Characterizing patterns of cell-ECM architecture in lung tumor tissue using imaging

Aaron Chiou, Ph.D.
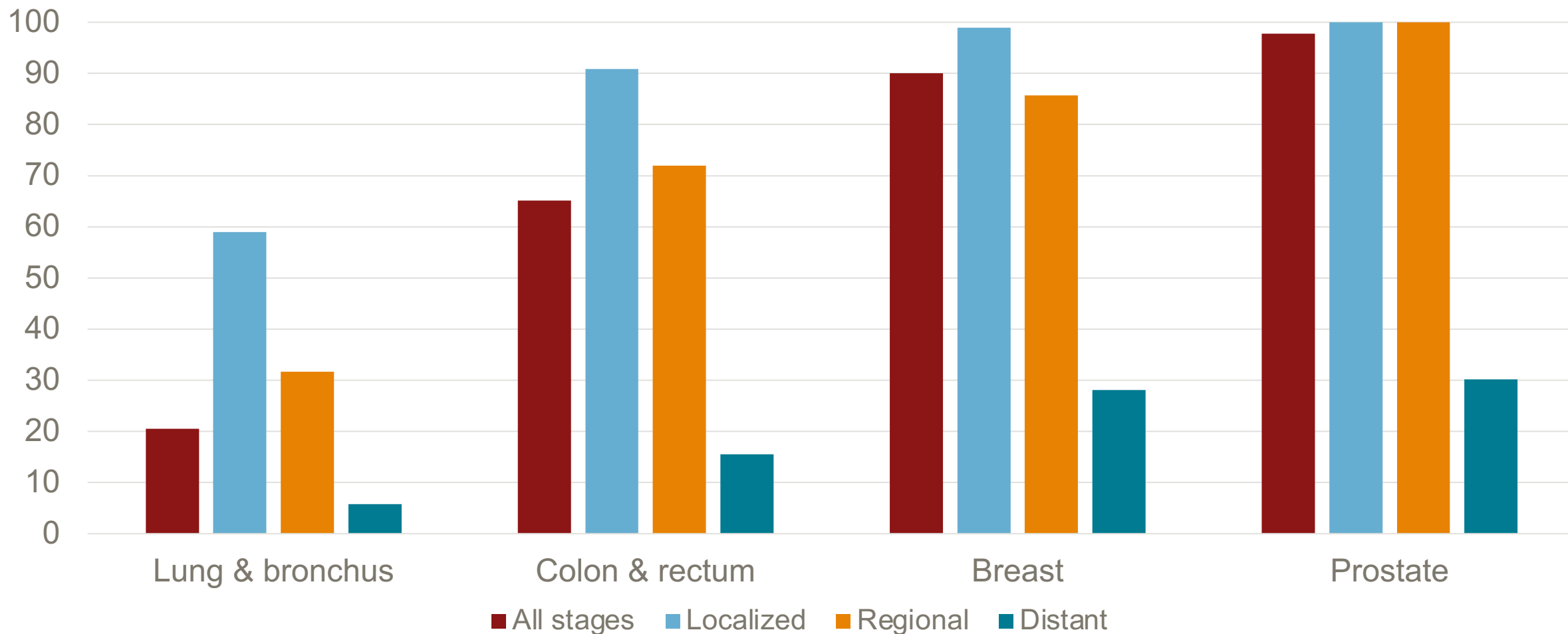
Mentors: Sylvia Plevritis, Ph.D.; Tushar Desai, M.D.
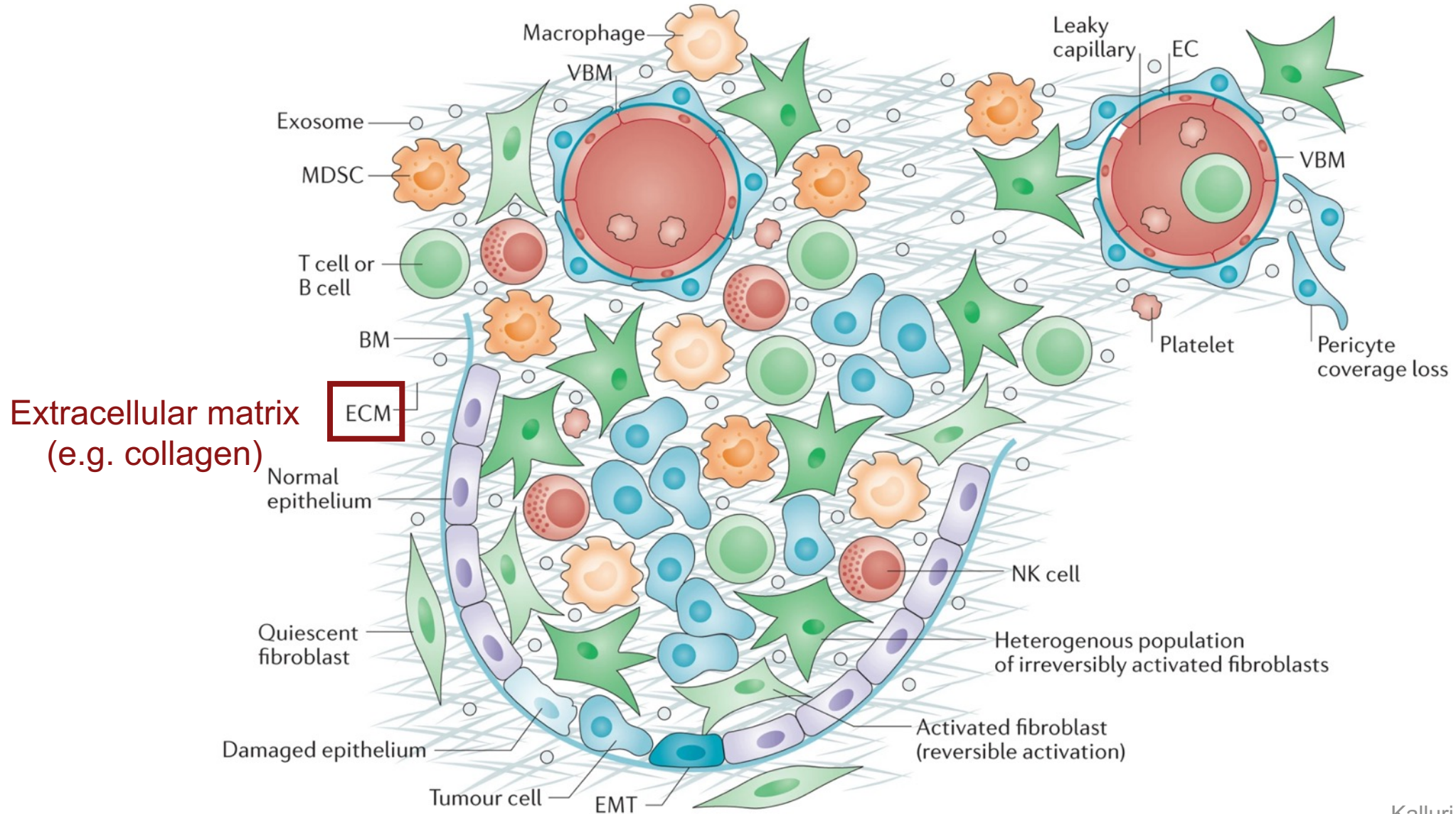
Stanford Cancer Imaging Training (SCIT) Seminar

January 12, 2022

Lung cancer survival lags behind other common cancers

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

Legend: All stages, Localized, Regional, Distant

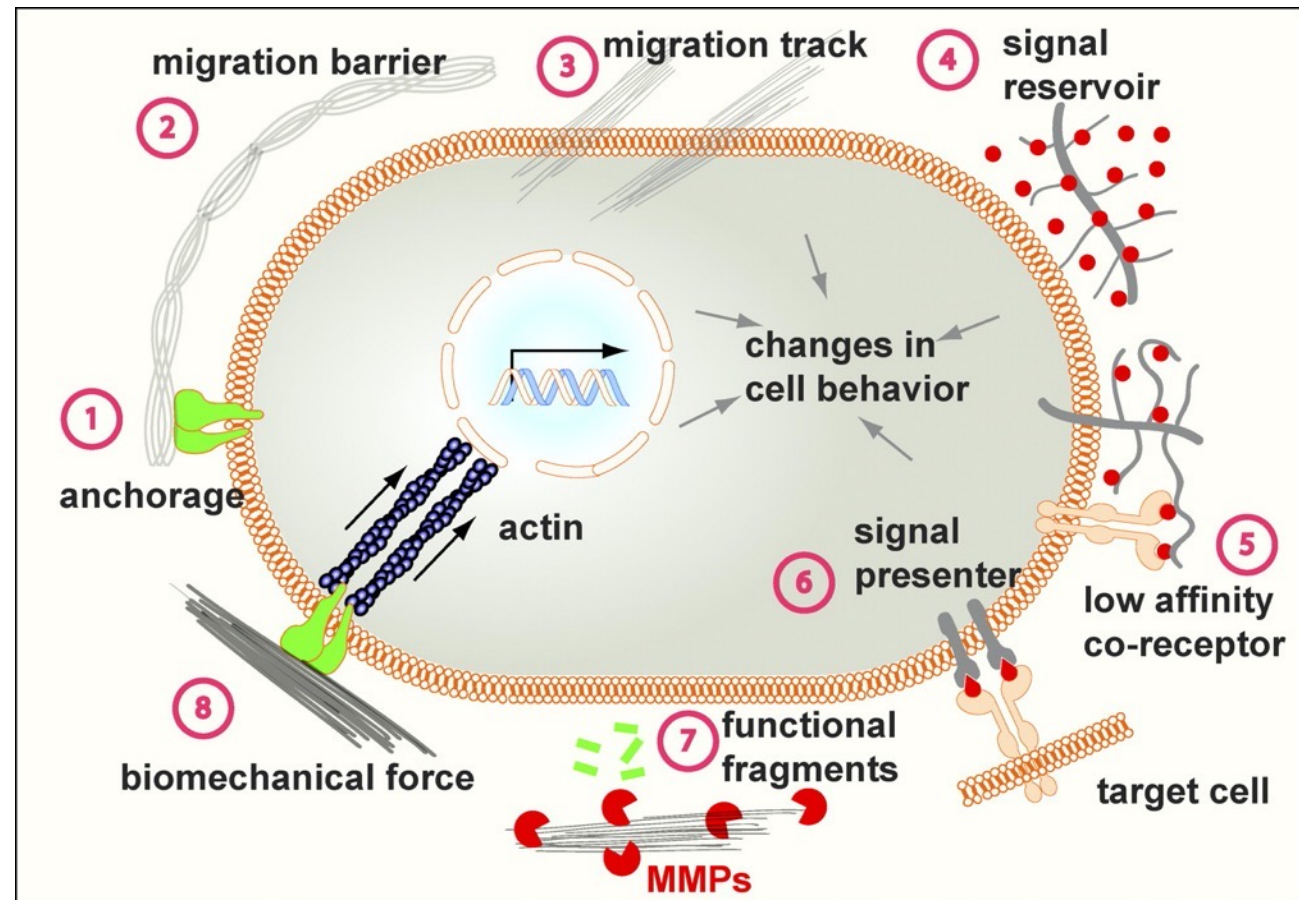Extracellular matrix (e.g. collagen)

Extracellular matrix (ECM) impacts cell behavior

- Meshwork of proteins etc. outside the cell
- Deposited, remodeled, degraded by cells

Provides:
- Structural support to tissues
- Anchorage for cells
- Biochemical and physical cues

Lu et al. *J Cell Biol* 2012

ECM and cancer

- ECM is altered in cancer
  - Amount
  - Organization
  - Composition

- Largely deposited and remodeled by cancer-associated fibroblasts (CAFs), which stiffens ECM and drives further signaling

- Physically guides cancer cell migration

- Blocks T cell infiltration into tumor

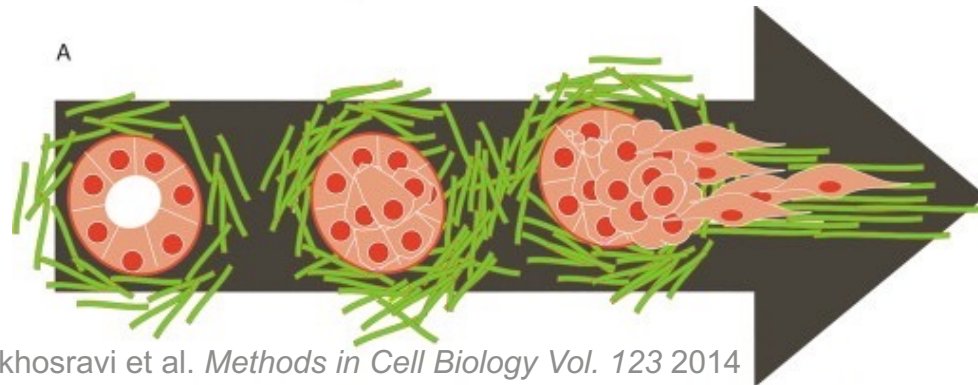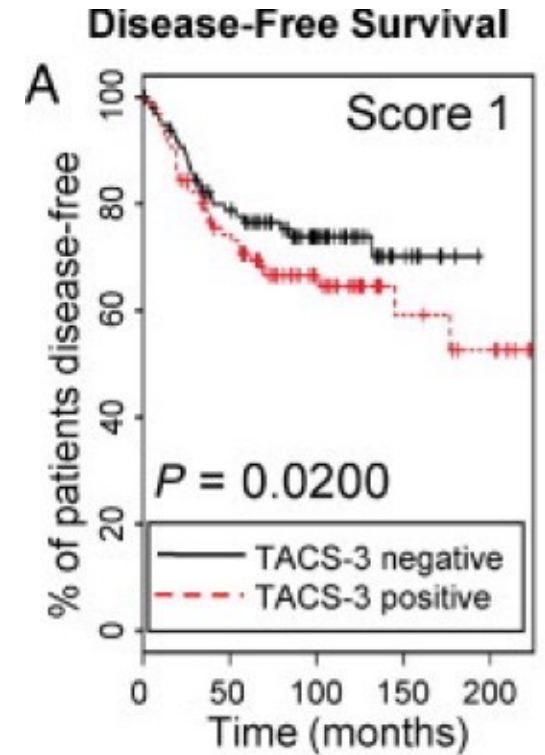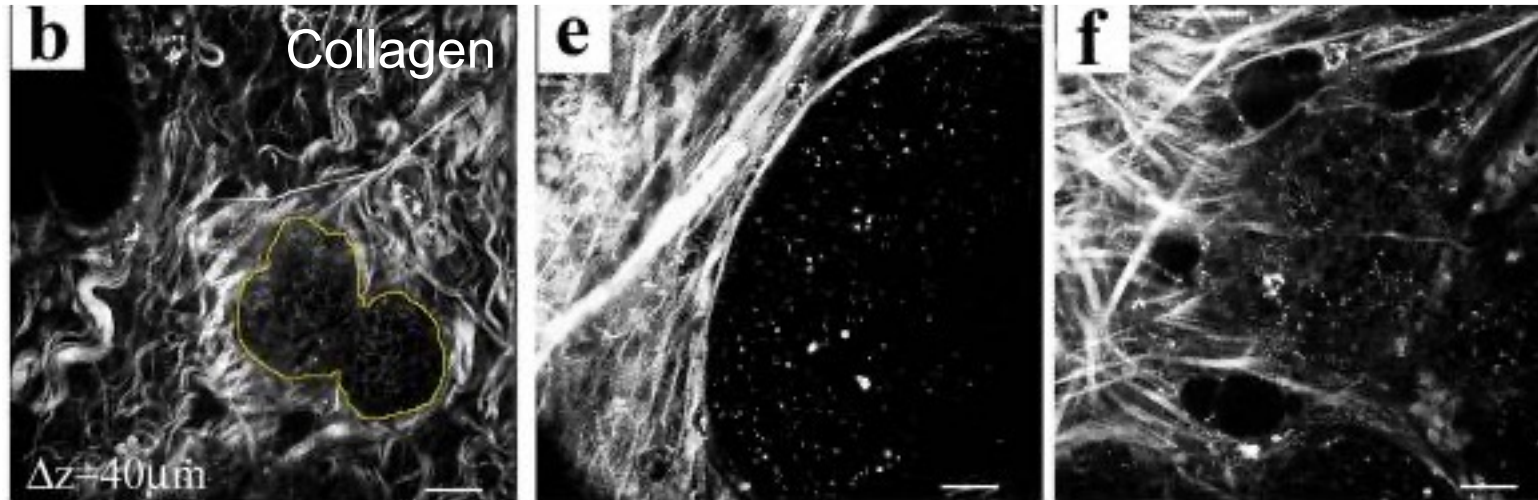- Increases drug resistance by blocking drug diffusion

Gocheva 2017; Golaraei 2020; Navab 2016

Aligned collagen is prognostic for breast cancer
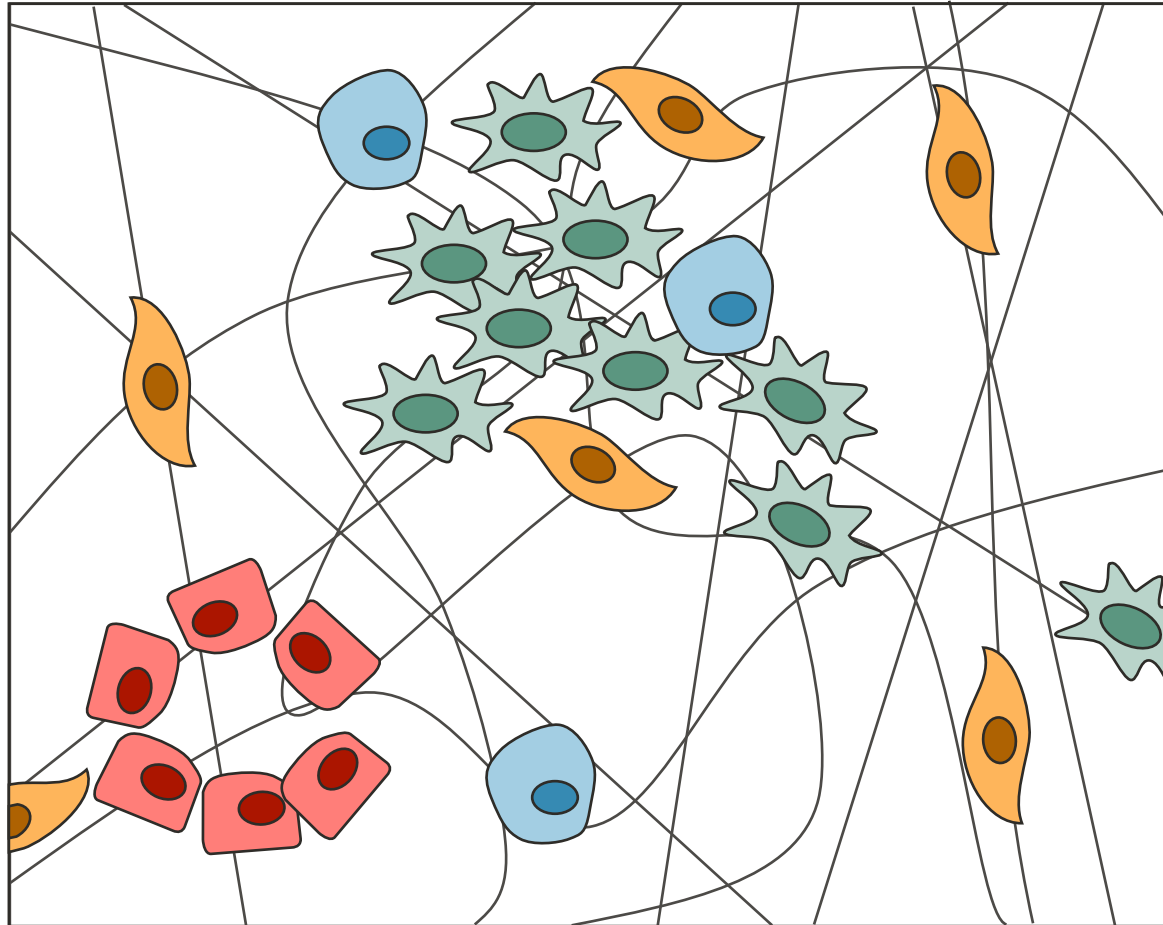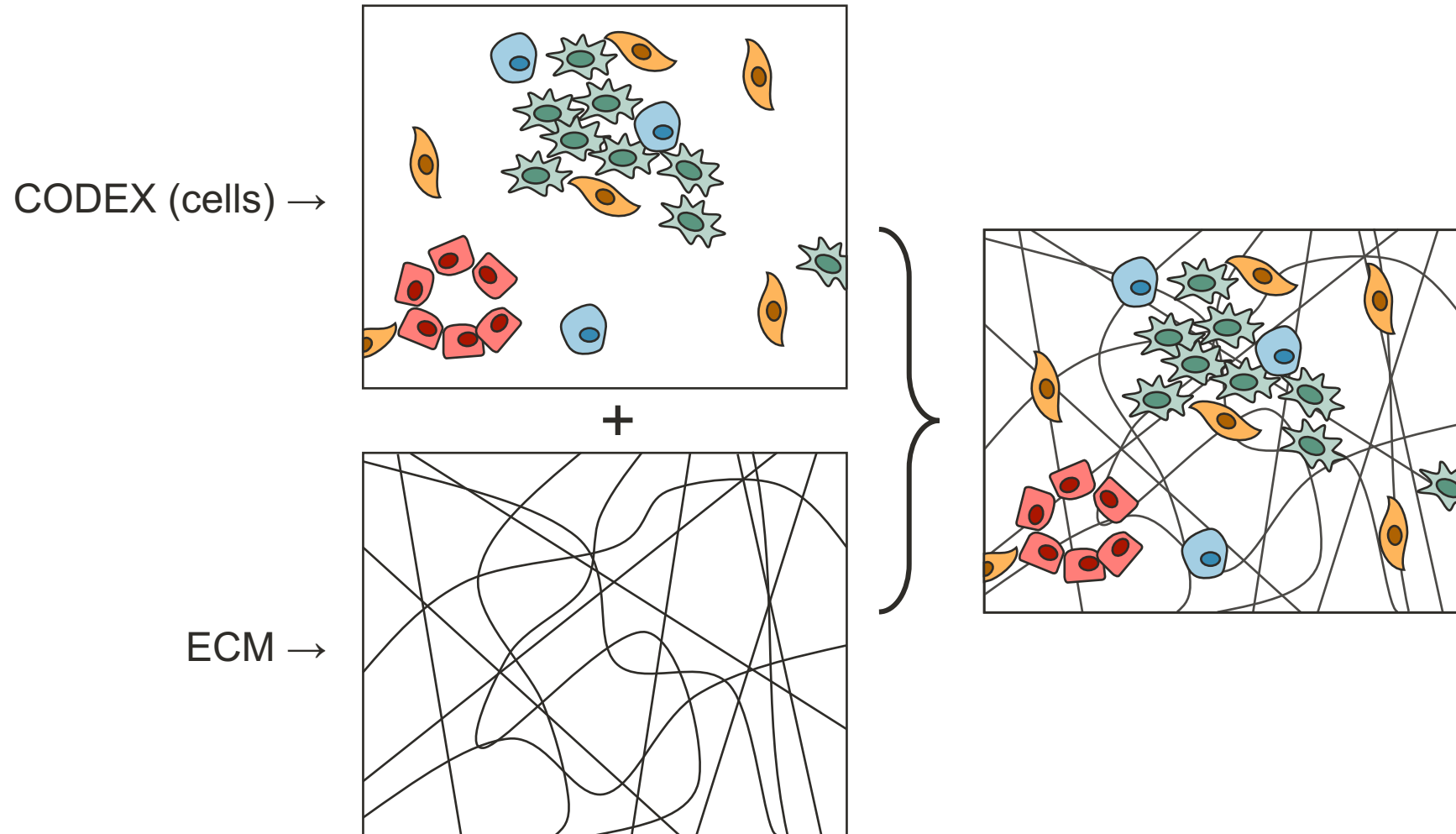
TACS: tumor-associated collagen signature

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

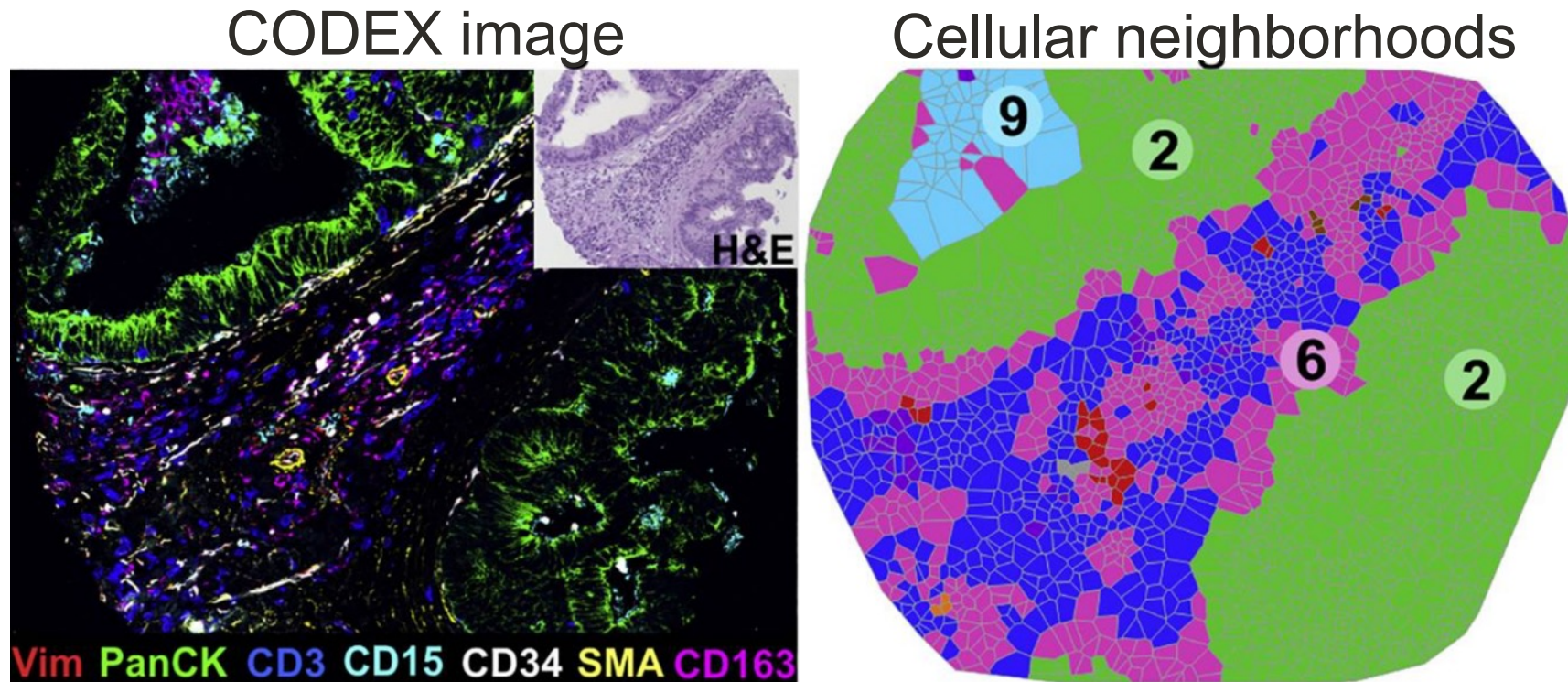Provenzano et al. *BMC Med* 2006; Provenzano et al. *BMC Med* 2008; Conklin et al. *Am J Path* 2011

Overall goal: characterize spatial patterns of cell-ECM interactions in lung cancer using imaging
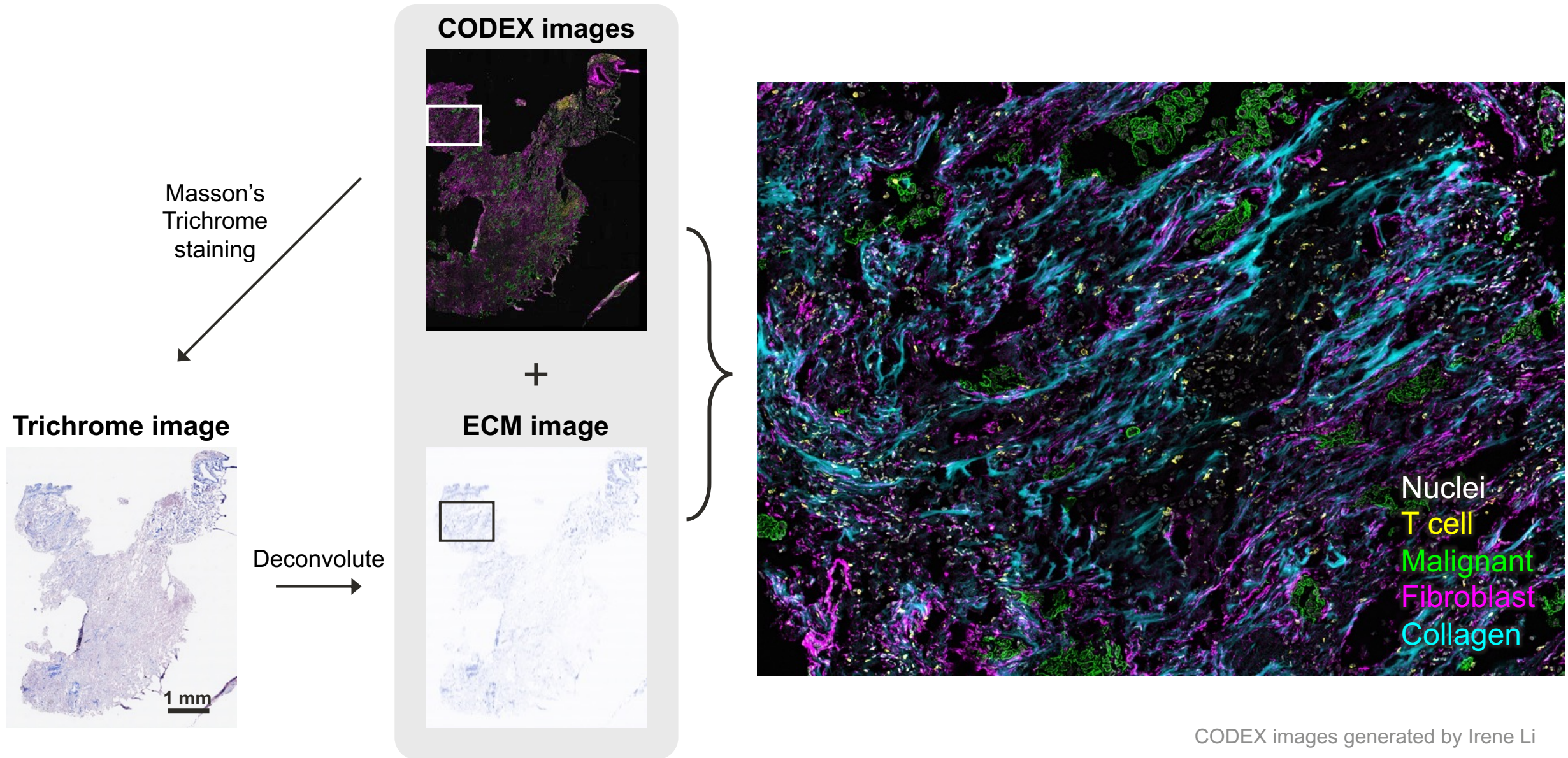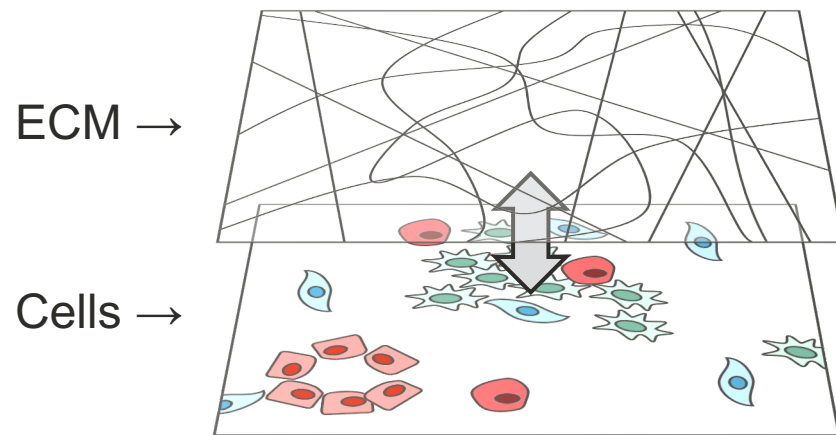
Part 1: integrating ECM imaging with CODEX

CODEX (cells) →

+

ECM →

CODEX reveals cellular spatial heterogeneity

CODEX image

Cellular neighborhoods

Vim PanCK CD3 CD15 CD34 SMA CD163

Collagen ECM visualized by Masson's Trichrome staining

CODEX images

Masson's Trichrome staining

Trichrome image

Deconvolute

+

ECM image

Nuclei
T cell
Malignant
Fibroblast
Collagen

1 mm

CODEX images generated by Irene Li

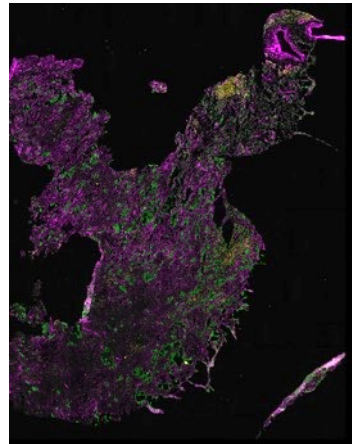# Part 2: characterizing cell-ECM architecture

ECM →

Cells →

Are ECM and cellular features associated?
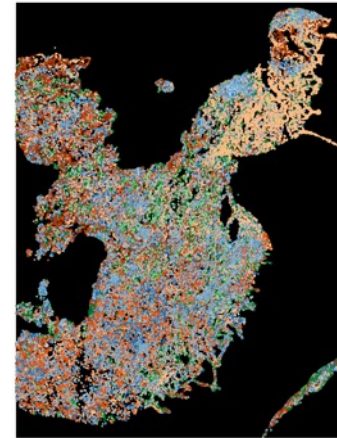
Current image analysis pipeline – same tissue section
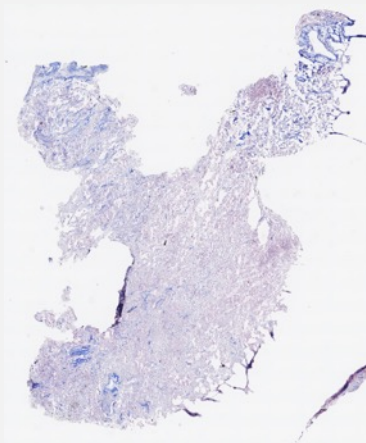
with Irene Li, Weiruo Zhang

CODEX images

Cell type identification

Process → Segment →

→ Cell-ECM analysis

Register Invert

Trichrome image

ECM image

Deconvolute →

→ Patch →

ECM feature extraction

100 μm x 100 μm patches
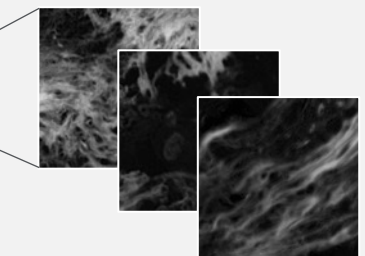
Features →

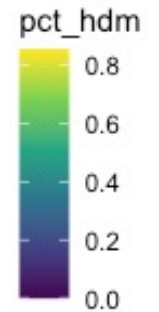| Patches ↓			
52.828	0.732	0.1030	…
81.648	0.193	0.0629	…
35.056	0.306	0.5303	…
…	…	…	…

TWOMBLI overview: FIJI macro to quantify ECM patterns
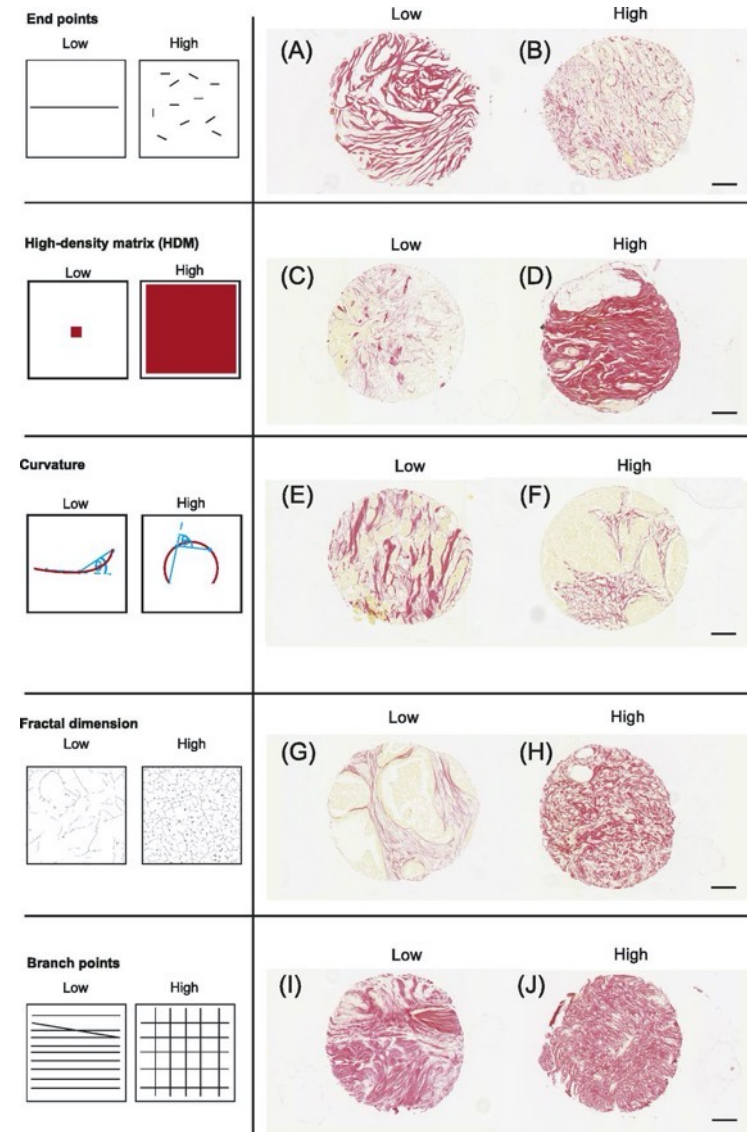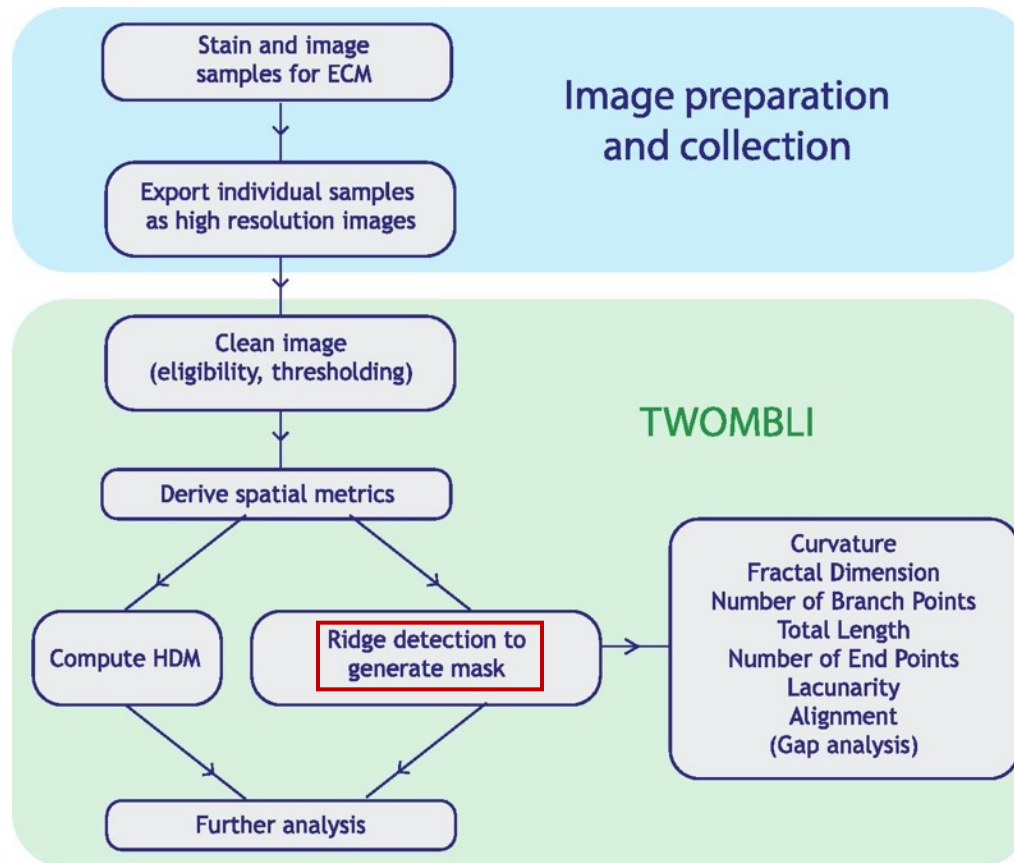
Patch-based ECM features: percent high-density matrix
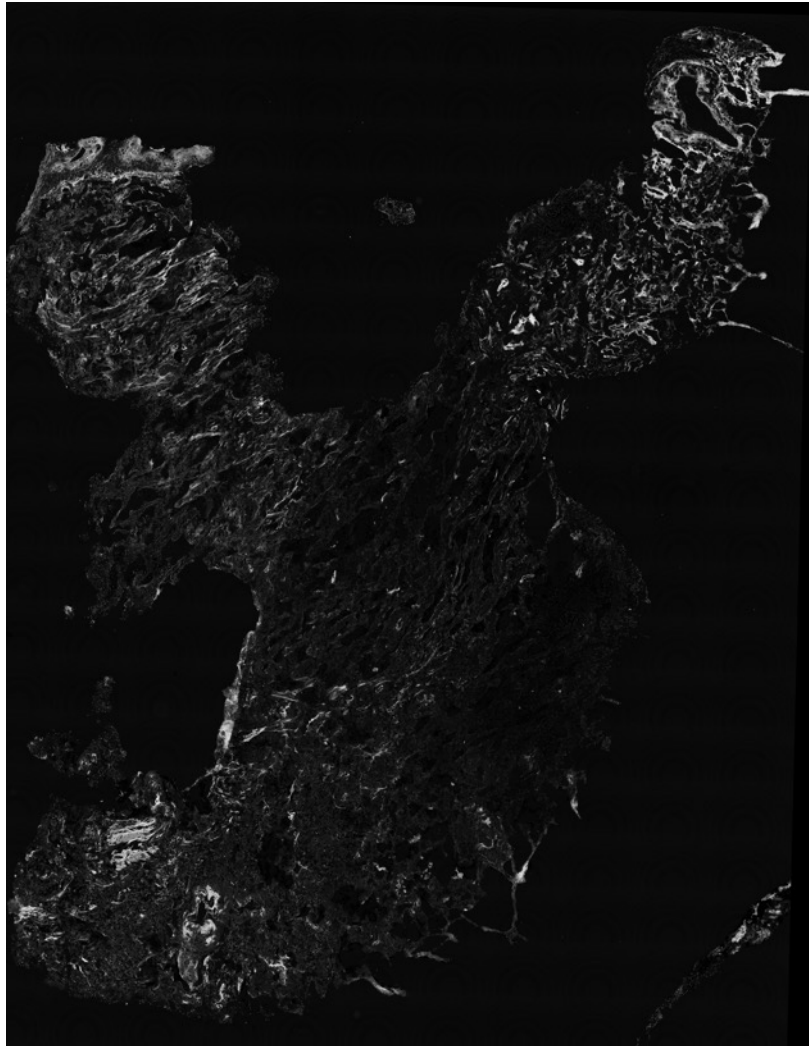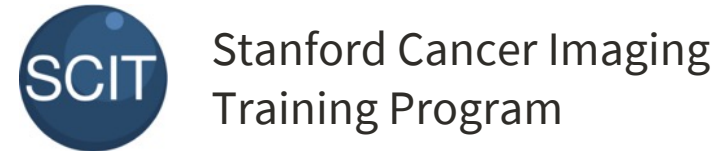

1803 patches

Thank you!

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