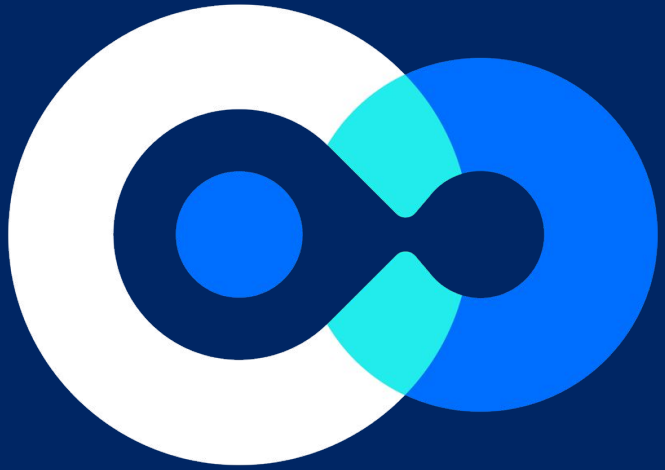
Spatial Multi-Omics for Cancer Systems Biology
Experimental & Computational Methods II

Session introduction and relating spatial features across assay platforms



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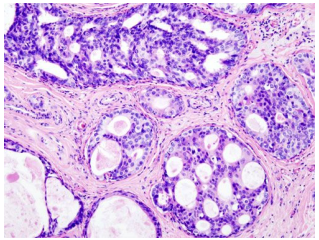
Institute for Systems Biology, Seattle

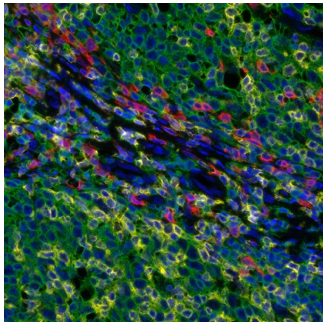
Experimental & Computational Methods II

- Robert Krueger (NYU) Visual analytics for imaging-based spatial biology profiling
- Joe Beecham (NanoString Technologies) - Spatial molecular imaging of FFPE cancer samples at any spatial-plex allows true systems biology understanding
- Lyla Atta (Johns Hopkins) - Evaluating normalization approaches for imaging-based spatial profiling technologies

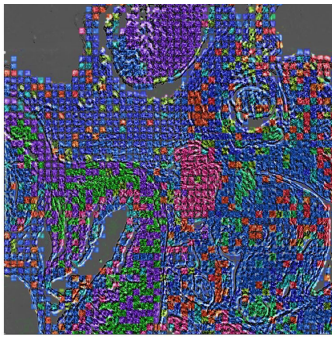
Relating spatial features across spatial biology platforms

Hematoxylin and Eosin - H&E





Immunohistochemistry (IHC)
Immunofluorescence (IF)



Spatial multi-omics

Hematoxylin and eosin (H&E) staining and images

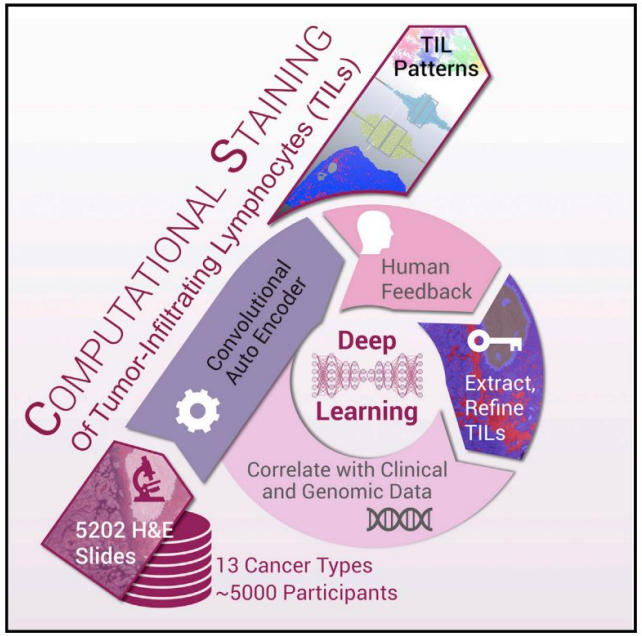
- The most widely used stain in medical diagnosis
- Hematoxylin stains cell nuclei blue
- Eosin stains the extracellular matrix and cytoplasm pink
- H&E shows the general layout and distribution of cells and provides a general overview of a tissue sample structure
- “Whole slide” gigapixel images, e.g 100,000 x 100,000 pixels
- Stored in 3 (R,G,B) channels as tiled TIFF / SVS format

Machine Learning Prediction from H&E Images

- Immune cell regions from H&E images
- Cancer cell regions from H&E images, informed by IHC/IF
  - P53 - HEMnet
  - panCK - SHIFT
- Immune cell regions from H&E, informed by IHC/IF
  - CD45

Immune cells from H&E, informed by pathologist

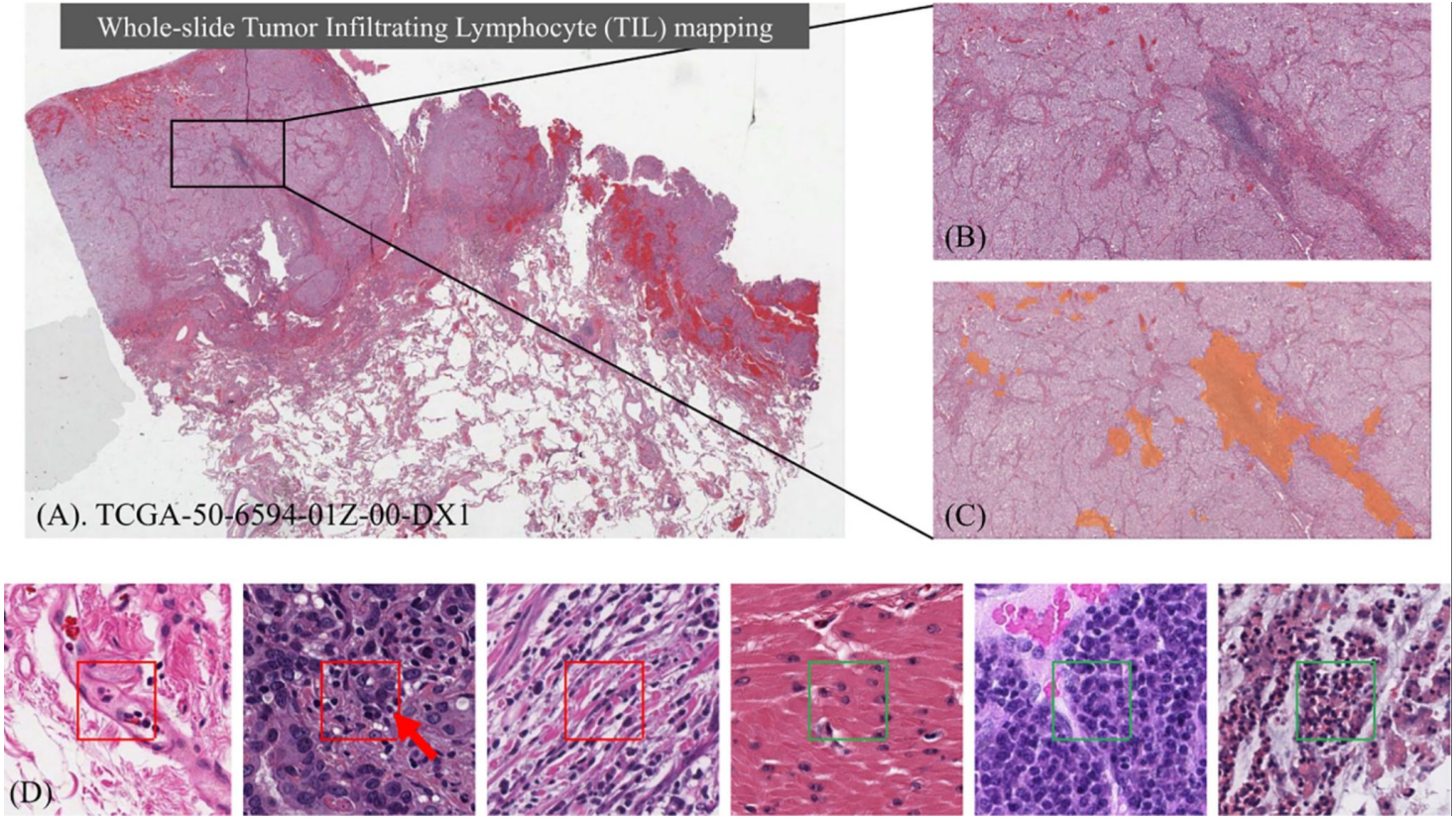
TIL Map: Tumor Infiltrating Lymphocyte Map, Computational staining



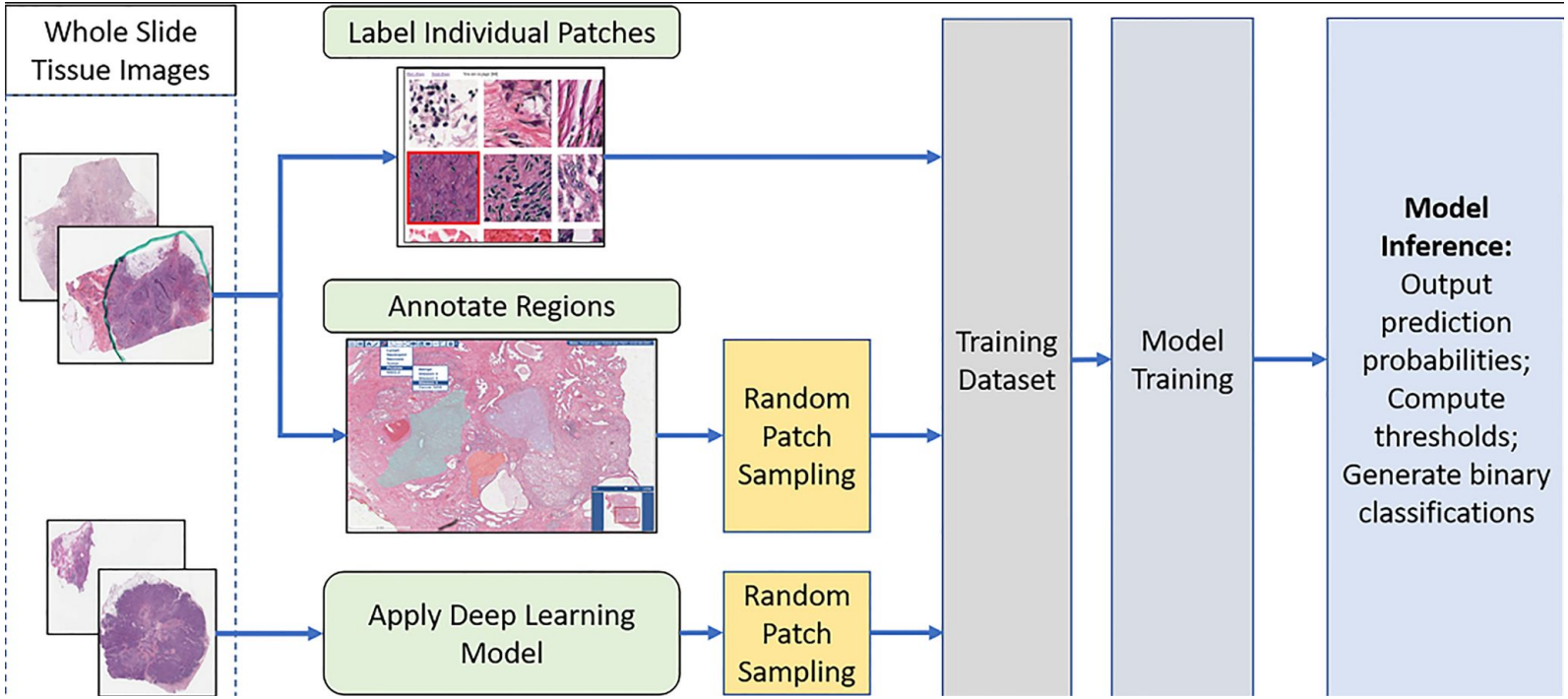
- Predict lymphocytes from H&E
- H&E stained sections from The Cancer Genome Atlas (TCGA)
- Predictions on tiles/patches: 100 × 100 pixel (50 x 50 micrometer)
- Neural networks (VGG-16,ResNet-34 Inception-V4)
- 13 human cancers (2018)
- 23 human cancers (2022)

Cell Reports **2018** Apr 3;23(1):181-193. Joel Saltz *et al.*
Front. Oncol., 15 Feb. **2022** Volume 11 - 2021 ; Shahira Abousamra *et al.*

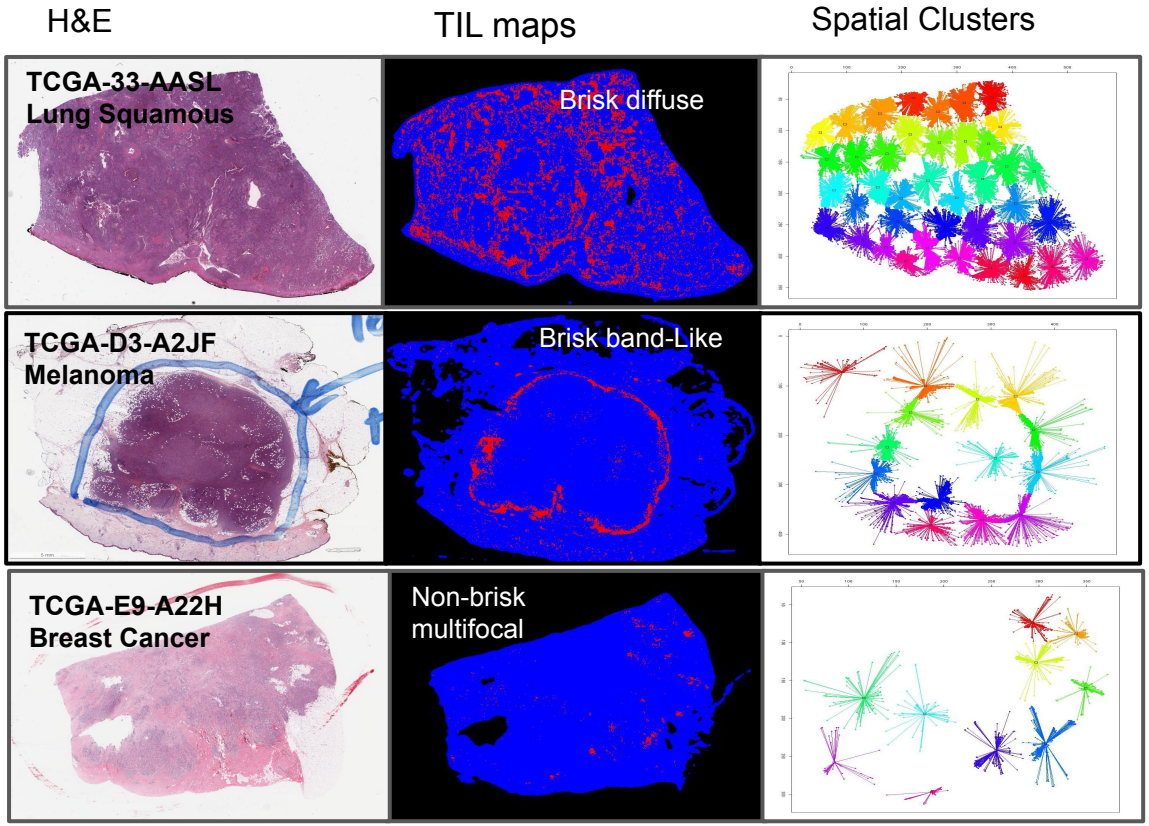
TIL Map - prediction



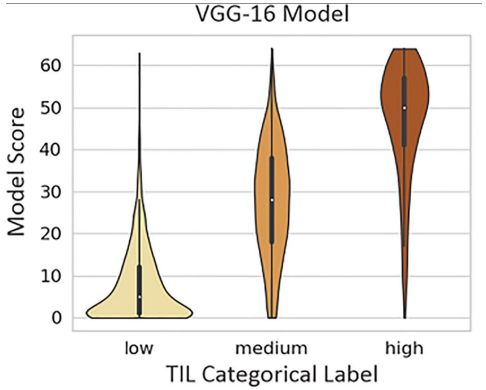
TIL Map - training

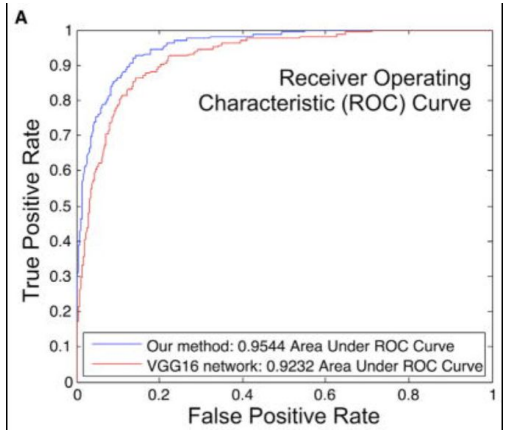


TIL Map - predictions and structure

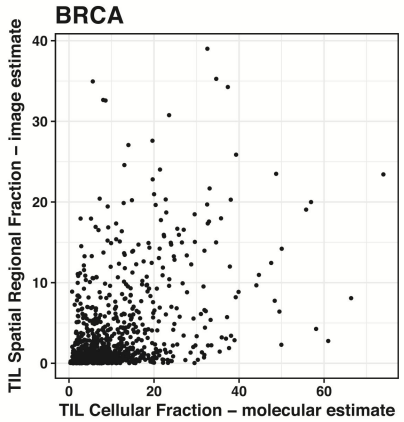


TIL Map assessment and correlates

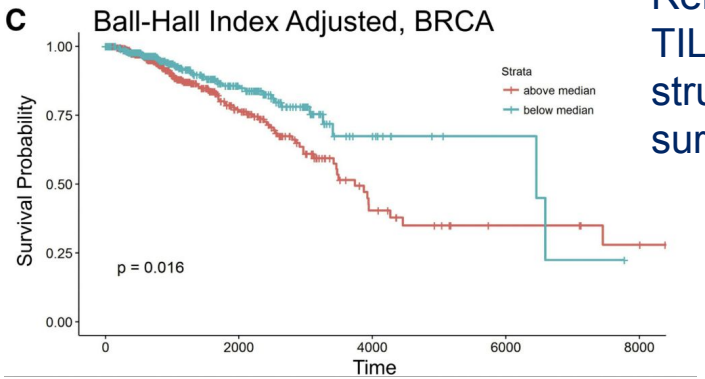




Statistical assessment



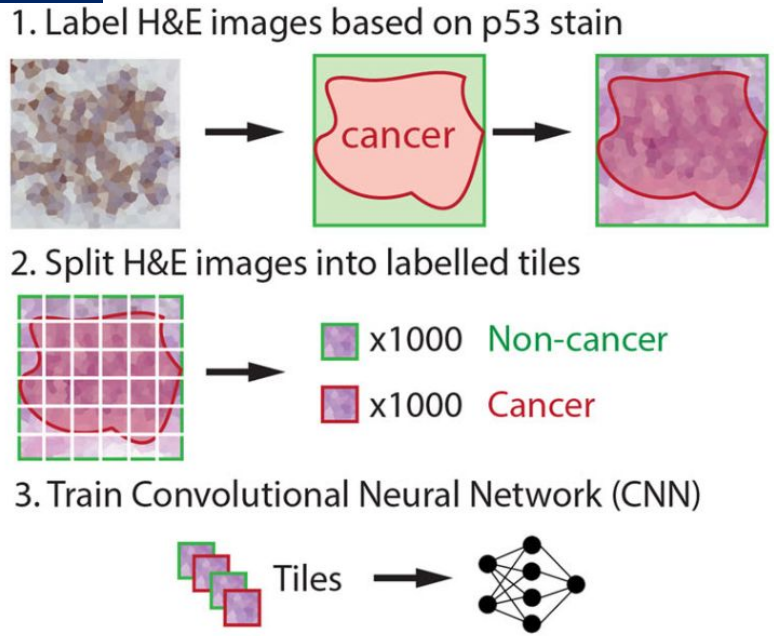
Relate to estimates from bulk genomic sequencing



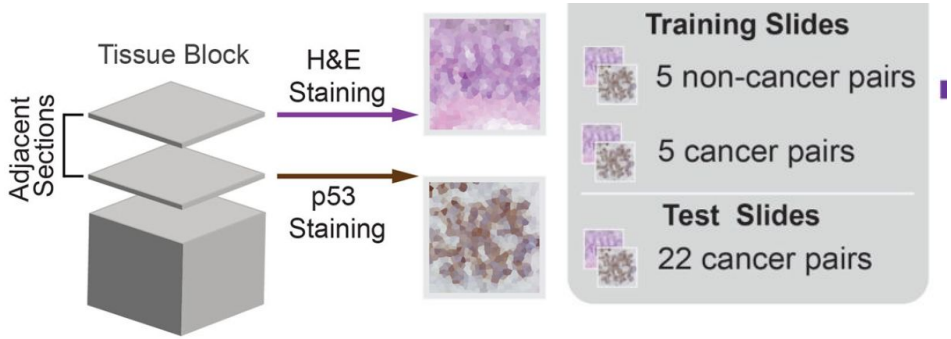
Relate to outcome: TIL Map cluster structure vs overall survival

Cancer cells from H&E, informed by IHC - HEMnet

HEMnet: H&E Molecular neural network

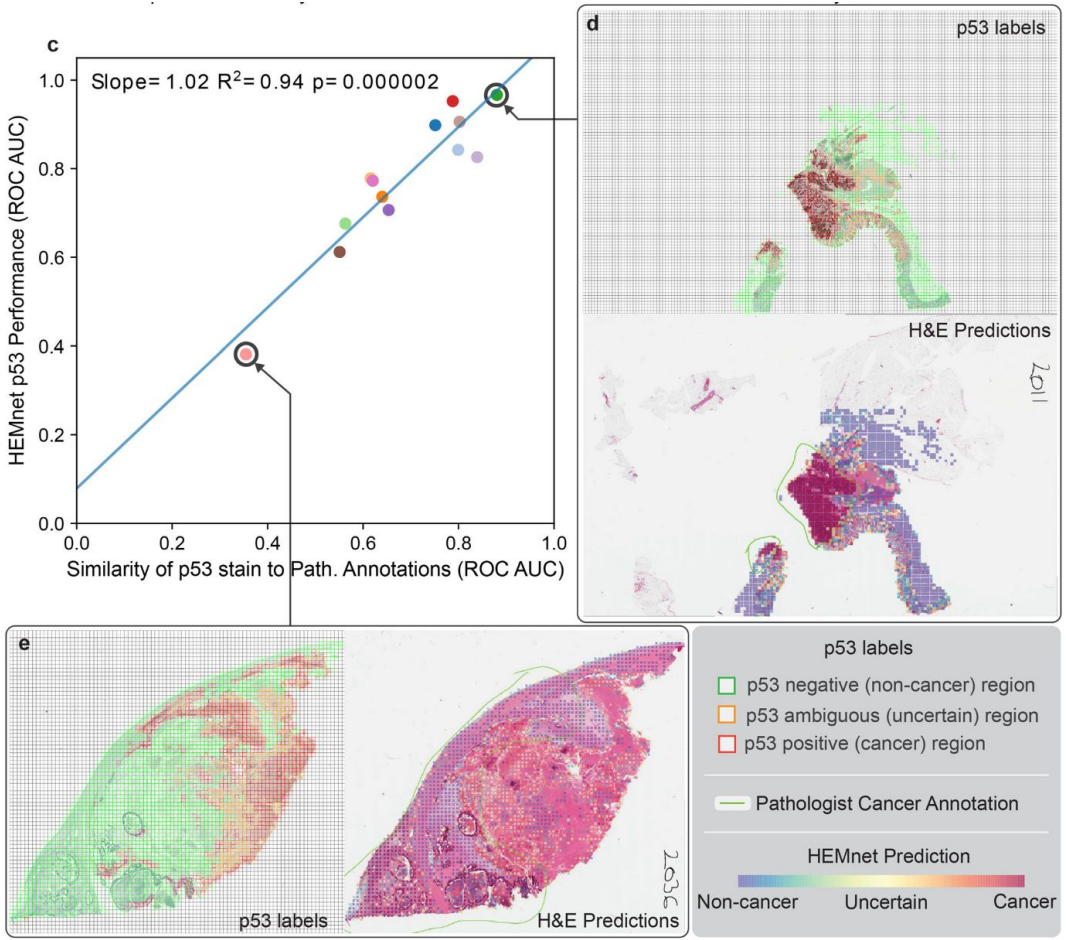


- Predict p53 (cancer) from H&E
- H&E and IHC of adjacent tissue sections
- Predictions on tiles: 224 × 224 pixel
- Convolutional Neural Network (CNN)
- Human colon cancer



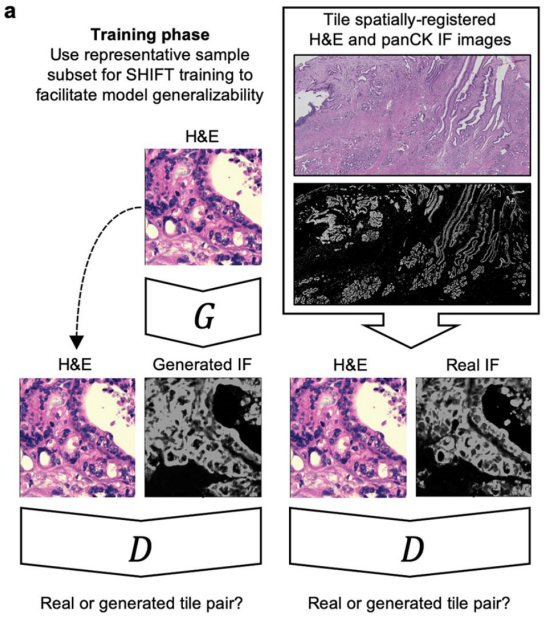
npj Precision Oncology (**2022**) 6:14 ; Andrew Su *et al.*

HEMnet - Assessing performance



Cancer cells from H&E, informed by IF - SHIFT

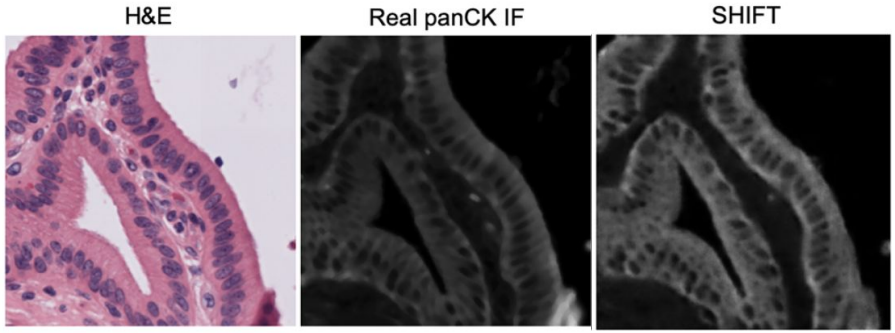
SHIFT: **s**peedy **h**istological-to-**i**mmuno**f**luorescent **t**ranslation, a deep learning-based method for virtual IF staining of images containing histologically-stained tissues.



- Predict PanCK (cancer) from H&E
- Human pancreatic cancer
- H&E and IF of same section of tissue
- Predictions on tiles: 256x256 pixel
- Generative Adversarial Network (GAN)
- Generator network G generates virtual IF tiles conditioned on H&E tiles.
- The discriminator network D learns to discriminate between real and generated image pairs.

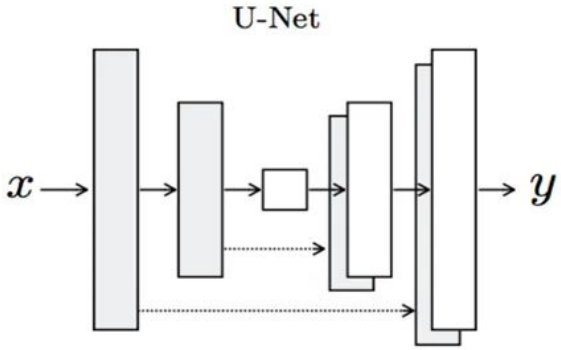
Nature Scientific Reports (**2020**) 10:17507, Erik A. Burlingame *et al.*

Prediction, Testing, and Architecture - SHIFT

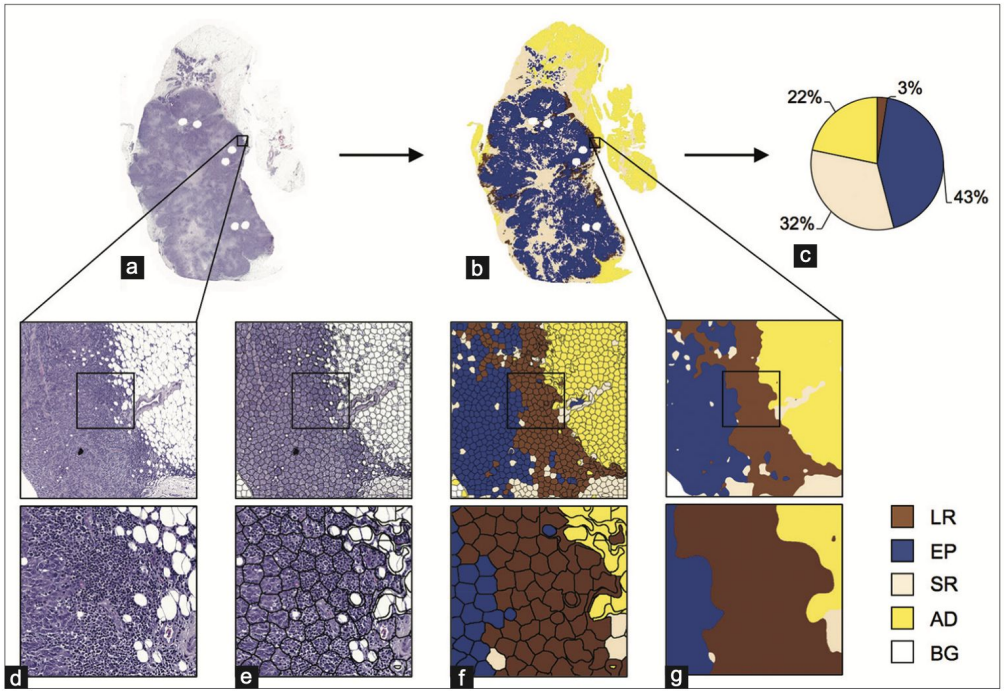


Conditional GAN: ***G*** has extra element to fool ***D***

G Network architecture --->



Immune cells from H&E, informed by IHC



- Train on CD45 (leukocytes)
- Prediction of tissue categories on “superpixels”
- Human breast cancer
- H&E and IHC of adjacent tissue sections
- Convolutional Neural Network (CNN)

LR: Leukocyte-rich, EP: Epithelium, SR: Stroma, AD: Adipose, and BG: Background

J Pathol Inform Volume 7, Issue 1, January–December 2016, 38; Riku Turkki *et al.*

Very important things that we skipped completely

- Antibody properties/quality
- Multiplexed labeling and imaging
- Image quality
- Image normalization
- Image registration and alignment
- Selection of regions
- Selection of tiles
- Selection of training and test sets
- Machine learning architectures
- Scoring/evaluation methods
- Other methods/publications
- …

Experimental & Computational Methods II

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- Lyla Atta (Johns Hopkins) - Evaluating normalization approaches for imaging-based spatial profiling technologies
- 15-minute Q&A - All Speakers from Session Two