The NCI Human Tumor Atlas Network (HTAN)

HuBMAP Annual Meeting

September 25, 2019

Shannon Hughes (NCI) & Mike Snyder (Stanford)

NIH NATIONAL CANCER INSTITUTE

NCI CANCER MOONSHOT

Human Tumor Atlas Network
A program of the National Cancer Institute
of the National Institutes of Health

The Cancer Moonshot Initiative (2016)

2016 State of the Union Address

Goals

- *Accelerate progress in cancer, including prevention & screening*

  From cutting-edge basic research to wider uptake of standard care

- *Encourage greater cooperation and collaboration*

  Break down silos within and between academia, government, and the private sector

- *Enhance data sharing*

  NCI Cancer Data Ecosystem

  Annotated patient-level clinical data and ‘omics

Blue Ribbon Panel Recommendations

A. Network for **Direct Patient Engagement**

B. Cancer **Immunotherapy** Clinical Trials Network

C. Therapeutic Target Identification to **Overcome Drug Resistance**

D. A National Cancer **Data Ecosystem** for Sharing and Analysis

E. Fusion Oncoproteins in **Childhood Cancers**

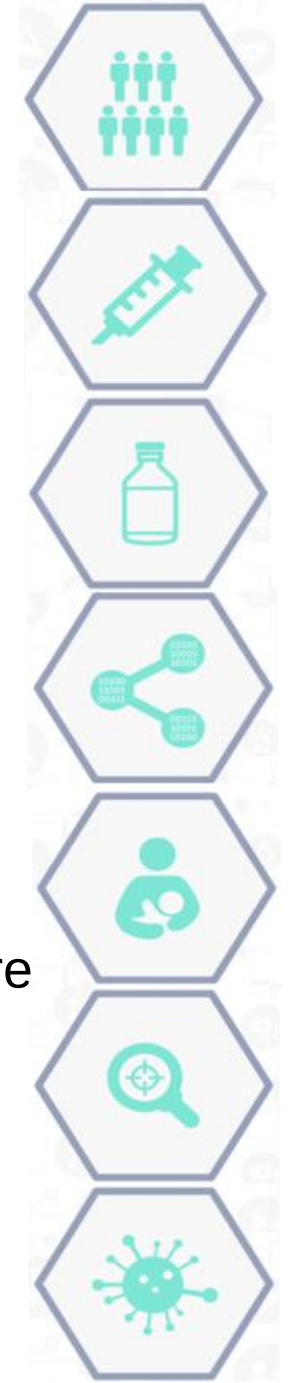
F. Symptom Management Research

G. Prevention and Early Detection: Implementation of Evidence-Based Approaches

H. Retrospective **Analysis of Biospecimens** from Patients Treated with Standard of Care

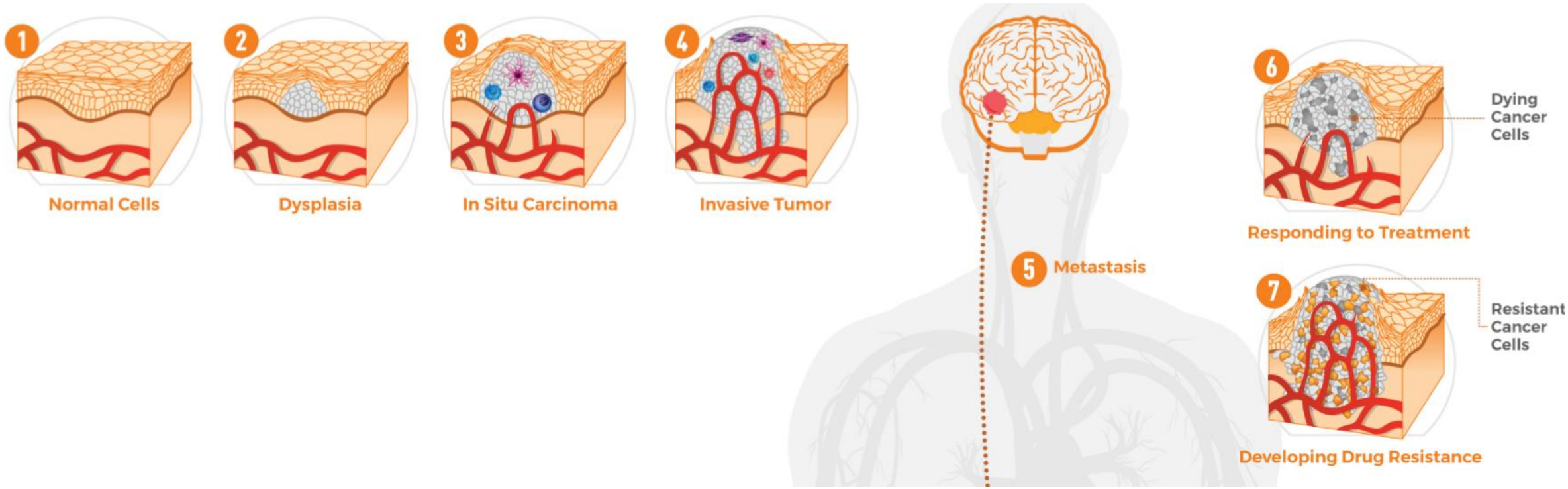
I. Generation of **Human Tumor Atlases**

J. Development of New Enabling **Cancer Technologies**



Recommendation I: *Generation of Human Tumor Atlases*

Create dynamic 3D maps of human tumor evolution to document the genetic lesions and cellular interactions of each tumor as it evolves from precancerous lesion to advanced cancer.

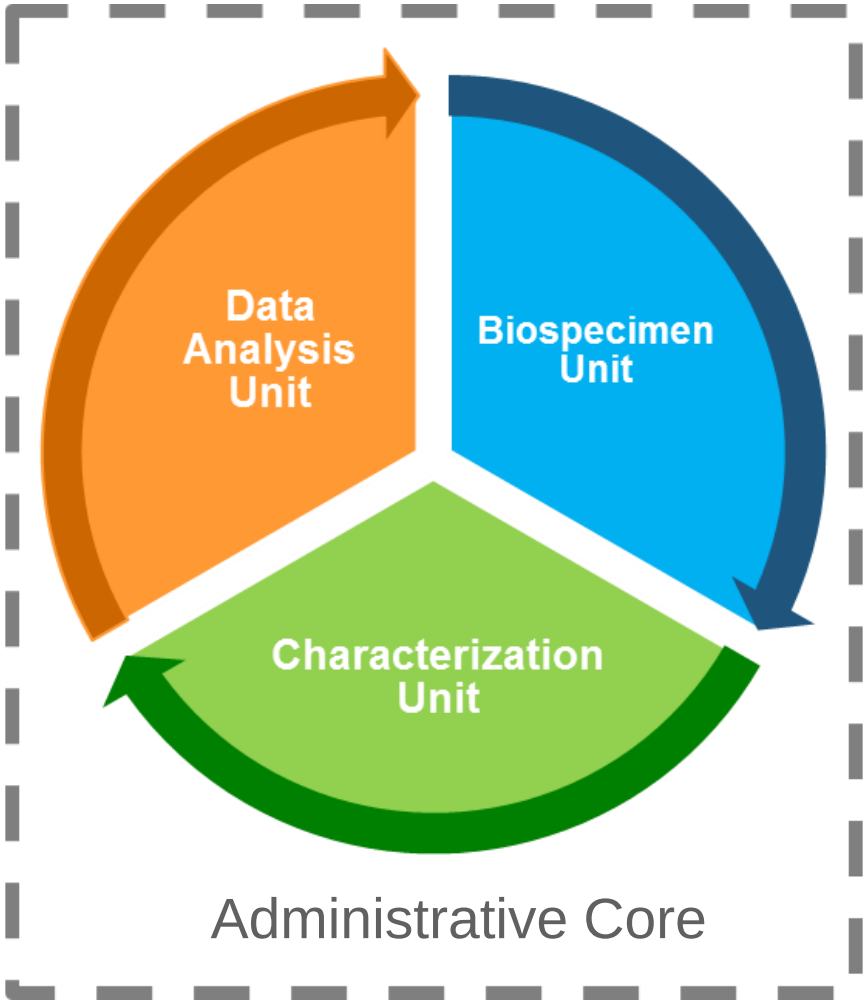


Adapted from "Cancer and the Human Tumor Atlas Network"
NCI's Annual Plan and Budget for Fiscal Year 2020

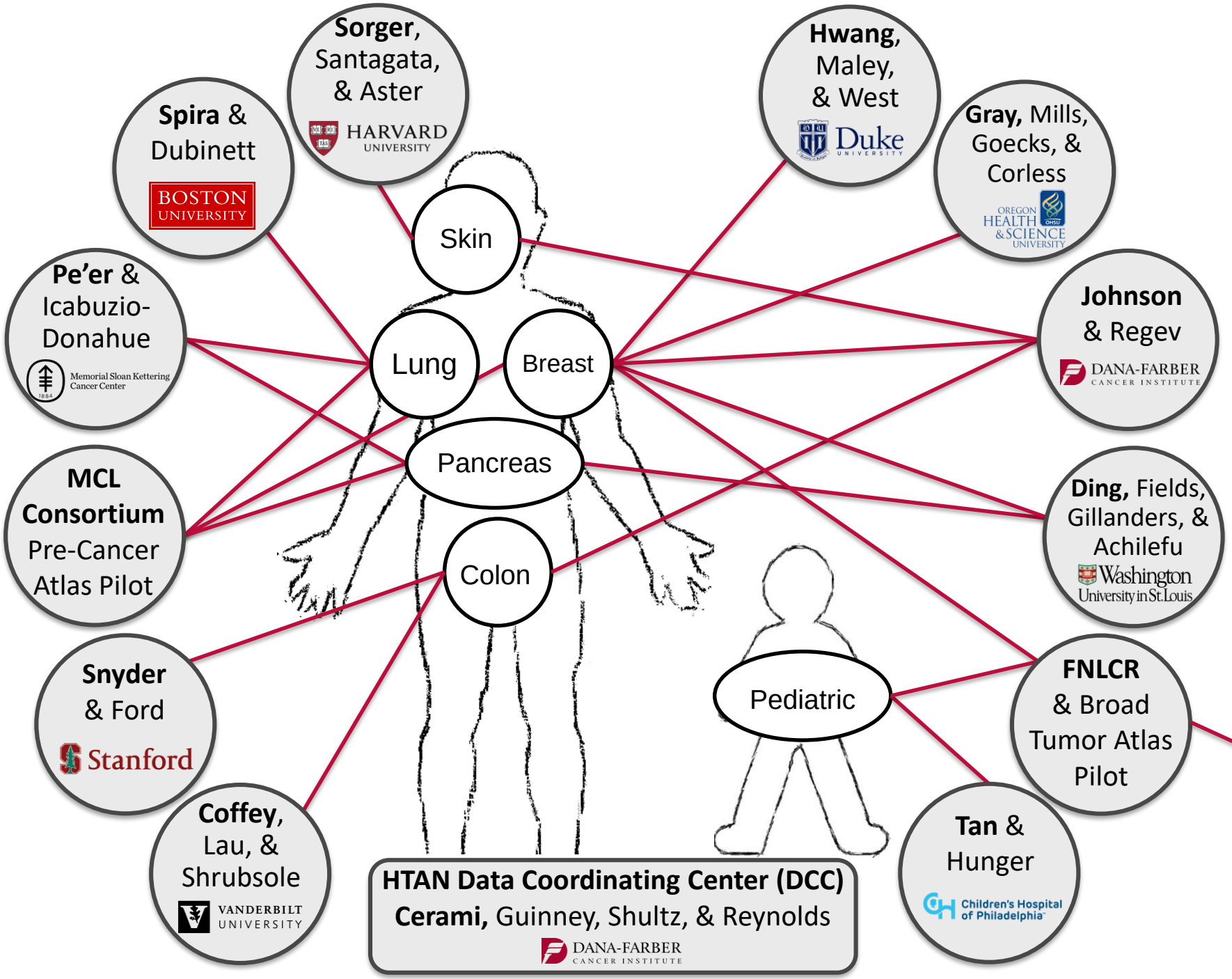
The NCI Human Tumor Atlas Network (HTAN)

- 10 U2C **Research Centers**
- 2 Pilot Cancer Atlases
- A U24 **Data Coordinating Center**
- A highly **multidisciplinary team of investigators**, including pathologists, clinical oncologists, cancer biologists, systems biologists, bioinformaticians, technology developers, computer scientists, etc.

Organization of HTAN Research Centers

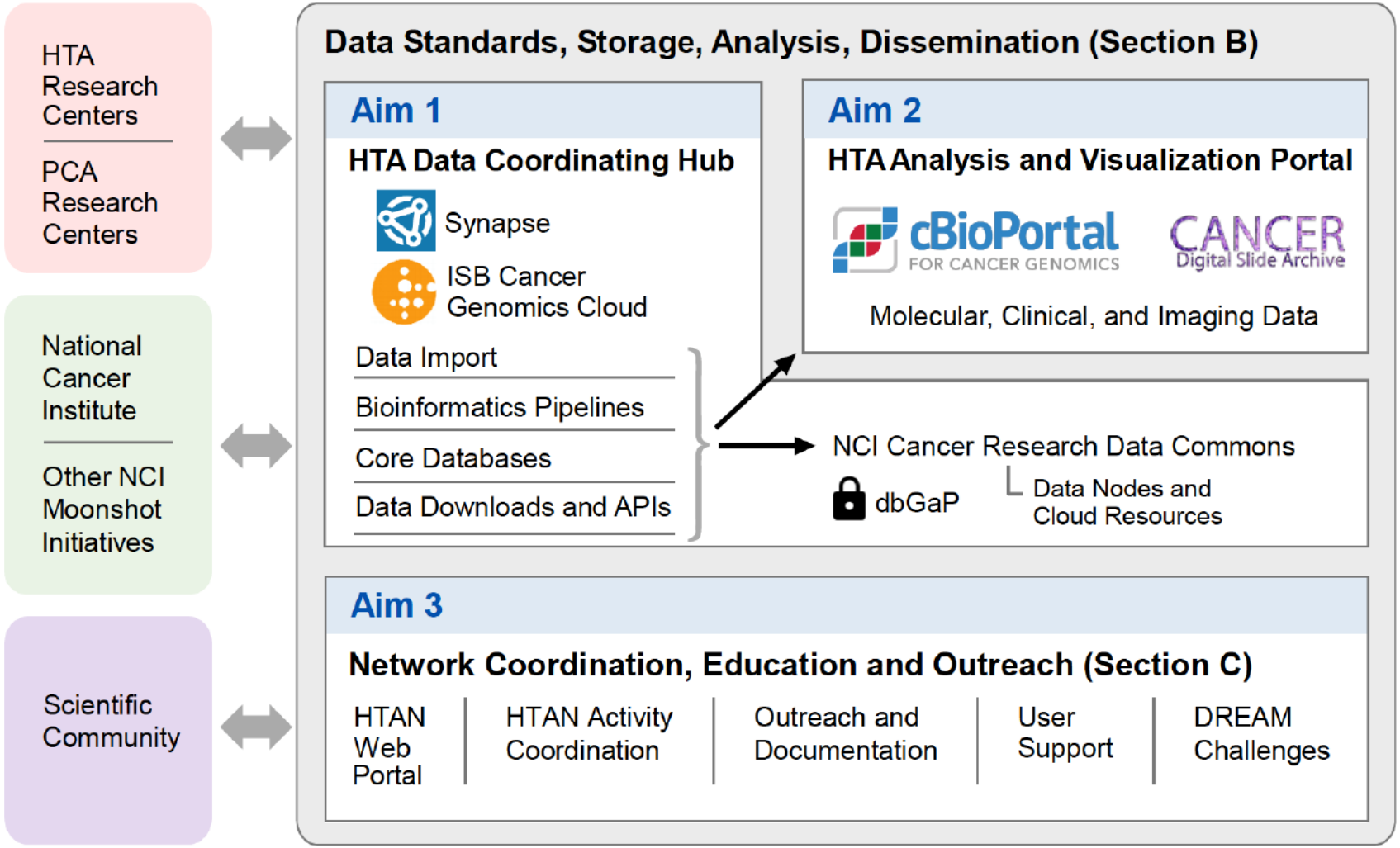


HTAN Research Centers and Tumor Atlases



A single-cell and single-nucleus RNA-seq toolbox for fresh and frozen human tumors
Slyper, Porter, Ashenberg, et al. bioRxiv; Sept 12 2019 (https://doi.org/10.1101/761429)

The HTAN Data Coordinating Center (DCC)



HTAN DATA COORDINATING CENTER (DCC)

Ethan Cerami, Justin Guinney, Nikolaus Shultz, & Vésteinn Thorsson

Dana-Farber Cancer Institute, Sage Bionetworks, Memorial Sloan Kettering Cancer Center, & Institute for Systems Biology

Image courtesy of Ethan Cerami

HTAN Data

Host level (microbiome, circulating factors)

Medical imaging modalities (MR, CT, PET)

Histology; Highly multiplexed 2D and 3D imaging

Metabolomics (Mass Spec, MALDI Imaging)

Proteomics (Mass Spec, Imaging Approaches)

Transcriptomics (RNA-Seq, in situ/FISH, etc.)

DNA-seq (whole genome, whole exome) and Epigenetics

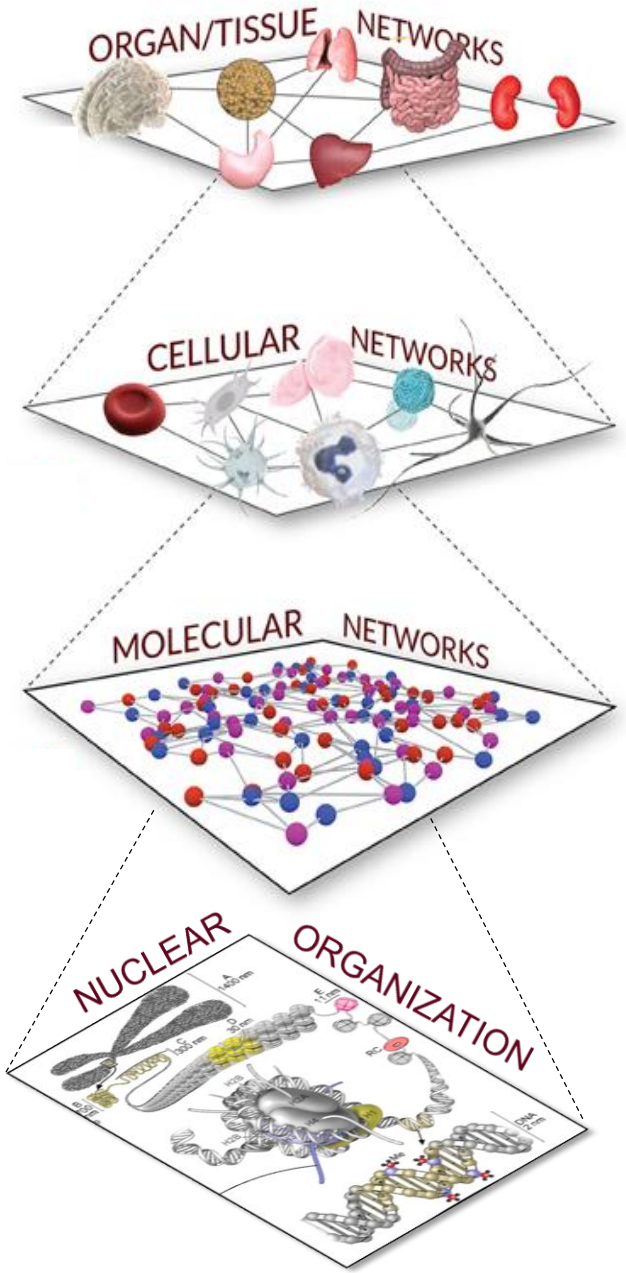
EM imaging (2D, 3D)

Sample of data types common with HuBMAP

CODEX, CyCIF, mIHC, MIBI, IMC, Slide-seq

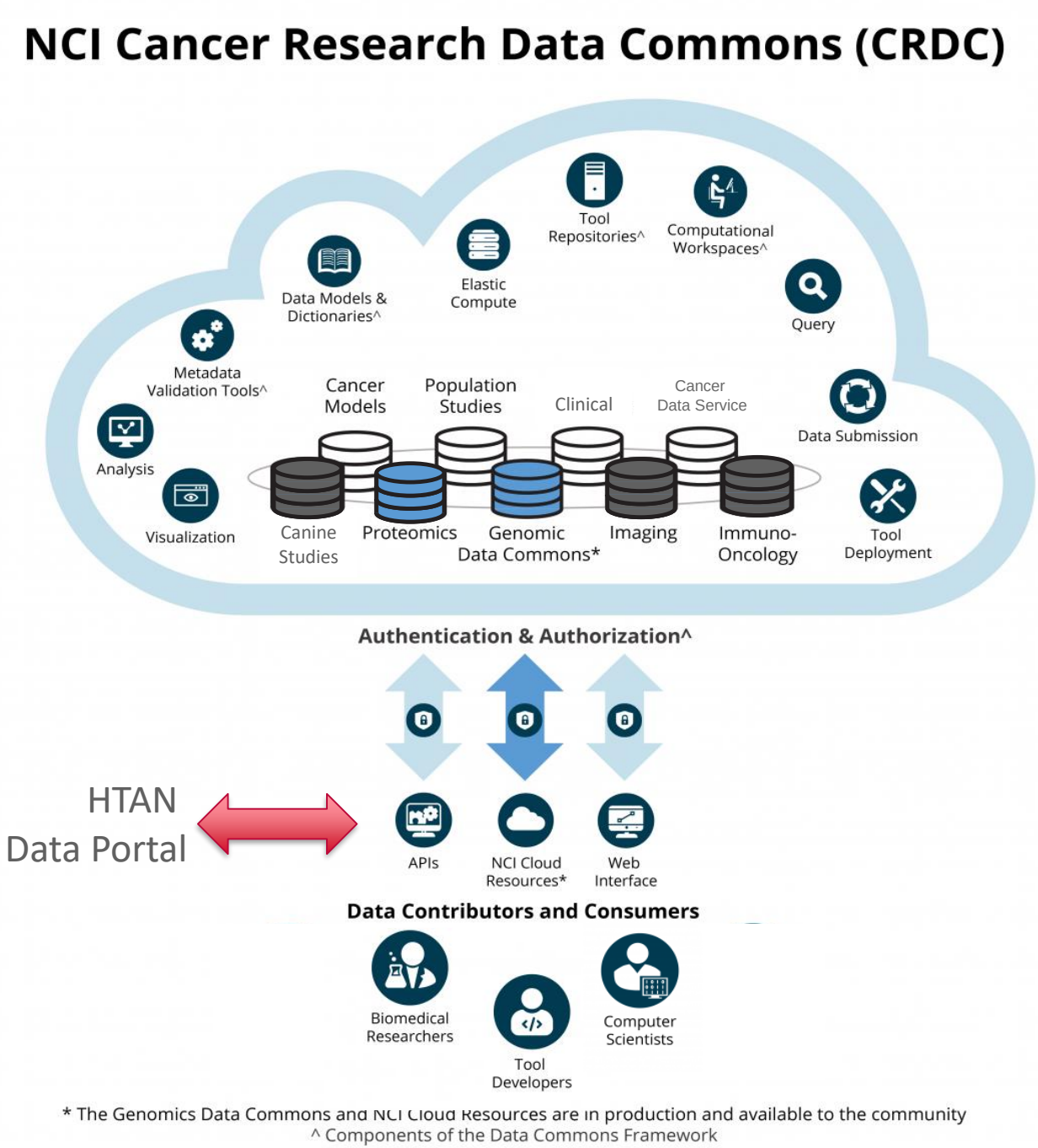
sc/sn 10X inDrops SMART-seq2 MERFISH

scATAC-seq scTHS-seq (+bulk)



HTAN data will be accessed through the NCI CRDC

- Data access is controlled through a common Authentication and Authorization mechanism that secures the data.
- Data are stored in domain-specific repositories, called Data Nodes (e.g., genomic, proteomic, imaging, etc.).
- Researchers can bring their own data and tools to the cloud, and combine with the data in the CRDC for integrative analysis.



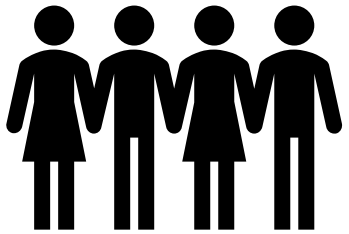
Slide from Eve Shalley, NCI CBIIT

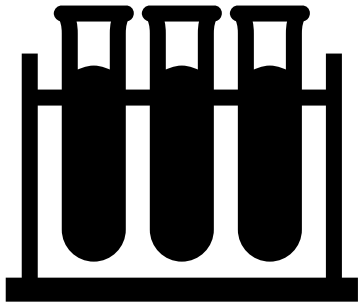
HTAN Policy Working Group

- **Mission:** Establish policies that **optimize sharing of data and information** within HTAN and the broader research community.
- **Co-Chairs:** Aviv Regev, Broad Institute; Bruce Johnson, DFCI; Justin Guinney, Sage
- **Current Priorities:**
  - Data Access & Release Policy (including DUA & MTAs)
  - ✓ Protocol Sharing Policy
  - ✓ Publication Policy

HTAN Clinical and Biospecimen Working Group

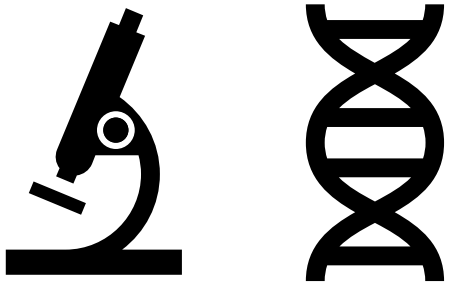
- **Mission:** Build consensus and provide guidance to enable implementation of **standardized collection, processing, handling, preservation/storage, sharing/tracking, de-identification, and annotation** of cases, samples, and clinical images across HTAN.
- **Co-Chairs:** Warren Kibbe, Duke; Dan Merrick, University of Colorado; Asaf Rotem, DFCI
- **Subgroups**
  - Clinical Annotations (CDEs)
  - Collection and Processing
  - Trans-Network Projects





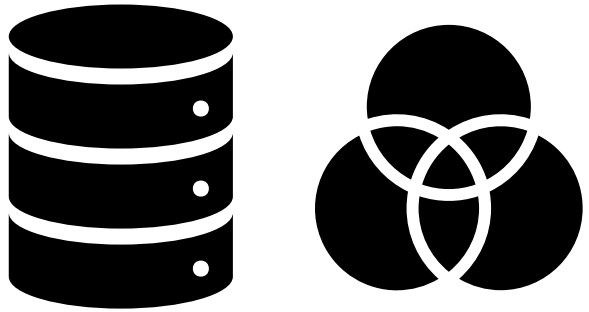
HTAN Molecular Characterization Working Group

- **Mission:** Help discover, develop, and distribute methods for data collection within HTAN. This will include development of **best practices, quality-control metrics, workflows, reagent/data standards, and procedures** (ultimately SOPs).
- **Co-Chairs:** Peter Sorger, Harvard; Orit Rozenblatt-Rosen, Broad; Ken Lau, Vanderbilt
- **Current Priorities:** *within the context of a Trans-network Project*
  - Integrative imaging data standards and imaging data sharing systems
  - Reference samples and preanalytical variables
  - NGS approaches on FFPE



HTAN Data Analysis Working Group

- **Mission:** Define, share, and integrate **best practices that support rigorous, reproducible data analysis and open science**. Serve as an interface between HTAN Research Centers and DCC with respect to data processing and analysis pipelines.
- **Co-Chairs:** Li Ding, WUSTL; Dana Pe'er, MSKCC; Kai Tan, CHOP
- **Subgroups**
  - Single-cell/Single-nucleus Sequencing Pipelines
  - Multiplex IHC/IFC Image Processing Pipelines
  - Cell Type Signatures
  - Emerging Technologies - scATAC-Seq/Methylation
  - Emerging Technologies - Radiology/Radiomics
  - Bulk Sequencing (methylation/RNA/DNA) & Proteomics/Metabolomics



HTAN Tumor Atlases will Facilitate Cancer Research

At the end a successful 5-year HTAN effort, we expect a preliminary set of human tumor atlases that:

- **Helps define tumor heterogeneity** within and across patients in high-priority adult and pediatric cancers
- **Quantifies the 3D architecture** of the tumor ecosystem during important transitions
- **Facilitates predictive modeling** that leads to development of new risk stratification methods, better treatment options for patients, and improved understanding of disease mechanisms
- **Provides direction for future atlas building efforts**

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What are the challenges?

- Many
- Consensus analysis pipelines for common assays
- How to handle, analyze, display/navigate multiplex images
- Balancing biology versus cataloging
- 3D

What are the most productive intersections between atlas efforts?

www.humantumoratlas.org

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