The NCI Human Tumor Atlas Network (HTAN)  
*Pre-application webinar slides for RFA-CA-17-036*

“Human Tumor Atlas Network: Data Coordinating Center (U24)”

Connection information for webinar:  
[NOT-CA-18-015](#)

The webinar will start at 4:05pm EST

Please note:
All participants are muted upon entry
The webinar will be recorded

NIH NATIONAL CANCER INSTITUTE

November 20, 2017
The Cancer Moonshot Initiative

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
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.

Figure adapted from Carr et al. 2016 EMBO Molecular Medicine
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 (PCA) Research Centers (U2C)** focused on characterization of pre-malignant lesions.  
   **RFA-CA-17-035**

3. **HTAN Data Coordinating Center (HTAN-DCC) (U24s)** focused on HTAN data and Network coordination.  
   **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 $\rightarrow$ Cancer  
Invasive $\rightarrow$ Metastatic  
Responsive $\rightarrow$ Resistant
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.
From the FOA:

Tumor atlases ... 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**

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

*(Non)Responsive to immunotherapy

*Highly metastatic

*High-risk hereditary

*Pediatric

**Transitions:**

Pre-cancer → Cancer

Invasive → Metastatic

Responsive → Resistant
From the FOA:

A human pre-cancer atlas is 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.
The HTAN-DCC will have two major areas of responsibility: (1) Data Standards, Storage, Analysis, and Dissemination (2) Consortium Coordination

The DCC will work closely with the U2C Research Centers to collect, store, curate, and disseminate all data, metadata, analysis and visualization tools, computational models, and completed atlases generated by the HTAN. The DCC will lead the development of HTAN data and analysis standards. The DCC will also coordinate HTAN activities including Network Steering Committee meetings and working groups.

Since it is difficult to predict the exact volume and types of data that will be generated by the HTAN, the HTAN-DCC will need to be flexible in their implementation of HTAN data coordination.

Human Tumor Atlas Network

High Priority Tumors for HTA Research Centers:
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Proposed data flow for HTAN:
Mechanism of support: **U24**, Resource-Related Research Projects--Cooperative Agreements

*To support research projects contributing to improvement of the capability of resources to serve biomedical research.*

**Application Type:** New applications only

**Budget:** Not to exceed **$1.0M direct costs per year** for years 1 & 2, and **$2.35M direct costs per year** for years 3-5.

**Project Period:** Not to exceed **5 years**.
Do not use standard Research Strategy subsections (Significance, Innovation, Approach), instead address the following sub-sections:

**Sub-section A: DCC Vision and Management** – This section will describe the overall goals and vision of the DCC, how progress will be monitored, and how communication will be handled within the DCC and across the HTAN.

**Sub-section B: Data Standards, Storage, Analysis, and Dissemination** – This section will describe how data will be managed and shared, interactions with data producers, and data dissemination.

**Sub-section C: Network Coordination and Outreach** – This section will describe approaches for coordinating Network activities interacting with outside collaborators.

**Sub-section D: Health Disparities** – If applicable, this section will describe how the proposed research address questions in minority or health disparities.
Sub-section A: DCC Vision and Management

- **Overview and Goals** – Describe goals and quantitative deliverables of the HTAN-DCC.
- **Milestones and Progress** – Describe milestones with metrics that will document progress towards the achievement of the ultimate goals.
- **Management and Communication Plan** – Describe how the DCC will manage the proposed project, who will oversee the day-to-day activities, and how the management structure will support achievement of the proposed goals and milestones.
Sub-section B: Data Standards, Storage, Analysis, and Dissemination

• **Data Portal Development** – describe development of a data portal that supports submission of and access to HTAN data, tools, computational, models, and atlases

• **Data Security** – describe approaches for adhering to all data security requirements

• **Data Storage & Access** – describe approaches for storing and managing access to HTAN data

• **Information Technology & Technology Development** – describe IT approaches for managing HTAN Data

• **Interactions with HTAN Data Producers** – describe approaches for interacting with data producers to establish data standards, common data processing pipelines, etc.

• **Data Wrangling** – how will the DCC work with data producers to ensure timely data submission

• **Implementation of Analysis & Visualization Tools** – plans to implement widely used tools

• **Centralized Access and Comparative Analysis of Atlases** – describe approaches for sharing and disseminating completed atlases

• **Data Export and Dissemination** – Describe plans to deposit data in public databases
Sub-section C: Network Coordination and Outreach

- **Web Portal Development** – describe a plan for developing and maintaining the main HTAN Web Portal that will constitute the main entry point for the sharing of resources and information related to HTAN activities.

- **HTAN Activity Coordination** – describe plans to provide the administrative infrastructure necessary to facilitate and coordinate all common activities of the HTAN.

- **Outreach, Documentation and User Support** – describe plans to provide outreach to the user communities to educate the community about the HTAN and its data, resources, tools, and completed atlases and provide user support.

Sub-section D: Health Disparities

- If applicable, address how health disparity populations or data will be integrated into the proposed studies.
All applications must include a data sharing plan

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 Moonshot℠ 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 here.** The data sharing plan will become a term and condition of award. Data and computational tool sharing by HTAN members will follow FAIR (findable, accessible, interoperable, and reusable) principles as defined [here](https://fairguidingprinciples.org/).

**NCI Cancer Moonshot Public Access and Data Sharing Policy**

[The FAIR Guiding Principles for scientific data management and stewardship](https://fairguidingprinciples.org/)
From the FOA:

**Leadership Effort Commitment:** The HTAN-DCC contact PD/PI must commit and maintain through the life of the award a minimum of **1.8 person-months of effort**. For applications with multiple PDs/PIs, a minimum effort of 1.8 person-months is required for the Contact PD/PI and **1.2 person-months of effort per additional** PD/PI is required.

**HTAN DCC Administrator:** Based on the complexity of the HTAN-DCC, the DCC PD(s)/PI(s) are **strongly encouraged to propose and budget for an HTAN-DCC Administrator** to manage day-to-day operations and work with the DCC PD(s)/PI(s), NCI staff, and HTAN Investigators to manage and coordinate the DCC activities.

**Travel Funds:** The budget should include funds to support travel for HTAN activities, including but not limited to supporting the travel and participation of PD(s)/PI(s) and other HTAN-DCC members at the semi-annual HTAN Steering Committee meeting and annual site visits.
## Human Tumor Atlas Key Dates

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<td>RFA-CA-17-036</td>
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RFA-CA-17-036: HTAN-DCC – 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:

• If possible, submit LOI prior to December 18
Consider the **FOA-specific review criteria** defined in Part 2, Section V

Applications will compete for available funds with all other recommended applications submitted in response to this FOA. Following initial peer review, recommended applications will receive a second level of review by the National Cancer Advisory Board.

**The following will be considered in making funding decisions:**

- Scientific and technical merit of the proposed project as determined by scientific peer review.
- Availability of funds.
- Relevance of the proposed project to program priorities.
- **Compliance with Beau Biden Cancer Moonshot Open Access and Data Sharing Policy**

Applications will be **reviewed by a Special Emphasis Panel** convened by the NIH Center for Scientific Review.
Contact Information

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Contact information for all HTAN RFAs:

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Human Tumor Atlas (HTA) Team (RFA-CA-17-034): NCI_HTAN_HTAU2C@mail.nih.gov
Pre-Cancer Atlas (PCA) Team (RFA-CA-17-035): NCI_HTAN_PCAU2C@mail.nih.gov

Slides and FAQs will be available
Search terms: Moonshot HTAN (scroll to bottom of page)