A Recommendation of the Cancer Moonshot Blue Ribbon Panel

HTAN

THE HUMAN TUMOR ATLAS NETWORK

Building Dynamic 3D Human Tumor Atlases to Advance Cancer Research

Blue Ribbon Panel's Recommendation:

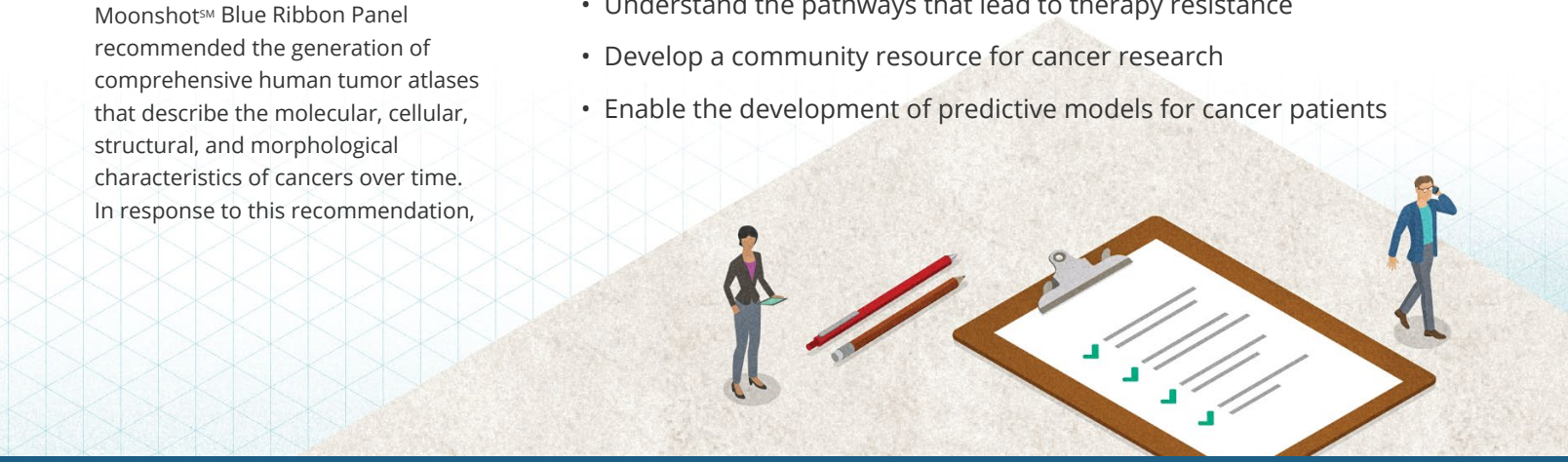
Develop 3D Cancer Atlases

Tumors are ecosystems that continuously evolve. Despite advances in understanding interactions within the cancer ecosystem, we know little about how the tumor architecture reflects progression from premalignant lesions to metastasis or how resistance to therapy develops.

To address this challenge, the Cancer Moonshot℠ Blue Ribbon Panel recommended the generation of comprehensive human tumor atlases that describe the molecular, cellular, structural, and morphological characteristics of cancers over time. In response to this recommendation, NCI launched the Human Tumor Atlas Network (HTAN). This collaborative network is using emerging technologies to create dynamic 3D human tumor atlases at single-cell resolution. Like Google Earth, these atlases can be viewed as interactive 3D maps showing the features of a tumor across multiple space and time scales. By providing insights about the composition, structure, and function of the various cells within the evolving tumor ecosystem, these human tumor atlases will enable predictive modeling to inform cancer treatment and prevention options for cancer patients.

WHY DO WE NEED HUMAN TUMOR ATLASES?

- Define the cellular and molecular architecture of human tumors
- Model tumor progression from pre-cancer to metastasis
- Understand the pathways that lead to therapy resistance
- Develop a community resource for cancer research
- Enable the development of predictive models for cancer patients



What is a **Human Tumor Atlas**?

A comprehensive human tumor atlas is defined as a multidimensional molecular, cellular, and morphological survey of human cancers over space and time. It can be thought of as a virtual 3D map of an evolving tumor ecosystem that shows the locations of individual molecules, cells, and tissues. A human tumor atlas provides visualization of the structure, composition, and multiscale interactions as a tumor grows, metastasizes, or responds to cancer therapy.

Like geographical mapping websites or apps that predict the best route to a new location and account for changing travel conditions, detailed human tumor atlases could be used to predict cancer patient responses to a treatment or to identify individuals for cancer prevention who are at increased risk for cancer.

HOW HTAN IS BUILDING HUMAN TUMOR ATLASES

HTAN is constructing dynamic 3D tumor atlases that describe important transitions in cancer. The network is specifically focusing on the evolution from the precancerous state to malignancy, the progression from a localized tumor to metastatic disease, the change in tumors during response to therapy, and the development of resistance to treatment.

The Human Tumor Atlas Network focuses on high-risk cancers: tumors that are sensitive or resistant to immunotherapy, hereditary cancers, and aggressive pediatric cancers. This involves the construction of atlases representing melanoma and cancers of the lung, pancreas, breast, and colon in adults, as well as brain cancers, neuroblastoma, sarcoma, and very high risk acute lymphoblastic leukemia in children. The atlases will represent a diverse population, including minority and underserved patients with cancer.

In order to create human tumor atlases, HTAN researchers need to collect and integrate single-cell resolution data from tumors. HTAN researchers are leveraging technological advances to comprehensively analyze single cells within a cancer ecosystem. Unlike previous efforts, HTAN tumor atlases take into account the spatial information of components within the tumor. Since many single-cell technologies require the dismantling of tumors which results in a loss of spatial relationships, HTAN investigators are using emerging, spatial imaging technologies to study the intact tumor architecture. By combining individual data from hundreds to thousands of single cells with spatial information about the cellular architecture of tumors, researchers can determine the location and function of individual cells within the complex tumor environment. This information is expected to advance basic and translational cancer research, such as the identification of biomarkers for cancer prevention and early detection.

There are other altas-building initiatives in biomedical research, and HTAN complements, yet is also distinct from, these projects. HTAN is unique in that it focuses on a range of cancers and examines how the spatial interactions of tumor components change over time. This is achieved through longitudinal sample collection and extensive analysis of clinical data that, together, will inform our understanding of disease progression and therapy resistance.

HOW HTAN IS ORGANIZED

HTAN consists of collaborative, interdisciplinary research teams from institutions across the country. Ten Human Tumor Atlas Research Centers of the network are creating detailed 3D atlases of cancers and pre-cancers. Additionally, two HTAN Pilot Projects are developing approaches and standard operating procedures for tumor tissue collection and data analysis that will be used across the network. The HTAN Data Coordinating Center manages the sharing of data and compilation of atlases generated by the network. This center also makes HTAN community resources available to the broader research community.

HTAN GOALS

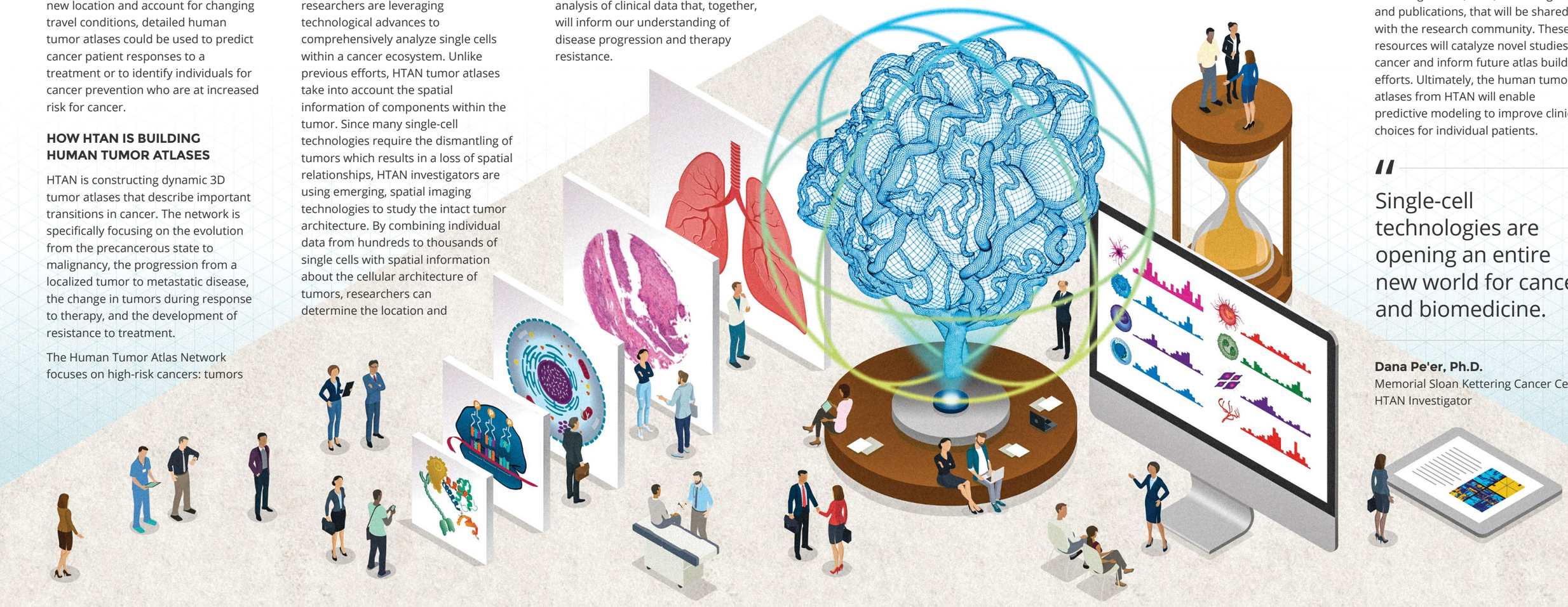
- Generate publicly available dynamic 3D human tumor atlases
- Enable predictive modeling of cancer across space and time
- Promote aggressive public data and resource release timelines
- Identify emerging technologies that will inform cancer research
- Develop standard operating procedures for future atlas efforts

HOW HTAN CONTRIBUTES TO THE CANCER MOONSHOT

HTAN is part of the Cancer Moonshot, which aims to accelerate progress in cancer research, encourage collaboration, and enhance data sharing. HTAN is a collaborative network that is contributing to these goals by generating resources, including atlases, data, technologies, and publications, that will be shared with the research community. These resources will catalyze novel studies of cancer and inform future atlas building efforts. Ultimately, the human tumor atlases from HTAN will enable predictive modeling to improve clinical choices for individual patients.

> "Single-cell technologies are opening an entire new world for cancer and biomedicine."

Dana Pe'er, Ph.D.
Memorial Sloan Kettering Cancer Center
HTAN Investigator



HTAN **Consortium**

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PANCREAS

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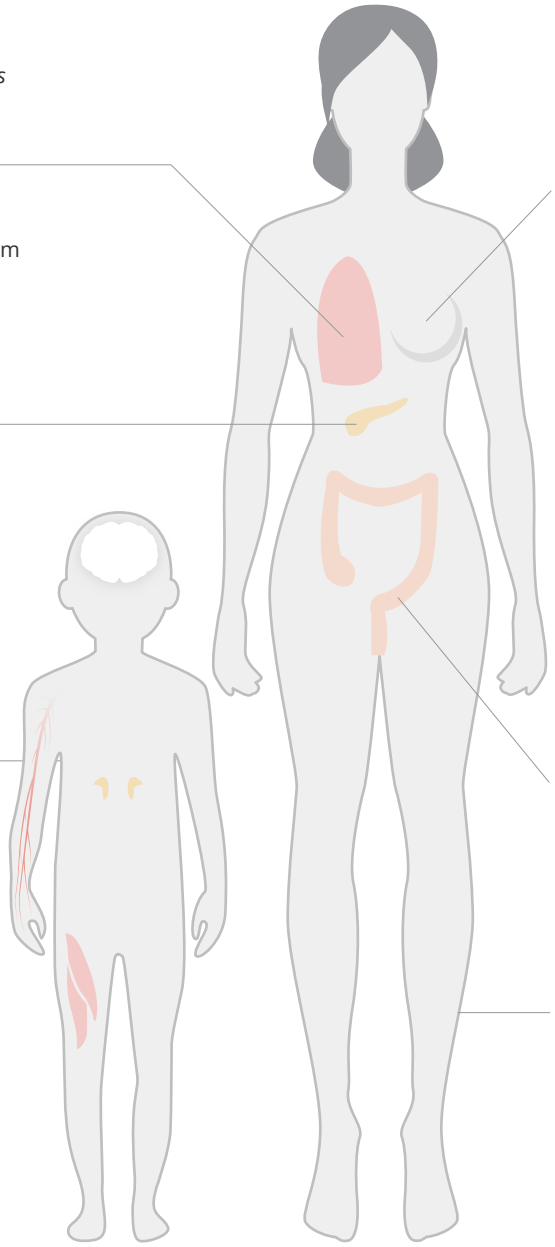
PEDIATRIC

FNLCR & Broad Institute
Tumor Atlas Pilot
Glioma, neuroblastoma, and sarcoma (organs commonly affected by these cancers include the brain, adrenal glands, and muscle)

Kai Tan and Stephen Hunger
Children's Hospital of Philadelphia
Glioma, neuroblastoma, and very high risk acute lymphoblastic leukemia (organs commonly affected by these cancers include the brain, adrenal glands, and blood)



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NIH NATIONAL CANCER INSTITUTE

LEARN MORE ABOUT **HTAN**

Find information about HTAN community resources, including 3D human tumor atlases:
humantumoratlas.org | cancer.gov/htan
@NCIHTAN | cancer.gov/brp

NCI CANCER MOONSHOT
Human Tumor Atlas Network
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