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ANNUAL MEETING 2025 CHICAGO
APRIL 25–30
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Human Tumor Atlas Network Precancer Atlas (PCA) Research Centers

A Transformational Program Charting A Course To Intercept Cancer And Drive Precision Medicine

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Disclaimers and Disclosures Information

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Indu Kohaar

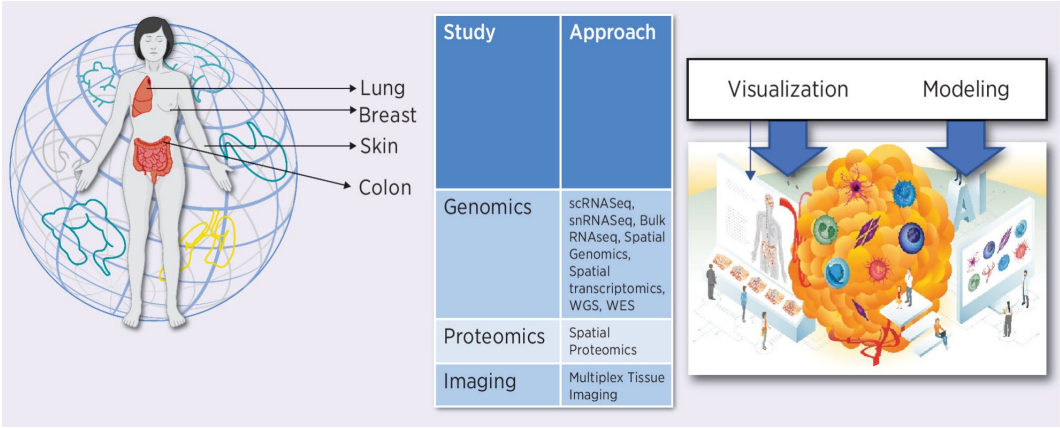
- I have no financial relationships to disclose.

- Opinions expressed are mine alone and should not be interpreted as representing the official viewpoint of the U.S. Department of Health and Human Services, the National Institutes of Health, the National Cancer Institute, or the Division of Cancer Prevention.

Precancer Atlas

Gateway to comprehensive knowledge of

- alterations in the microenvironment
- their interplay, which drives cancer progression at its earliest stages



Srivastava et al, Cancer Prev Res (Phila). 2023

Systematic efforts to

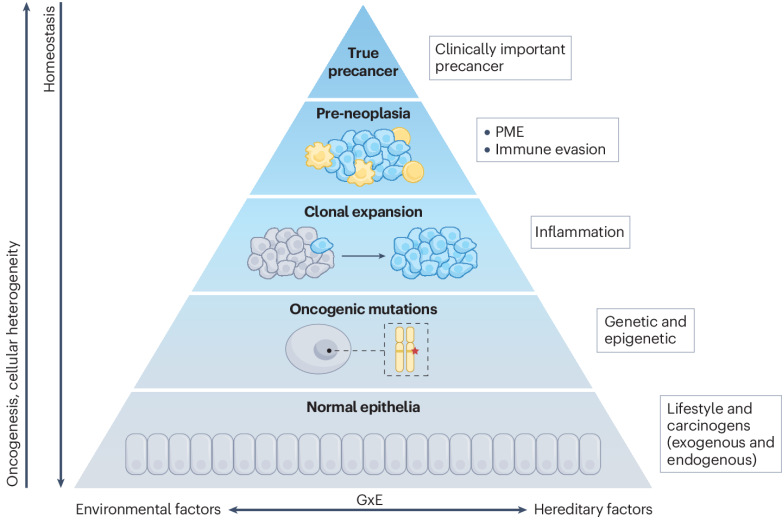
- longitudinally collect and
- perform molecular and cellular profiling of premalignant lesions in time and space as they progress towards frank malignancy

Definition of Precancer

Precancerous lesions are regions of histologically and/or molecularly abnormal tissues that more often progress to invasive carcinoma than healthy or normal tissue.

Precancers can be defined as lesions

- that may or are likely to progress to invasive cancer
- where there is clear evidence of an association with increased risk of invasive cancer
- which are different from normal cells and share molecular and phenotypic features with invasive cancer



Faupel-Badger, J., Kohaar, I., Srivastava, S. et al. Nat Rev Cancer, 2024

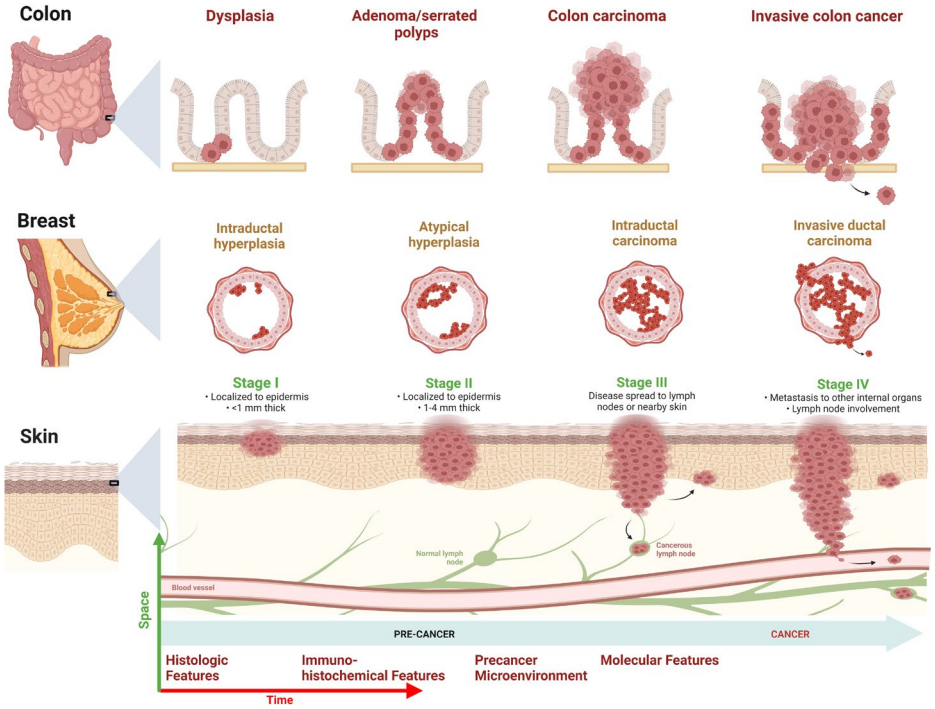
Examples of Precancerous Lesions

Precancers of solid tumors

- Barrett's Esophagus
- DCIS (HTAN Phase 1)
- Colon polyps (HTAN Phase 1)
- Oral Submucous Fibrosis
- PanIN (HTAN Phase 2)
- Cervical Dysplasia

Precancers of hematological malignancies

- MGUS (HTAN Phase 2)
- Smoldering myeloma



Kohaar et al, Hematol Oncol Clin North Am. 2024

Precancer Many Unknowns!!!

- Which biological, molecular, radiological, and pathological features should be considered when defining precancer?
- Individuals at high risk: What special considerations should be included in defining precancer? How do germline variants influence the risk or incidence of precancer?
- How do somatic mutations in phenotypically normal tissue and their consequences affect the analysis of precancer?
- How early do somatic mutations interface with the microenvironment? What is the interplay between somatic mutations and the microenvironment?
- Which biological, molecular, immunological, and pathological features distinguish progressors from non-progressors?

The integration of molecular/cellular data with quantitative imaging data as well as clinical data is necessary

Purpose of Pre-Cancer Atlases

- Clinical Needs: More precise risk assessment, prevention and early detection

- Objective: A multidimensional cellular, morphological and molecular mapping of pre-malignant tumors along with geospatial information to understand
  - heterogeneity of tumors
  - when pre-cancers progress or regress to consequential cancers
  - key cellular and molecular features that can predict progression
  - targets for cancer interception and early detection
  - use/development of computational tools for atlas construction and visualization

Seminal Discoveries: HTAN PCA Phase 1

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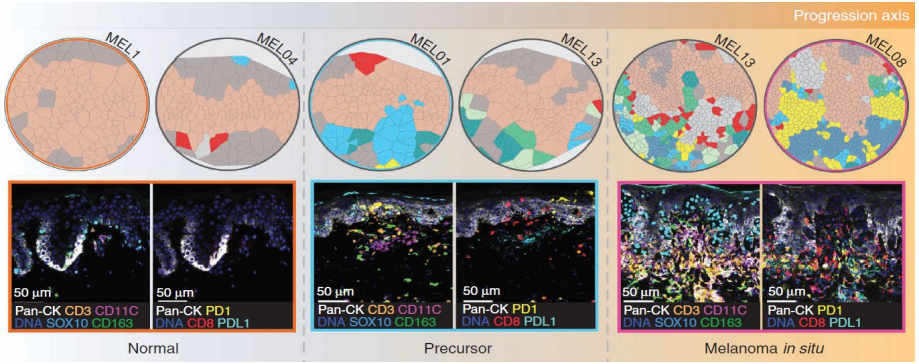
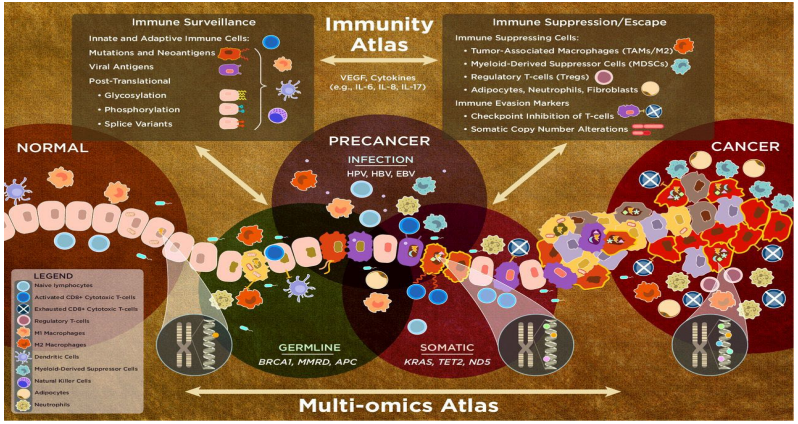
- A genomic classifier based on the epithelial and stromal features predicts both recurrence and invasive progression in primary DCIS
- Intestinal stem cells found to drive growth trajectory in FAP polyps
- Identification of novel targets in infant leukemia via paired single-cell epigenomics and transcriptomics



Adapted from Nirmal, Maligna, Vallius et al. Cancer Discovery 2022



Campbell et al., Cancer Prevention Research, 2016

- Immune landscape is poorly understood for screen-detected and interval lesions and the changes within their immune milieu over time during critical transitions in cancer.
- Immune cell infiltration is noted as early as the pre-proliferative state of LUSC
- Spatially restricted multicellular immune networks differentiate MMRd and MMRp colon cancer and drive progression

HTAN PCA Phase 2

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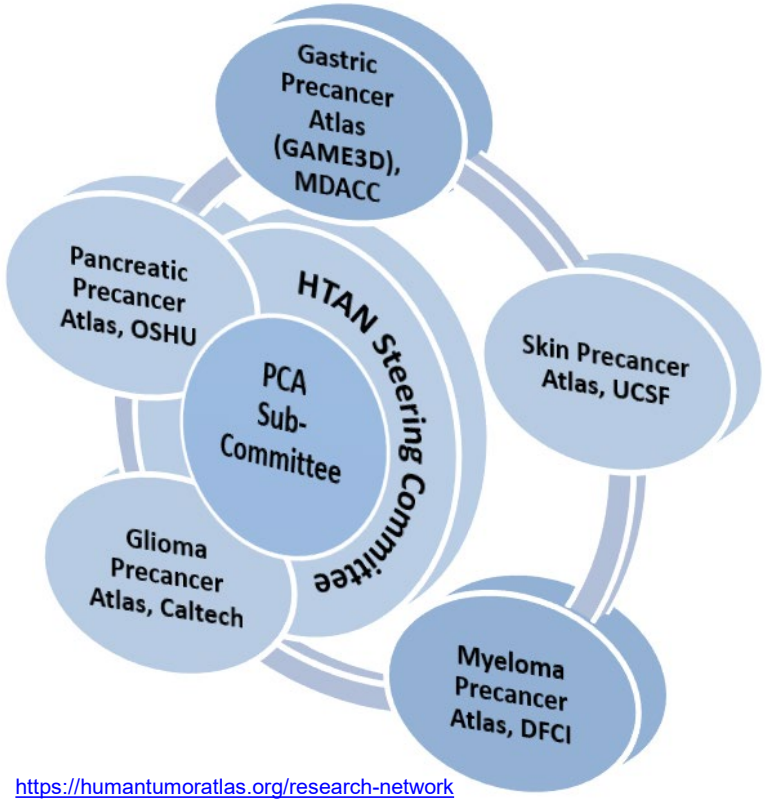
- Five PCA centers under HTAN Phase 2: Skin, Glioma, Myeloma, Pancreas, and Gastric
- 2-D/3-D Atlas building using state-of-the-art technologies for spatial genomics/transcriptomics, imaging, and proteomics in bulk and single cell analysis
- Rich biospecimen resources and computational tools for atlas building



https://humantumoratlas.org/research-network

PCA- Key to Early Disease Detection and Interception

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Expected Outcomes of PCA Research Centers

- Improved understanding of disease initiation and progression
- Characterize heterogeneity
- Quantify the dynamics and multidimensional architecture
- Identify novel biomarkers
- Predictive modeling of pre-malignant to malignant transition

How can you be part of the HTAN?

- Associate Membership:
  - HTAN offers researchers not currently funded by HTAN the opportunity to apply to join the program as non-voting Associate Members.
  - For Associate Membership, contact HTAN Data Coordinating Center (htan.dcc@ds.dfci.harvard.edu)
  - Engage in HTAN Consortium activities through working groups, annual meetings, and developing collaborations
- Freely available HTAN Data use
- Educational Training, Workshops, and Networking
- Participation in the PCA Subcommittee as an Ad hoc/Associate Member


Translational WG


Advisory Committee for Data Coordination


Computational Alignment WG


Methods WG


Visualization WG


Outreach WG

HTAN PCA Program Contact: NCI_HTAN_PCAU2C@mail.nih.gov

Important Resources

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- HTAN PCA Program:

  Scan to view HTAN PCA Program →

- HTAN Data Portal:

  Scan to view data portal →

PCA Subcommittee listserv:
PCA-SUB-COMM@LIST.NIH.GOV

Please feel free to reach out:
indu.kohaar@nih.gov ; srivasts@mail.nih.gov

Check out HTAN PCA Presentations in AACR 2025

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- Method Workshop Session (MW01) - Integrating Computational Pathology, AI, and Spatial Multi-Omics in 2D and 3D (April 26, 2025, 8:00 AM - 9:30 AM; Room S102 - McCormick Place South; Level 1)
  - Precision mapping of tumor ecosystems via computational pathology and spatial multi-omics (Linghua Wang)
  - AI-driven 3D spatial mapping of the tumor immune microenvironment for precision oncology (Tae Hyun Hwang)
- Single-cell spatial multi-omics for mapping cell organization, interactions, and functional niches (Linghua Wang; Session: Advances in Technologies; Session AT04 - Integrating Multi-Omics and Spatial Technologies for Discovery and Prediction)
- Inflammation and cancer: From basic mechanisms to therapeutic targets (Lisa M. Coussens; Session SY48 - Targeting Innate Immune Cell Subsets)
- Modeling emergent cell behaviors in the TME with virtual cells (Elana Judith Fertig; Session MW02 - Application of AI and Natural Language Processing to Advance Cancer Research and Treatment)
- Modeling the progression to pancreatic tumor invasion from in silico to human fibroblast-epithelial interactions (Elana Judith Fertig; Session Type: Advances in Prevention Research; Session APRV05 - New Game Plan for Cancer Prevention: Tackling Neoplasms by Intercepting the Host Microenvironment)

THANK YOU!

Please feel free to reach out:

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