The Human Tumor Atlas Network

Concept Presentation
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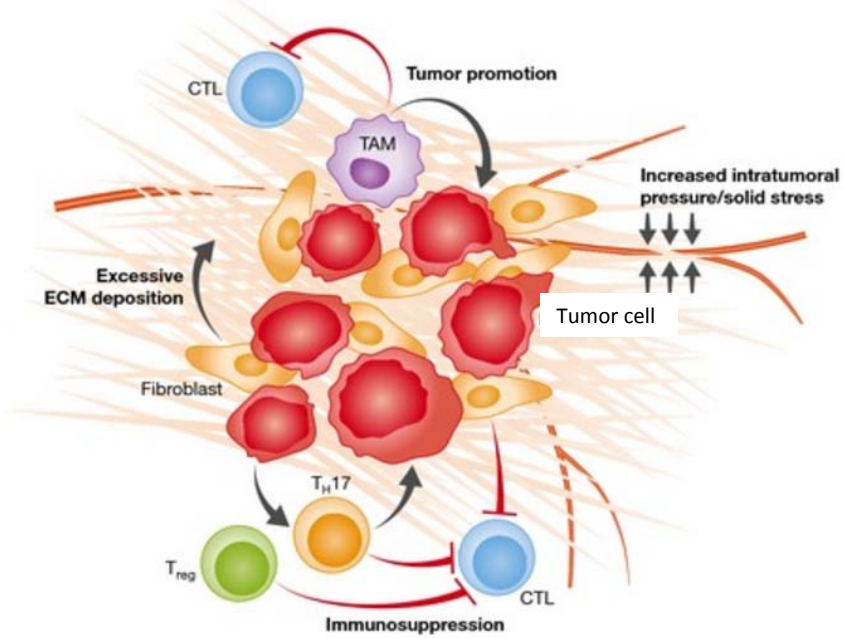
On behalf of the Generation of Human Tumor Atlases Implementation Team

We lack a comprehensive view of the tumor ecosystem

- Molecular, cellular and tissue-level interactions facilitate critical transitions in cancer.
- Gaps in our knowledge make it difficult to predict prognosis or develop risk stratification, precision screening and treatment strategies.

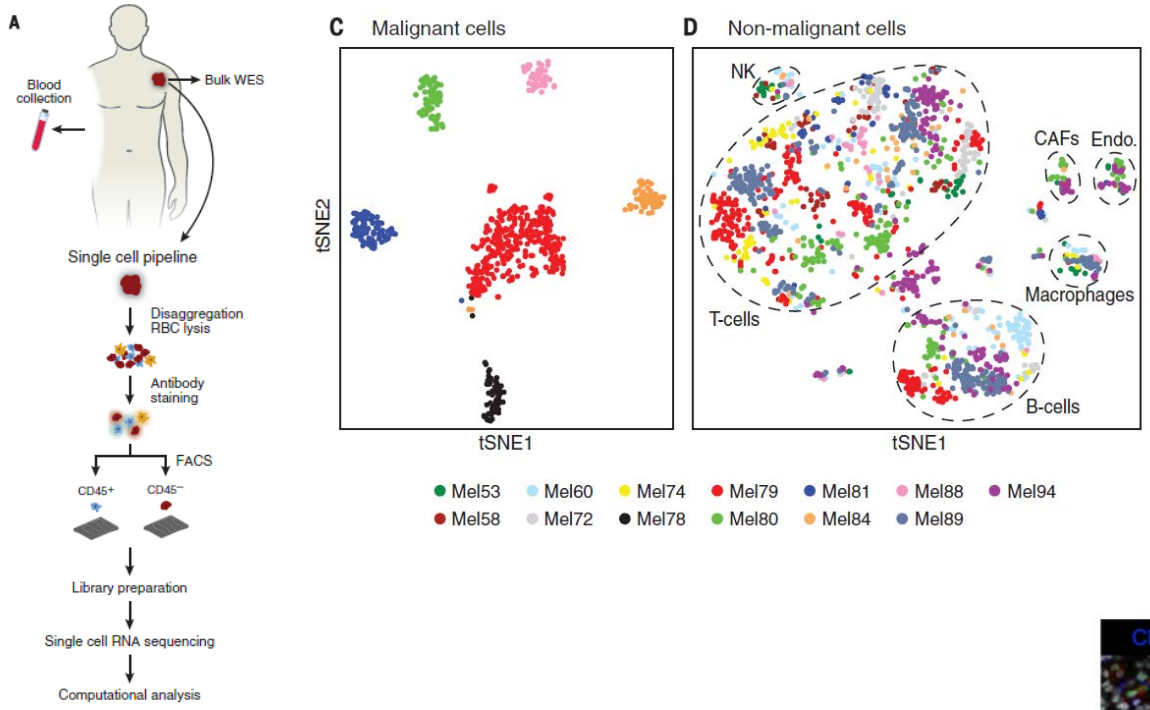


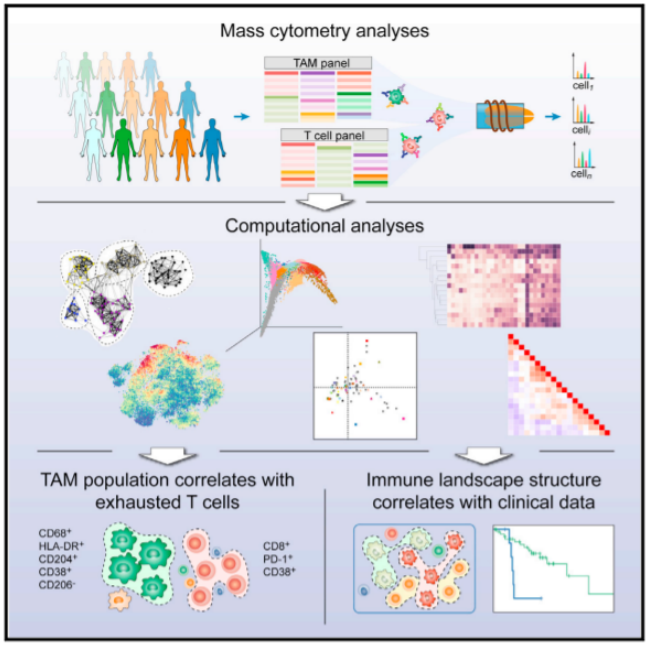
A **comprehensive** view will improve:

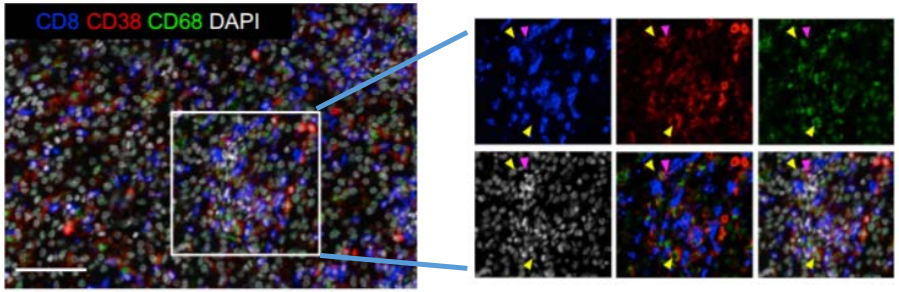
- Understanding of tumor heterogeneity and evolution
- Contribution of non-tumor components, such as stromal and immune cells, ECM
- Identification of markers of progression and drug resistance
- Development of early intervention strategies and robust therapies.

Figure adapted from Carr et al. 2016 EMBO Molecular Medicine

Transformative technologies and computational approaches can now facilitate a comprehensive view of cancer







Figures from:
Tirosh et al. Science April 2016
Chevrier et al. Cell May 2017

Recommendation I: Generation of Human Tumor Atlases

Combined recommendation from the Cancer Immunotherapy and Prevention, the Pediatric Cancer, and the Tumor Evolution and Progression BRP Working Groups

- A high-resolution map of the dynamic 3-dimensional architecture of an individual tumor over time, that
- Describes the molecular, cellular and physiological events that occur within individual cancer cells, the cancer mass, the tissue of origin and sites of metastasis, including the molecular, cellular and soluble components that can influence the immune response to the cancer, in order
- To enable predictive modeling to refine therapeutic choices for patients.
- Specific critical time points are mentioned: transition from premalignant to cancer, metastasis and response to and development of resistance to therapy.
- Initial focus on exemplary pediatric and adult cancers, including at least one adult cancer in which immunotherapy responses have been good and one in which such responses have been poor.

The Human Tumor Atlas Network

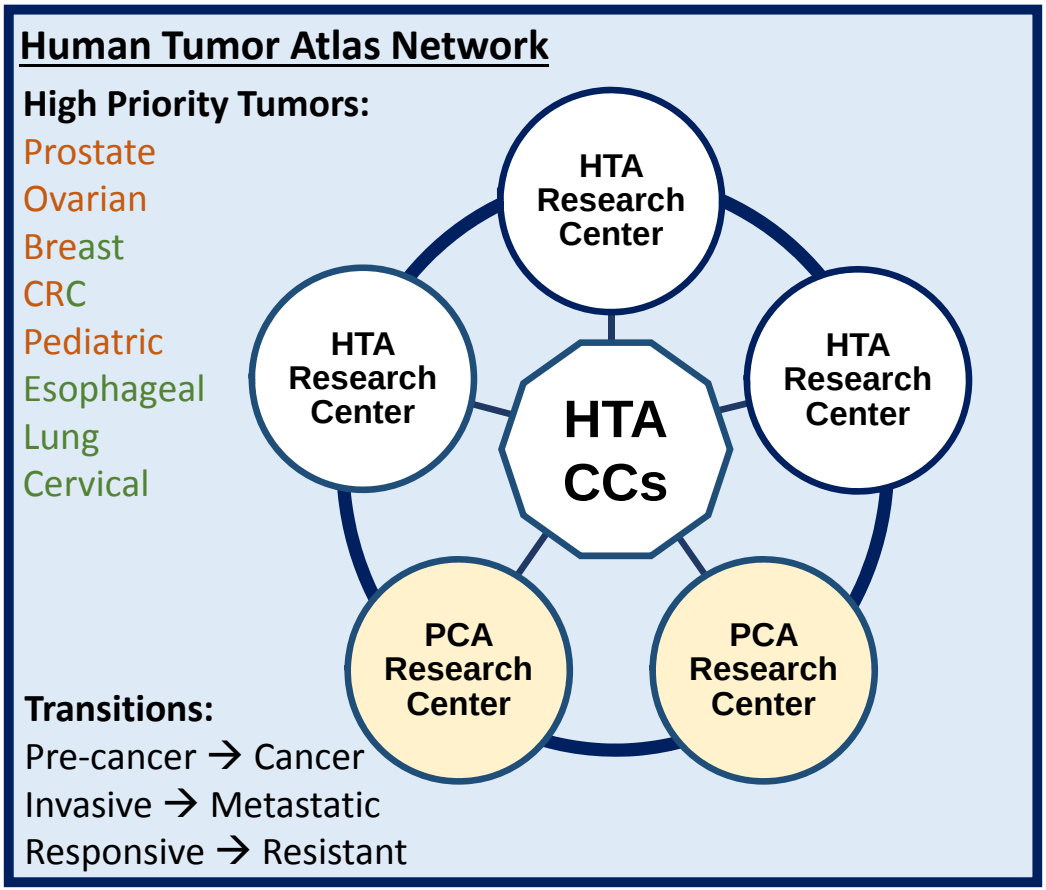
Goal: Pilot-scale, high-priority human tumor atlases that facilitate basic and clinical scientific discovery regarding important transitions during tumorigenesis.

Components:

1. Highly-integrated **HTA Research Centers** (UM1) focused on construction of dynamic 3D tumor atlases.

2. Complementary **Pre-Cancer Atlas Research Centers** (UM1) focused on characterization of pre-malignant lesions.

3. HTA **Coordinating Centers** (U24) focused on integration of the HTA Network through administrative and scientific support.



Orange = Focus of HTA Research Centers

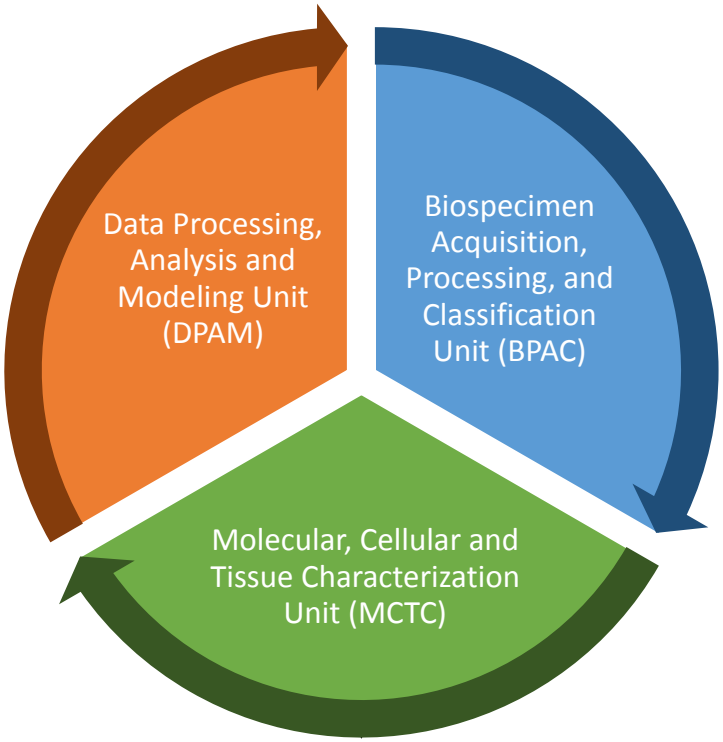
Green = Focus of PCA Research Centers

Structure of HTA and PCA Research Centers

The HTA Network will include **UM1 HTA and PCA Research Centers** whose research activities span the full range of atlas-building activities, including:

1) Development and transfer of SOPs for tissue acquisition, preservation, and processing.
2) Multi-scale, multi-parameter data collection using samples collected over time during important transitions in cancer.
3) Data integration, analysis and visualization to deliver a final atlas 'product'.

A highly multi- and interdisciplinary team of investigators is required, including pathologists, clinical oncologists, cancer biologists, systems biologists, bioinformaticians, technology developers, computer scientists, etc.

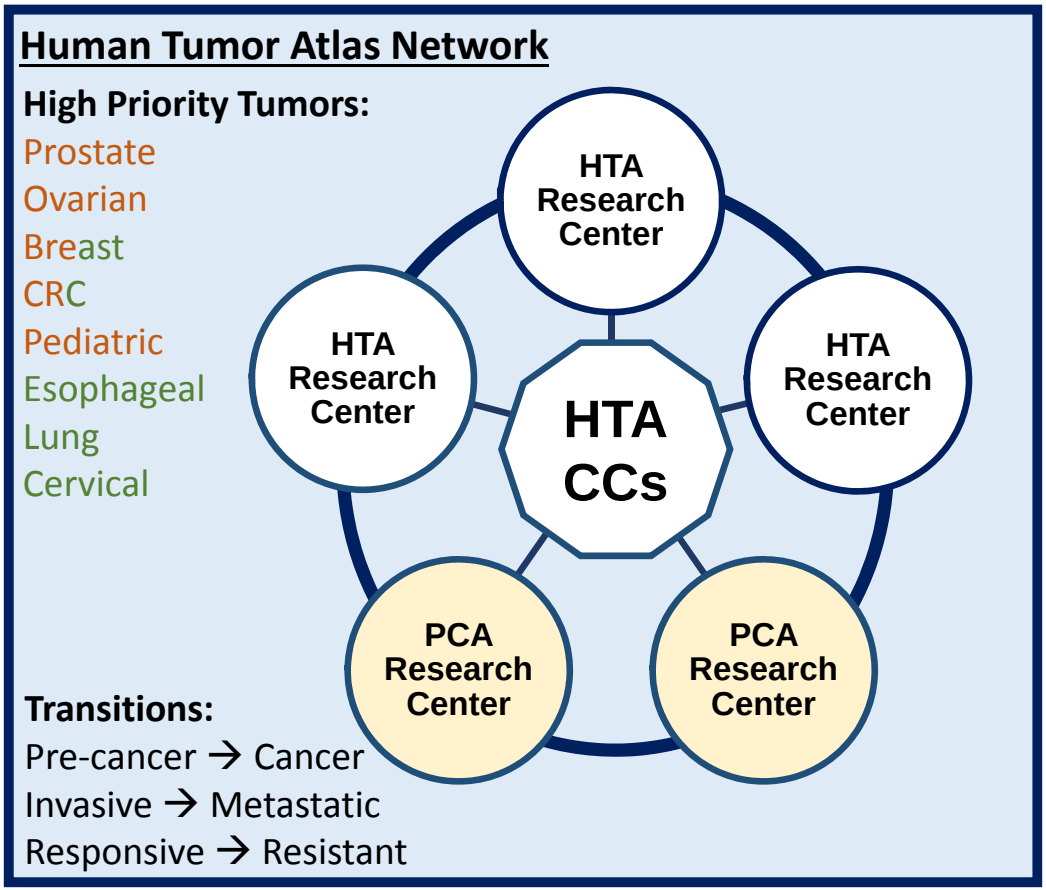


Human Tumor Atlas Network Coordinating Centers

The HTA Network will be supported by two **HTA Network Coordinating Centers**:

1) HTA Data Coordinating Center (HTA-DCC)
   - via **U24 Cooperative Agreement**
2) HTA Tissue Coordinating Center (HTA-TCC)
   - FY19

Fruitful interaction and collaboration between HTA/PCA Research Centers, HTAN Coordinating Centers, NCI Staff, and outside partners is key to success of the HTAN.



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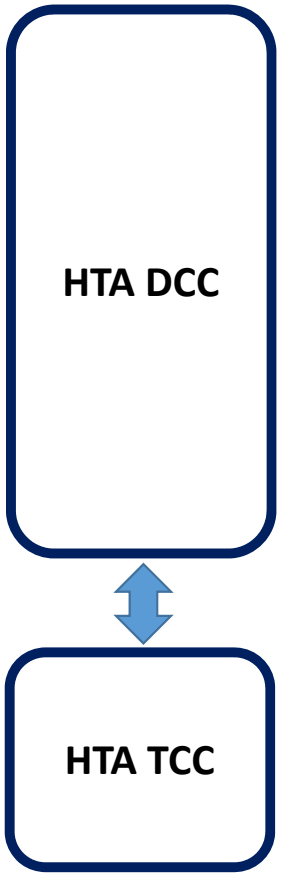
HTA Network Coordinating Centers:

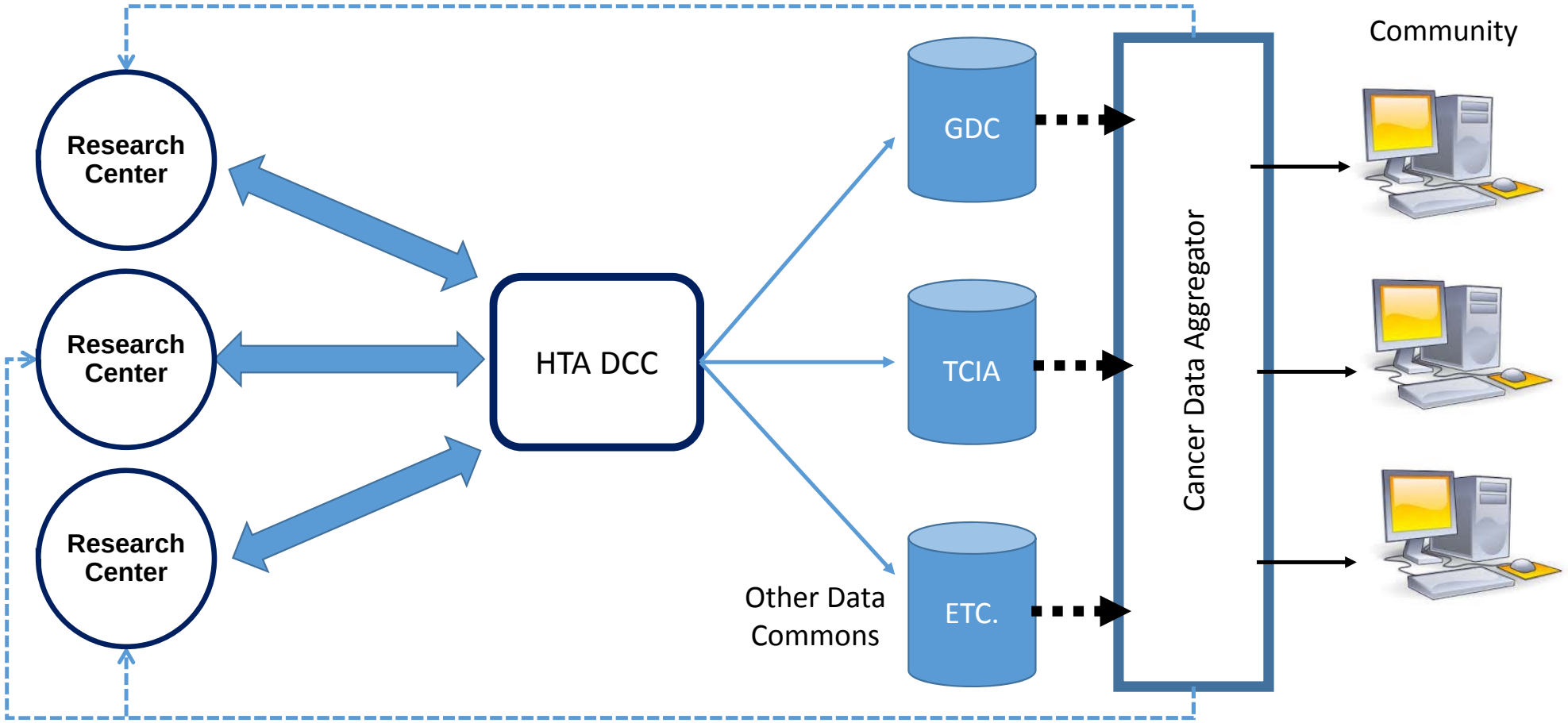
Oversight by NCI Program Staff and HTA Steering Committee:



- Coordinate policy and science-focused WGs, lead Outreach efforts
- Administrative support for Steering Committee meetings, Network-wide meetings and workshops
- Create and maintain a public presence for the HTA Network (website, etc)
- Coordination of WGs for metadata practices, and computational analysis pipelines
- Facilitate data ingest and distribution to the HTA Network (and partners)
- Facilitate data distribution to NCI-approved repositories / data commons

- Coordinate exchange of SOPs across tumor types/UM1s
- Oversee tracking and distribution of HTA biospecimens, models, and resources
- Will likely be a virtual resource

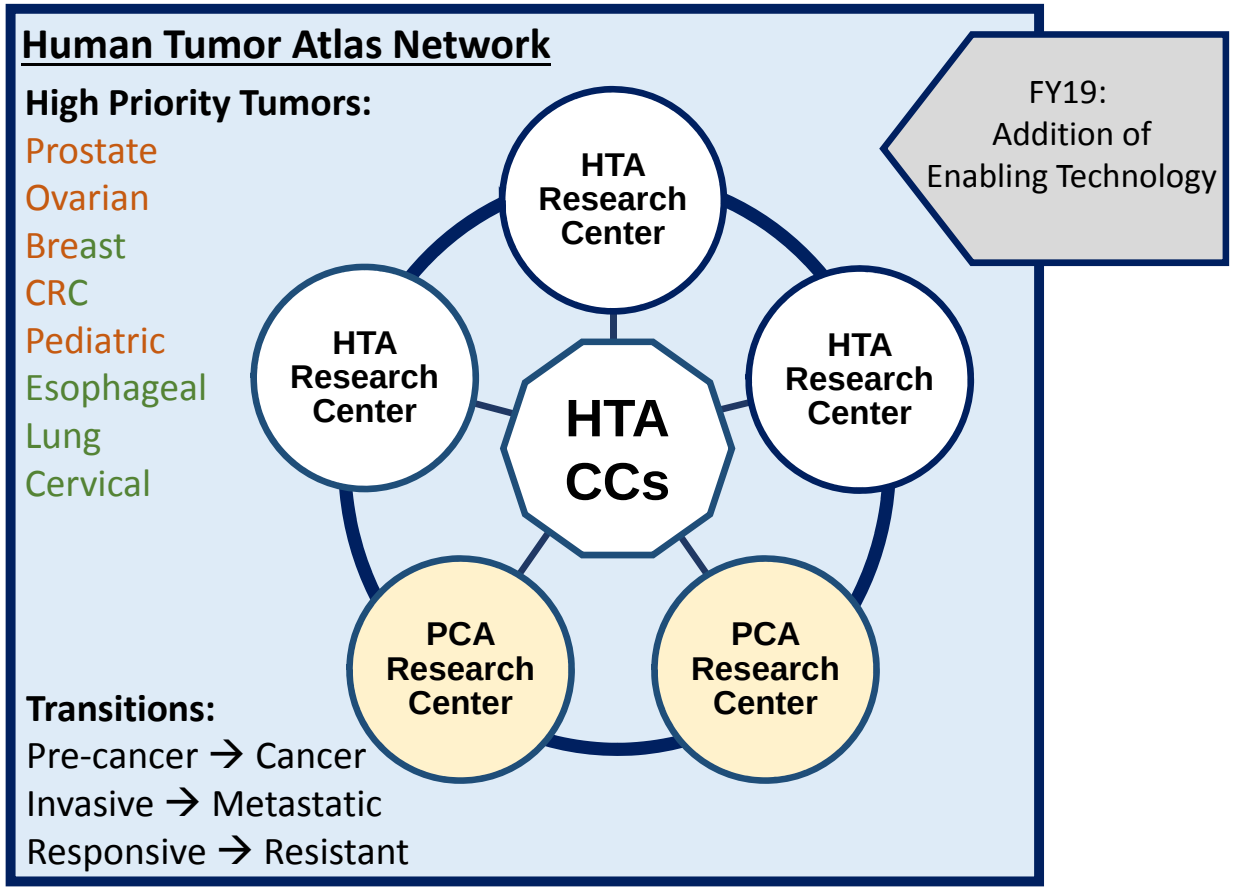
Proposed data flow for HTA Network:



Addition of Enabling / Emerging Technologies

A joint effort with the **Enabling Technologies CMIT** starting in **FY19** will provide experimental and computational approaches that enrich the HTA Network:

- Workshops led by NCI to identify needs within the HTA Network
- Enabling technologies added through **Administrative Supplements** to ongoing grants



Human Tumor Atlas Network: Deliverables

Measures of success:

- Five 'live' tumor atlases that are intuitive, searchable, and informative for the research, clinical, and patient communities
- Searchable database of harmonized, multi-scale data that are easily accessible to the research community – and statistics that indicate the data is being used
- A catalog of validated SOPs for tissue acquisition, data collection, and open source analysis workflows – including those focused on integration of omics data and functional or molecular imaging

Human Tumor Atlas Network: Outcome

At the end a successful initial 5-year HTA effort, a preliminary set of comprehensive human tumor atlases that:

- Define tumor heterogeneity within and across patients in high-priority adult and pediatric cancers
- Quantify the dynamics and 3D architecture of the tumor ecosystem during important transitions
- Facilitate predictive modeling that leads to development of new risk stratification methods, better treatment options for patients, and improved understanding of disease mechanisms

Portfolio Analysis – *towards* Atlas efforts

NCI Programs:

TARGET

APOLLO Network

Blood PAC

CPTAC3 (PGDACs, 5 – U24s)

MCL – 6 U01

IMAT – R21/R33

CSBC – 2 U54

NCI Grants/Contracts:

Cancer Sampling Index (CaSIX) Contract *(PS-ON)* – physical characterization + multi-omics of colon cancer PDX models; some spatial information

Other NIH Efforts:

HuBMAP Common Fund Program – goal is to build spatially-resolved, multi-scale maps of normal human organs (upcoming)

Kidney Precision Medicine Project (*NIDDK*) – spatially-resolved, multi-scale maps of kidney pathologies (applications currently under review)

Non-NIH Efforts: Human Cell Atlas Consortium; IVY Glioblastoma Atlas Project (Allen Brain Institute); **CRUK Efforts**

Budget: Human Tumor Atlas Network

Component	Number of Awards	Cost per Award	Total Cost per Year (M)
HTA Research Centers (UM1)	3	$2.35 DC / $3.375 TC	$10.125
PCA Research Centers (UM1)	2	$2.35 DC / $3.375 TC	$6.25
HTA-TCC Tentative start FY19	1	$0.5M	$0.5 (FY19-22)
HTA-DCC (U24)	1		$1.5 FY18-19 $3.5 FY20-22
Total			**$18.375 FY18** **$18.875 FY19** **$20.875 FY20-22**

Thank you

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