

# Human Tumor Atlas Network (HTAN) Frequently Asked Questions (FAQs)

We appreciate your interest in the NCI Human Tumor Atlas Network (HTAN) and hope that you and your team will choose to submit an application. To maximize your chances of success, we would like to provide some guidance that may be helpful. For additional clarification of these or other issues, we encourage you to contact the appropriate HTAN team via email:

Pre-Cancer Atlas (PCA) Team ([RFA-CA-17-035](#)): [NCI\\_HTAN\\_PCAU2C@mail.nih.gov](mailto:NCI_HTAN_PCAU2C@mail.nih.gov)

Human Tumor Atlas (HTA) Team ([RFA-CA-17-034](#)): [NCI\\_HTAN\\_HTAU2C@mail.nih.gov](mailto:NCI_HTAN_HTAU2C@mail.nih.gov)

HTAN Data Coordinating Center Team ([RFA-CA-17-036](#)): [NCI\\_HTAN\\_Data@mail.nih.gov](mailto:NCI_HTAN_Data@mail.nih.gov)

## **Information about the Human Tumor Atlas Network**

### **1. What is the Beau Biden Cancer Moonshot<sup>SM</sup> Initiative?**

The Beau Biden Cancer Moonshot<sup>SM</sup> Initiative is part of an effort initiated by former President Obama in his 2016 State of Union Address to accelerate cancer research. NCI convened a Blue Ribbon Panel (BRP) in 2016 that was charged with assessing the state of the science in specific areas and identifying major research opportunities that could uniquely benefit from the support of the Cancer Moonshot and could lead to significant advances in our understanding of cancer and in how to intervene in its initiation and progression. The recommendations focused on areas in which a coordinated effort could profoundly accelerate the pace of progress in the fight against cancer and were not intended to replace existing cancer programs, initiatives, and policies already underway. The [BRP final report](#) was approved by the National Cancer Advisory Board and included a recommendation for the *Generation of Human Tumor Atlases* (BRP Recommendation I). The [21st Century Cures Act](#) was signed into law in December 2016 dedicating new funds to support efforts associated with the [Beau Biden Cancer Moonshot<sup>SM</sup> Initiative](#).

### **2. What is the goal of the NCI Human Tumor Atlas Network (HTAN)?**

The goal of the HTAN is the construction of human tumor atlases that describe the multidimensional (i.e. 3D) cellular, morphological and molecular mapping of human cancers over time for informing future cancer research and, ultimately, clinical decision-making. The human tumor atlases resulting from the HTAN efforts will lend support for evidence-based expansion of the HTAN after completion of the initial 5-year pilot phase.

HTAN investigators will work together as a single consortium to accomplish HTAN goals. Two types of atlas-building initiatives spanning the entire continuum of cancer will be supported by the HTAN:

- The Human Tumor Atlas (HTA) Research Centers ([RFA-CA-17-034](#)), that will construct atlases describing the transition from locally invasive to metastatic cancer, dynamic response to therapy, and development of therapeutic resistance.
- The PreCancer Atlas (PCA) Research Centers ([RFA-CA-17-035](#)) that will construct atlases describing how and when premalignant lesions progress to invasive cancer or regress or obtain a state of equilibrium.

The atlas-building initiatives will be supported by:

- An HTAN Data Coordinating Center (HTAN-DCC; [RFA-CA-17-036](#)), that will be responsible for data storage, harmonization, distribution, and compilation of the final human tumor atlas collection.
- An HTAN Tissue Coordinating Center (HTAN-TCC; anticipated to be developed in Fiscal Year 2019), that will provide a virtual resource for the investigators to identify and share available biospecimens across the HTAN.

### **3. What is the relationship between HTAN and The Cancer Genome Atlas (TCGA)?**

HTAN is a stand-alone, fixed-term NCI-sponsored consortium focused on generating comprehensive, multidimensional tumor atlases describing key transitions during tumorigenesis. The HTAN effort builds upon and extends the efforts of The Cancer Genome Atlas (TCGA) which provided genomic and transcriptomic characterization of many tumor types, resulting in an important resource for the scientific and clinical communities while promoting advances in associated technologies and bioinformatic approaches. The HTAN will focus on longitudinal studies of pre-cancer, metastasis, and drug resistance with an emphasis on collecting comprehensive clinical data over time. Furthermore, the tumor atlases generated by the HTAN will facilitate understanding of interactions within multidimensional architecture of the tumor microenvironment, including the role of the immune system, normal cells, and non-cellular components. HTAN will build upon the lessons learned from TCGA, address its limitations, and use evolving state-of-the-art information technology and other emerging technologies to achieve its goal.

### **4. What is the relationship between HTAN and other similar programs?**

The NCI HTAN Program Staff works closely and shares members with other NIH programs that aim to build similar atlases across normal and disease tissues, including the BRAIN Initiative, the Common Fund HuBMAP Program, and the NIDDK Kidney Precision Medicine Program. Each NIH program has specific goals and areas of interest, though there is significant interest in sharing expertise, developing synergies and building collaborations among the NIH-funded programs.

The Human Cell Atlas (HCA) initiative is an international investigator-organized, grass-roots organization with the mission of creating comprehensive reference maps of all human cells. While there is regular communication between HCA and NIH/NCI, the HTAN does not formally participate in the HCA and the focus, goals, and management of the HTAN are separate to those of HCA. Review and funding of HTAN applications is led by the NIH and involvement in the HTAN will not require participation in the HCA.

## **Questions about the science within the HTAN**

### **5. What is a human tumor atlas?**

Within the HTAN, a human tumor atlas is generally 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. Tumor atlases constructed within the HTAN should describe the dynamics of cancer, focusing on the transition from pre-cancer to malignancy, from local

invasion to distant metastasis, and in response to or during the development of resistance to therapy. Please see the HTAN U2C RFAs for more information.

**6. Will specific tumor types or organ sites be given funding priority within the HTAN?**

No. The HTA and PCA Research Center Funding Opportunity Announcements (FOAs) do not require applicants to propose atlas construction of specific, pre-determined tumor types or organ sites. However, high-priority tumor characteristics were defined by the Working Groups of the Cancer Moonshot Blue Ribbon Panel and projects that address those characteristics will be viewed with high programmatic priority upon review of applications in response to the HTA Research Center FOA ([RFA-CA-17-034](#)). In a complementary manner, applications in response to the PCA Research Center FOA ([RFA-CA-17-035](#)) should address the four specific criteria outlined in that FOA as justification of choice of organ site.

**7. What level of tumor characterization is minimally expected?**

It is minimally expected that multiparameter data collected from multiple molecular assays and/or imaging modalities will be employed to characterize each tumor, such that the multidimensional architecture of the tumor and its environment, including cells and non-cellular components, will be represented.

**8. What methods for biospecimen characterization are within the scope of the program?**

The HTAN supports application of assays that generate high quality quantitative data for characterizing cells and extracellular structures at micron resolution. One focus of the program is in-situ analysis of the biomolecular composition, morphology, and architecture of tumor tissue, using unbiased, qualitative assays that can be readily multiplexed with other assays and used for analyzing multiple human tumors. Methods which require significant pre-processing of the tumor and surrounding tissue, that result in significant biomolecular degradation, or that work with dissociated or fragmented cells and do not accurately recover spatial organization will be considered lower priority if proposed in the absence of characterizations that report on tumor architecture.

Although the focus is on technologies that provide quantitative readout of the spatial organization of specific biomolecules, such as proteins, RNA, DNA and metabolites, projects can propose generating data from technologies that will enhance scientific and clinical understanding, including from, but not limited to, MRI, micro-CT, photoacoustic imaging, Raman spectroscopy, histology, and mechanical imaging.

**9. Will the HTAN support projects that do not use human clinical biospecimens to construct the final proposed tumor atlas?**

No. It is recognized that biospecimens from non-human models or *in vivo* and *ex vivo* platforms derived from human tumors, such as tumor organoids, patient-derived xenograft models, and other systems that maintain native tumor architecture may be useful during development of standard operating procedures for tissue processing, preservation, and characterization. However, it is expected that data contained within the final tumor atlas deliverables of the HTAN will be derived from human clinical biospecimens, preferably prospectively collected.

## **Questions about the HTAN RFAs:**

### **10. What are cooperative agreements?**

A cooperative agreement funding mechanism supports projects to be performed by investigators in an area representing their specific interest and competencies, and is used when substantial NIH programmatic involvement is anticipated. In addition to a Program Director from the National Cancer Institute, each award will be assigned a Project Scientist from NIH who will participate with the Principal Investigators on a Steering Committee.

### **11. Are Foreign Institutions eligible for funding?**

No and Yes. Foreign Institutions or non-domestic components of U.S. Organizations may not apply as the primary awardee. However, foreign components to U.S. led applications are allowed, provided that they are justified (i.e., justified in terms of expertise).

### **12. Can research teams span institutions?**

Yes. Team members may span multiple institutions, and it is possible that the full range of expertise needed for a proposal may not exist at one institution. Teams are expected to assemble the expertise across labs, disciplines, and institutions needed to achieve the goals of the project and the HTAN.

### **13. How much should be budgeted for travel to required HTAN meetings, in general?**

A rule of thumb is that it costs an estimated \$2,000 per investigator per meeting to travel.

### **14. What is the page limit for the Research Strategy section?**

For the HTA and PCA U2C RFAs: 6 pages for the Admin Core Research Strategy section; 12 pages for **each** of the Overall, Biospecimen Unit, Characterization Unit, and Data Analysis Unit Research Strategy sections.

For the HTAN-DCC U24 RFA the Research Strategy section is limited to 30 pages.

### **15. Are milestones the same as specific aims?**

No, a milestone is a defined event, achievement, or important stage that is used to indicate the progress of a project. Milestones are expected to be:

- Major steps or events (e.g., activities or outcomes) with a clearly defined purpose.
- Specific targets that depict progress toward project goals.
- Descriptive of what will be done and when it will be completed.
- Collectively organized in a logical order (e.g. sequentially, simultaneously, or iteratively).
- Associated with a timeframe (e.g., end of the fiscal year).

Milestones should not be presented as specific aims or broadly aspirational statements of what a project is expected to achieve. See each of the HTAN FOAs for specific instructions regarding milestone requirements.

### **16. Who is responsible for building the final human tumor atlas?**

The HTA and PCA Research Centers are responsible for, among other things, integrating individual multi-dimensional tumor maps into atlases representing the relevant transition in tumorigenesis proposed by that Research Center. The HTAN Data Coordinating Center is responsible for, among other things, integrating these individual tumor atlases together into a body-wide resource of functional, structural and biomolecular data that will enable comparative studies across tumor sites and types.

#### **17. What consortia agreements are expected in the HTAN Program?**

HTAN awardees will form a single consortium, with the overarching mission to build dynamic, spatially-resolved, tumor-specific atlases that can be utilized to build predictive models of tumorigenesis to inform future cancer research and, ultimately, clinical decision making. In addition to completing the research goals outlined in their applications, successful applicants will be expected to work collaboratively with all members of the HTAN, including the HTA ([RFA-CA-17-034](#)) and PCA ([RFA-CA-17-035](#)) Research Centers, the HTAN Data Coordinating Center ([RFA-CA-17-036](#)), the future HTAN Tissue Coordinating Center (expected Fiscal Year 2019), and NCI Program Staff, to help develop common standards, metrics for data generation and storage, and data analysis and visualization tools that can be used by the members of the HTAN and the broader scientific community. The NCI will facilitate the initiation of new collaborative research projects across the entire network. HTAN Consortia agreements, such as policies governing joint publications, material transfer agreements, etc, will be discussed and voted upon by the HTAN Steering Committee upon its assembly after awards are made.

HTAN investigators will be required to attend the initial HTAN Kickoff meeting, as well as semi-annual HTAN investigator meetings and regular teleconferences with Network members and NIH Program Staff for the duration of the funding cycle. Further details of the responsibilities of the HTAN investigators, including those associated with the HTAN Steering Committee, can be found in Section VI. Award Administration Information under “Cooperative Agreement Terms and Conditions of Award” in each HTAN FOA.

#### **18. What are the plans for data and resource sharing for this program?**

All awards made under the Beau Biden Cancer Moonshot are expected to follow the data and resource sharing policies outlined in the [NCI Cancer Moonshot Public Access and Data Sharing Policy](#). Awardees will work collectively with the NIH to develop and implement an appropriate rapid HTAN internal data release policy that will be applicable to all awardees in the Consortium.

#### **19. What is the role of the HTAN Steering Committee?**

Once HTAN awards have been made, a single HTAN Steering Committee composed of HTAN PD/PIs and NCI Program Staff that is responsible for joint governance of HTAN activities will be constituted (see Section VI. Award Administration Information under “Cooperative Agreement Terms and Conditions of Award” in each HTAN FOA.). The HTAN Steering Committee will be tasked, among other things, with establishing agreements that address the following issues: (1) procedures for data sharing among HTAN members, data sharing with the scientific community outside of the HTAN, and data sharing with industry partners; (2) procedures for safeguarding confidential information, including without limitation, any data generated by HTAN members as well as information and/or data received from external collaborators; (3) procedures for addressing ownership of intellectual property resulting from aggregate multi-party data; (4) procedures for sharing tools and reagents under an overarching MTA amongst HTAN members that operationalizes material transfer in an efficient and expeditious manner; (5)

publication policy for the entire HTAN, determining timing, authorship, and content of co-publications, in order to facilitate collaborations and co-publications by Network members while protecting each HTAN investigator's primary ownership and authorship of their data and discoveries.

**20. Is funding based on a payline?**

No. Funding decisions are based on scientific merit and programmatic needs, as defined in the funding announcement, and on the availability of funds.

**21. What role does the NIH/NCI have in the HTAN?**

The role of NCI staff in the HTAN is spelled out in each FOA and will be defined further in the terms and conditions of award. In brief, the HTAN NCI Program Staff will have significant scientific and programmatic involvement during the project period through technical assistance, advice, and coordination.

**22. Can changes be made to the Research Plan during the project period?**

Since this is an actively managed cooperative agreement-based consortium, investigators should expect that their goals and budgets will be modified during the project period. For example, funds may be withheld each year and released only when consortium-wide activities have been proposed and approved. To promote synergy and collaboration between projects in the HTAN, NIH staff may also work with awardees to amend and refine goals and milestones. As tools and techniques are developed within the HTAN and other programs, investigators may also be asked to cross-validate these approaches. Investigators can also propose minor changes to the research approach as needed during the course of the project.