The Cancer Moonshot

CSR Advisory Council
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Dinah S. Singer, Ph.D.
Deputy Director
National Cancer Institute, NIH

Goals of the Cancer Moonshot

- Accelerate progress in cancer, including prevention & screening
  - From cutting edge basic research to wider uptake of standard of care
- Encourage greater cooperation and collaboration
  - Within and between academia, government, and private sector
- Enhance data sharing

(Presidential Memo 2016)

Blue Ribbon Panel

- "The Blue Ribbon Panel … will provide expert advice on the vision, proposed scientific goals, and implementation of the National Cancer Moonshot. ..The panel may also recommend other cancer research activities to enhance this effort.

- "The Panel will provide an intensive examination of the opportunities and impediments in cancer research…

(Presidential Memo 2016)

Blue Ribbon Panel

- 28 Members
  - Clinicians, researchers, advocates, representatives from pharma and IT
  - Three face-to-face meetings to identify "Moonshot" recommendations
- 7 Working Groups
  - Clinical trials, enhanced data sharing, cancer immunology, tumor evolution, implementation science, pediatric cancer, precision prevention and early detection
  - Each group had 12-15 members. In total, ~150 individuals were actively involved
  - Met weekly for 6 weeks to generate 2-3 recommendations/working group of major scientific opportunities "poised for acceleration"

Scientific and Community Outreach Activities

Goal:

- Provide opportunities for the public and experts ways to submit ideas
- Increase the public's participation in the Cancer Moonshot

Approaches:

- Online public idea repository – over 1600 ideas submitted
- One-on-one public input: email
- BRP Listening sessions
- Professional conferences

Response:

- Over 1600 ideas received

Overview of Blue Ribbon Panel Report

- The Report summarizes the recommendations of exceptional research opportunities that could lead to powerful advances in our understanding of cancer

- The online Report includes all recommendations in their entirety at **www.cancer.gov.brp**

Blue Ribbon Panel Recommendations

A. Network for direct patient engagement

B. Cancer immunotherapy translational science network

C. Therapeutic target identification to overcome drug resistance

D. Creation of a national cancer data ecosystem

E. Fusion oncoproteins in pediatric cancer

F. Symptom management research

G. Precision prevention and early detection

H. Retrospective analysis of biospecimens from patients treated with standard of care

I. Creation of human tumor atlas

J. Development of new enabling technologies

Cross Cutting Themes: Health disparities, prevention, data sharing, partnerships

www.cancer.gov/brp

Summary of the Recommendations

A. Network for direct patient engagement:

- Enlist patients in federated network where patients can "pre-register" for clinical trials and contribute their tumor profile data to expand knowledge about what therapies work and in whom.

B. Cancer immunotherapy translation network.

- Organize a network to discover and evaluate novel immune-based approaches for adult and pediatric cancers, and eventually develop vaccines.

C. Therapeutic target identification to overcome drug resistance.

- Launch interdisciplinary studies to delineate mechanisms that lead cancer cells to become resistant to previously effective treatments.

D. Creation of a national cancer data ecosystem.

- Create an ecosystem to collect, share, and interconnect datasets.

Summary of the Recommendations (continued)

E. Fusion oncoproteins in pediatric cancer.

- Improve understanding of the abnormal fusion proteins that result from chromosomal translocations and drive many pediatric cancers.

F. Symptom management research.

- Support research to accelerate development of guidelines for management of patient-reported symptoms to improve quality of life and adherence to treatment regimens.

G. Precision prevention and early detection:

- Implementation of evidence-based approaches. Conduct implementation science research to encourage broader adoption of HPV vaccination, colorectal cancer screening, and tobacco cessation.

Summary of the Recommendations (continued)

H. Retrospective analysis of biospecimens from patients treated with standard of care.

- Analyze biopsies to learn which features predict outcome to better plan treatment for future patients.

I. Creation of human tumor atlas.

- Catalog the evolution of genetic lesions and cellular interactions in tumor/immune/other cells in tumor microenvironment from the earliest detected lesions to metastasis and develop predictive models

J. Development of new enabling technologies.

- Support development of technologies to accelerate testing of therapies and tumor characterization.

Cancer Funding in 21st Century Cures Act

- **The cancer research portion is named the Beau Biden Cancer Moonshot Initiative**

- **$1.8 billion over 7 years**
  - **$300 million for FY17**
  - **$300 million for FY18**
  - **$400 million for FY19**
  - **~$200 million FY20-23**
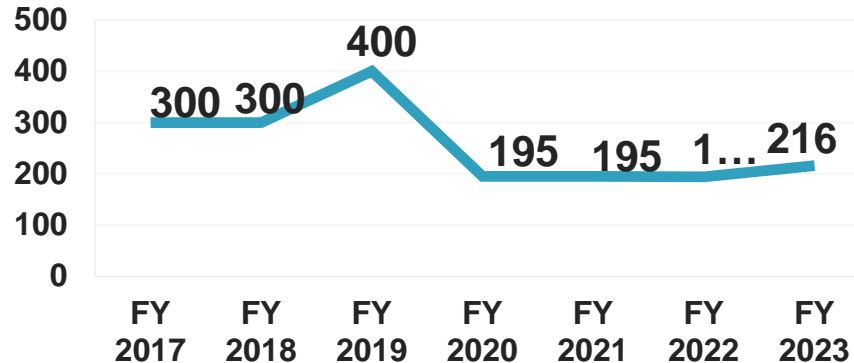
- *"To support cancer research, such as the development of cancer vaccines, the development of more sensitive diagnostic tests for cancer, immunotherapy and the development of combination therapies, research that has the potential to transform the scientific field that has inherently higher risk, and that seeks to address major challenges associated with cancer."*

Cancer Moonshot Implementation Teams

- Network for Direct Patient Engagement
- Cancer Immunotherapy Network
  - Pediatric Immunotherapy
  - Adult Immunotherapy
- Overcome Drug Resistance
- National Data Cancer Ecosystem
- Fusion Oncoproteins in Pediatric Cancer
- Symptom Management
- Prevention and Early Detection
  - High Risk Cancers
  - Prevention & Screening
- Human Tumor Atlases
- Retrospective Analysis of Biospecimens
- New Enabling Cancer Technologies

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Cancer Moonshot Initiatives
2017-2020

2016 Blue Ribbon Panel

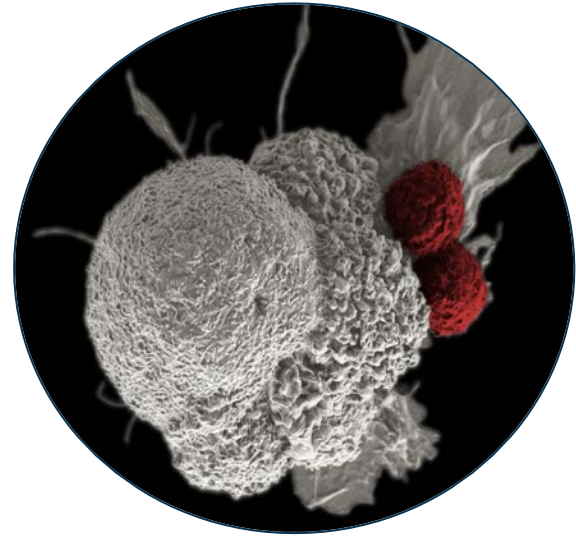| Category	FY17	FY18	FY19	Proposed for FY20
Network for Patient Engagement	Biobank (R&D)	CCR Rare Tumor Patient Engagement Network (IR)	Portal to Support Patient Engagement (R&D)	Patient Engagement for Priority Cancer Sequencing (PE4PC)
Immuno-therapy Network	Canine Immunotherapy Trials; Immunotherapy Related P01s; Pancreatic Cancer Microenvironment Network; Characterizing Sequelae w/ Immunotherapy (Admin Supp); Metabolic Reprogramming to Improve Immunotherapy; Enhancing Applicability of Mammalian Models; Cancer Immunotherapy Trials & Network - Pediatric; National Center for Cell-Based Therapy (IR)	Pediatric Immunotherapy Discovery & Development Network; Immuno-Oncology Translation Network (IOTN): Data Centers; IOTN Immunoprevention & Immunotherapy Research Projects	IOTN Immuno-Engineering for Immunotherapy (i3) Centers; IOTN Immunoprevention Projects; Discovery and Dissemination of TCR Gene Therapy (IR); IOTN Reissuance; PI-DDN Reissuance	Advancing Immunotherapy by Mitigating Immune-Related Adverse Events (irAEs); Cancer Moonshot Collaborative Meeting; PI-DDN Supplements
Overcome Drug Resistance	Drug Resistance and Sensitivity Research Centers; Drug Target Related Grants (P01s & STTRs); Human Cancer Models Initiative – HCMI (R&D)	Research to Identify & Treat Cancer Sensitivity/Resistance (Admin Supp); MasterLymph: Precision Medicine to Improve DLBCL Therapy (IR & R&D)		Mechanisms of Cancer Drug Resistance (Competing Revisions)
Cancer Data Ecosystem	Data Ecosystem Support for GA4GH (Admin Supps); CIMACs and Data Commons; Office of Data Sharing (R&D); Data Ecosystem (R&D); Expand Data Commons and Sharing (R&D)	GENIE Supplements; Cancer Data Aggregator (R&D)	Imaging for APOLLO (R&D); De-Identification of Narrative Text in Clinical Documents (R&D)	
Drivers of Childhood Cancers	Fusion Oncoproteins of Childhood Cancer (APRC); Ewing Sarcoma R21; Pediatric Core (R&D) R21	Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium	FusOnC2 Reissuance	FusOnC2 Supplements
Symptom Management	Dissemination & Implementation Research	Analyzing and Interpreting Clinician and Patient Adverse Event Data; Improving Management of symPtoms Centers (IMPACT); Understanding Chronic GVHD (IR)	PRO Measures to Address Accrual Barriers to Underserved (R&D); STAR Act: Improving Outcomes for Pediatric & AYA Cancer Survivors; Optimizing Management and Outcomes for Cancer Survivors	
Prevention & Detection Strategies	Tobacco Use Treatment in Cancer Patients (Admin Supp); Smoking Cessation Program; HPV Vaccine Trial (IR); Comparing Colon Cancer Detection (R01 & Admin Supp)	Accelerating CRC Screening with Implementation Science (ACCSIS); Approaches to Identify and Care for Inherited Cancer Syndromes; Prostate Cancer in Men of African Ancestry (RESPOND); Dissemination of CRC Screening for Native Americans (Admin Supp)	Implementation Science Centers for Cancer Control (ISC³); Communication & Decision Making for Inherited Cancer Syndromes; Accelerated Control of Cervical Cancer (IR); ACCSIS Reissuance; Approaches to Identify and Care for Inherited Cancer Syndromes Reissuance	
Retrospective Analysis of Biospecimens	Retrospective Tumor Analysis (R&D)			
Human Tumor Atlases	Integrative Oncogenomics of Multiple Myeloma P01; Tumor Atlas Pilot Program (R&D)	Molecular Profiling to Predict Responses - MP2PRT (R&D); Human Tumor Atlas Research Centers & Coordinating Center; Pre-Cancer Atlas Research Centers	Human Tumor Atlas Research (Admin Supp)	
New Cancer Technologies	PDX Development and Trial Centers (PDTCs); Integration & Validation of Technologies (SBIR Grants); Advancing BRP Highlighted Technologies (APTRC Supp); Cancer Detection Technologies (SBIR/STTR Grants/Contracts); Models for Cancer Disparities (SBIR Contracts)	Minority-PDTCs	Activities to Promote Human Immune-Representing Oncology Models (APHIROM) (Admin Supps); PDXNet Supplements Reissuance; Technology Prize Competitions for Cancer Moonshot Priorities	APHIROM Exploratory and Developmental Research Projects; HCMI: Next Gen Technology for Next Gen Cancer Models; SBIR Contracts for New Tech
Partnerships	Partnership for Accelerating Cancer (PACT); NCI-DOE Collaborations (Pilots, JDACS4C, and ATOM); APOLLO with DOD and VA	PDXNet (Admin Supp); PSMA-PET of Prostate Cancer (IR)	CCR NCI Program for Natural Product Discovery (IR)	

Created by C.E. McCarthy, Ph.D., Division of Cancer Biology

Highlights of the 2018 Cancer Moonshot Initiatives

- **Pediatric Immunotherapy Discovery and Development Network**

- **Immuno-Oncology Translation Networks**

- **Fusion Oncoproteins in Childhood Cancers Consortium**

- **Drug Resistance and Sensitivity Network**

- **National Cancer Data Ecosystem**

- **Symptom Management Research**

- **Accelerating CRC Screening & Follow-up through Implementation Science (ACCSIS)**

- **Human Tumor Atlas Network**

Pediatric Immunotherapy Discovery and Development Network (PI-DDN)

Recommendation: Develop a pediatric immunotherapy translational network that would facilitate the testing of new immunotherapy approaches in *childhood cancers.*

Implementation: PI-DDN

PI-DDN Centers and Projects - Advancing translational research of immunotherapy approaches for children and adolescents with cancer:

Awards (6):

- Identification of antigenic epitopes and development of optimized epitope-targeting therapeutic reagents

- Identification and therapeutic targeting of cancer cell-intrinsic and -extrinsic mechanisms of immune evasion in the tumor microenvironment

Barriers to the Development of Immunotherapies for Childhood Cancers
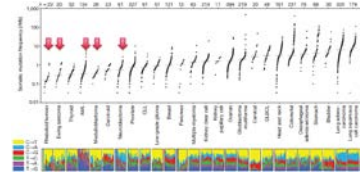
Low mutation burdens

HER2
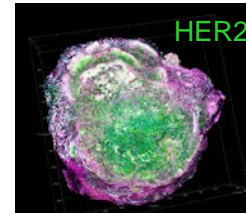
Target antigens expressed in *adult* cancers
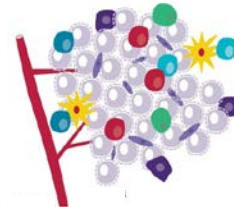
Immunosuppressive tumor microenvironment

Immuno-Oncology Translational Network (IOTN)

- **Recommendation:** Accelerate translation of basic discoveries to clinical applications to improve <u>immunotherapy</u> outcomes for both **"hot"** and **"cold"** cancers

- **Implementation:** Leverage the expertise and resources of a collaborative *network* of investigators focused on improving immunotherapy approaches:

  - Investigate the innate and adaptive immune mechanisms contributing to tumor progression or suppression

  - Identify factors contributing to tumor escape from immune surveillance

  - Discover and evaluate new immunotherapy strategies

  - Investigation of intrinsic and extrinsic pathways leading to acquired resistance to immune-modulating regimens.
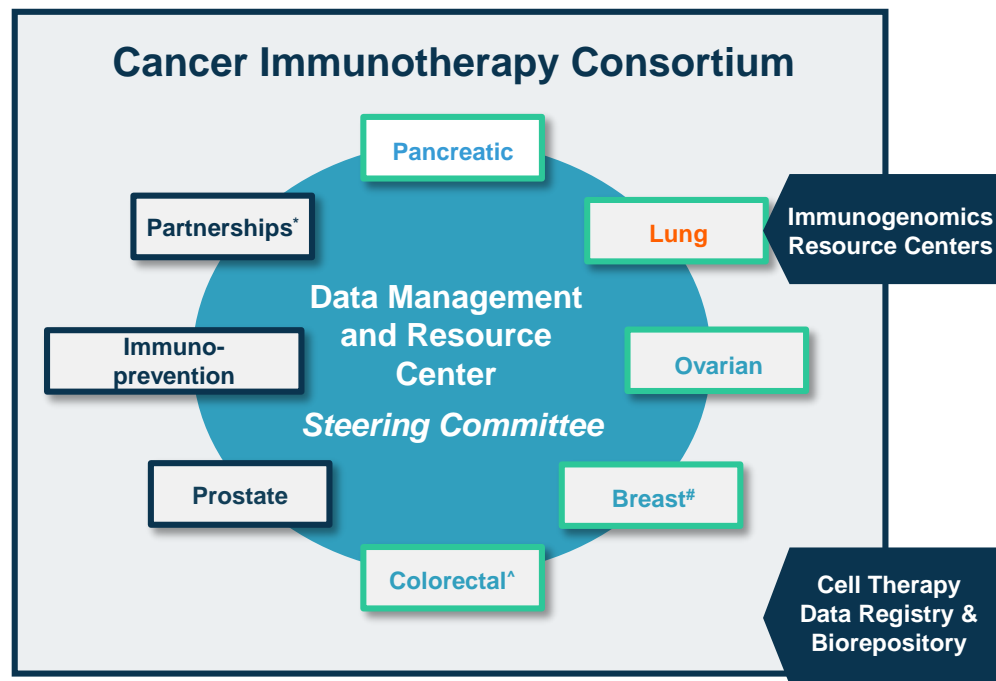
#TNBC
^MSI^{hi}
*GBM, Head & Neck, etc.
□ Sync'd with Tumor Atlas Group

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Fusion Oncoproteins in Childhood Cancers

Recommendation: Improve our understanding of fusion oncoproteins in pediatric cancer.

Implementation: Fusion Oncoproteins in Childhood Cancers (FusOnC2) Consortium

FusOnC2 Research Centers (U54s) – Advancing biological research in the area of pediatric fusion oncoproteins and informing the development of targeted therapies for childhood cancers.

- Focus on fusion oncoproteins found in tumors that have a *high-risk* of treatment failure:

> A) EWSR1-FLI1/EWSR1 (Ewing sarcoma) (2)
>
> B) SS18-SSX (synovial sarcoma) (2)
>
> C) Fusion-positive rhabdomyosarcoma
>
> > Intramural – Barr, Kahn
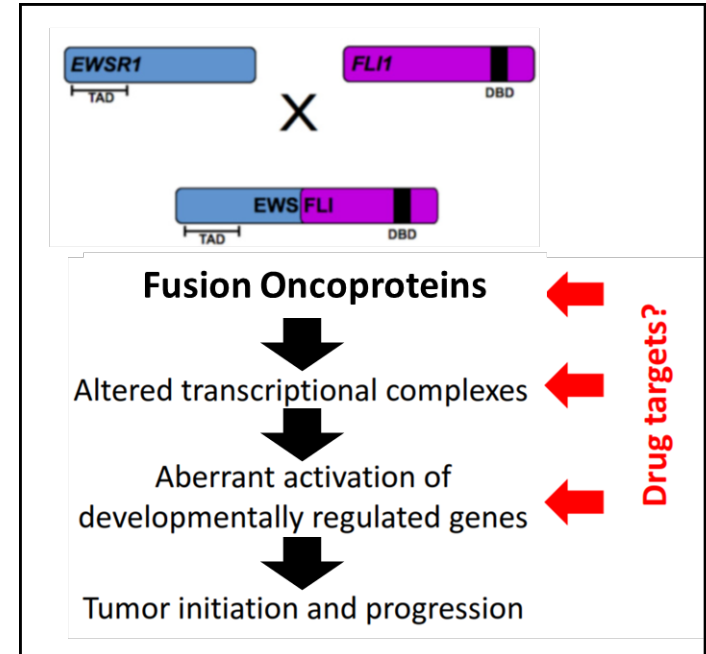
Drug Resistance and Sensitivity Network (DRSN)

Recommendation: Establish multidisciplinary research teams to determine cancer cell vulnerabilities that can be used for the development of new therapies that prevent or overcome therapeutic resistance.

Implementation: DRSN and DiCoCo

- *Drug Resistance and Sensitivity Centers of the DRSN* – preclinical and collaborative studies to understand and combat mechanisms of tumor resistance and/or to exploit tumor sensitivity to anti-cancer therapies.

- *CCR Lymphoma Basket Trial: Divide and Conquer with Combinations (DiCoCo)* - testing combinations of targeted treatments and measuring biomarkers in patients with lymphoma to identify effective combinations of drugs that can treat the disease and overcome drug resistance.

Drug Resistance and Sensitivity Network

Multiple Myeloma

Mayo Clinic - Arizona

Prostate

MSKCC-UW/ Fred Hutch

DRSN Steering Committee

OHSU

UCSF/Stanford

AML

Massachusetts General Hospital

Lung

CRC, Melanoma, Lung
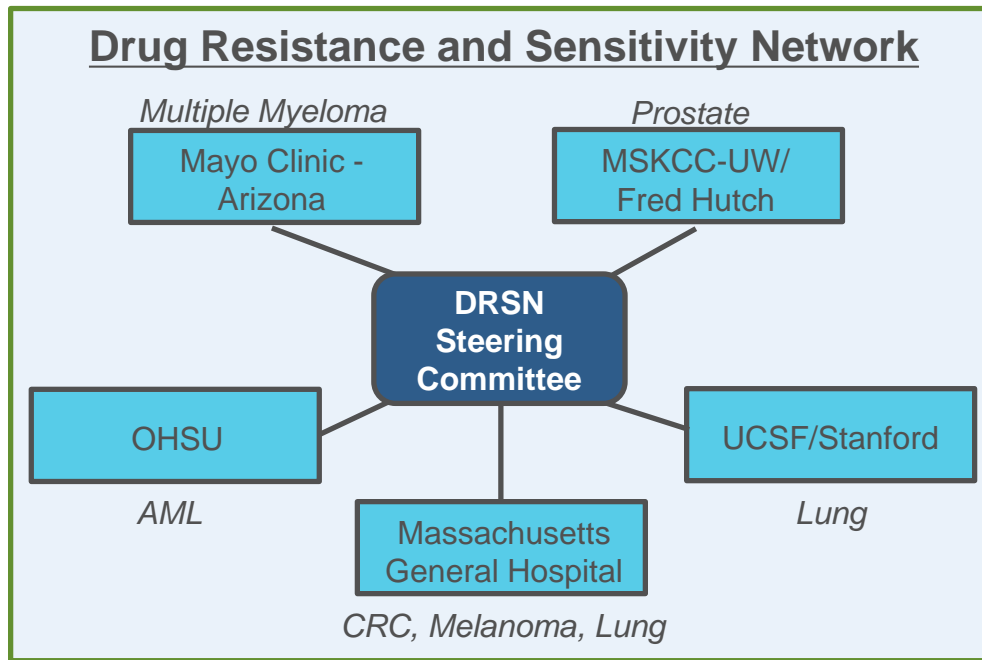
LYMPHOMA BASKET TRIAL: DIVIDE AND CONQUER WITH COMBINATIONS (DICOCO)

National Cancer Data Ecosystem

Recommendation: Build a National Cancer Data Ecosystem for sharing and analyzing data from cancer studies.

Implementation: National Cancer Data Ecosystem

- ***NCI Cancer Research Data Commons (CRDC)*** - Part of a data science infrastructure that connects data collections with analytical tools.

- ***NCI Office of Data Sharing***

- ***Privacy Preserving Patient Record Linkage Software*** – Developing unique patient identifiers that link to individual patient data from different sources.

- ***NCI Genomics Evidence Neoplasia Information Exchange (GENIE) Supplements -*** Promoting genomic and clinical data sharing.

- ***NCI Metadata Annotator*** - improved identification and use of high-quality metadata.

- ***NCI Imaging Support to the APOLLO Network -*** Supporting an APOLLO image library of clinical cancer tissues.
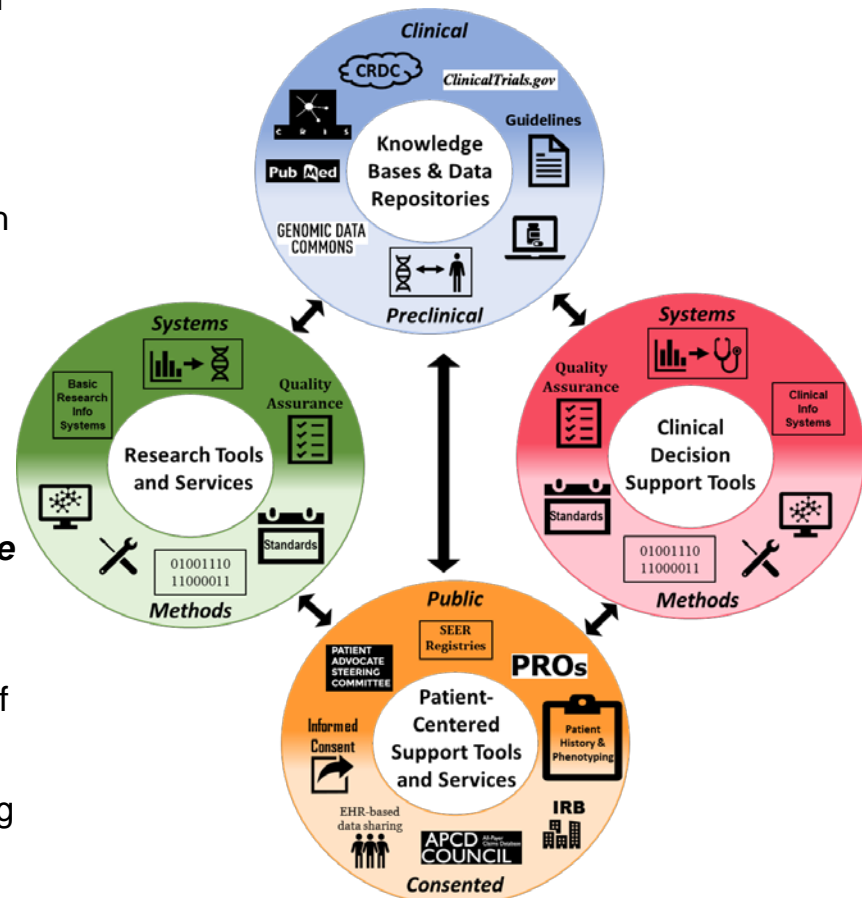
Symptom Management Research

Recommendation: Develop guidelines for managing patient-reported symptoms to minimize debilitating side effects of cancer treatment.

Implementation: Symptom Management Research Projects

- *Analyzing and Interpreting Clinician and Patient Adverse Event Data to Better Understand Tolerability* - Developing new methods for collecting and analyzing PROs in cancer clinical trials to improve the understanding of harmful side effects.

- *Improving Management of symPtoms Centers (IMPACT)* - Setting up integrated symptom monitoring and management systems in clinics and testing the impact of the systems on patient outcomes.

- *CCR Graft-Versus-Host Disease (GVHD) Symptom Management –* Developing a pediatric chronic symptom scale (PCSS) for GVHD to improve the understanding and management of GVHD symptoms.
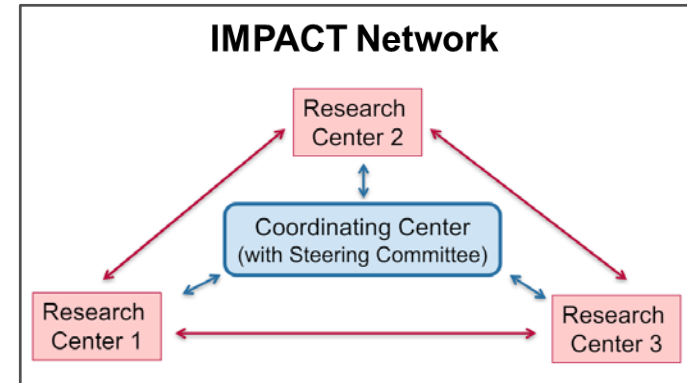
IMPACT Network

Research Center 2

Coordinating Center (with Steering Committee)

Research Center 1

Research Center 3

GRAFT-VERSUS-HOST DISEASE (GVHD) SYMPTOM MANAGEMENT

Prevention and Screening

Smoking Cessation Programs

Recommendation: Conduct implementation research to accelerate the adoption and deployment of sustainable, evidence-based cancer prevention and screening interventions at multiple levels and in different settings.

Implementation: Prevention and Screening Research Projects

- *Tobacco Cessation Treatment in Cancer Patients at NCI Cancer Centers* -

- *Improving Smoking Cessation in Socioeconomically Disadvantaged Populations via Scalable*

- *CCR Cervical Cancer Control and HPV Vaccine Trials*

- *Accelerating Colorectal Cancer Screening and Follow-up through Implementation Science (ACCSIS)* -

- *Dissemination of a Colorectal Cancer Screening Program Across American Indian Communities*

ACCSIS Signature Trial
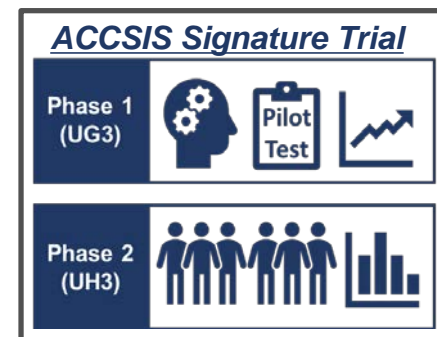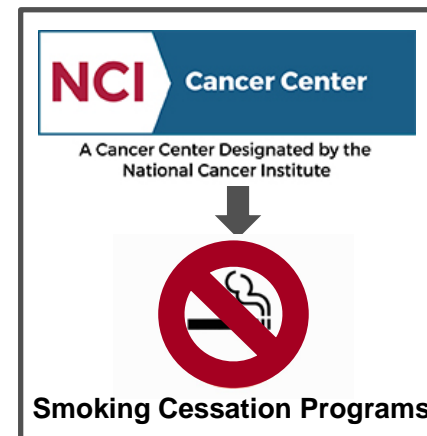
Human Tumor Atlas Network (HTAN)

Recommendation: Create dynamic 3D maps of human tumor evolution.

Implementation: HTAN

HTAN - Constructing 3D atlases of the multidimensional cellular, morphological, molecular features of human cancers over time.

- Focus on *high-risk* cancers; including those responsive/non-responsive to immunotherapy; pediatric cancers

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

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

Human Tumor Atlas Research Centers - Generating organ-specific human tumor atlases.

PreCancer Atlas Research Centers – Constructing atlases of precancerous lesions and their microenvironment.

HTAN Data Coordinating Center – Ensuring interoperability of HTAN data and dissemination of results to the scientific community

Experimental Measurements   **Computational Analysis**
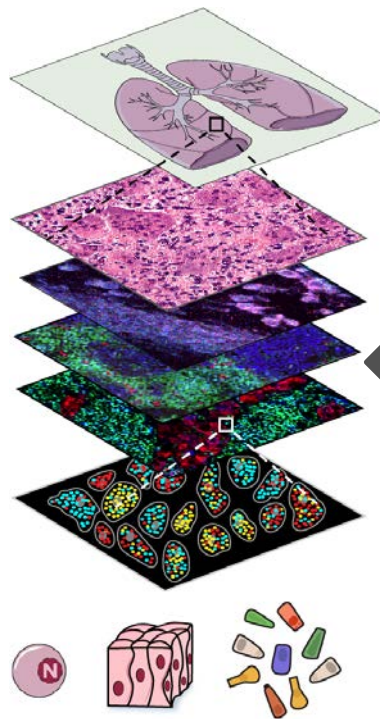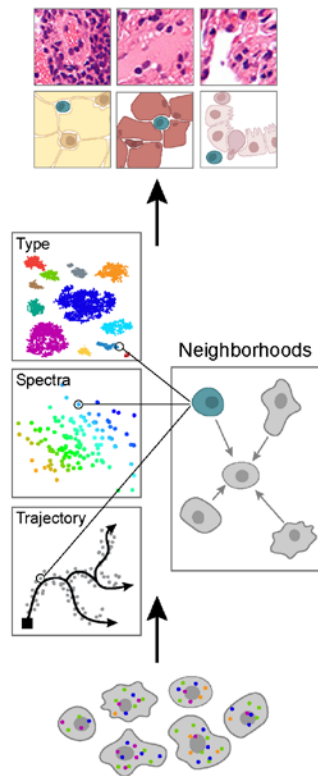
Figure from A. Regev and HTAPP Team

Cancer Moonshot FOAs

https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding

Questions?

www.cancer.gov/moonshot