*Intensify research on the major drivers of childhood cancers*

Goal: To learn more about the **molecular mechanisms** of transformation driven by fusion oncoproteins and apply this knowledge to **target identification, small molecule inhibition**, and **pre-clinical testing**.

**Multidisciplinary team science approach:**
- proteomics
- structural biology
- genomics/epigenomics
- medicinal chemistry
- experimental therapeutics
- cancer biology

Figure: examples of translocations currently being studied

Content courtesy of Keren Witkin, PhD, Division of Cancer Biology, NCI
Shared Mechanism of Fusion-Driven Oncogenesis: Co-opting the Transcriptional Regulation Machinery

- SS18-SSX
- NUP98-rearrangements
- ZTFA-RELA

Data Sharing is Critical to Achieving our Goals

Available to the global scientific community via the Cancer Research Data Commons:

- **Repositories** (Genomic Data Commons, Imaging Data Commons, etc.)
- **Infrastructure**
- **Cloud Resources**

Fueled by the Cancer Moonshot and in service of the National Cancer Plan’s goals

Learn more: [datacommons.cancer.gov](http://datacommons.cancer.gov)
Genomic Data Commons

Harmonized Cancer Datasets
Genomic Data Commons Data Portal

Get Started by Exploring:

Projects | Exploration | Analysis | Repository

Search e.g. BRAF, Breast, TCGA-BLCA, TCGA-A5-A0G2

Data Portal Summary

<table>
<thead>
<tr>
<th>Projects</th>
<th>Primary Sites</th>
<th>Cases</th>
</tr>
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<tbody>
<tr>
<td>78</td>
<td>68</td>
<td>86,962</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Files</th>
<th>Genes</th>
<th>Mutations</th>
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<tr>
<td>931,947</td>
<td>22,501</td>
<td>2,885,293</td>
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QDC Applications

The GDC Data Portal is a robust data-driven platform that allows cancer researchers and bioinformaticians to search and download cancer data for analysis. The GDC applications include:

Data Portal | Website | API | Data Transfer Tool | Documentation | Data Submission Portal | Publications

https://www.cancer.gov/gdc
Actions laid out by the White House to drive us toward ending cancer as we know it today:

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

https://www.whitehouse.gov/cancermoonshot/
Cancer Cabinet

The first Cancer Cabinet Meeting, at the White House on March 16, 2022.

“[The Cancer Cabinet will] drive a whole-of-government effort to unleash every possibility within our power, within their jurisdictions.”

—President Joe Biden
Reignited Cancer Moonshot Activities

Telehealth Research Centers of Excellence (TRACE)

Cancer Moonshot Scholars

Multi-Cancer Detection (Vanguard Study)

Learn more: cancer.gov/moonshot
Achieving the Cancer Moonshot Goals

REDUCE CANCER MORTALITY BY AT LEAST 50% over the next 25 years and improve the experience of people and their families living with and surviving cancer.

CANCER DEATH RATES MUST DECLINE FASTER

<table>
<thead>
<tr>
<th>Current Rate of Decline</th>
<th>Needed Rate of Decline</th>
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<td>2.3% PER YEAR</td>
<td>2.7% PER YEAR</td>
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National Cancer Plan

• **Long-term vision** for ending cancer as we know it
• **A framework for collaboration**
• **All-of-government** approach
• **All-of-society** approach
• **Inclusive of everyone** (organizations and individuals)

• Not a medium-term strategic/action plan
• Not confined to research – includes care, advocacy, policy, individual behaviors

Learn more: [NationalCancerPlan.cancer.gov](http://NationalCancerPlan.cancer.gov)
<table>
<thead>
<tr>
<th>GOALS</th>
<th>What success looks like</th>
<th>NationalCancerPlan.cancer.gov</th>
</tr>
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<tbody>
<tr>
<td><strong>Prevent Cancer</strong></td>
<td>All people and society adopt proven strategies that reduce the risk of cancer</td>
<td>Deliver Optimal Care</td>
</tr>
<tr>
<td><strong>Cancers are detected and treated at early stages, enabling more effective treatment and reducing morbidity and mortality</strong></td>
<td>The health care system delivers to all people evidence-based, patient-centered care that prioritizes prevention, reduces cancer morbidity and mortality, and improves the lives of cancer survivors, including people living with cancer</td>
<td></td>
</tr>
<tr>
<td><strong>Detect Cancers Early</strong></td>
<td>Engage Every Person</td>
<td></td>
</tr>
<tr>
<td><strong>Effective treatment, with minimal side effects, is accessible to all people with all cancers, including those with rare cancers, metastatic cancers, and treatment-resistant disease</strong></td>
<td>Every person with cancer or at risk for cancer has an opportunity to participate in research or otherwise contribute to the collective knowledge base, and barriers to their participation are eliminated.</td>
<td></td>
</tr>
<tr>
<td><strong>Maximize Data Utility</strong></td>
<td>Optimize The Workforce</td>
<td></td>
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<tr>
<td><strong>Eliminate Inequities</strong></td>
<td>The cancer care and research workforce is diverse, reflects the communities served, and meets the needs of all people with cancer and those at risk for cancer, ensuring they live longer and healthier lives</td>
<td></td>
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Examples of NCI’s Contributions to Our Shared Goals

- Pragmatica-Lung Study (S2302)
- Clinical Trials Innovation Unit (CTIU)
- Connecting Underrepresented Populations to Clinical Trials (CUSP2CT)
- Telehealth Research Centers of Excellence (TRACE)
- Childhood Cancer–Data Integration for Research, Education, Care, and Clinical Trials (CC-DIRECT)
- NCI Community Oncology Research Program (NCORP)
CC-DIRECT: Childhood Cancer Data Integration for Research, Education, Care and Clinical Trials program

Major components
• Standardized electronic health record
• Patient navigation services

Status
• Currently in planning stages
• As the project evolves, there will be opportunities for provider and advocacy communities to be involved

Stay informed: nciadvocacy@nih.gov

Collaborators:
• National Cancer Institute
• Centers for Medicare and Medicaid Services
• Office of the National Coordinator for Health Information Technology
• Alliance for Clinical Trials in Oncology
• American Cancer Society
• American Society of Clinical Oncology
• Children’s Oncology Group
• MITRE Corporation
Clinical Trials Innovation Unit (CTIU)

The CTIU will:

• Select a few high-priority studies for new study designs and operational procedures

• Help speed clinical testing to deliver new approaches for diagnosis, treatment, and prevention of cancer

• Accept inputs from the extramural research community

  ✓ First proposal submission deadline: June 12

CTIU leadership includes representatives from NCI, FDA, NCTN, and NCORP
Pragmatica-Lung Study (S2302)
A streamlined model for future cancer clinical trials

Designed to:
• Eliminate potential barriers to enrollment
• Increase diversity and enrollment in clinical trials
• Streamline processes for trial design and execution
• Use focused endpoints and efficient data collection
• Complete enrollment of 700 participants, by 2025

Led by SWOG Cancer Research Network, in collaboration with the Alliance for Clinical Trials in Oncology

Purpose: Evaluate whether ramucirumab + pembrolizumab combination therapy improves overall survival over standard treatment in people with advanced NSCLC.
Public Engagement

• Read the National Cancer Plan: nationalcancerplan.cancer.gov

• Follow @theNCI & @NCIDirector on social media and use #Every1HasARole and #NationalCancerPlan

• Subscribe for email updates to learn about ways to engage with the plan
Thank you!