

# Integrating multiplexed imaging with collagen imaging to characterize patterns of cell-extracellular matrix (ECM) architecture in lung cancer

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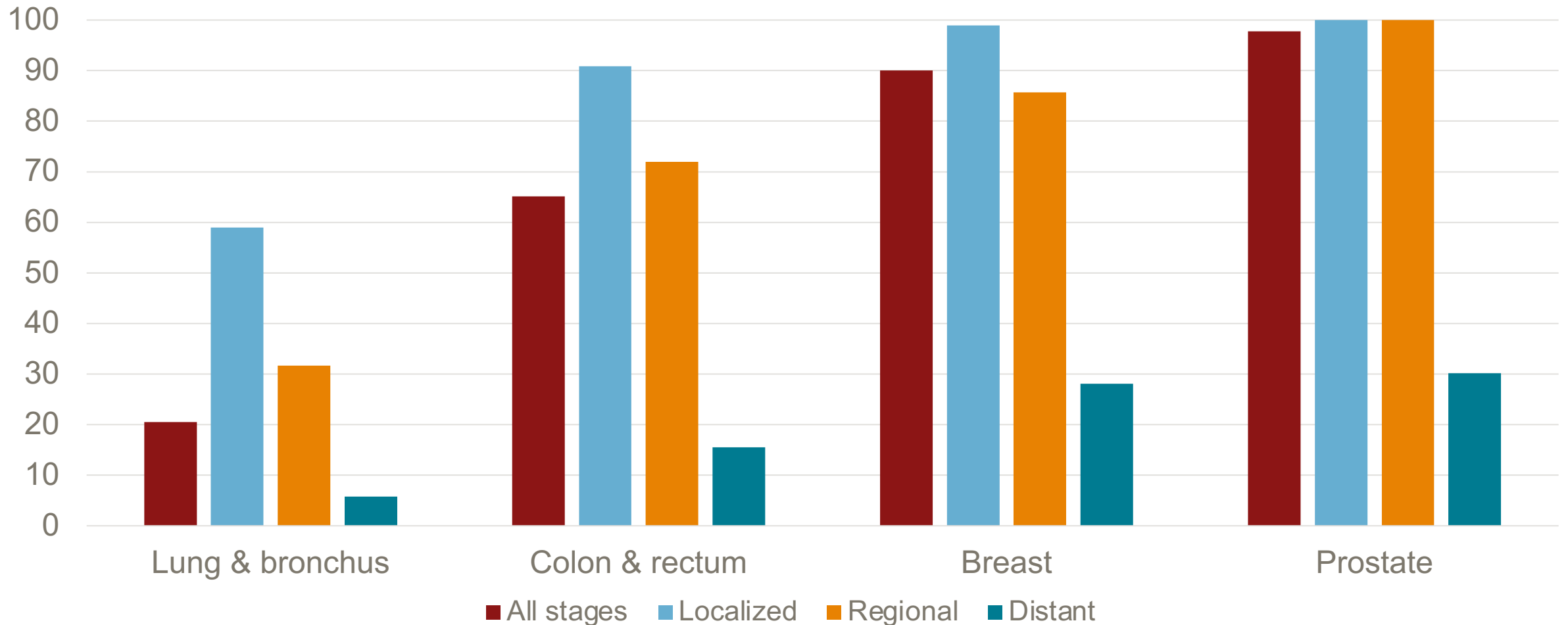
Stanford Cancer Imaging Training (SCIT) Seminar

July 6, 2022

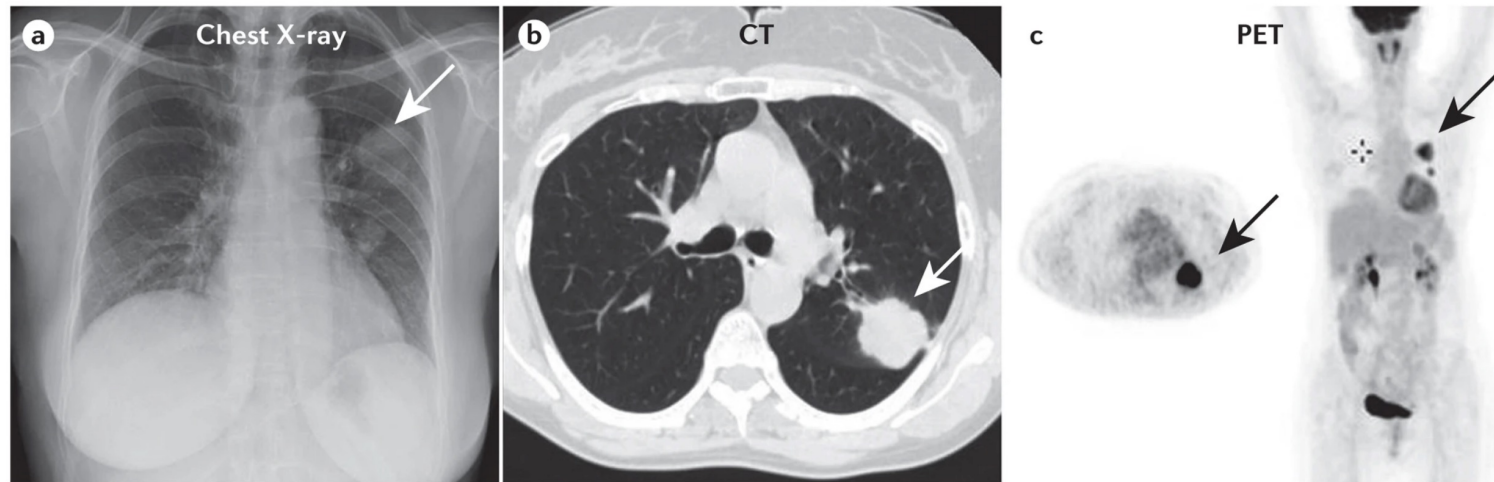


# Lung cancer survival lags behind other common cancers

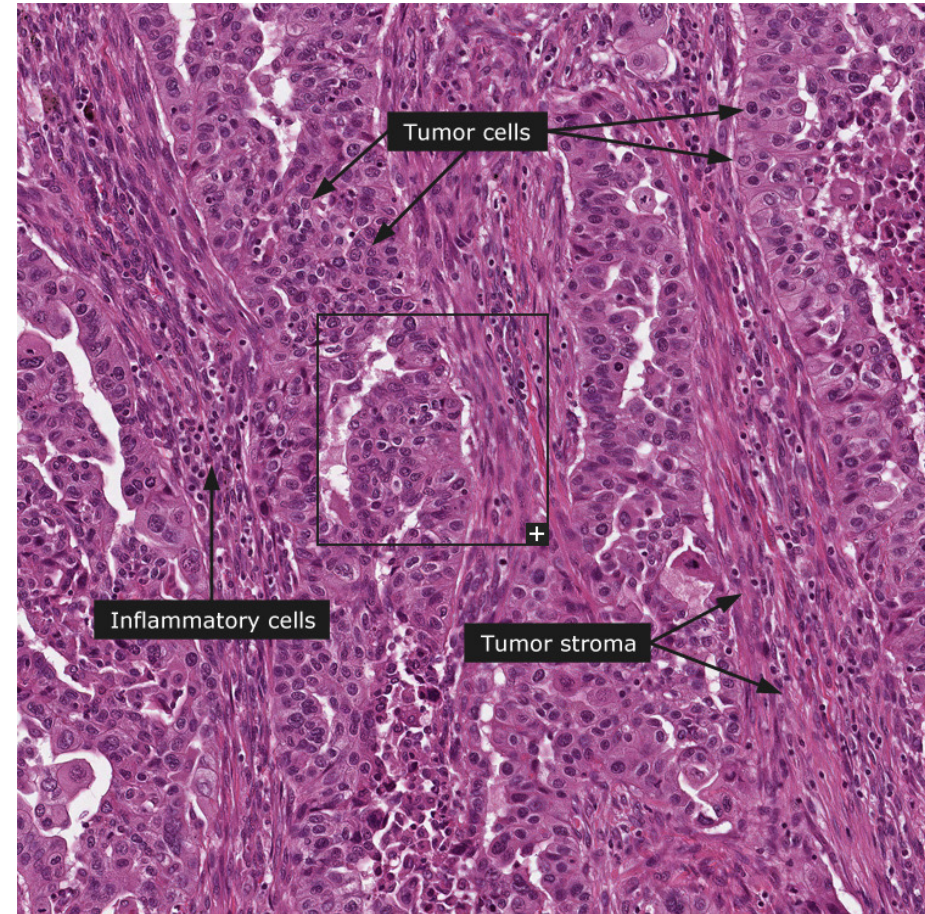
5-year survival rates (%) by cancer site and stage at diagnosis



# Diagnostic imaging and pathology

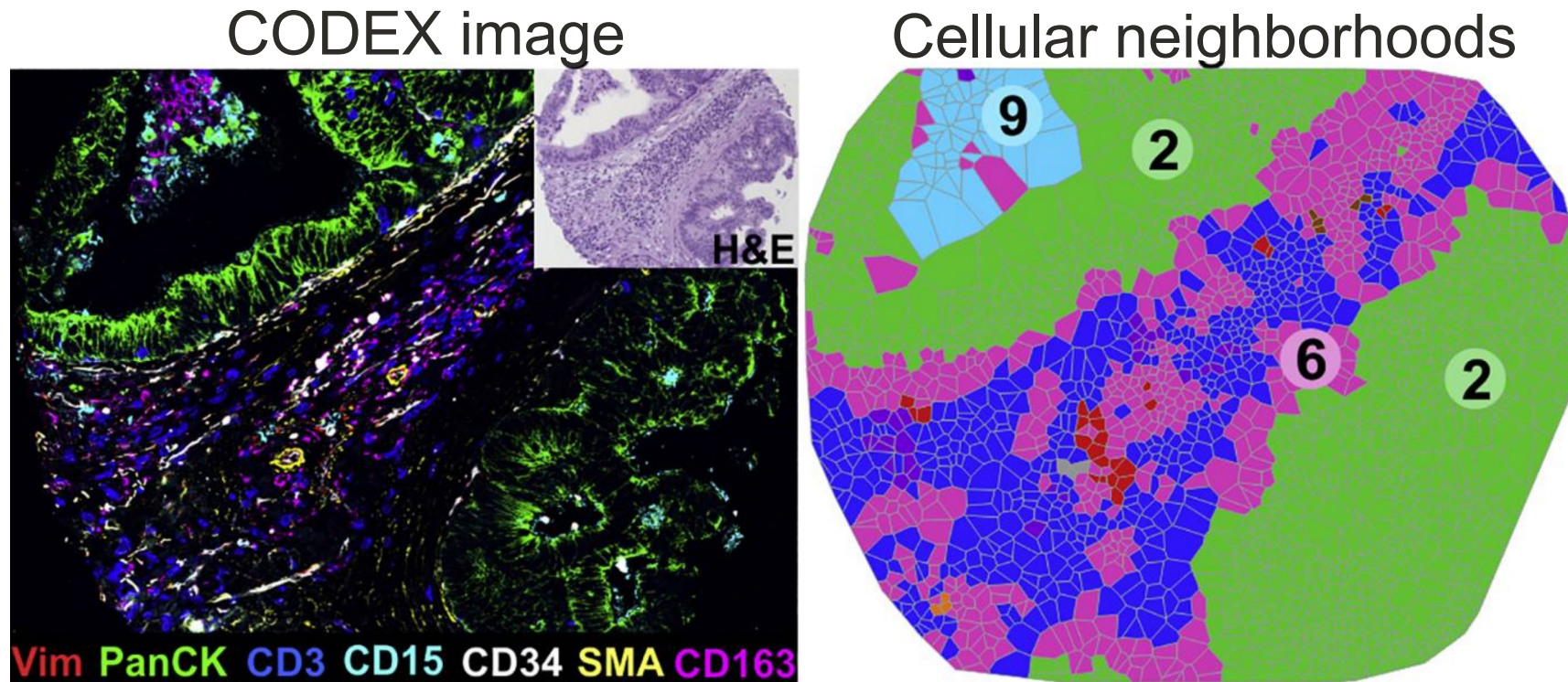


Gridelli et al., *Nature Rev Dis Primers* 2015



*The Human Protein Atlas*

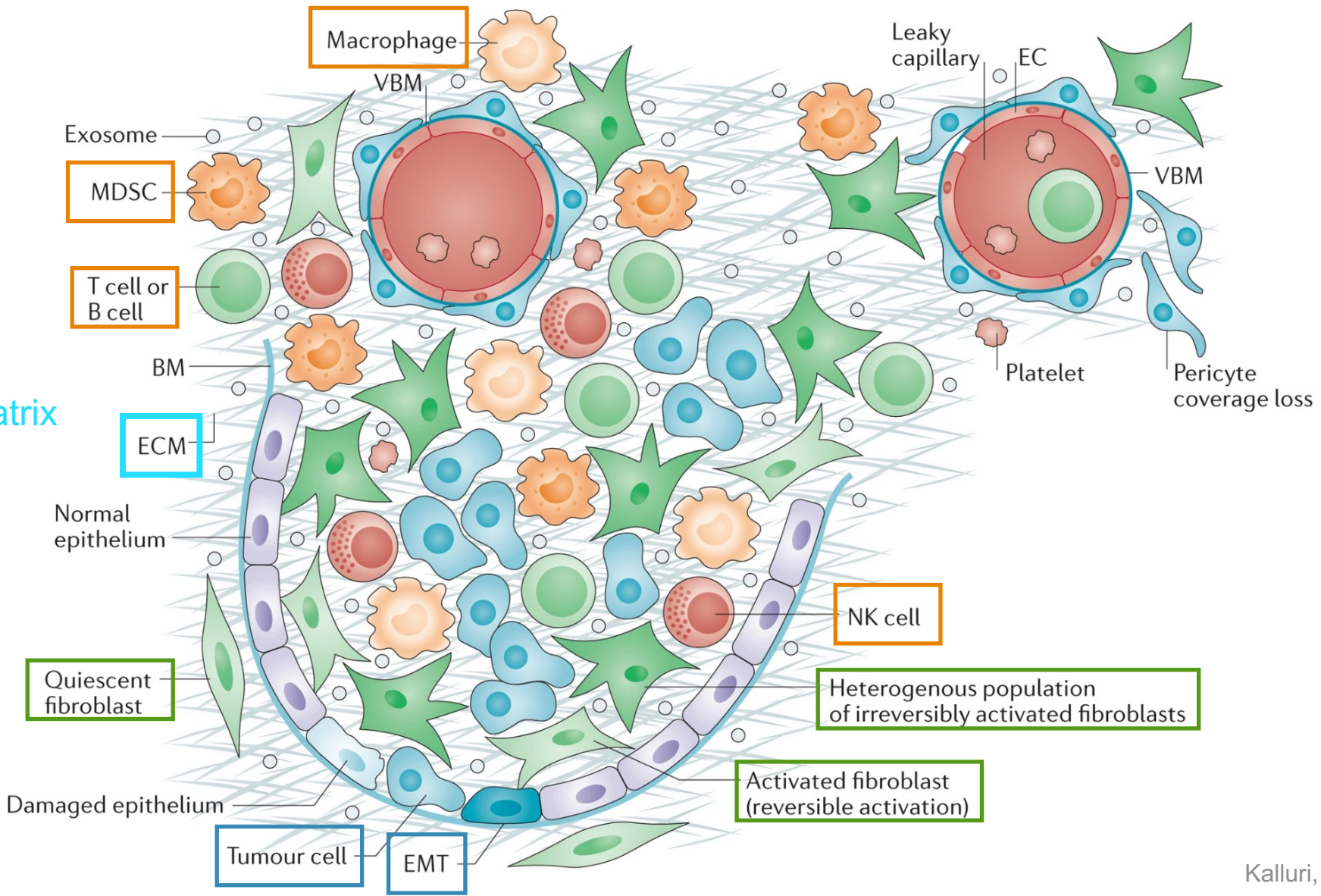
# CODEX reveals cellular spatial heterogeneity



# Heterogeneity in the tumor microenvironment

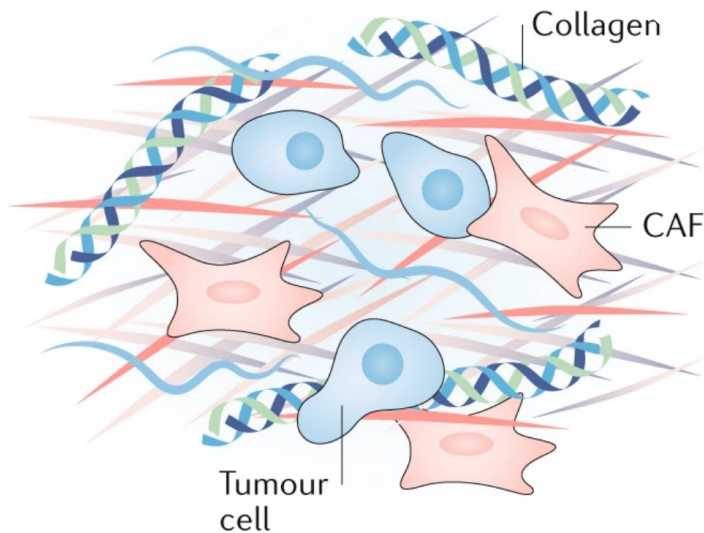
Tumor cells  
Immune cells  
Fibroblasts

Extracellular matrix  
(e.g. collagen)

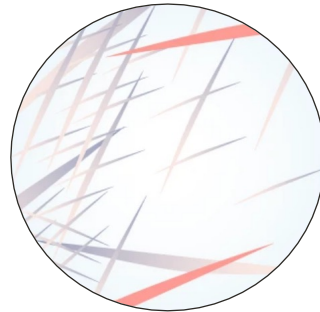


# Cancer-associated extracellular matrix (ECM) changes

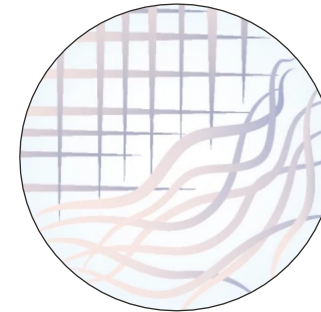
- **Extracellular matrix (ECM):** meshwork of proteins, etc. outside the cell
  - Provides structure and signals to cells
  - Deposited, remodeled, degraded by cells



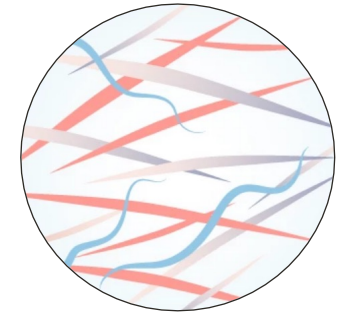
## Amount



## Organization



## Composition



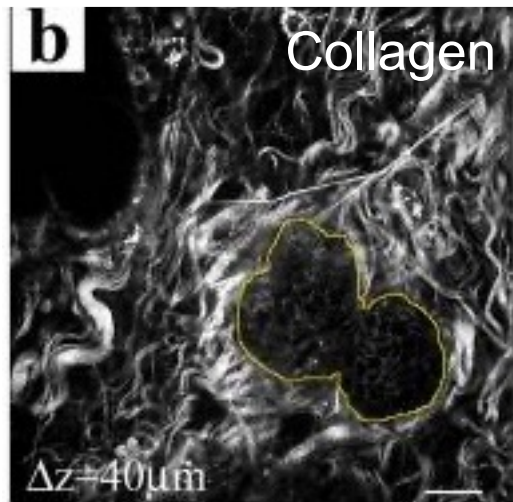
## Effects on cells in the tumor microenvironment:

- Remodeling by cancer-associated fibroblasts (CAFs)
- Physically guides cancer cell migration
- Blocks T cell infiltration into tumor
- Increases drug resistance by blocking drug diffusion

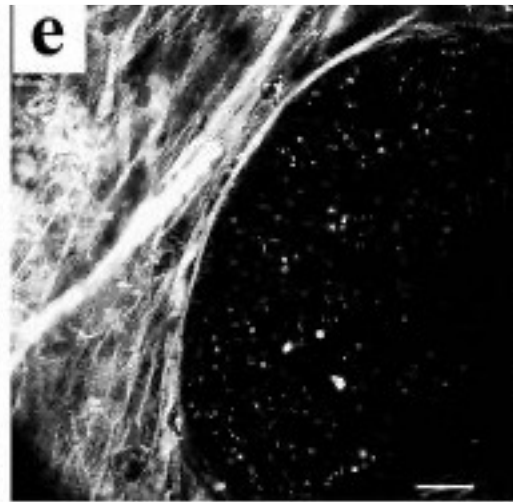
# Aligned collagen is prognostic for breast cancer

**TACS:** tumor-associated collagen signature

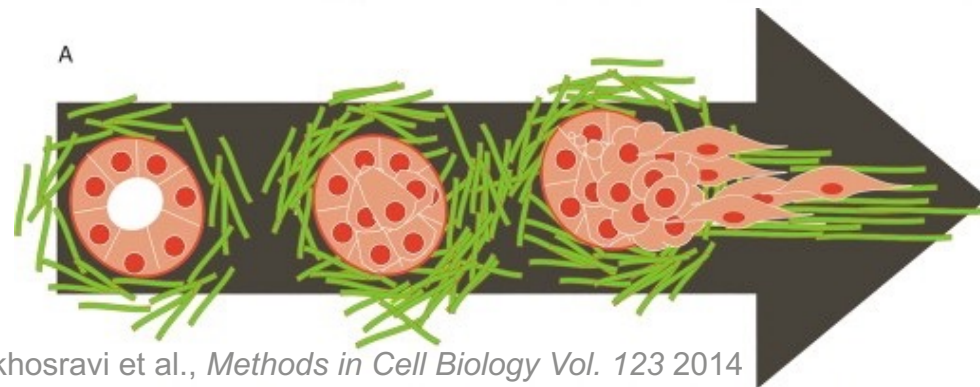
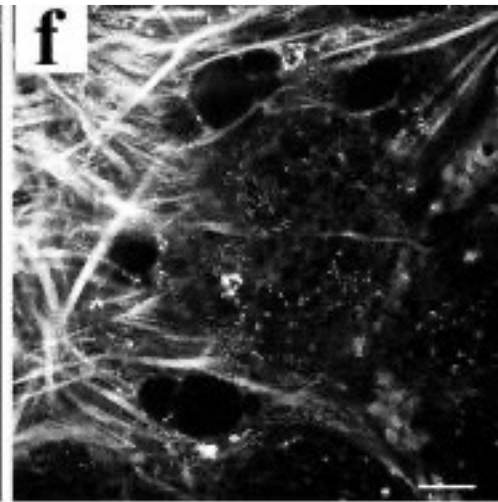
**TACS-1**



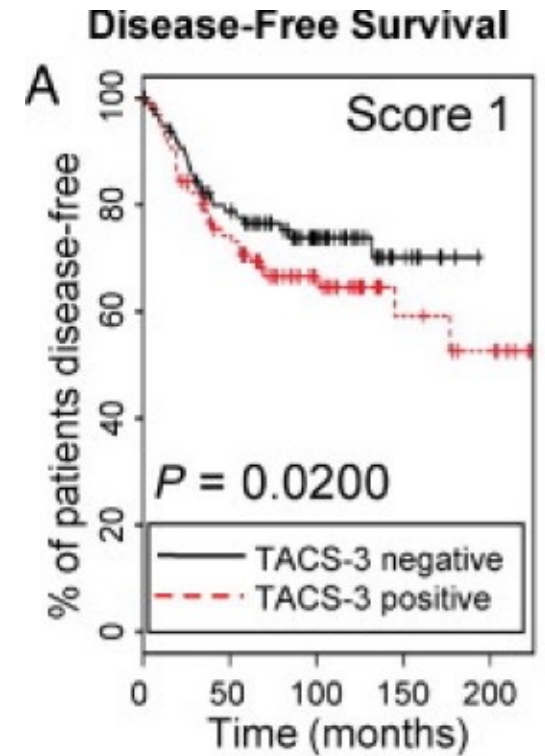
**TACS-2**



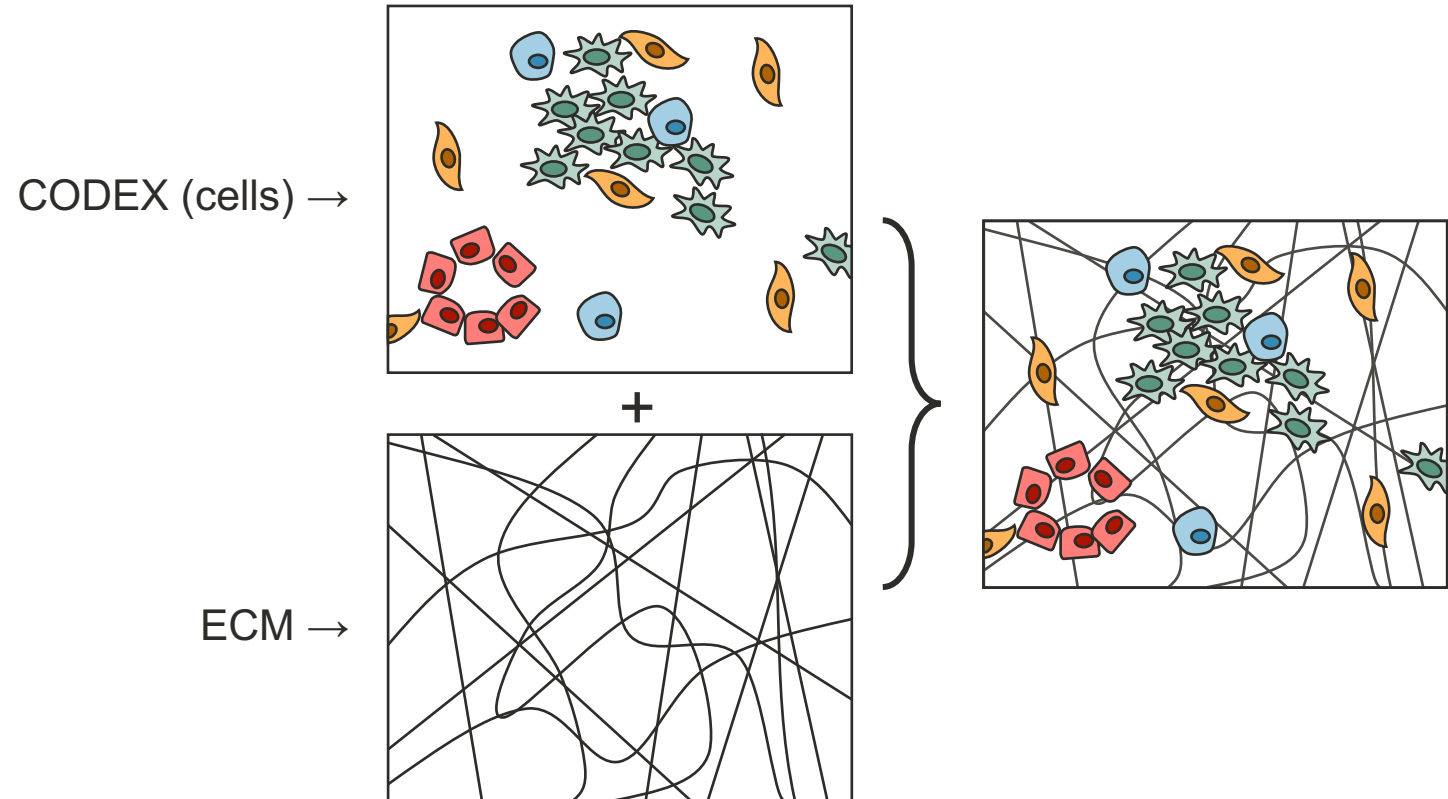
**TACS-3**



Keikhosravi et al., *Methods in Cell Biology* Vol. 123 2014



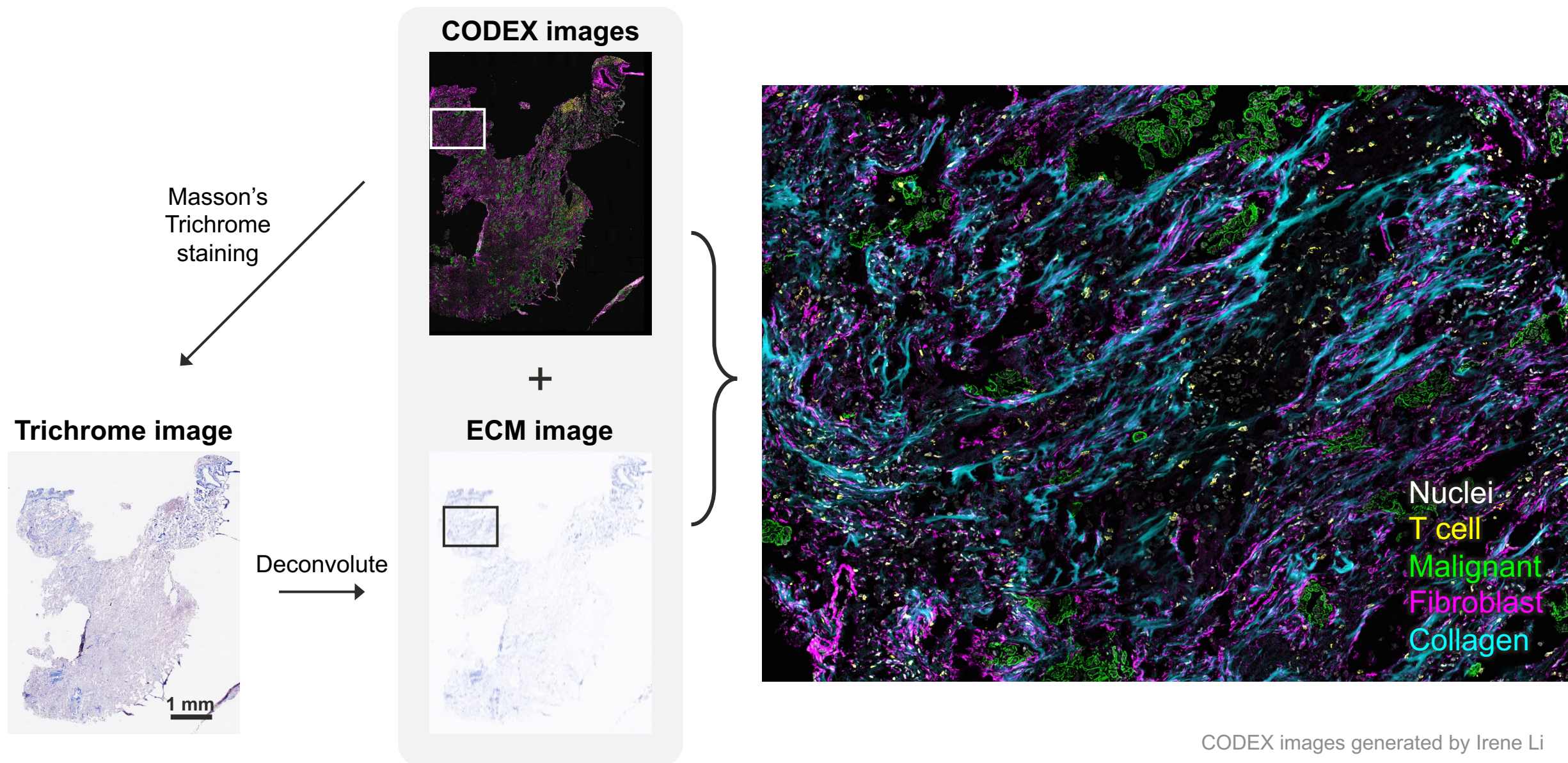
# Overall goal: characterize spatial patterns of cell-ECM associations in lung cancer using imaging





# Methods

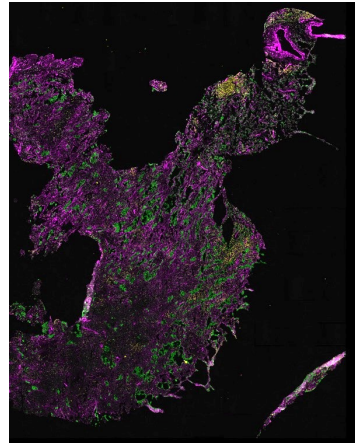
# Collagen ECM visualized by Masson's Trichrome staining



# Data collection and integration

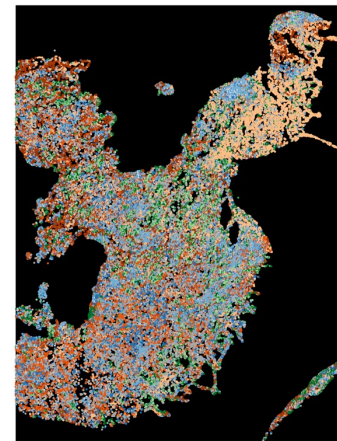
with Irene Li, Weiruo Zhang

**CODEX images**



Process → Segment

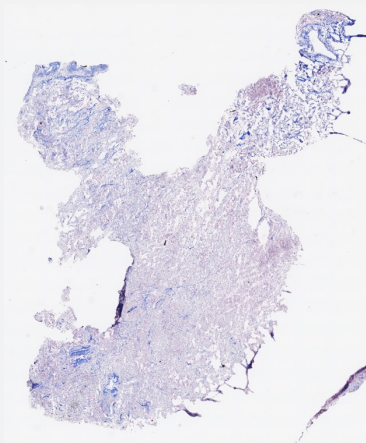
**Cell type identification (CELESTA)**



Zhang et al. *Nat Methods* 2022

Cell-ECM  
analysis

**Trichrome image**

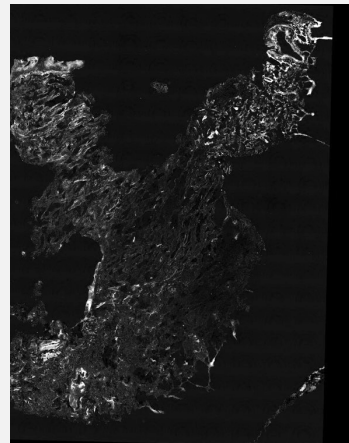


Deconvolute →

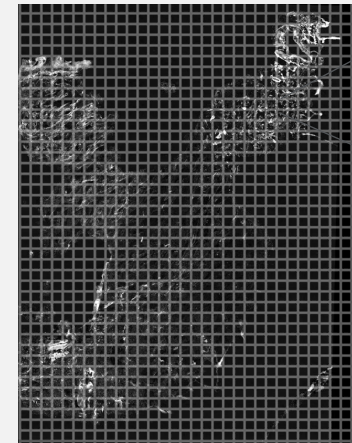
**ECM image**



Register  
Invert

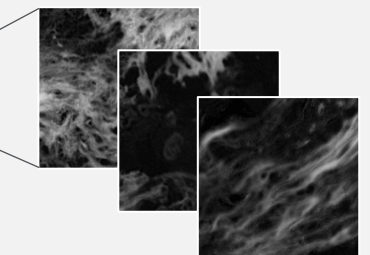


Patch →



100 µm x 100 µm patches

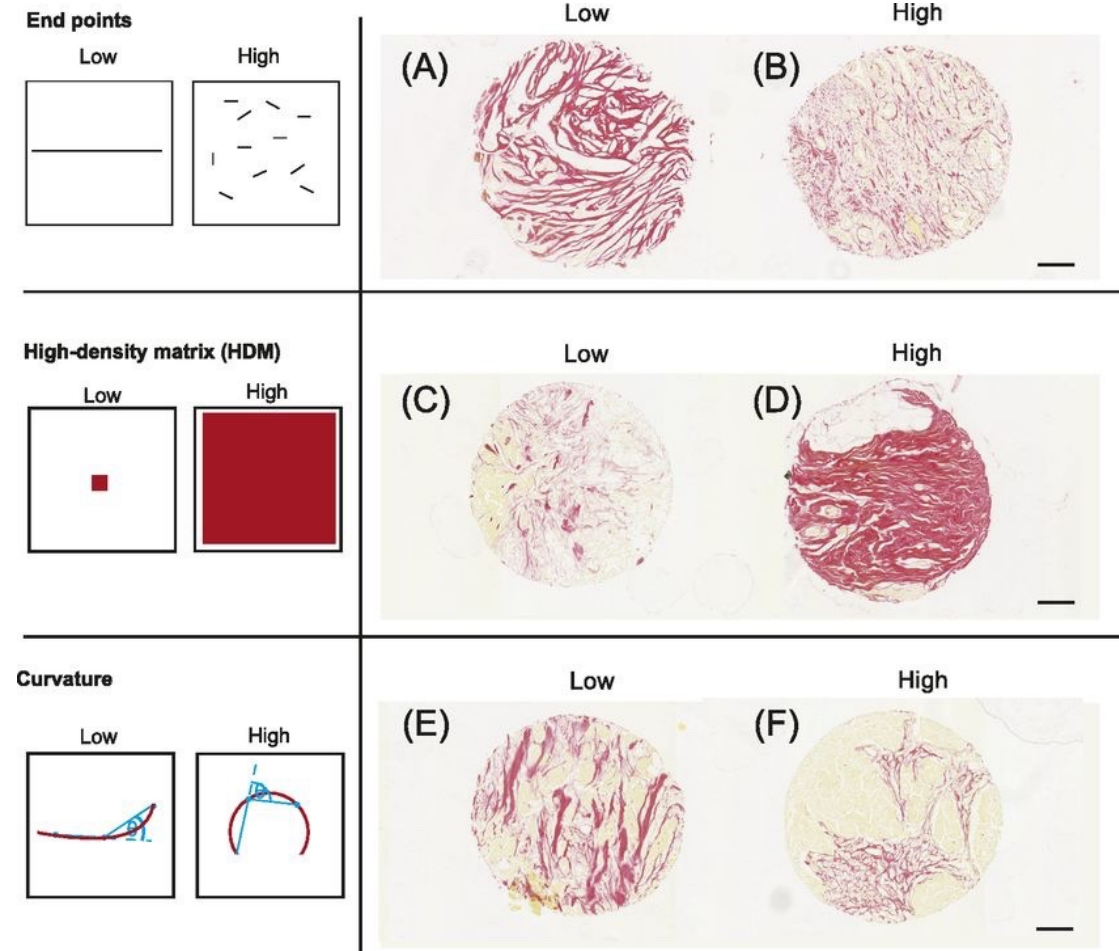
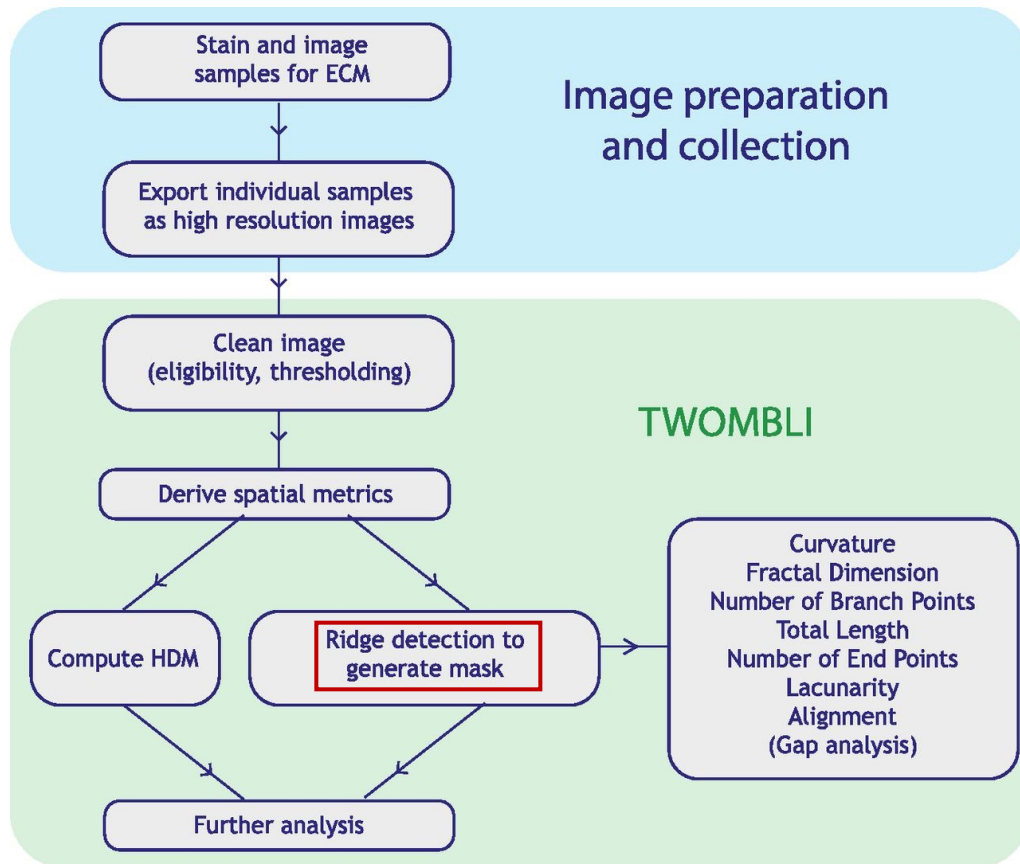
**ECM feature extraction**



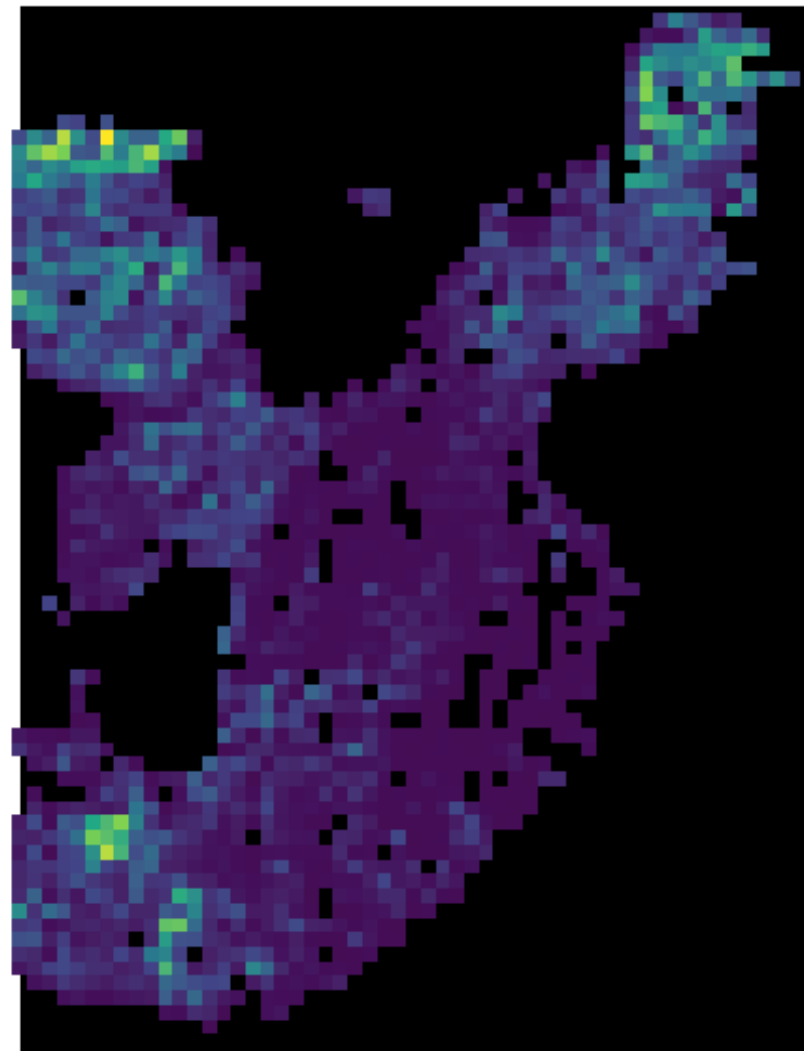
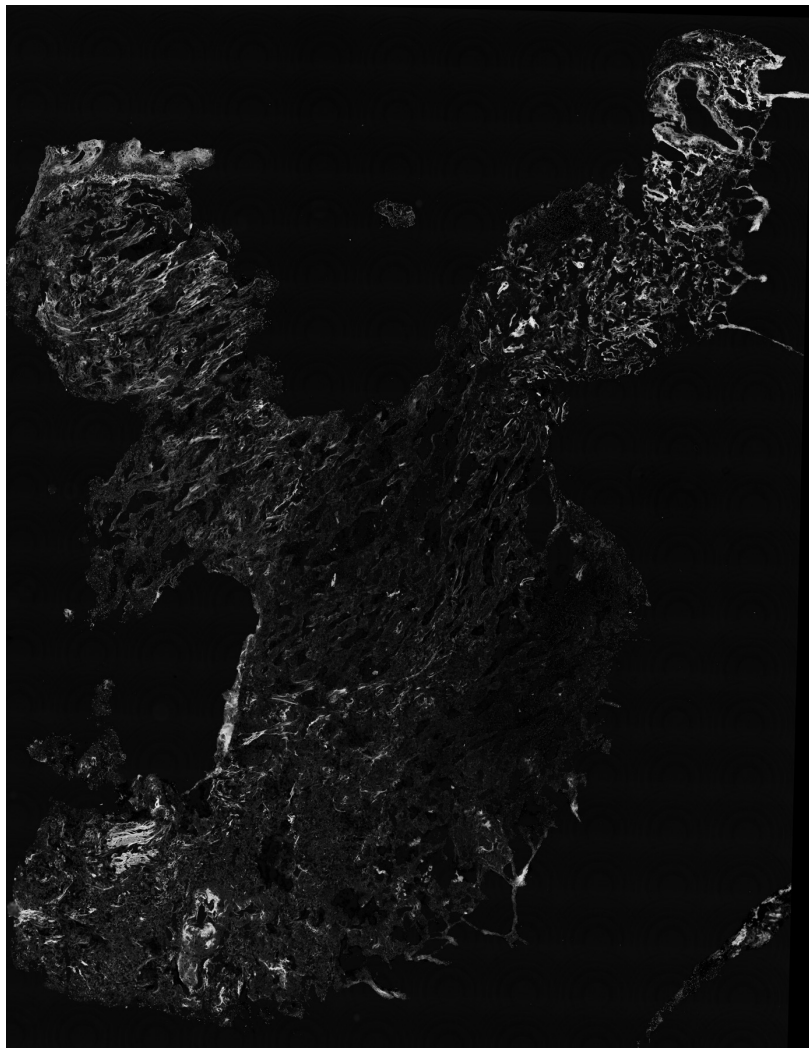
Features →

Patches ↓	52.828	0.732	0.1030	...
	81.648	0.193	0.0629	...
	35.056	0.306	0.5303	...
	...	...	...	...

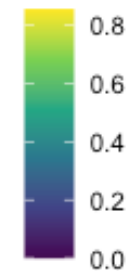
# TWOMBLI overview: FIJI macro to quantify ECM patterns



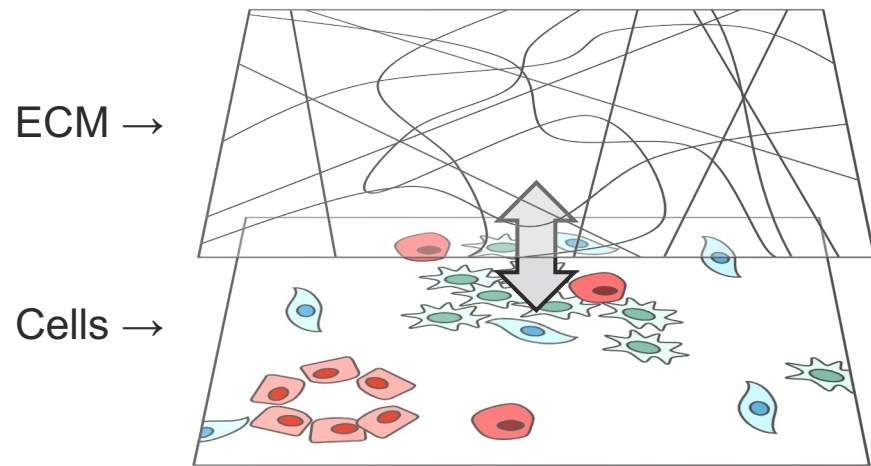
# Patch-based features: ECM density



1803 patches



# Summary



- Developing analysis pipeline to spatially profile cell-ECM associations
- ECM architecture varies by nodal status and is associated with shifts in cell type composition

**Next steps:** further characterization of spatial associations, validation

# Thank you!

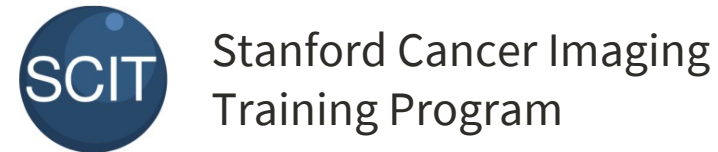
## Mentors

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Yuanyuan Li, Ph.D.  
Weiruo Zhang, Ph.D.



## Longaker Lab

## Thoracic Surgery

Joseph Shrager, M.D.



**Patients who have donated their tissue for research**