

The NCI Human Tumor Atlas Network

NCI HTAN Team

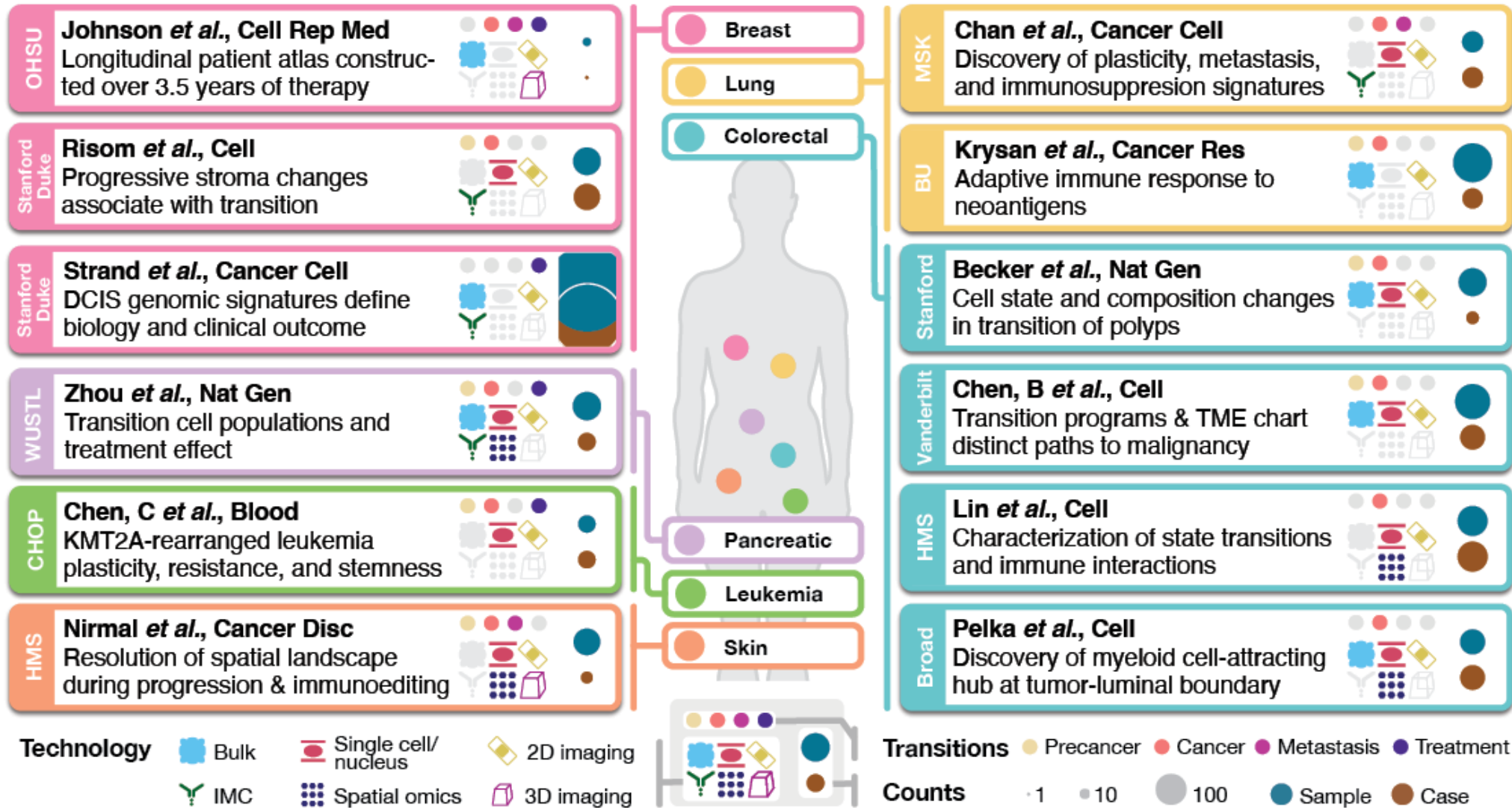
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BRP Recommendation I: “Generation of Human Tumor Atlases” directed the development of *“human tumor atlases for adult and pediatric cancers that map the evolution of human tumors by documenting the genetic lesions, molecular pathways, and cellular interactions that guide tumor development from pre-malignant tissue to primary cancer, progression to metastasis, response to therapy and acquisition of resistance.”*

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 Atlases as of April 2023



Plus, an additional 149 manuscripts, with 40% reporting and sharing new data analysis and integration approaches.

Figure courtesy of L. Ding, WUSTL HTAN

HTAN data and resources available for the cancer research community

<https://data.humantumoratlas.org/>

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

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

11

Atlases

50

Organs

1311

Cases

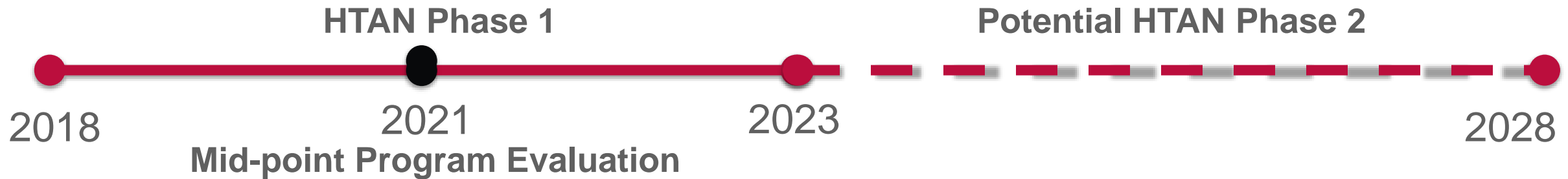
3821

Biospecimens



HTAN Timeline* and External Panel Recommendations

Panel findings included an appreciation for “the tremendous advances in technologies that enabled the construction of atlases, particularly those pertaining to imaging and computational efforts to quantify cellular neighborhoods and measures of intra- and intertumoral heterogeneity”.



External panel recommendations for future HTAN efforts included:

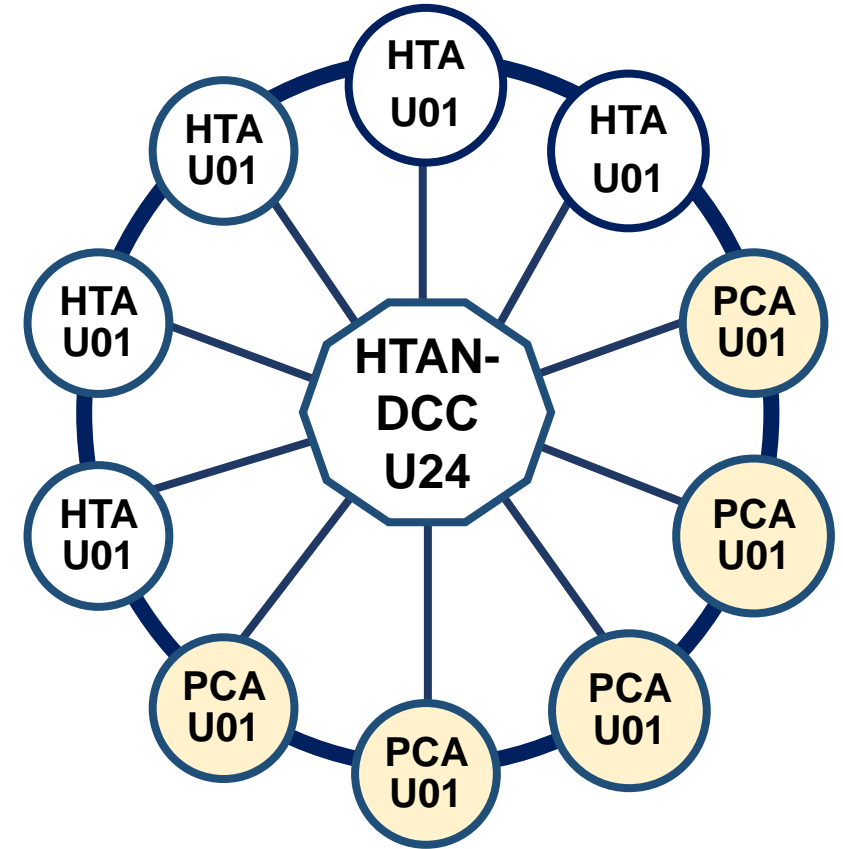
- Renewing a focus on **analysis of longitudinal samples**, especially in the precancer atlas
- Collection and harmonization of **multiple common data types** across atlases
- Renew the focus on collection of samples from a **diverse patient population**
- Continue to **lead the community in spatial atlas construction**

Request for reissuance of HTAN

Goal: Spatial precancer and tumor atlases that inform future development of prevention, interception, diagnosis and therapy options for patients.

Components:

1. **HTA Research Projects (U01)** creating **spatial atlases** mapping the dynamic tumor ecosystem.
2. **Pre-Cancer Atlas Research Centers (U01)** creating atlases that **comprehensively characterize** pre-malignant lesions.
3. **HTAN Data Coordinating Center (U24)** focused on network coordinating and facilitating FAIR data sharing and reuse.



HTAN Steering Committee
HTAN Working Groups
HTAN Junior Investigator Meetings
HTAN-NCI CRDC Collaboration

Human Tumor Atlas (HTA) and Precancer (PCA) U01 Research Projects

Request reissuance of RFA-CA17-034 & RFA-CA17-035

U01 Structure

Biospecimen
Collection & QC

Sample
Characterization

Data Analysis &
Atlas Construction

Each U01 awardee will:

Construct **one tumor atlas** that generates insights poised for translation. *Tumor/tissue site will not be specified, but projects adding significant new value to the current atlases will be prioritized.**

Include at least **two established HTAN data types** to facilitate cross-atlas analysis (one must be spatial).

Prioritize funding of projects that **include diverse patient samples** to increase the impact of atlas-derived insights.

Set-aside **15% of the budget in Y2-Y5** for collaborative and validation projects. Can include model systems.

Human Tumor Atlas (HTA) and Precancer (PCA) U01 Research Projects

Request reissuance of RFA-CA17-034 & RFA-CA17-035

PCA Research Projects

Use case must be driven by a **clear understanding of clinical context** in precancer.

Atlases should **utilize streamlined technology** to characterize an adequate number of samples. Single-cell analysis not required.

Wherever possible, **longitudinal sampling** from the same patient is desired.

Overall goal is to guide prevention and interception strategies.*

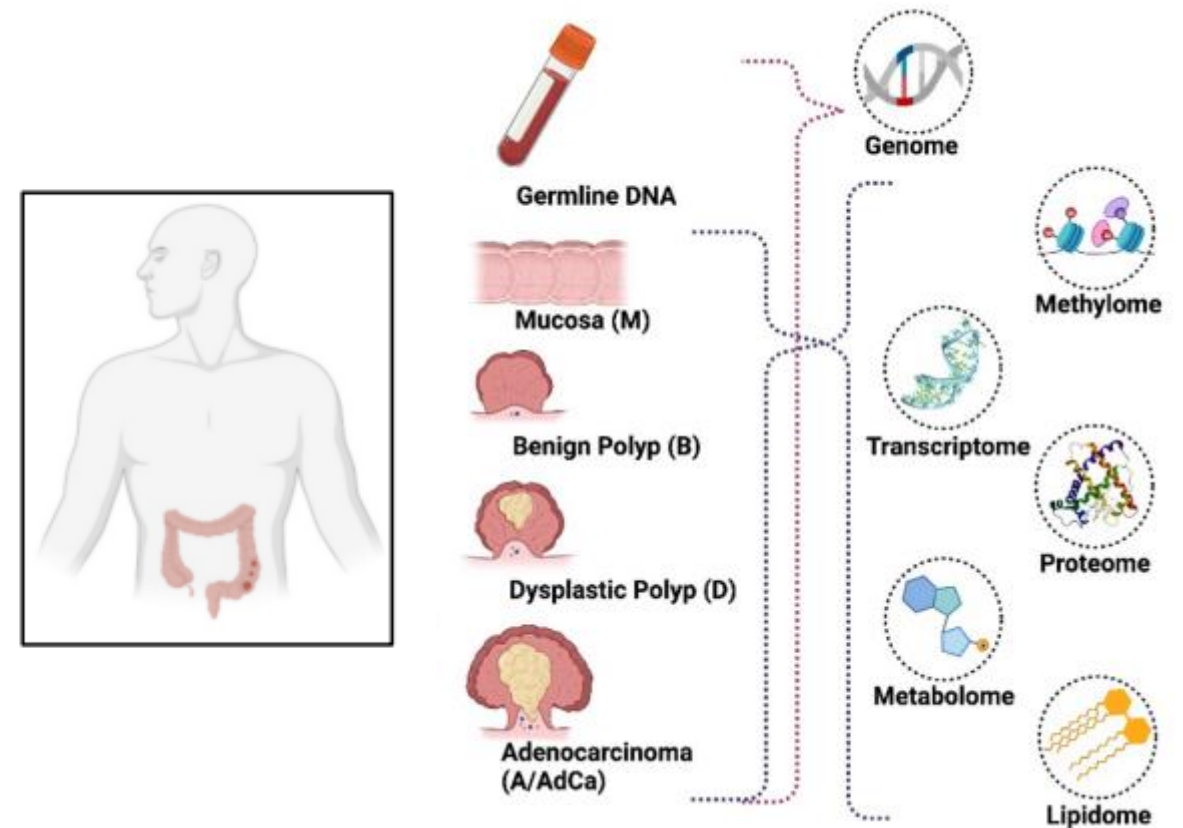


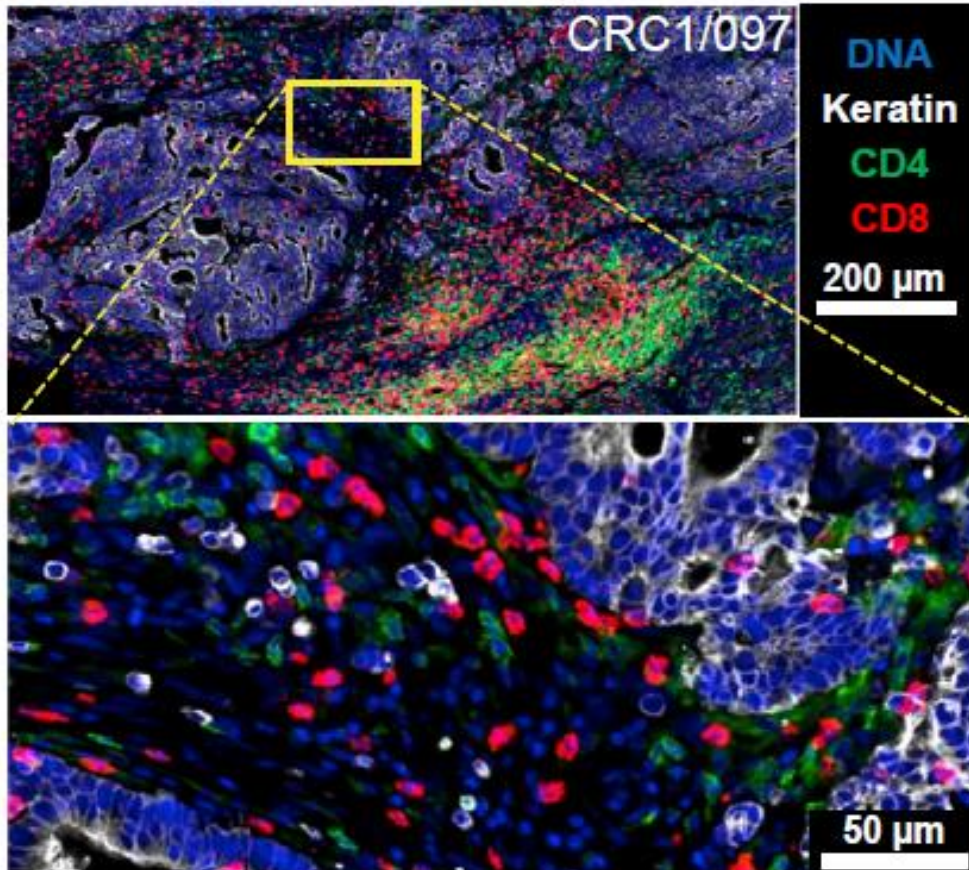
Figure modified from Horner et al.

<https://doi.org/10.21203/rs.3.rs-515393/v1>

Human Tumor Atlas (HTA) and Precancer (PCA) U01 Research Projects

Request reissuance of RFA-CA17-034 & RFA-CA17-035

Budding at tumor margin



HTA Research Projects

Atlases should **focus on spatial mapping** of multi-dimensional tumor architecture.

Single-cell genomics in a supportive role for spatial mapping and functional interpretation.

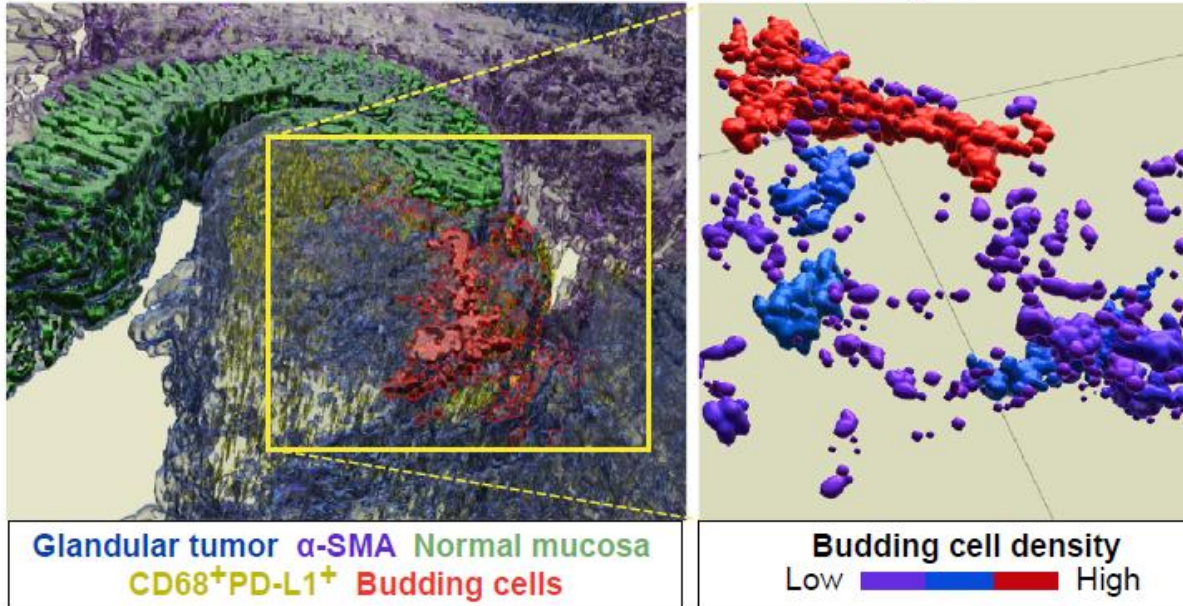
Use cases can **span all tumor transitions** (precancer, treatment, metastasis).

Overall goal is to map and validate spatial interactions as tumors develop and evolve.*

Human Tumor Atlas (HTA) and Precancer (PCA) U01 Research Projects

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3D overview of CRC1 at region A of the invasive margin



HTA Research Projects

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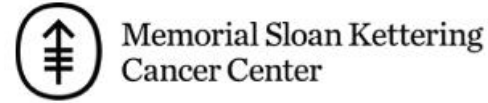
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Overall goal is to map and validate spatial interactions as tumors develop and evolve.*

HTAN Data Coordinating Center (HTAN-DCC) U24

Request Limited Competition reissuance of RFA-CA17-036



Achievements and highlights:

- Community-driven development of HTAN data standards and clinical data model.
- Ingest, harmonization and quality control of >200 TB of data representing >1500 patients, >7000 biospecimens, and 17 distinct assays.
- Key collaborator and driving use case for development of NCI Cancer Research Data Commons (new data types and HTAN tool/pipeline integration).

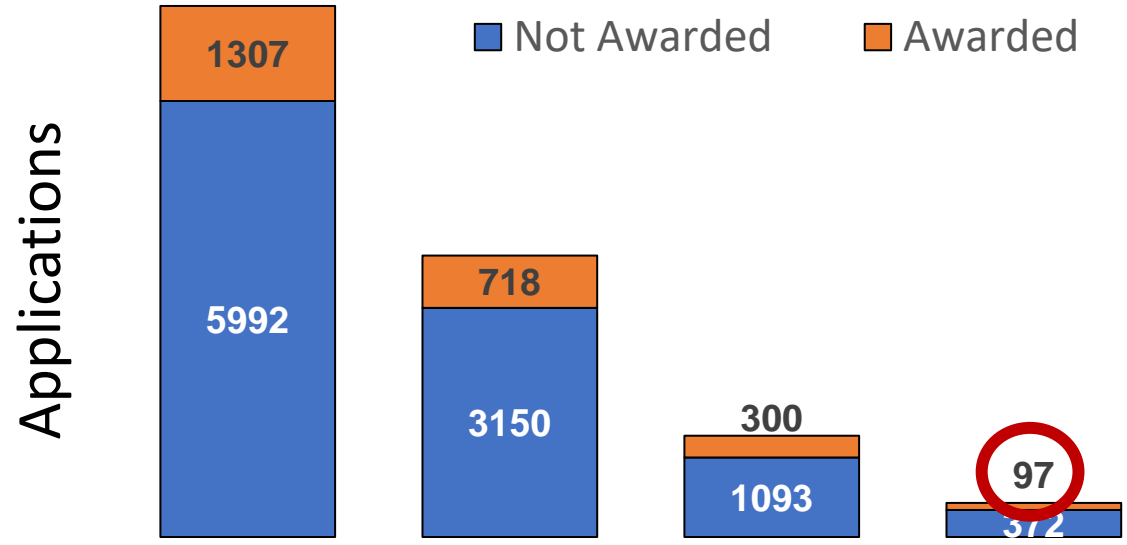
Focus for HTAN phase 2:

- Harmonization of common data analysis pipelines.
- Become an exemplar for FAIR sharing and use of spatial omics modalities.
- Expand community engagement and education efforts regarding use of HTAN data.

Portfolio Analysis (FY2013-2022)

10 U01 or U54 in ongoing NCI programs such as TBEL, MetNet, ARTNet, PSRC

8 R01s where atlas construction is proposed; no prospective collection

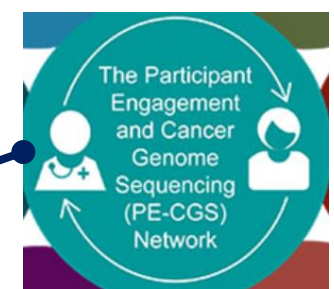
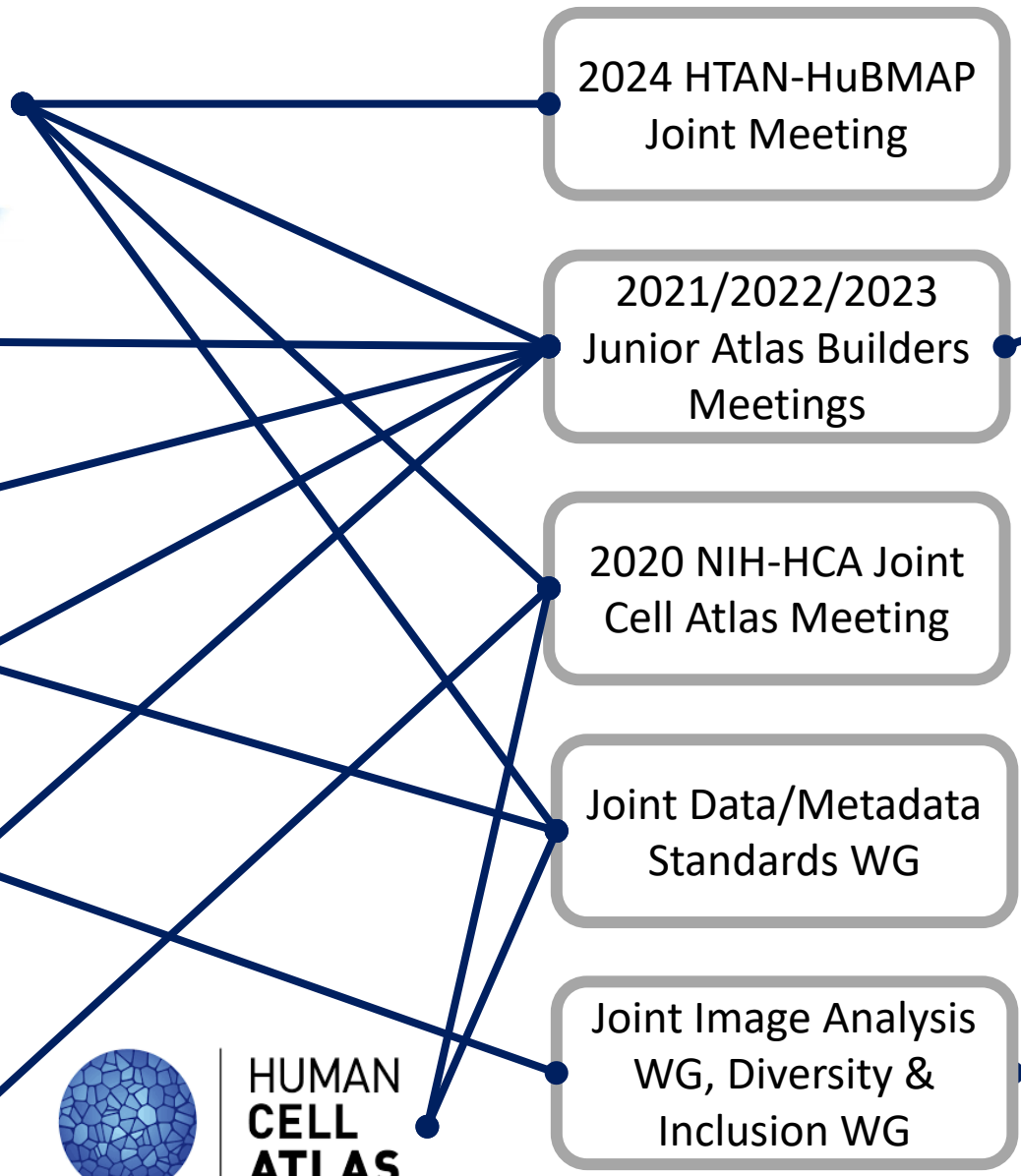
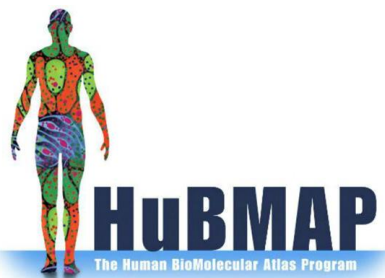


Unlike HTAN, these awards were not funded as community resources with a mandate to share well-labeled data with the research community.

Single Cell Seq	●		●	●
Spatial Omics		●	●	●
Atlas				●

("co-detection by indexing" OR mxIF OR "imaging mass cytometry" OR "codetection by indexing" OR CODEX OR "multiplexed ion beam imaging" OR MIBI OR "cyclic immunofluorescence" OR CyCIF OR "multiplex immunohistochemistry" OR mIHC OR "multiplex IHC" OR VECTRA OR MERFISH OR SeqFISH OR Visium OR "spatial transcriptomics" OR GeoMX OR CosMX OR FISSEQ OR "STARmap" OR DBiT-seq) AND ("single cell sequencing" OR "single-cell sequencing" OR "single cell RNA sequencing" OR "single-cell RNA sequencing" OR "single cell RNA-seq" OR "single-cell RNA-seq" OR "scRNA seq" OR "scRNA-seq" OR "single-cell ATAC-seq" OR "single cell ATAC-seq" OR "scATAC-seq" OR "scATAC seq" OR "sci-ATAC-seq" OR "single nucleus RNA-Seq" OR "single-nucleus RNA-Seq" OR "single nuclei RNA sequencing" OR "snRNA-Seq" OR "snRNA Seq" OR "sNuc-Seq" OR "Smart-3SEQ") AND (cancer OR tumor OR pre-cancer OR precancer)

HTAN contributes to the larger atlas building and using community*



Cancer Immunoprevention Network (CIP-Net)

PREVENT Cancer Preclinical Drug Development Program

Cancer Prevention-Interception Targeted Agent Discovery Program (CAP-IT)

Translational and Basic Science Research in Early Lesions (TBEL) Program



Evaluation criteria for HTAN

The success of a second phase of HTAN will be evaluated against specific program deliverables and benchmarks, including:

- **Candidate biomarkers for cancer risk** or molecular targets that are poised for validation within independent cancer cohorts and portend prevention strategies for diverse people.
- **Candidate biomarkers for diagnosis, prognosis, or response to therapy** that can be further investigated for useful correlations with clinical outcomes.
- **Quantitative maps of large-scale (2D and/or 3D) molecular characteristics** within tumors or premalignant lesions.
- **Easily accessible and analyzable atlas datasets** describing the spatial dynamics and/or 3D architecture of the tumor ecosystem during important transitions in pre-cancer and cancer.
- **Community use of HTAN atlases**, as evidenced by download and data access statistics, usage of atlas visualization tools, and publications and/or presentations citing HTAN resources.
- **Interoperability of HTAN datasets with other efforts** (i.e. normal atlases, SenNet, TBEL, etc.) that facilitates analysis across the normal to disease spectrum and/or allows for cross-testing of atlas-derived hypotheses.

Budget Request

<u>Component</u>	<u>Number of Awards</u>	<u>Cost per Award (TC)</u>	<u>Total Cost per Year (M)</u>	<u>Total Cost (5 years, M)</u>
HTA Research Projects (U01)	5	\$1.4M (\$800K DC)	\$7M	\$35M
PCA Research Projects (U01)	5	\$1.4M (\$800K DC)	\$7M	\$35M
HTAN-DCC (U24)	1	\$3.0M (\$1.8M DC)	\$3M	\$15M
Total			\$17M	\$85M

Questions from BSA review panel:

Questions addressed within the presentation*:

- Designated tumor or tissue types; specific/new goals of PCA and HTA U01 projects; interaction of HTAN with other programs; diversity of patient samples; HTAN timeline

Provide stronger justification for a Limited Competition RFA for the HTAN-DCC

- Capitalize on the **extensive NCI investment** in current HTAN Data Portal infrastructure and data sharing workflows.
- **Cost savings due to reuse** and improvements to existing infrastructure.
- Continue the **HTAN-DCC and NCI Cancer Research Data Commons collaboration** that is benefitting the larger NCI-supported research community (i.e. building of new FAIR data sharing processes).
- NCI Program staff will maintain **close collaboration through the Cooperative Agreement** structure to ensure continued high-quality performance and robust service to HTAN.

Thank you

Questions?