Human Tumor Atlas Network (HTAN)

2018 IMAT Investigators Meeting

November 29, 2018

Sean E. Hanlon

NIH NATIONAL CANCER INSTITUTE

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

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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**

Blue Ribbon Panel's Recommendation I
Generation of Human Tumor Atlases

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

Goal of the Human Tumor Atlas Network (HTAN):

Construction of **high-resolution, multidimensional, multiparametric, dynamic atlases** of individual tumors over time. Atlases should:

- Describe the **molecular, cellular, and physiological events** that occur during tumor evolution.

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

- Enable **predictive modeling** to refine preventive and therapeutic choices.

- Include critical time points — **transition from pre-malignancy to cancer, metastasis, response to therapy, and development of resistance to therapy**.

HTAN is a <u>Community Resource Program</u>

- Create a community resource that **catalyzes cancer research across disciplines**

- Promote aggressive **public data and resource release** timelines

- Facilitate and understanding of what **technologies and assays will be most informative** across tumor types

- Develop **standard operating procedures** that will allow meaningful comparison of data across these technologies

- Generate a **publicly available set of tumor atlases** describing transitions in cancer in a spatially-resolved manner for use by the cancer community

HTAN Atlases will describe critical transitions in cancer

…facilitated by collaboration across research centers and approaches.

A comprehensive human tumor atlas is defined as the **multidimensional molecular, cellular, and morphological mapping** of human cancers, **complemented with critical spatial information** (at the molecular, cellular, and/or tissue level) that **facilitate visualization of the structure, composition, and multiscale interactions** within the tumor ecosystem.
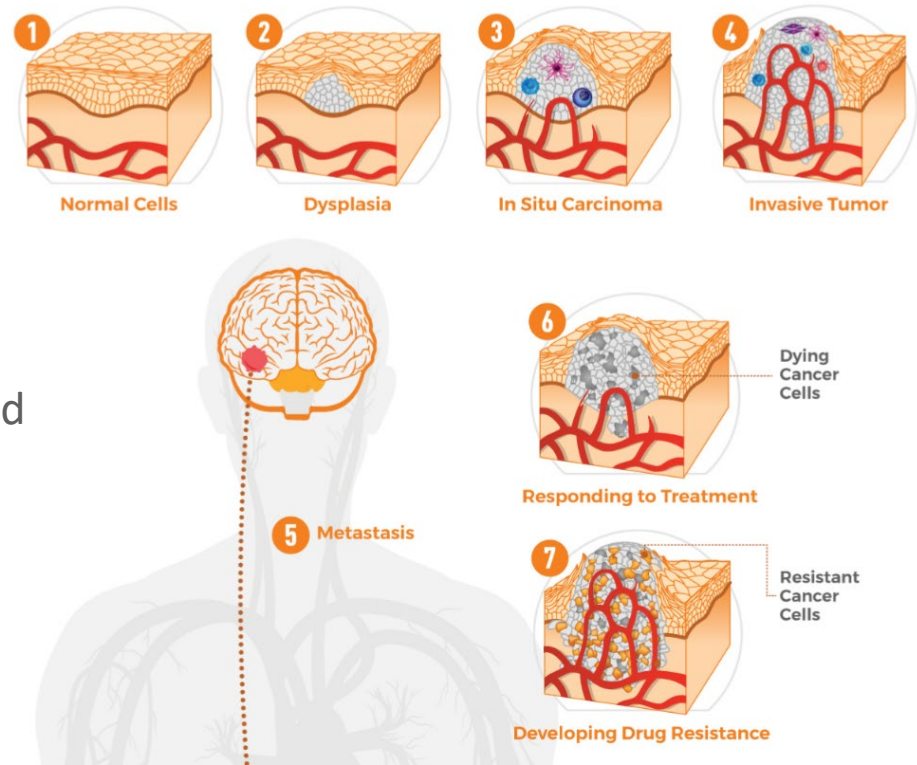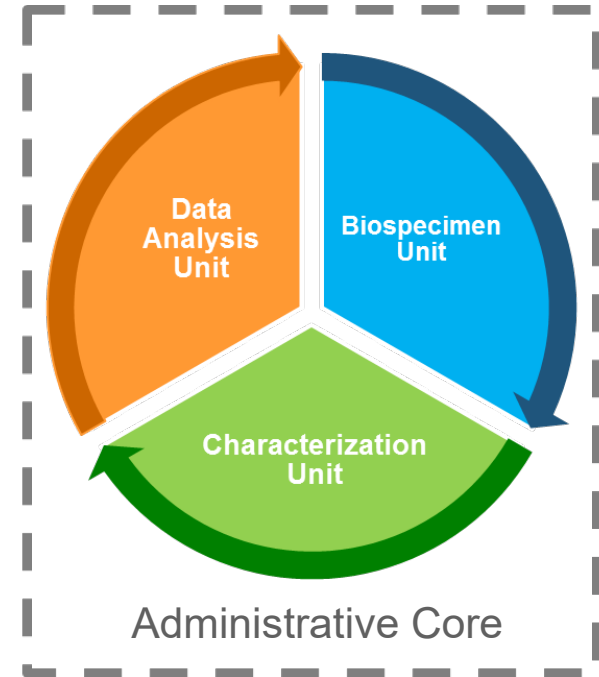

Adapted from "Cancer and the Human Tumor Atlas Network" NCI's Annual Plan and Budget for Fiscal Year 2020

The Human Tumor Atlas Network

- 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 U2C Research Centers

Data Analysis Unit

Biospecimen Unit

Characterization Unit

Administrative Core

The Human Tumor Atlas Network

Sorger, Santagata, & Aster — HARVARD UNIVERSITY

Spira & Dubinett — BOSTON UNIVERSITY

Hwang, Maley, & West — Duke UNIVERSITY

Gray, Mills, Goecks, & Corless — OREGON HEALTH & SCIENCE UNIVERSITY

Pe'er & Icabuzio-Donahue — Memorial Sloan Kettering Cancer Center

Haining & Regev — DANA-FARBER CANCER INSTITUTE

MCL Consortium Pre-Cancer Atlas Pilot

Ding, Fields, Gillanders, & Achilefu — Washington University in St. Louis

Snyder & Ford — Stanford

FNLCR & Broad Tumor Atlas Pilot

Coffey, Lau, & Shrubsole — VANDERBILT UNIVERSITY

Tan & Hunger — Children's Hospital of Philadelphia

HTAN Data Coordinating Center (DCC)
Cerami, Guinney, Shultz, & Reynolds — DANA-FARBER CANCER INSTITUTE

Skin, Lung, Breast, Pancreas, Colon, Pediatric

Focus of Atlases				
	Pre-Cancer	**Response to Therapy**	**Development of Resistance**	**Metastasis**
Pediatric cancers		Tan (NB; SOC) ** (NB; SOC) Tan (VHR-ALL; CAR-T)	Tan (Glioma; SOC) ** (Glioma; SOC)	
Breast	Hwang (DCIS) *	Ding (TNBC; αPD-L1) Gray (TNBC; αPD-L1 + αPARP)		** (ER+/PR+)
Breast	Hwang (DCIS) *		Gray (ER+/PR+; αCDK4/6) Haining (ER+/PR+; αCDK4/6)	** (ER+/PR+)
Colon	Snyder (FAP) Coffey	Haining (MSI Hi/Lo; αPD-L1 or αCTLA-4)		
Melanoma	Sorger	Haining (αPD-L1 or αCTLA-4)		
Lung	Spira *			Pe'er
Pancreas	*			Pe'er Ding

(Left side vertical label: Cancers in adults)

* = FY17 PCA Pilot Project (NCI MCL Consortium, not Moonshot funded)

** = FY17 HTA Pilot Project (Leidos/Broad Institute, Moonshot funded)

Note: Sorger center also pursuing CHIP pilot atlas

TNBC = Triple-Negative Breast Cancer
DCIS = Ductal Carcinoma In Situ
FAP = Familial Adenomatous Polyposis
NB = Neuroblastoma
VHR-ALL = Very High-Risk B-Cell Acute Lymphoblastic Leukemia
SOC = Standard of Care
MCL = Molecular and Cellular Characterization of Screen-Detected Lesions

We don't yet know the best data, but it is sure to be multi-dimensional

Microbiome

Medical imaging modalities (rad...

Histology

Metabolomics (LC-MS...

Protein imaging (...MIBI, IMC, cyclic-IF, etc.)

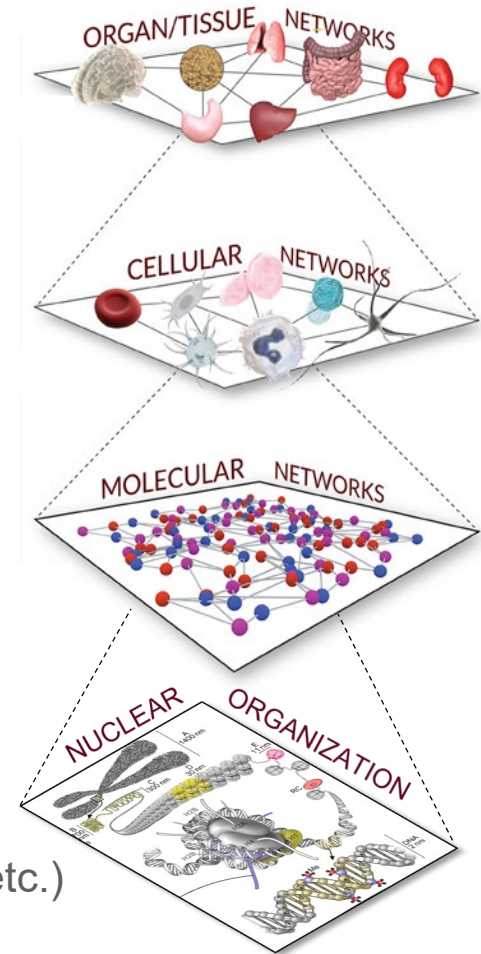Transcripto... ...Seq, MERFISH, etc.)

Whole ... whole exome, targeted DNA seq
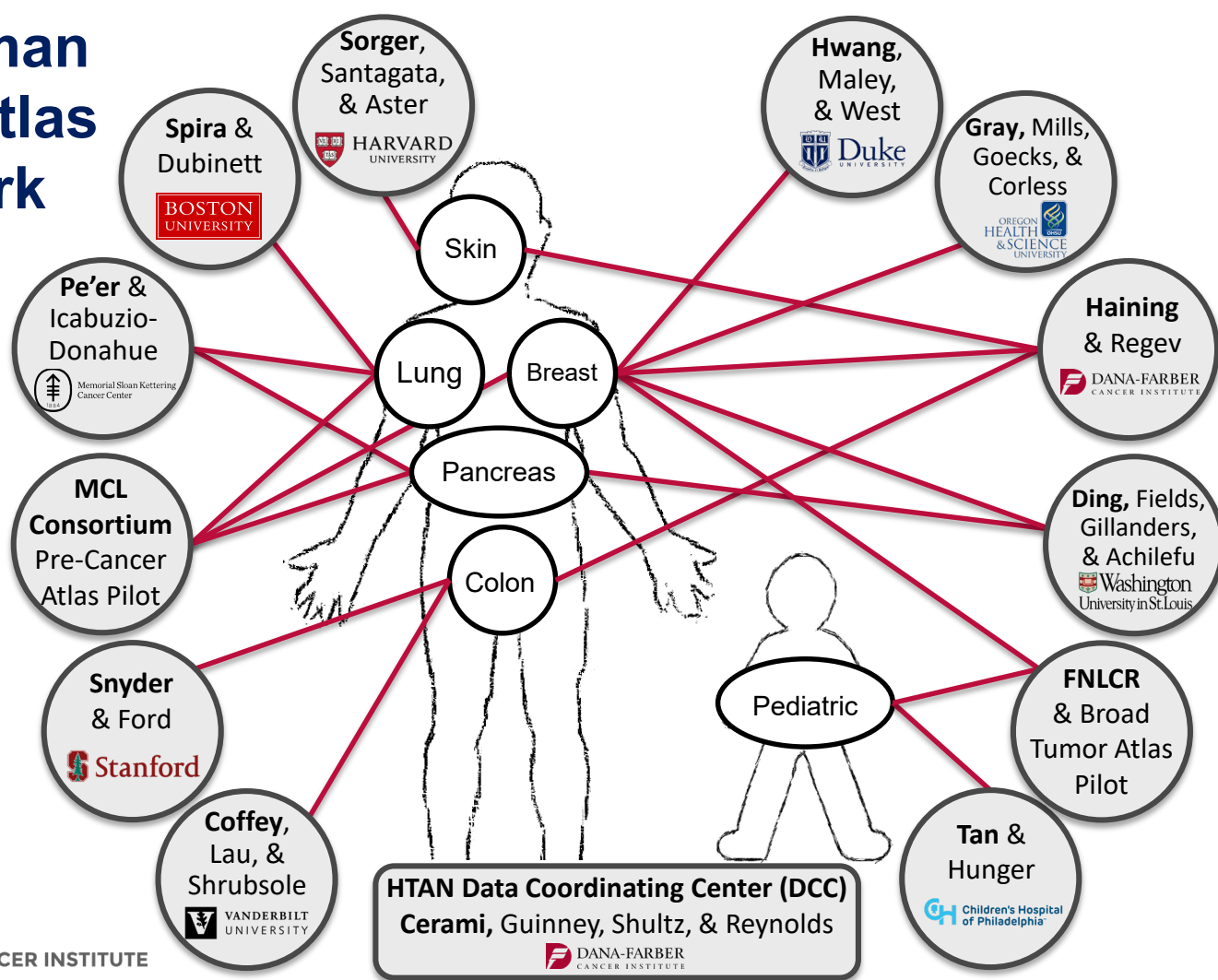
EM... (2D, 3D)

...e organization and epigenetics (ATAC-seq, BS-seq, etc.)

Many at single-cell resolution and/or with spatial information

ORGAN/TISSUE NETWORKS

CELLULAR NETWORKS

MOLECULAR NETWORKS

NUCLEAR ORGANIZATION

Multi-scale modeling!

Data Integration

The Human Tumor Atlas Network

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BOSTON UNIVERSITY

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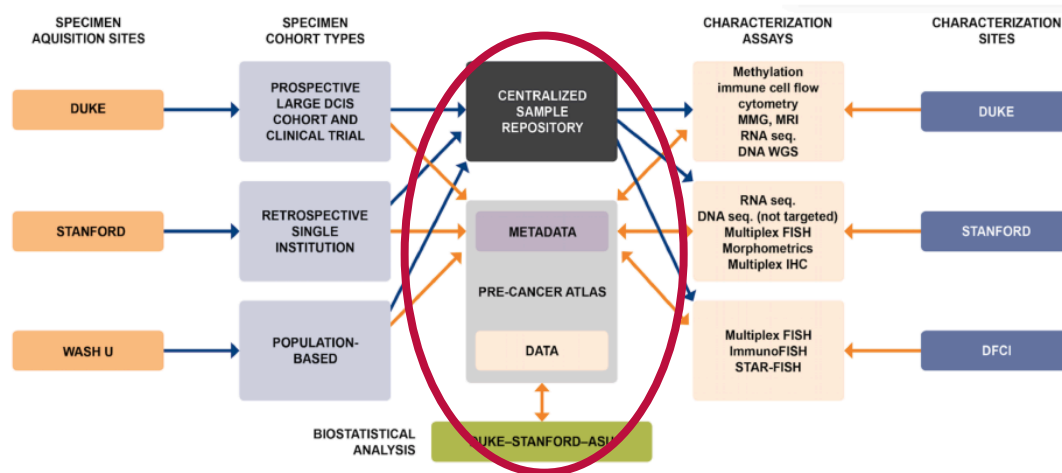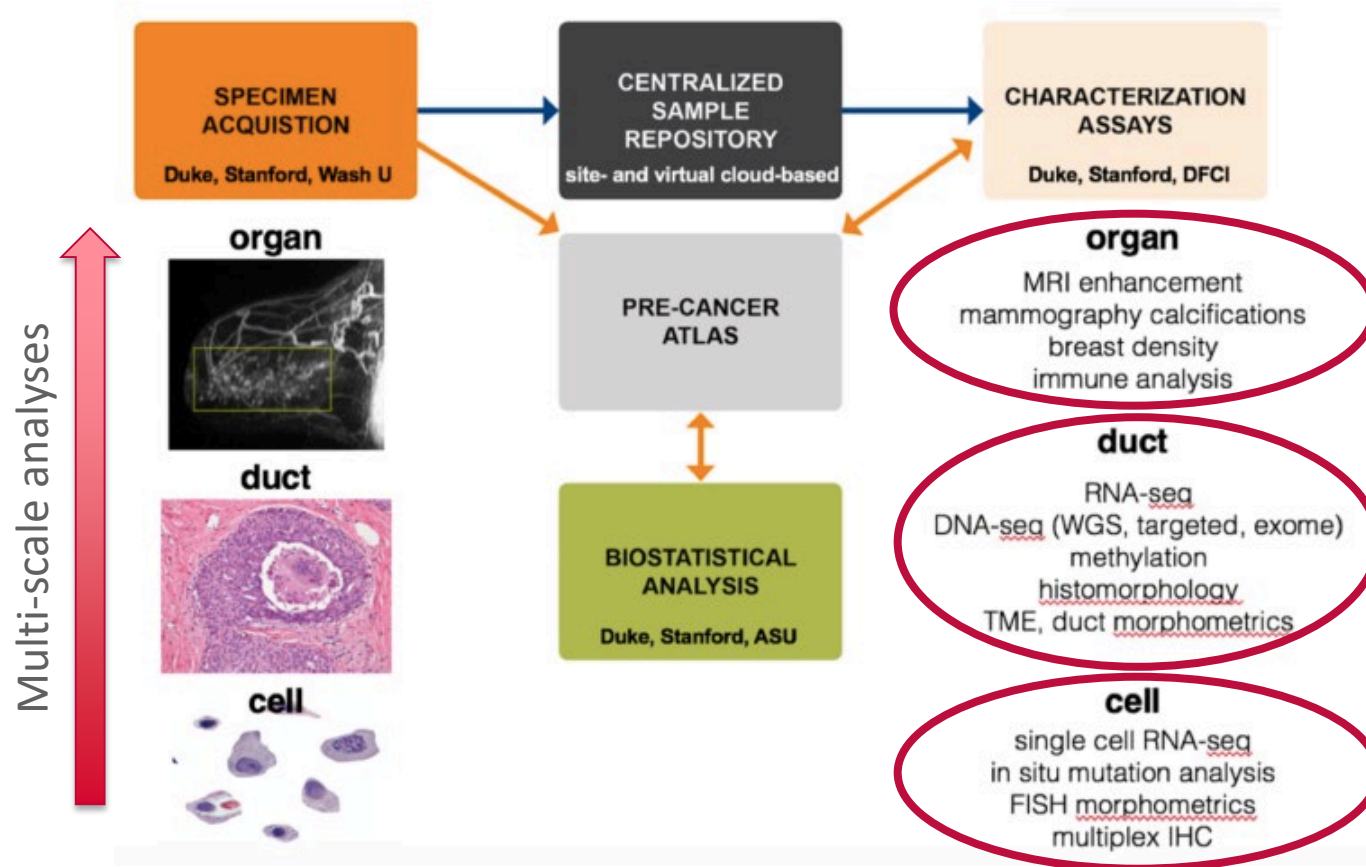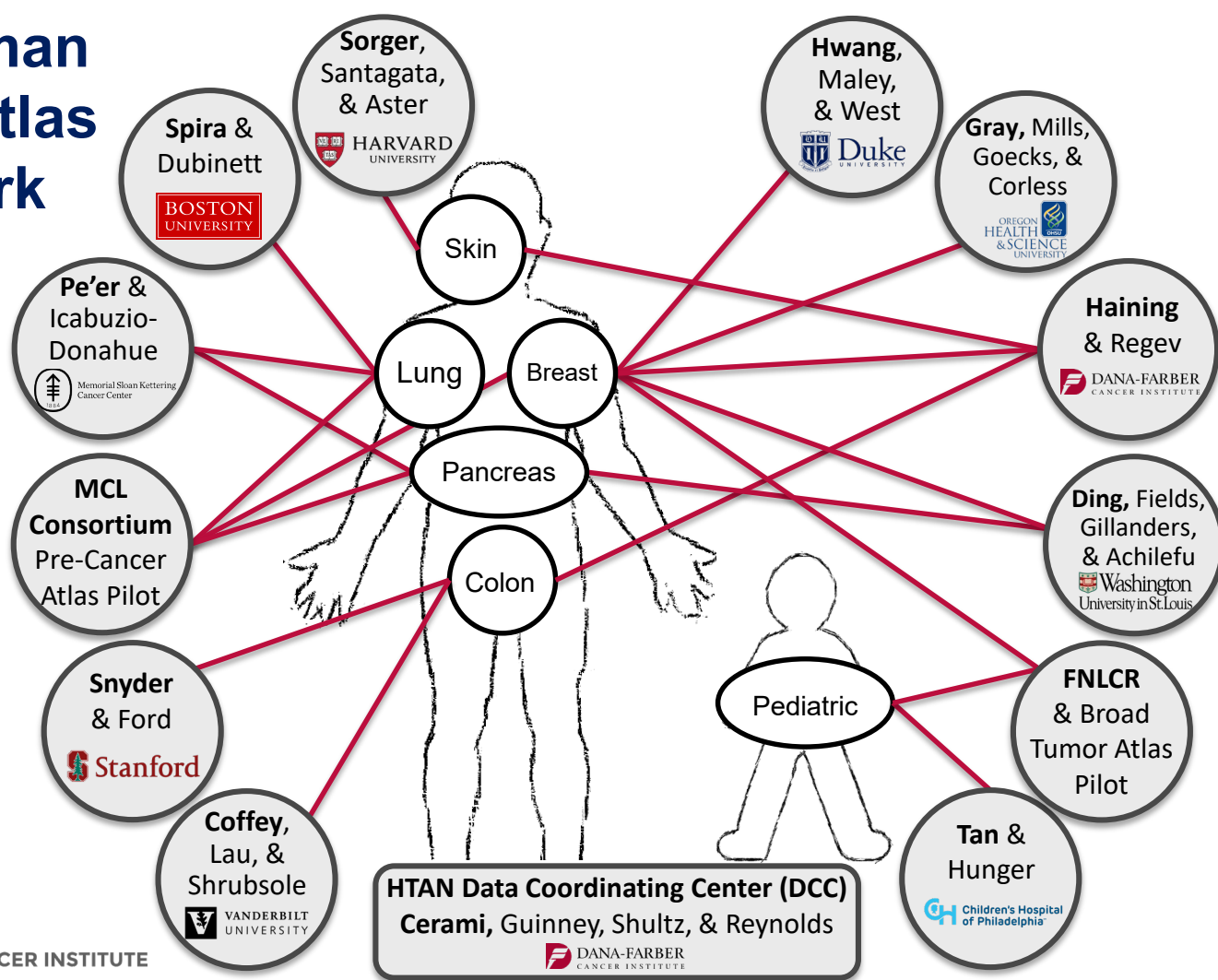
Duke Breast Pre-Cancer Atlas

- Aim 1: **Develop a platform** for organizing the three-dimensional, multi-modal data derived from a pre-cancer, that facilitates the discovery of the **natural history of the pre-cancer** and **predictors of progression**.

- Aim 2: **Populate that platform** with data from both retrospective and longitudinal (watchful waiting) cohorts of patients with DCIS and other breast precancers to **build a precancer atlas** and **test novel predictors of progression**.
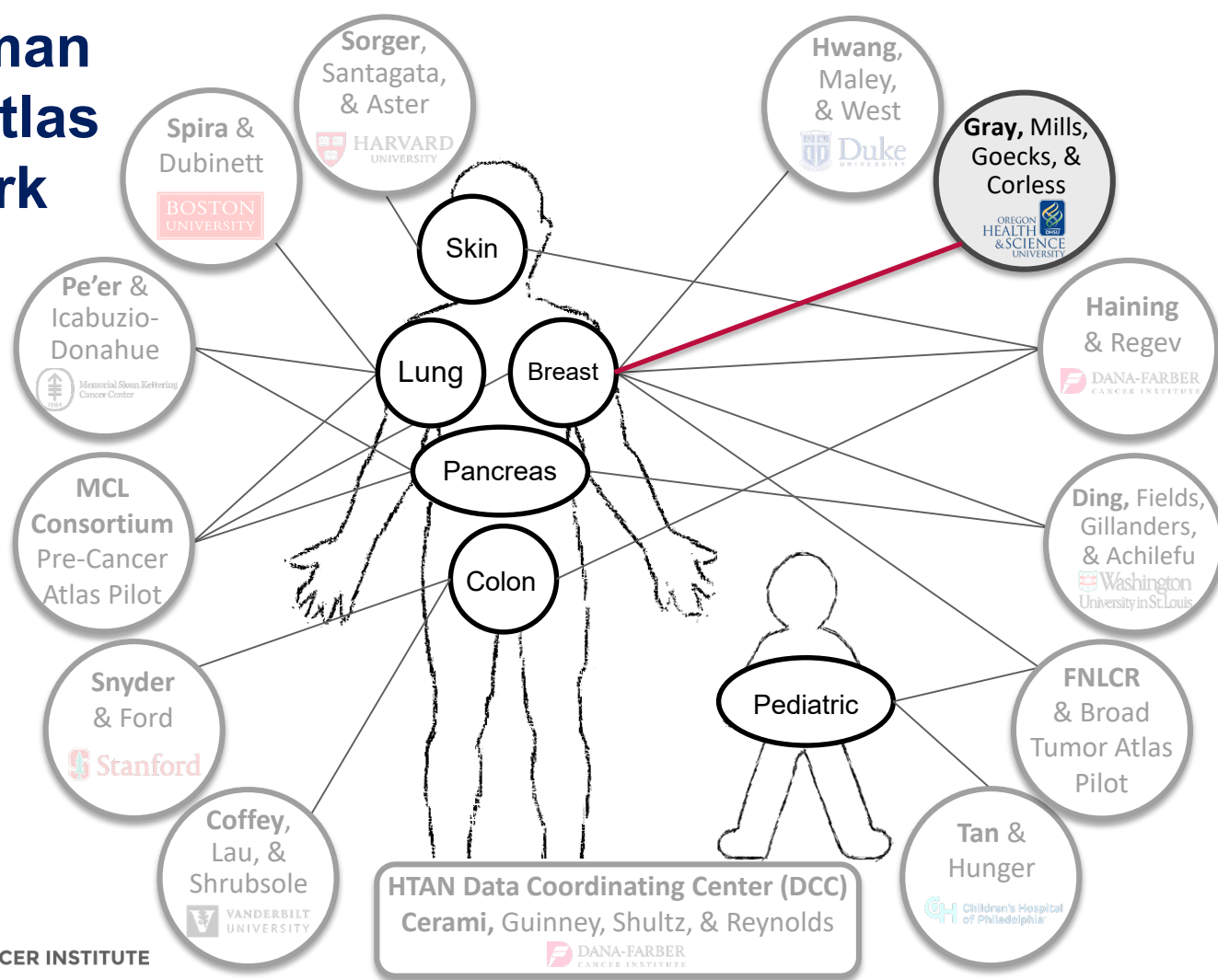

Courtesy of Shelly Hwang

Duke Breast Pre-Cancer Atlas

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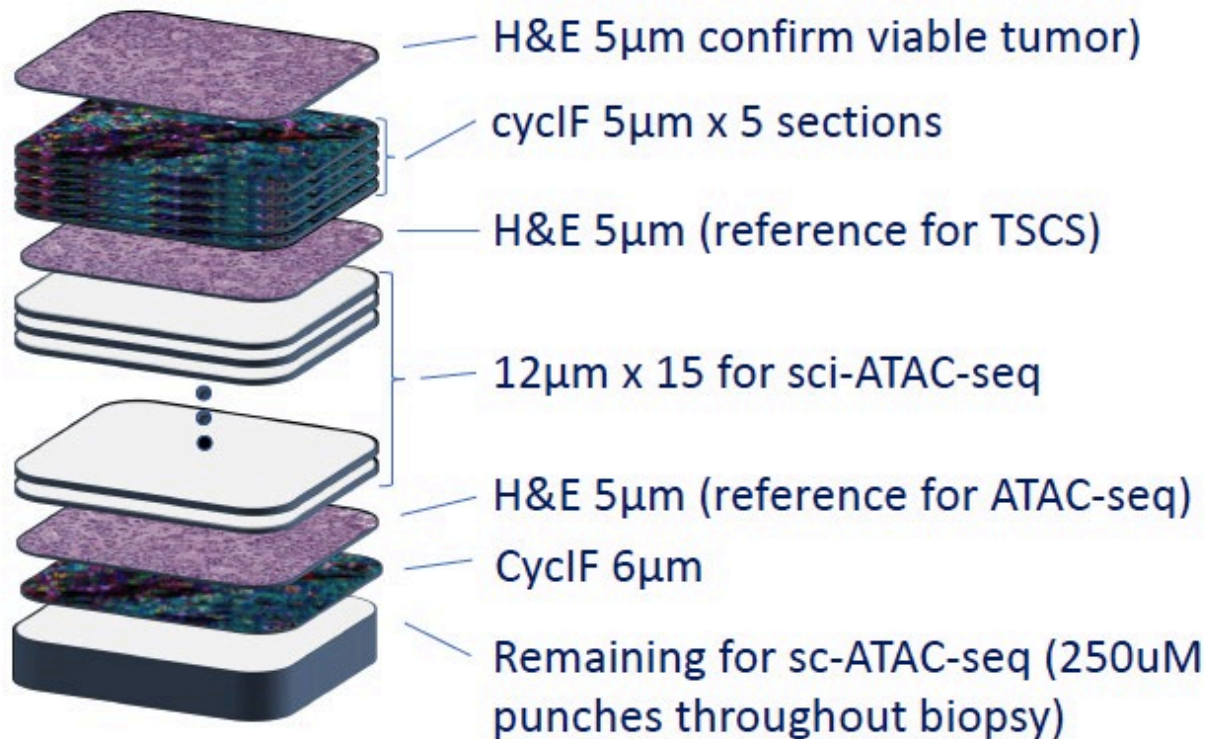
16

Omic and Multiscale Image (OMS) Atlas

Overarching goal: Identify **therapeutic vul**
mechanisms of **resistance** in evolving met
• HRBC treated with CDK4/6 inhibitors + anti-estr
• TNBC treated with PARP inhibitor + immune che

Lopez et al., Methods Cell Bio. 2017

Courtesy of Joe Gray

17
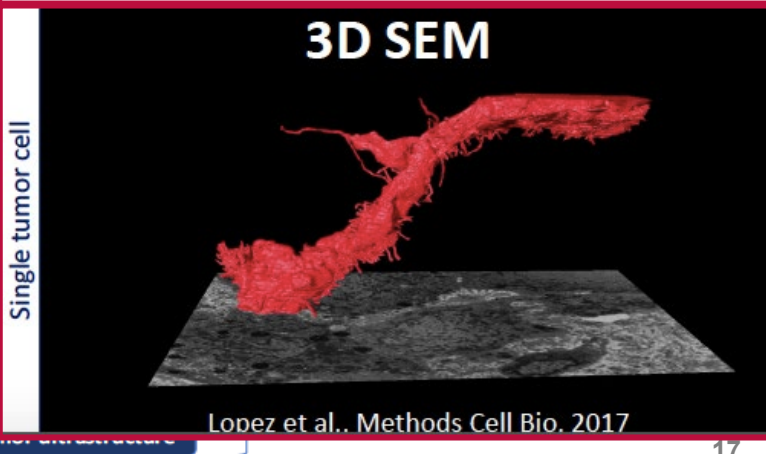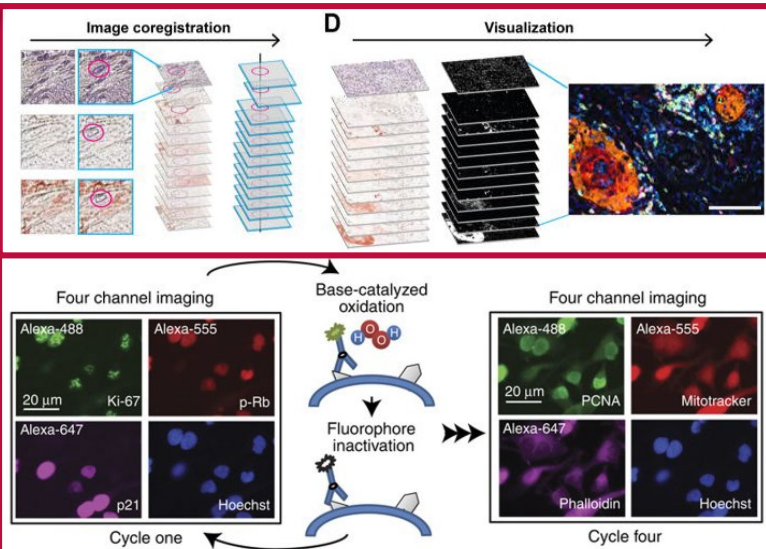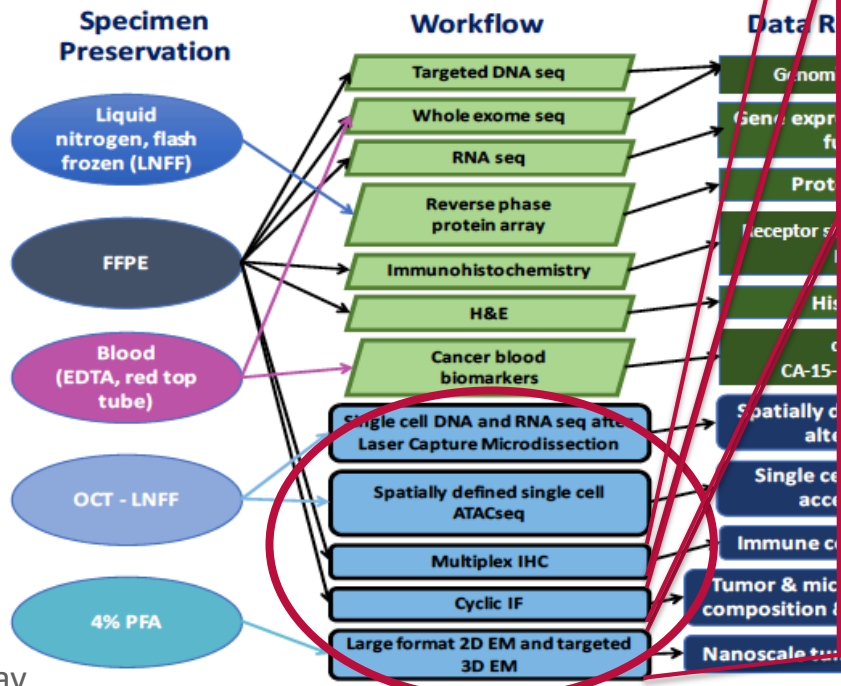
Tissue processing to facilitate spatial registration of cycIF, TSCS and sc-ATAC-seq

Frozen OCT

H&E 5µm confirm viable tumor)

cycIF 5µm x 5 sections

H&E 5µm (reference for TSCS)

12µm x 15 for sci-ATAC-seq

H&E 5µm (reference for ATAC-seq)

CycIF 6µm

Remaining for sc-ATAC-seq (250uM punches throughout biopsy)

HTAN Technology Challenges and Needs

- Additional imaging agents/approaches for **highly multiplexed molecular imaging**, including multiplex **tracers for in vivo imaging** (PET/CT/MR)

- **3D imaging capabilities** and ability to co-register images to **link 'omic' data with spatial location** in tumor

- Data **integration and visualization** approaches

- **Reducing amount of input** needed for assays to allow more measurements on small biopsies/samples

- Adapting assays to be compatible with a **variety of tissue preservation** approaches

- Possibly **liquid biopsy tools** or liquid biopsy storage agents

- Possibly **standard reference materials**