

Audio connection information for webinar:

<https://grants.nih.gov/grants/guide/notice-files/NOT-CA-18-015.html>

The webinar will start at 2:05pm

The NCI Human Tumor Atlas Network (HTAN)

Pre-application webinar for RFA-CA-17-034

“Human Tumor Atlas (HTA) Research Centers (U2C)”

Please note:

All participants are muted upon entry to the webinar

The webinar will be recorded



November 16, 2017

The Cancer Moonshot Initiative



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 Research Data Commons
 - Annotated patient-level clinical data and ‘omics

The Process



Vice President's Office



Federal Task Force



NIH/NCI

National Cancer Advisory Board

Blue Ribbon Panel (BRP)

BRP Working Groups (WG)

Cancer Immunology WG

Tumor Evolution and Progression WG

Pediatric Cancer WG

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**



Cancer Funding in 21st Century Cures Act

Impact

- *Allows for funding of the BRP Recommendations*

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

- *Specifies requirements for:*

Data sharing ([Cancer Moonshot Public Access and Data Sharing Policy](#))

Advancing health disparities research

“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 seeds to address major challenges associated with cancer.”

Recommendation I: Generation of Human Tumor Atlases

I. Develop a 3D cancer atlas

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

[BRP Pediatric Cancer Working Group Report \(pdf\)](#)

[BRP Cancer Immunology Working Group Report \(pdf\)](#)

[BRP Tumor Evolution and Progression Working Group Report \(pdf\)](#)

[Final Blue Ribbon Panel Report \(pdf\)](#)



The Human Tumor Atlas Network (HTAN)

Implementation of the combined recommendation from the Cancer Immunology, the Pediatric Cancer, and the Tumor Evolution and Progression BRP Working Groups

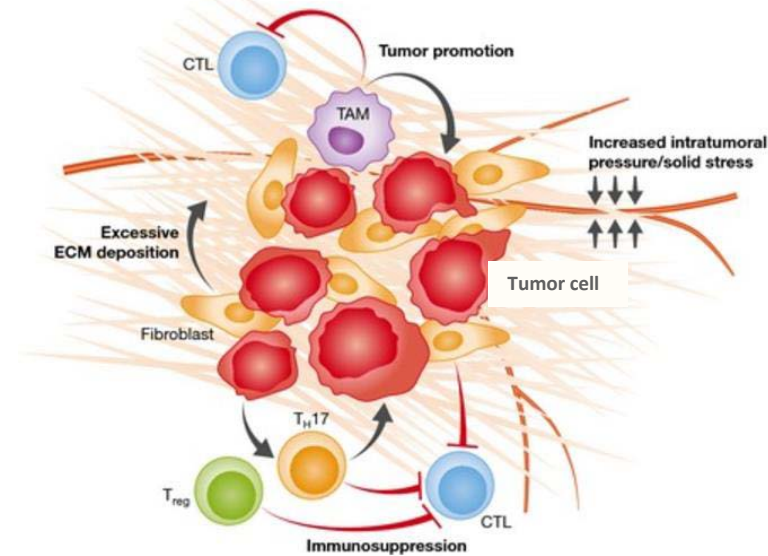
- **High-resolution maps** of the dynamic 3-dimensional architecture of an individual tumor, that
- Describes the **molecular, cellular and physiological events** that occur within individual cancer cells, the cancer mass, the tissue of origin and sites of metastasis, including the molecular, cellular 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 premalignancy to cancer, locally invasive to metastatic, and the 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.

Spatial context is emphasized in the BRP recommendation

- 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 tumor atlas** will inform:

- 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.



The Human Tumor Atlas Network (HTAN)

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

Components of the HTAN:

1. **Human Tumor Atlas (HTA) Research Centers (U2C)** focused on construction of dynamic 3D tumor atlases.
[RFA-CA-17-034](#)
2. **Pre-Cancer Atlas Research Centers (U2C)** focused on characterization of pre-malignant lesions.
[RFA-CA-17-035](#)
3. **Coordinating Centers (U24s)** focused on integration of the HTA Network through administrative and scientific support.
[RFA-CA-17-036](#)

Human Tumor Atlas Network

High Priority Tumors for HTA Research Centers:

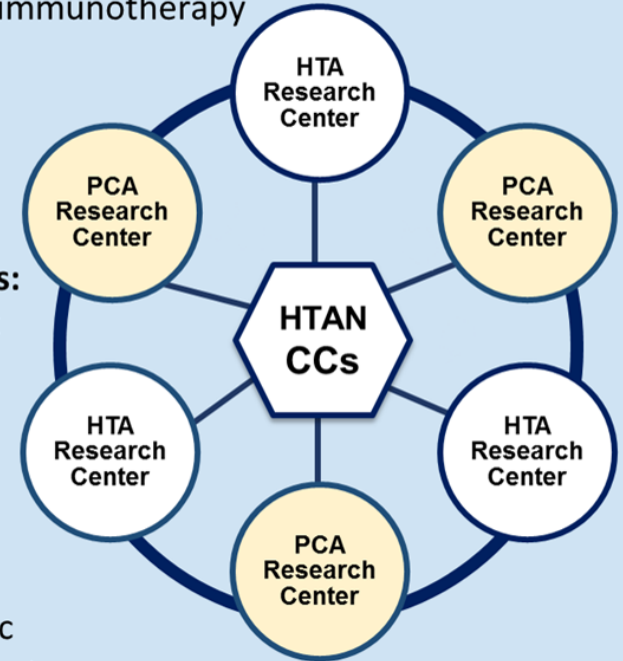
- * (Non)Responsive to immunotherapy
- * Highly metastatic
- * High-risk hereditary
- * Pediatric

Tumor Criteria for PCA Research Centers:

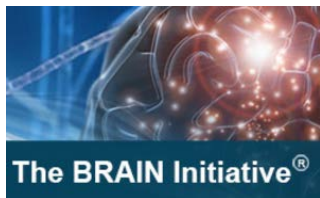
- * Public health impact
- * Access
- * Feasibility
- * Partnerships

Transitions:

- Pre-cancer → Cancer
- Invasive → Metastatic
- Responsive → Resistant

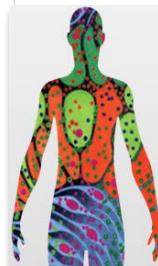
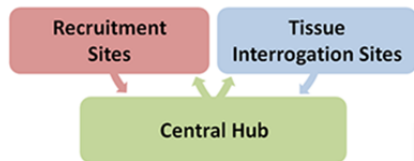


The HTAN in the context of other “Atlas” initiatives:



Kidney Precision Medicine Project (NIH/NIDDK)

Identifying critical human cells, pathways, and targets for new therapies in acute and chronic kidney diseases.



The Human BioMolecular
Atlas Platform (HuBMAP)
NIH Common Fund Program



Human Tumor Atlas Network

- Emphasis on spatial relationships and interactions
- Prospective/longitudinal sample collection (time)
- Extensive clinical data
- Atlases describing disease transitions

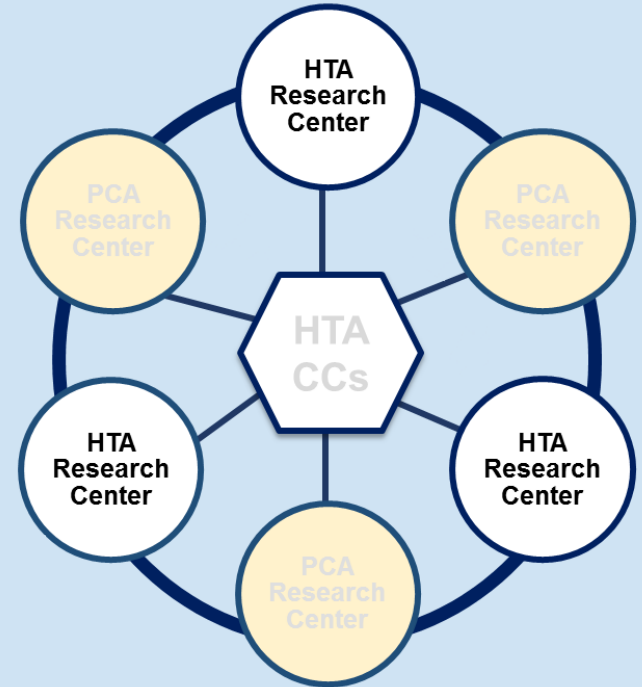


RFA-CA-17-034: Human Tumor Atlas (HTA) Research Centers

What is a human tumor atlas?

For the purposes of this FOA, 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.

Human Tumor Atlas Network



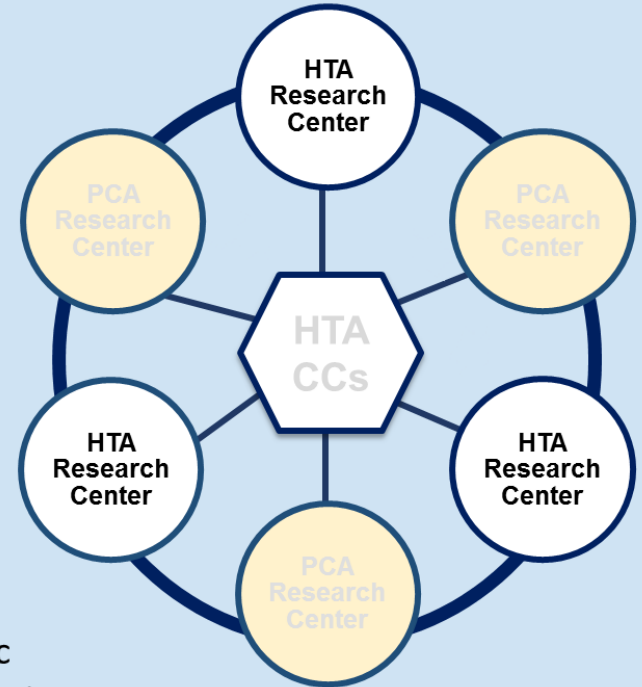
RFA-CA-17-034: Human Tumor Atlas (HTA) Research Centers (Cont.)

From the FOA:

Tumor atlases supported under this FOA must focus on one of the following three important transitions in cancer:

- **The transition from locally invasive to metastatic cancer** ... atlases characterizing multiple metastatic sites, atlases describing the transition into or out of tumor dormancy, atlases capturing colonization of early disseminated tumor cells at distant sites.
- **The dynamic response to therapy** ... atlases describing a positive response to traditional, targeted and/or immuno-therapies, atlases that describe no response, incomplete response, or negative response to traditional, targeted and/or immuno-therapies.
- **The development of therapeutic resistance**, ... atlases describing the transition from responsive to traditional, targeted, and/or immuno-therapy to resistant to that therapy.

Human Tumor Atlas Network



Transitions:

Pre-cancer → Cancer

Invasive → Metastatic

Responsive → Resistant

RFA-CA-17-034: Human Tumor Atlas (HTA) Research Centers (Cont. 2)

High-priority tumor characteristics:

The [HTA Research Centers] aim to build comprehensive tumor atlases through the characterization of **tumors representing a diverse patient population, including minority and underserved patients**, with a focus on pediatric and adult cancers that are highly metastatic,... **promising candidates for immunotherapy**,... **refractory to immunotherapy**,... and **high-risk hereditary tumors**.

...NIH programmatic preference will be given to tumor choices that satisfy the **high priority categories** listed above.

Note: Max 3 organ-specific tumors; Max 3 tumor atlases proposed per application

Human Tumor Atlas Network

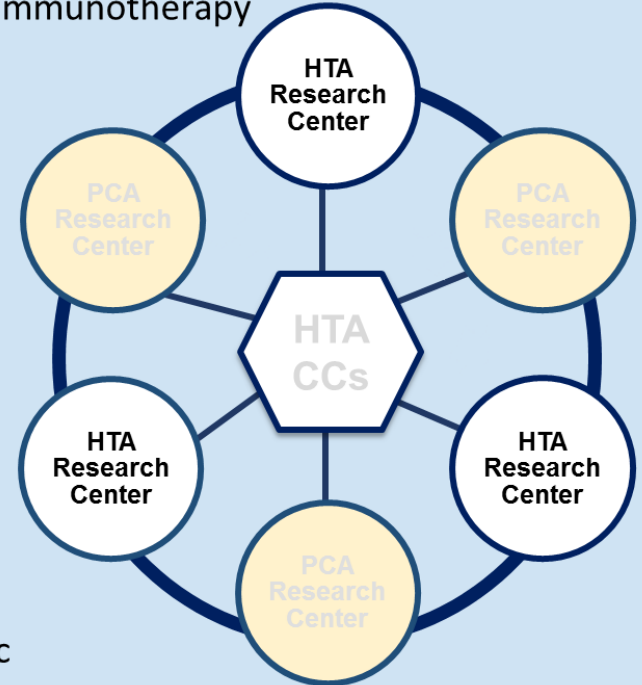
High Priority Tumors (for RFA-CA-17-034):

- *(Non)Responsive to immunotherapy
- *Highly metastatic
- *High-risk hereditary
- *Pediatric

See FAQs for more information.

Transitions:

- Pre-cancer → Cancer
- Invasive → Metastatic
- Responsive → Resistant



Mechanism of Support & Funding: U2C Research Center

Mechanism of support: U2C, Resource-Related Research Multi-Component Projects and Centers Cooperative Agreements

To support multi-component research resource projects and centers that will enhance the capability of resources to serve biomedical research. Substantial federal programmatic staff involvement is intended to assist investigators during performance of the research activities, as defined in the terms and conditions of the award.

Application Type: New applications only

Budget: Not to exceed **\$2.25M per year (direct costs)** per Center. *Cap is exclusive of 3rd party F&A costs.*

Project Period: Not to exceed **5 years**.

Application and Submission Information

Component Types Available in ASSIST	Research Strategy Page Limits	Required number of Components
Overall	12	1
Admin Core (use for Administrative Core)	6	1
Functional Unit (use for Biospecimen Unit, Characterization Unit, Data Analysis Unit)	12 (Each Unit)	3

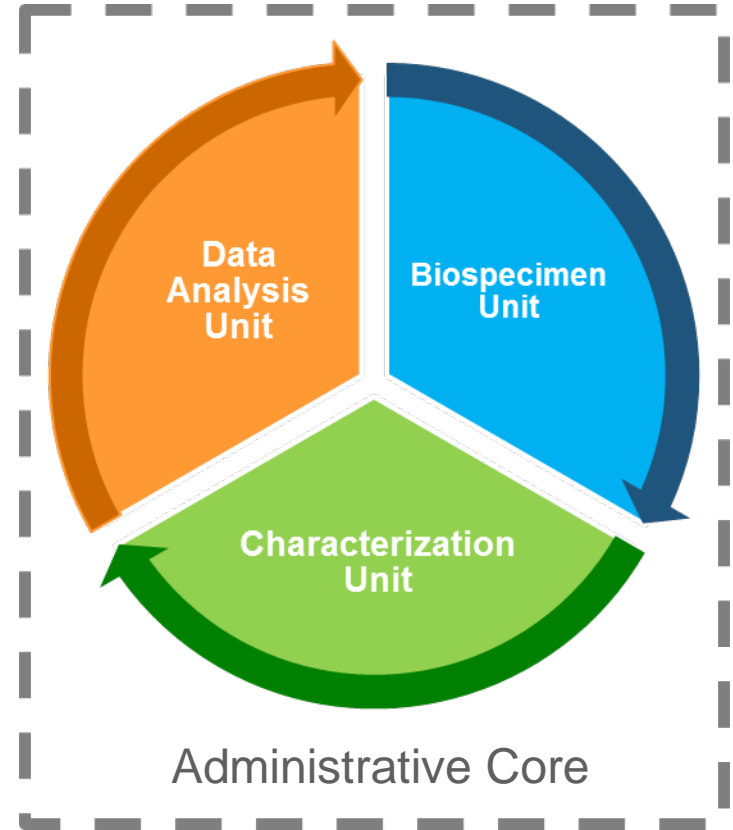
Applications that do not contain all required components will not be reviewed.

Organization of HTA and PCA U2C Research Centers

The HTA Network will include **U2C 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 anticipated, including pathologists, clinical oncologists, cancer biologists, systems biologists, bioinformaticians, technology developers, computer scientists, etc.



HTA U2C Research Center Leadership Expertise

From RFA-CA-17-034:

Leaders and senior investigators of the [HTA Research Center] **must have relevant expertise** in the various aspects of tumor atlas construction, especially **clinical oncology, pathology, cancer biology, data analysis, and mathematical/computational modeling**.

Given the multidisciplinary expertise required for exemplary response to the objectives of the HTA Network, **this FOA encourages the use of the multi-PD/PI option**. Foreign components are allowed.

Effort commitment requirement: **1.8 person-months per year for Contact PD/PI**

1.2 person-months per year for multiple PD/PI (2+)

Note: 1.8 person-month commitment remains for Contact PD/PI

Overall Component

Research Strategy (12 page limit, FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

Sub-section A: Proposed Human Tumor Atlas(es) – Define the tumor atlas(es) that will be constructed within the HTA Research Center. Outline the significance and impact provided by the creation of the atlas(es). Succinctly describe the envisioned final structure of the atlas(es). Preview the use case proposed within the Data Analysis Unit.

Sub-section B: Research Center and Team Organization -- Provide a concise description of the team structure of the Research Center.

Sub-section C: Research Units -- Provide an overview of the preliminary data included in the application demonstrating the capabilities and expertise included within each Unit.

Sub-section D: Project Milestones – Describe Overall Center Milestones and Interim (semi-annual) Center Milestones.

Sub-section E: Health Disparities -- If applicable, address how health disparity populations or data will be integrated into the proposed studies.

Overall Component (Cont.)

Data Sharing Plan

All applications must include a data sharing plan

The Data Sharing Plan should be provided only under the Overall component but it should cover all the activities of the Center.

Addressing the Cancer Moonshot Open Access Pilot Program: Utilizing the provision outlined in the 21st Century Cures Act, NCI has established a data sharing policy for projects that are funded as part of the Beau Biden Cancer MoonshotSM Initiative that requires applicants to submit a Public Access and Data Sharing Plan that: (1) describes their proposed process for making resulting publications and to the extent possible, the underlying primary data immediately and broadly available to the public upon publication and; (2) if applicable, provides a justification to NCI if such sharing is not possible. **NCI will give competitive preference and funding priority to applications that comply with the strategy described at [NCI Cancer Moonshot Public Access and Data Sharing Policy](#).** The data sharing plan will become a term and condition of award.

Administrative Core

Budget

Administrative Core Budget specifics:

Center Administrator. Based on the complexity of the HTA Research Center, applicants are expected to propose and budget for a Center Administrator to manage day-to-day operations.

Funds for Trans-Network Projects: A minimum of \$200,000 in direct costs per year must be allocated to a restricted fund for support of post-award collaborative projects between HTAN Research Centers. These funds should be presented in the Other Direct Costs category under the heading "HTAN Collaborative Project Fund". Funds will be released pending approval by NCI following discussion of proposed projects by the HTAN Steering Committee.

Travel Funds: The budget should include funds to support travel for Network activities, including but not limited to supporting the travel and participation of PD(s)/PI(s) and other HTA Center members in the semi-annual HTAN Steering Committee meeting and annual site visits.

Administrative Core (Cont.)

Research Strategy (6 page limit: FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

Sub-section A: Leadership and HTA Research Center Organization -- address the major responsibilities of the Administrative Core

Sub-section B: Center logistics and communication -- describe the strategies for communication and resource/data/tool exchange

Sub-section C: Evaluation of Interim Center Milestones– outline plans for critically evaluating and revising the Interim Center Milestones specified in the Overall Component.

Biospecimen Acquisition, Processing and Characterization Unit (Biospecimen Unit)

Research & Related Senior/Key Person Profile

Unit Leads are expected to include investigators with hands on experience in collection, annotation and characterization of clinical biospecimens, including oncologists and pathologists with medical doctoral degrees and others with molecular pathology expertise. Other key personnel may include, but are not limited to, a research coordinator, surgical nursing staff and/or laboratory technicians.

Biospecimen Unit

Research Strategy (12 page limit, FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

Sub-section A: Overview and Biological Motivation -- Provide an overview of how the Biospecimen Unit will collect biospecimens that are reflective of the racial/ethnic diversity of the United States for use in constructing the proposed tumor atlas(es).

Sub-section B: Sample Acquisition Pipeline – Provide a comprehensive roadmap for sample acquisition, processing, and characterization. The strongest applications will demonstrate the proposed sample acquisition pipeline through presentation of preliminary data.

Sub-section C: Clinical Data and Metadata – Describe plans for collection of appropriate clinical and epidemiological data.

Sub-section D: Informed Consent – Provide details about the breadth of informed consent obtained from patients.

Sub-section F: Benchmarks of Unit Progress – Provide a clear set of tentative semi-annual quantitative benchmarks for the Biospecimen Unit.

Biospecimen Unit

Research Strategy (12 page limit, FOA Part 2 – Section IV)

NOTE: Applicants are to upload examples of patient consent forms for biospecimen collection **in the Appendix** using the filename “*Sample Consent Forms*”.

Please note that during the webinar on November 16th, it was *incorrectly* stated that the consent forms should be uploaded under “Other Attachments”. Please upload them in the Appendix.

Molecular, Cellular, and Tissue Characterization Unit (Characterization Unit)

Research & Related Senior/Key Person Profile

Unit Leads are expected to include investigators with significant experience leading multidisciplinary teams with hands on experience in collection of multidimensional, multiparameter data sets from tissue samples.

Characterization Unit

Research Strategy (12 page limit, FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

Sub-section A: Overview and Biological Motivation -- Provide a general overview of the various data types that will be collected within the Characterization Unit.

Sub-section B: Proposed Data Collection -- Provide a comprehensive description of the proposed molecular, cellular and tissue characterization.

Sub-section C: Preliminary Data – Present preliminary data demonstrating current capabilities within the Center, including novel combination or integration of methods.

Sub-section D: Quality Assurance/Quality Control -- Describe a strategy to monitor and ensure the quality of instrument performance and data generated across the HTA Research Center.

Sub-section F: Benchmarks of Unit Progress – Provide a clear set of tentative semi-annual quantitative benchmarks for the Characterization Unit.

Data Processing, Analysis, and Modeling Unit (Data Analysis Unit)

Research & Related Senior/Key Person Profile

Unit Leads are expected to include investigators with significant experience leading multidisciplinary teams with hands on experience in analysis of multidimensional, multiparameter data sets from tissue samples.

The Unit must have senior/key investigators with expertise in biostatistics, data analysis, data processing, bioinformatics, and computational and mathematical modeling.

Data Analysis Unit

Research Strategy (12 page limit, FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

Sub-section A: Biological Motivation and Proposed Atlas Use Case -- Provide a brief overview of the various data processing, analysis and modeling techniques that will be utilized within the Data Analysis unit, concentrating on type of biological insight that can be gained through employment of those techniques.

Provide plans for completion of at least one use case example that will demonstrate how the resulting human tumor atlas dataset can be utilized to build a predictive computational model of cancer. Describe the clinical or biological insight that will be gained from the modeling effort.

Sub-section B: Biostatistics -- Describe the type of biostatistical analyses to be performed by the Data Analysis Unit for use by investigators within the Data Analysis, Biospecimen, and Characterization Units.

Sub-section C: Data Processing -- Describe and demonstrate any existing or proposed data processing pipelines to be employed within the HTA Research Center.

Data Analysis Unit (Cont.)

Research Strategy (12 page limit, FOA Part 2 – Section IV)

Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

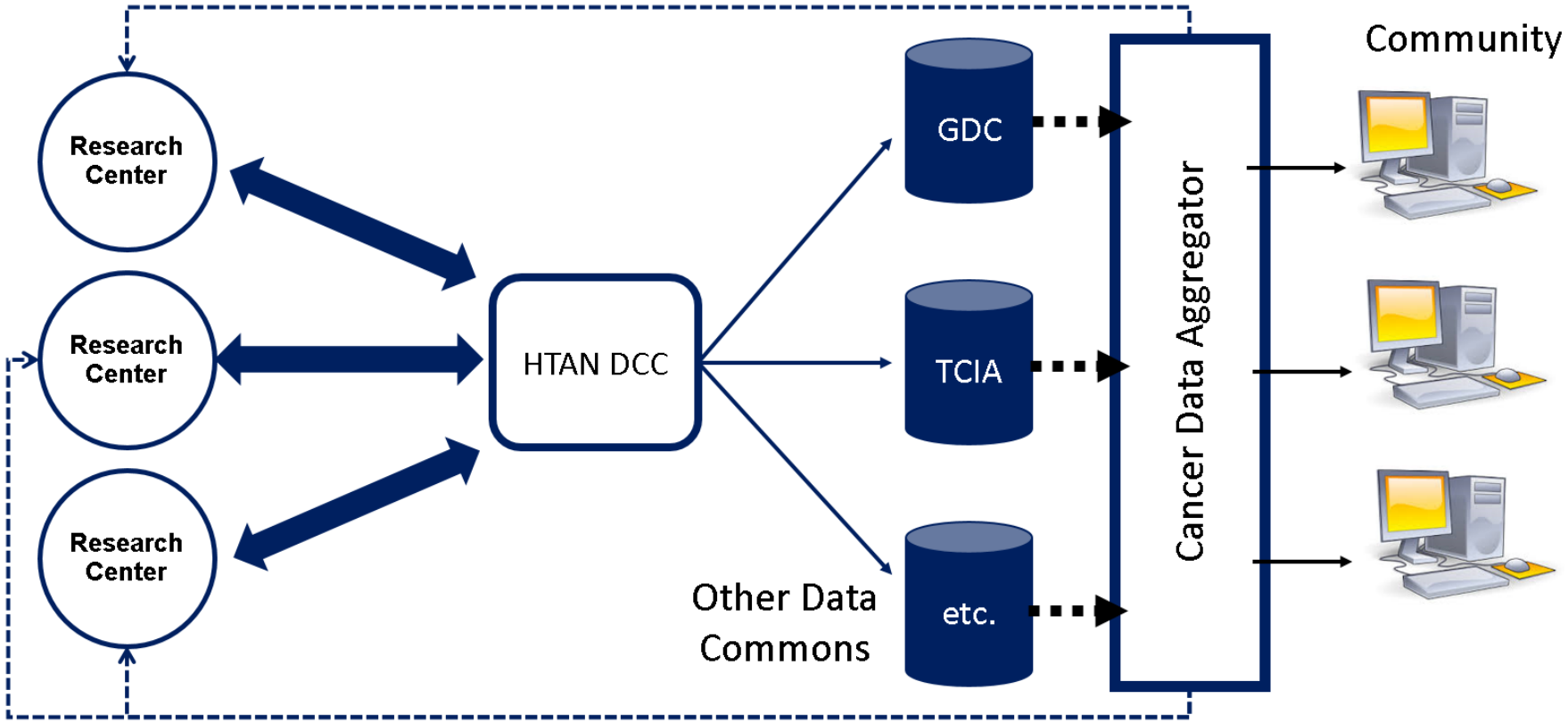
Sub-section D: Data Analysis -- Describe and demonstrate the computational approaches to be employed within the Data Analysis Unit that will result in the generation of dynamic multi-dimensional tumor maps from high-content, multi-parameter imaging and omics assays conducted by the Characterization Unit.

Sub-section E: Atlas Construction -- Describe and demonstrate plans to aggregate and integrate data and metadata from the broad range of experimental and computational approaches outlined throughout the application into a tumor atlas utilizing the tumor maps described in the previous section.

Sub-section F: Network-wide Collaboration -- Describe plans to collaborate with the HTAN Data Coordinating Center and other HTAN Research Centers in developing common data formats and interoperable tools and procedures allowing seamless integration and presentation of the atlases across the entire HTAN.

Sub-section G: Benchmarks of Unit Progress – Provide a clear set of tentative semi-annual quantitative benchmarks for the Data Analysis Unit.

Proposed Data Flow for HTAN



Information about HTAN Data Coordinating Center (U24)

[RFA-CA-17-036](#)

The DCC will work closely with the HTA and PCA Research Centers.

The HTAN-DCC will have **two major areas** of responsibility: (1) **Data Standards, Storage, Analysis, and Dissemination** (2) **Consortium Coordination**

The HTAN-DCC will collect, **store, curate, and disseminate** all data, metadata, analysis and visualization tools, computational models, and [completed atlases](#) generated by the HTAN. Additionally, the DCC will **lead the development of common data elements, data and metadata standards, clinical and epidemiological data requirements, and data processing pipelines**. The DCC will also **coordinate HTAN activities** including in-person and virtual Network Steering Committee meetings and working groups.

Pre-application webinar: Monday, November 20th 4:00 pm ET

Information about PCA Research Centers (U2C)

RFA-CA-17-035

From the FOA:

A human pre-cancer atlas is defined as a multidimensional cellular, morphological and molecular mapping of **human pre-malignant tumors**, complemented with critical **spatial information** (at cellular and/or molecular level) that facilitate visualization of the structure, composition, and multiscale interactions within the tumor ecosystem **over time** resulting in progression or regression of the tumors.

Each PCA Center will lead the construction of **at least one pre-cancer atlas**.

Selection of organ sites must be based on the following **four criteria**: **Impact on Public Health**; **Access to Technologies and Biospecimens**; **Feasibility of Atlas Construction**; **Synergistic Partnerships for Maximizing Resources**.

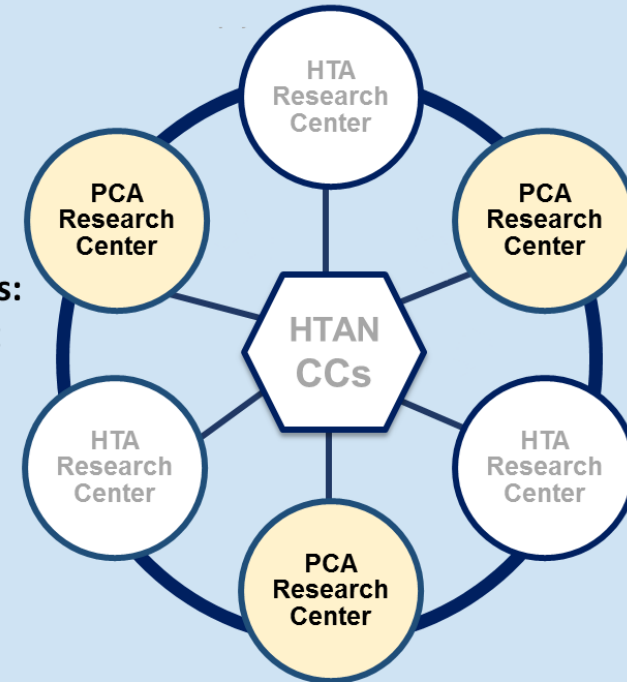
Human Tumor Atlas Network

Tumor Criteria for PCA Research Centers:

- *Public health impact
- *Access
- *Feasibility
- *Partnerships

Transitions:

Pre-cancer → Cancer



Key Dates

	Pre-Application Webinars	Letters of Intent Due Dates	Application Due Dates	Review Dates	Earliest Anticipated Start Dates
RFA-CA-17-034	November 16, 2017	Dec 18, 2017	Jan 18, 2018	Spring 2018	September 2018
RFA-CA-17-035	November 14, 2017	Dec 18, 2017	Jan 18, 2018	Spring 2018	September 2018
RFA-CA-17-036	November 20, 2017	Dec 18, 2017	Jan 18, 2018	Spring 2018	September 2018

Letter of Intent (LOI)

Due date: **December 18, 2017**

Highly encouraged, but not required

Required elements:

- Descriptive title of HTA Research Center
- Name(s), address(es), telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating Institution(s)
- Number and title of funding opportunity

Additional recommended information:

- **Provide a brief description of the proposed tumor atlas(es), including tumor type and transition being addressed**
- **If possible, submit LOI prior to December 18**

Application Review Information

- Consider the **FOA-specific review criteria** defined in Part 2, Section V
- Overall impact scores provided for Overall Component, Administrative Core, Biospecimen, Characterization, and Data Analysis Units.
- Individual Criterion Scores provided for Overall Component include:
 - Significance
 - Approach
 - Investigator(s)
 - Environment
 - Innovation
 - **Integration**
- An overall impact score for the Admin Core and each Functional Unit will be based on bulleted lists defined in Part 2, Section V.

Applications reviewed by a Center for Scientific Review Special Emphasis Panel

Scientific Review Officer: Dr. Lambratu (Bree) Rahman Sesay (rahmanl@csr.nih.gov)

Submission Information

Electronic submission is required for RFA-CA-17-034

NIH's **Application Submission System & Interface for Submission Tracking (ASSIST)** is available for the electronic preparation and submission of multi-project applications through Grants.gov to NIH. Applications to this FOA must be submitted electronically; paper applications will not be accepted. ***ASSIST replaces the Grants.gov downloadable forms*** currently used with most NIH opportunities and provides many features to enable electronic multi-project application submission and improve data quality, including: pre-population of organization and PD/PI data, pre-submission validation of many agency business rules and the generation of data summaries in the application image used for review.

ASSIST [Website](#)

ASSIST [Webinar](#)

Problems accessing or using ASSIST?

Contact the [eRA Commons Help Desk](#)

Submission Information (Cont.)

Electronic submission is required for RFA-CA-17-034

You are strongly encouraged to upload and test your application in ASSIST at least five days prior to the application deadline. This will allow time to correct any formatting or technical errors. Once the deadline passes (5:00 PM local time on January 18th) you will *no longer be able to access your application to correct errors.*

ASSIST Website:

- Familiarize yourself with ASSIST early.
- Pay attention to the order of the application components to save time and reduce errors.

Problems accessing or using ASSIST?

Contact the [eRA Commons Help Desk](#)

Contact Information

Scientific/Research Contact(s) for RFA-CA-17-034:

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Pre-Cancer Atlas (PCA) Team ([RFA-CA-17-035](#)):

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Human Tumor Atlas (HTA) Team ([RFA-CA-17-034](#)):

NCI_HTAN_HTAU2C@mail.nih.gov

HTAN Data Coordinating Center Team ([RFA-CA-17-036](#)):

NCI_HTAN_Data@mail.nih.gov

[Slides and FAQs are available on Cancer.gov](#)

<https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/funding/upcoming#hta>

Search terms: Moonshot upcoming funding opportunities