The NCI's Human Tumor Atlas Network

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The NCI Human Tumor Atlas Network

Overarching program goal: Construct dynamic 3D atlases of human cancers

- Integrate molecular, cellular, and tumor tissue composition and architecture, including the microenvironment and immune milieu
- Describe *transitions during cancer:* premalignant lesions to malignancy, locally invasive to metastatic cancer
- Enable *predictive modeling* to refine detection and therapeutic choices



HTAN Marker Paper. Rozenblatt-Rosen et al., Cell 2020

3

HTAN Phase 2: building on the goals of HTAN Phase 1

A publicly available set of spatially-resolved tumor maps describing transitions in cancer for use by the cancer research community



Highlights from the HTAN Nature Collection

- One study examined the interactions among cancer and non-cancer cells in breast, colon, pancreas, kidney, uterus, and bile duct cancers. The study identified distinct substructures, which they called microregions, within many tumors. They found that cells in different microregions within the tumors often have different activities and interactions.
- Several studies focused on colorectal cancer, including two that defined early molecular-level events that drive the transformation of precancerous lesions in the colon into cancer.
- Two studies focuses on breast cancer. One used single-cell RNA sequencing to profile metastatic cancer from 60 individuals with this disease, and another described the underlying genetic networks that define breast cancer subtypes based on profiles of thousands of cells from each of 37 tumors.

Common Themes Across Tumor Types and Analyses

- Recurring cellular spatial patterns that typify co-evolution of tumor and stroma emerging as drivers for progression and resistance
- Discovery of rare, transitional, dedifferentiated and/or plastic tumor cell types - often conserved across tumor subtypes and correlated with poor outcome
- Deep exploration of stroma, immune and tumor cell interactions
 - Regulation of tumor growth via immune-suppressive signaling circuits and cancer subtype-specific spatially organized immune-malignant cell networks
 - Cancer-associated fibroblasts (CAFs) act as CAF-subtype-specific TME remodelers that impact immune responses

~200 Total HTAN publications & preprints





Diverse HTAN Tumor Types: Phase 1

LUNG

Avrum Spira and Steven Dubinett Boston University and University of California Los Angeles

Dana Pe'er and Christine Icabuzio-Donahue Memorial Sloan Kettering Cancer Center

PANCREAS

Dana Pe'er and Christine Icabuzio-Donahue Memorial Sloan Kettering Cancer Center

Li Ding, Ryan Fields, William Gillanders and Samuel Achilefu Washington University in St. Louis

COLON

Michael Snyder and James Ford Stanford University

Robert Coffey, Ken Lau and Martha Shrubsole Vanderilt University

Bruce Johnson Dana-Farber Cancer Institute and Broad Institute

FNLCR and Broad Institute Tumor Atlas Pilot

https://data.humantumoratlas.org/



BREAST

Shelley Hwang, Carlo Maley and Robert West Duke University, Arizona State University and Stanford University

Joe Gray, Gordon Mills, Jeremy Goecks Oregon Health and Science University

Bruce Johnson Dana-Farber Cancer Institute and Broad Institute

Li Ding, Ryan Fields, William Gillanders and Samuel Achilefu Washington University in St. Louis

Frederick National Laboratory for Cancer Research (FNLCR) and Broad Institute Tumor Atlas Pilot

Peter Sorger, Sandro Santagata an Jon Aster Harvard University and Brigham and Women's Hospital

Bruce Johnson and Aviv Regev Dana-Farber Cancer Institute and Broad Institute

PEDIATRIC

FNLCR and Broad Institute Tumor Atlas Pilot glioma / neuroblastoma / sarcoma

Kai Tan and Stephen Hunger Children's Hospital of Philadelphia

glioma / neuroblastoma / very high risk acute lymphoblastic leukemia



7

Diverse HTAN Tumor Types: Phase 1 and Phase 2

SKIN

Melanoma and Cutaneous Squamous Cell Carcinoma Alan Shain, Boris Bastian and Iwei Yeh University of California, San Francisco

PANCREAS

Rosalie Sears, Elana Fertig, Jonathan Brody and Laura Wood Oregon Health & Science University

BRAIN

Long Cai, Richard Everson, Matthew Thomson and Barbara Wold California Institute of Technology

GASTRIC

Linghua Wang, Tae Hyun Hwang, Mingyao Li and Paul Mansfield MD Anderson

MULTIPLE MYELOMA

Irene Ghobrial Dana Farber Cancer Institute

https://data.humantumoratlas.org/

PROSTATE

Li Ding, Feng Chen, Eric Kim and Russell Pachynski Washington University in St. Louis

COLON

Ken Lau and Jeffery Spraggins Vanderbilt University

OVARY

Samuel Mok, Michael Birrer and Sammy Ferri-Borgogno MD Anderson

LYMPHOMA

Rong Fan, Stephanie Halene, Zongming Ma and Mina Xu Yale University

PEDIATRIC SOLID TUMORS

Rhabdomyosarcoma, Neuroblastoma and Wilms Tumor Shahab Asgharzadeh, James Amatruda and Long Cai University of California, Los Angeles



The NCI Human Tumor Atlas Network



HTAN Principles

- **Community Resource** create a community resource that catalyzes cancer research across disciplines
- **Complementary approaches** strengths and weaknesses will be discovered as a Network; expect to work together
- Open communication accelerate science by breaking down walls; strive towards inter-operability
- **Data & Resource sharing** requirement for success; expect aggressive public data/resource release timelines

HTAN Data Jamborees

- Virtual HTAN Jamboree, Dec 2023 & In-Person HTAN Jamboree, Nov 2024
 - ~200 total participant applications
 - ~30 total project pitch submissions
- ~90 participants selected to work on 12 projects, each addressing a specific scientific question or technical challenge using available HTAN data
 - ✓ Promote the access and reuse of HTAN data
 - Promote collaborations to expand the HTAN community
 - Promote development of new methods and tools for HTAN data analysis
 - Identify gaps and limitations of existing HTAN data and resources





HTAN Jamboree Participants



BioData Sage

26

HTAN Associate Membership

- Associate Members are expected to contribute to HTAN by:
 - generating, sharing or analyzing data;
 - jointly developing software or algorithms;
 - developing mutually beneficial resources, protocols or reagents;
 - and/or coordinating development of standards, formats or metadata
- Associate Members are encouraged to actively engage in HTAN activities
- Associate Member must abide by all HTAN policies
- Applications for Associate Membership require:
 - A letter of support from a current HTAN member
 - A recent biosketch
 - A letter of intent from the applicant describing their planned contributions to HTAN



Upcoming HTAN-BTEP Presentations



April 2, 2025: Fabian Seidl, General Dynamics Information Technology

- Title: Analyzing HTAN scRNASeq data accessible in BigQuery with CellTypist
- Description: This tutorial will demonstrate how to access HTAN single cell expression data directly from ISB-CGC BigQuery tables. It will then show how to perform a CellTypist analysis in Python.
- April 9, 2025: Rowan Beck, Velsera
 - Title: Accessing and Analyzing HTAN Data using the Cancer Genomics Cloud
 - Description: This session will provide an overview of accessing HTAN data on the Cancer Genomics Cloud (CGC) and demonstrate how to process and analyze these datasets using scalable pipelines and interactive apps.

□ May 7, 2025: Fabian Seidl, General Dynamics Information Technology

- Title: Analyzing HTAN spatial data with BigQuery spatial analytics
- Description: This tutorial will demonstrate how to perform spatial analysis on HTAN single cell data identifying local cell neighborhoods directly with built in BigQuery functionality.