Multi-Scale Image Analytics for High Dimensional Spatial Mapping of Normal Skin Tissues

GE Research (GRC), University of Pittsburgh (UPitt)

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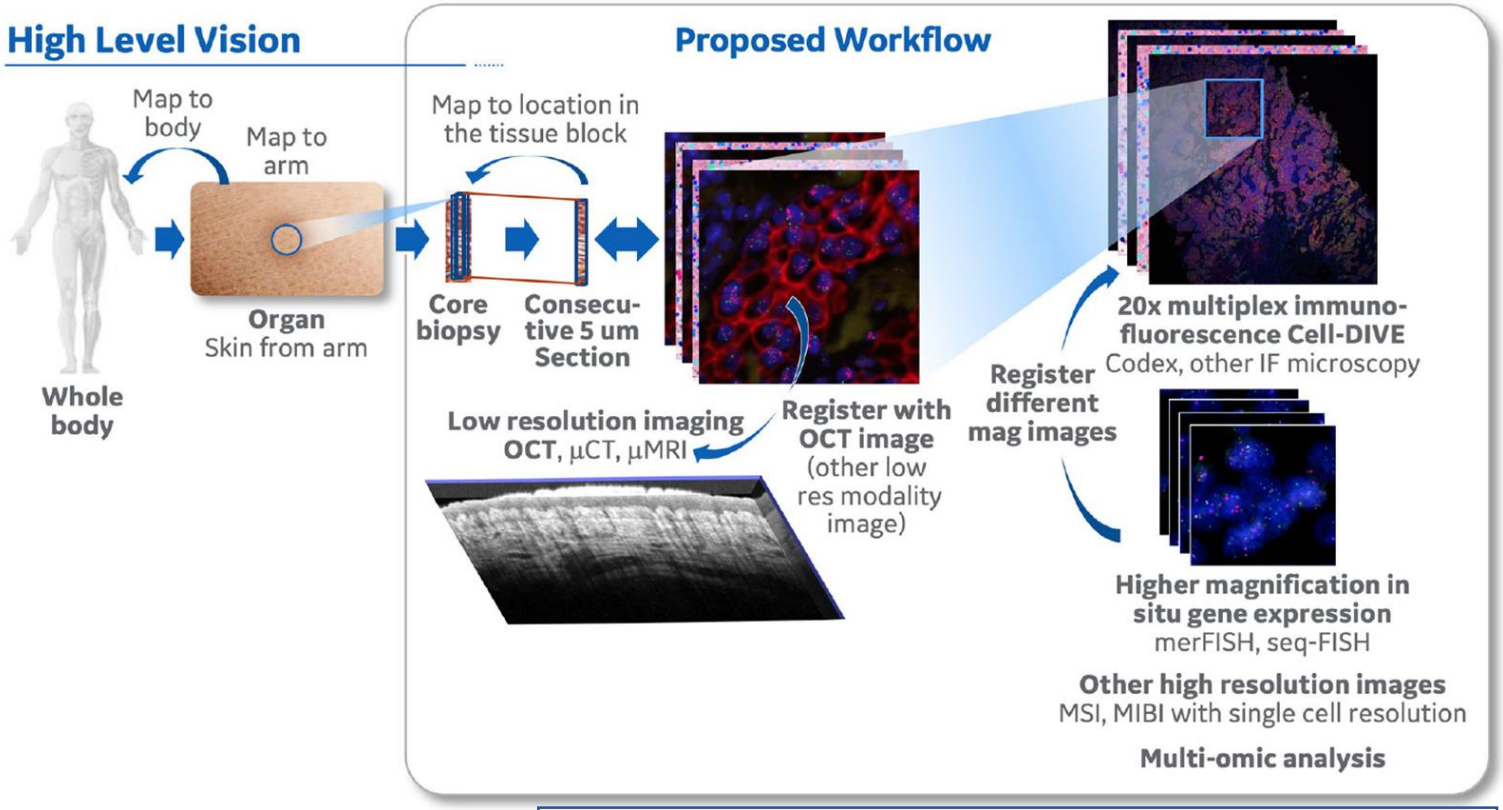
Project Overview



Objectives:

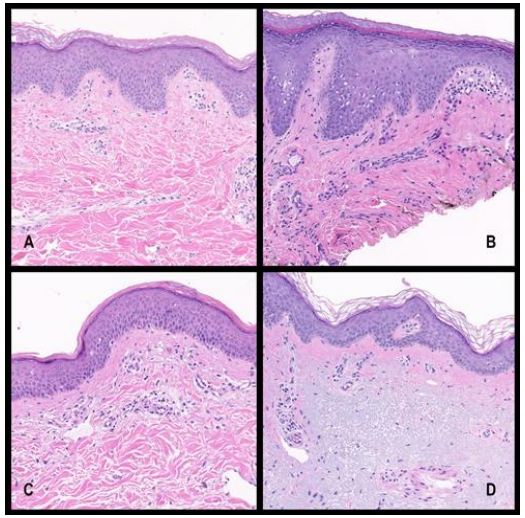
- Generate multi-modality and multi-resolution image dataset of normal skin tissue samples.
- Apply/develop algorithms for multi-modality/multi-resolution image registration (2-D to 3-D), segmentation and quantification.
- Evaluate changes in biomarker expressions and skin tissue structure as a function of aging and UV exposure.

Multi-modalities images to be used:

1. 2D highly-multiplexed (Cell DIVE™) images of skin tissue serial sections.
2. 3-D Optical coherence tomography (OCT) or micro-CT
3. Single cell in situ RNA on a small number of the serial sections (collaboration to be established)

Most exciting features of our project:

- Combining high-dimensional, multi-modality, multi-resolution and multi-omic data to gain insight about environmental and aging effects on normal skin tissue.



A) Non sun-exposed skin in a young patient

B) Sun-exposed skin in a young patient

C) non sun-exposed skin in an elderly patient

D) sun-exposed skin in an elderly patient showing marked photoaging effects including prominent solar elastosis.

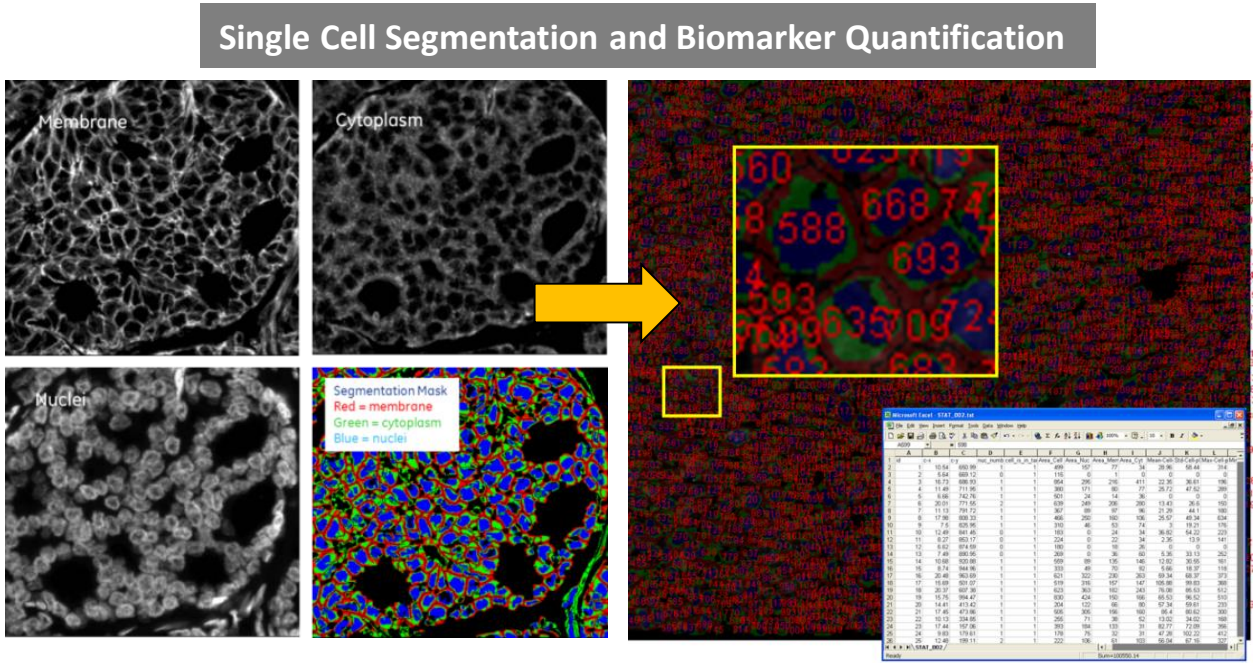
Year 1 Deliverables

1. **Data Generation**
   - OCT (or micro-CT) images of 12 skin tissue specimens (younger and older subjects; UV exposed and non-exposed regions).
   - Multiplexed images for **12** specimens (**20-25** sections; **15-20** biomarkers).
   - Single-cell segmentation and biomarker quantification for all multiplexed images.
   - Relevant OCT/micro-CT imaging features.

2. **Open Source Code**

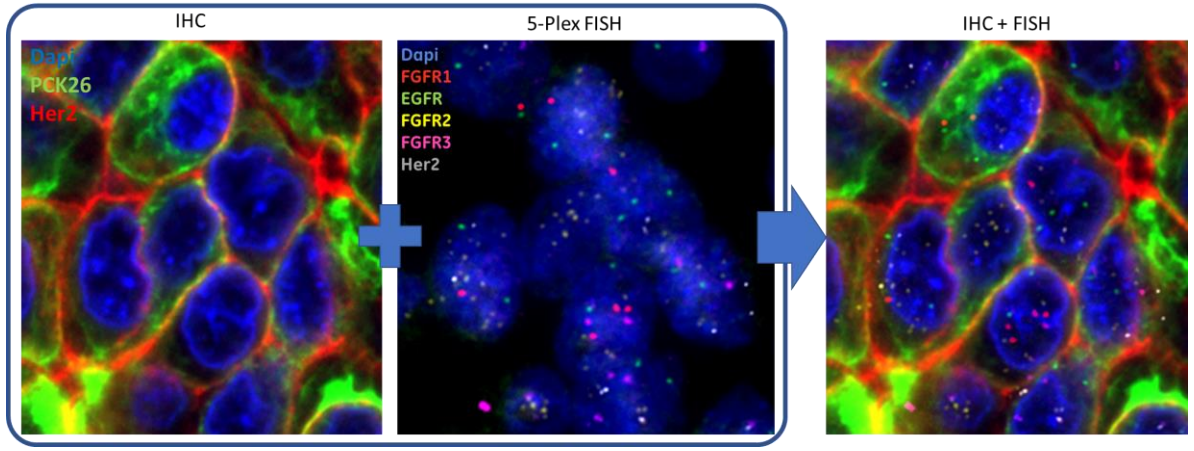
   2-D multiplexed image segmentation & quantification algorithms.
   Algorithms for mapping Multiplexed and OCT/micro-CT images.
   (stretch) An algorithm for registering multiplexed biomarker images (proteomics) with multiplexed RNA image.

3. **Reports summarizing data and analysis**



HuBMAP Collaborations

- Potential Collaborators:
  - Long Cai & Guo-Cheng; California Institute of Technology
  - HIVE projects (e.g. Rahul Satija; New York Genome Center)
  - Other RTI Projects



- Goals of collaboration:
  1. Work with Long Cai et al to link high-resolution cell-level multi-omic (proteomic + RNA FISH) images and volumetric imaging data (OCT/micro-CT)
  2. *(Stretch)* Work with Rahul Satija to enable integration of the multi-scale, high-resolution multi-omic maps into the HuBMAP CCF

- Collaboration status: started initial discussions during the preparation for the proposal

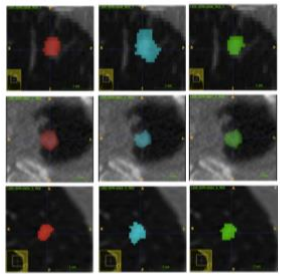
What should HuBMAP Do ?

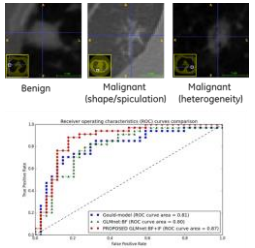
- Integration with other single cell efforts, e.g. Human Pre-Cancer Atlas, Human Tumor Atlas, Human Cell Atlas
- Broadening to international participation
- Integrate “normal” microbiome/other environmental factors (diet, exposure, etc.) analysis & effects on tissue organization/composition (particularly tissues exposed to microbes)
- Adopting best practices in SW engineering (e.g. Agile methodology, Data/Code repositories, etc.)

Multi-Scale Image Analysis at GE Research

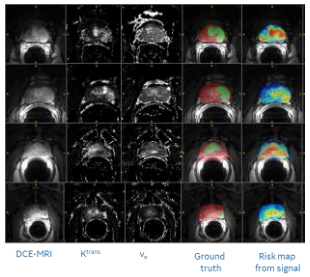
From In-vivo/Radiology → **To Tissue/ROI/Cell Population** → **To Single Cell & Sub-Cellular**

CT Lung Nodule Detection and Screening





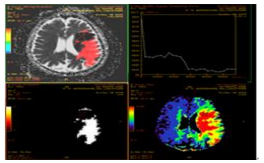
MRI Prostate Tumor Detection



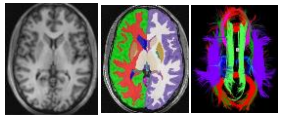
Ultrasound Organ Segmentation

Automated MRI Scan Planning

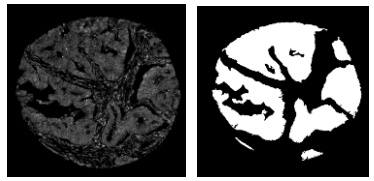
MRI Stroke Detection



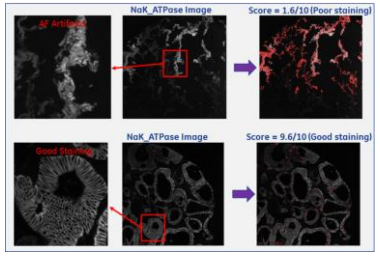
Brain Structures Segmentation



Tissue (epithelial) Segmentation



Staining and Segmentation QC



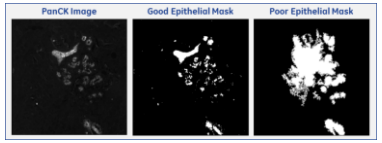
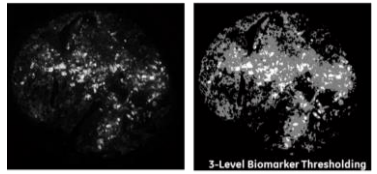
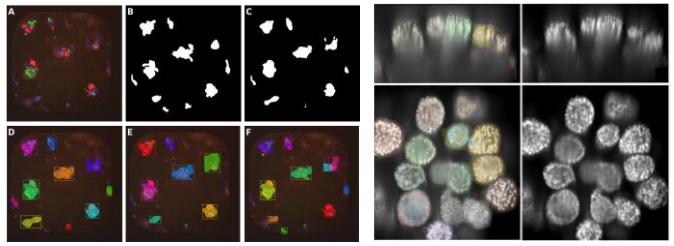


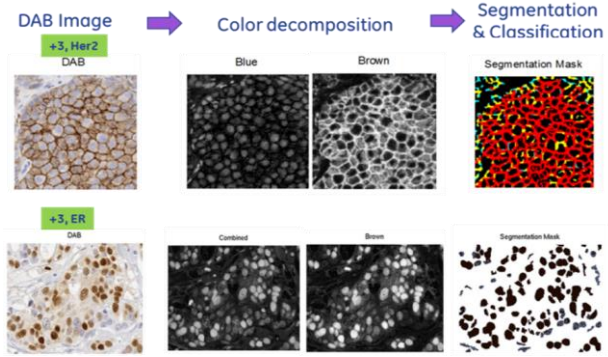
Image-level Biomarker Thresholding



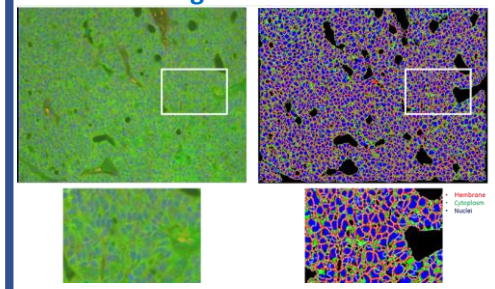
Deep Learning-based Organoids Segmentation



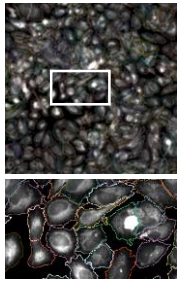
Digital Pathology (Image Scoring)



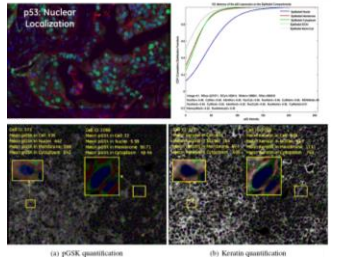
Multi-channel Single Cell Segmentation



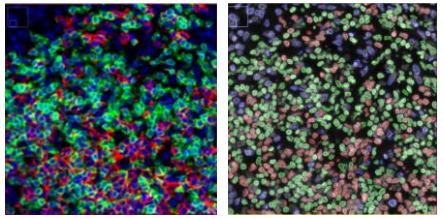
Deep Learning-based Single Channel Cell Segmentation



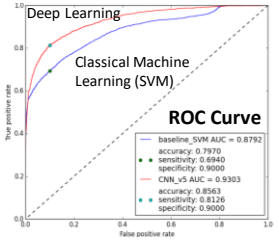
Biomarker Quantification



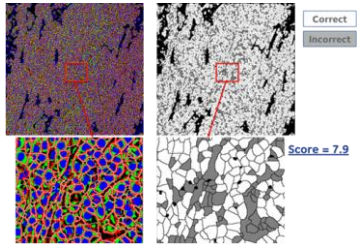
Deep Learning-based Immune Cell Classification



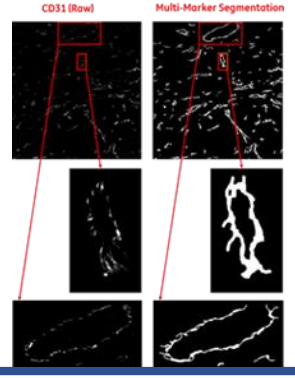
CD20 (red) , CD3 (green), double negative (blue)



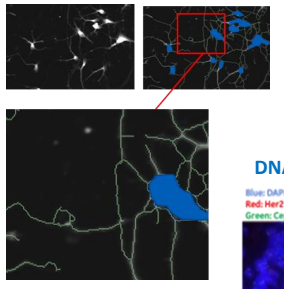
Cell Segmentation QC



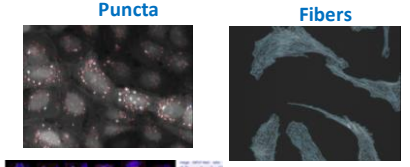
Blood Vessels Segmentation



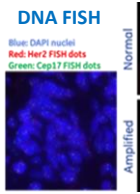
Neurites Segmentation

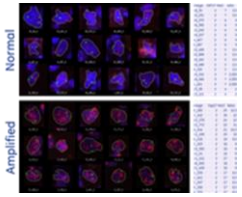


Sub-Cellular Analysis

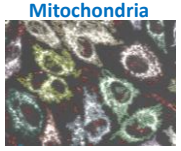


DNA FISH



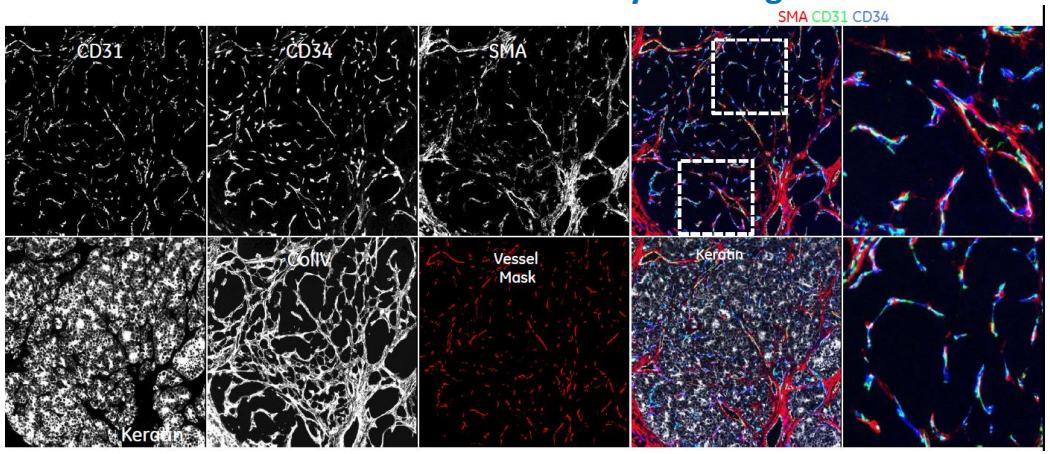


Mitochondria



Example Applications

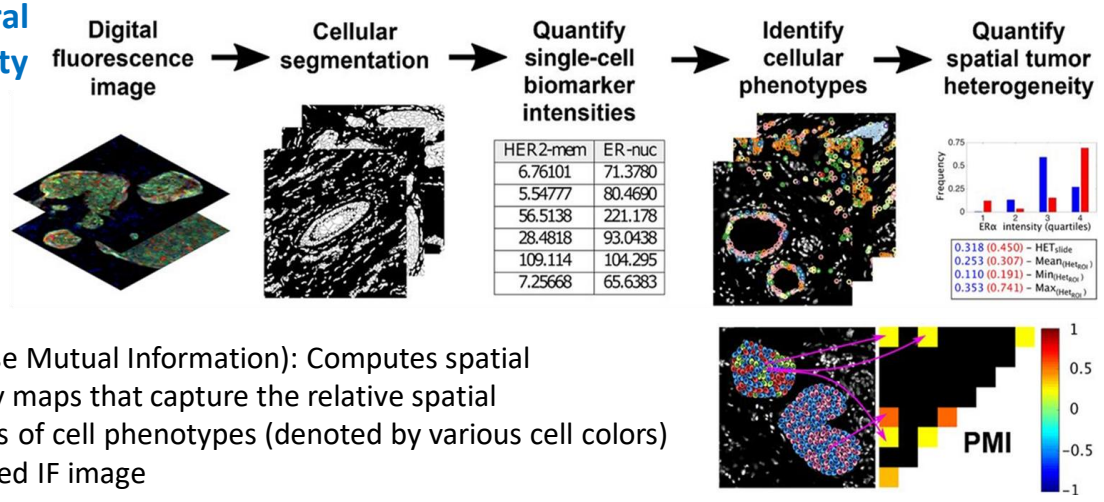
Tumor Blood Vessel Maturity Profiling



An example of using multi-channel vessel segmentation to investigate different stages of blood vessel maturity and molecular characteristics.

Uhlik et al (Clinical Cancer Research 2016)

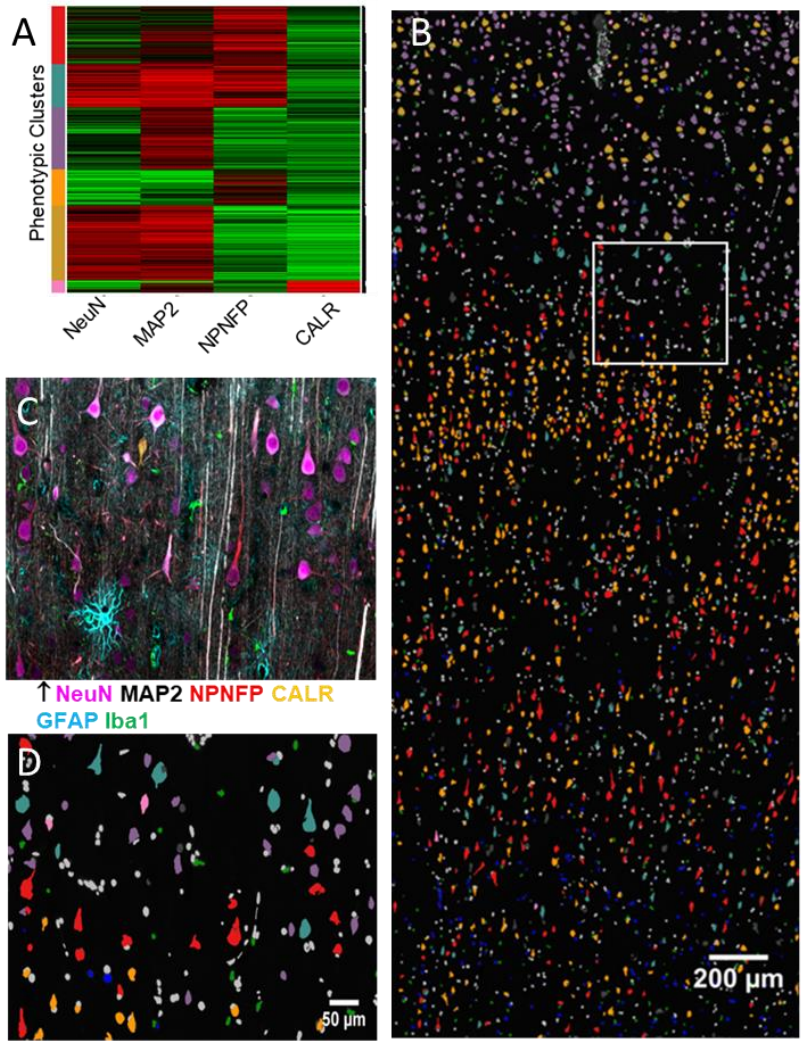
Intra-Tumoral Heterogeneity



PMI (Pointwise Mutual Information): Computes spatial heterogeneity maps that capture the relative spatial cooccurrences of cell phenotypes (denoted by various cell colors) in a multiplexed IF image

Spagnolo et al, J. Pathol Inform (2016)

Brain Tissues (Neuro) Analysis



An example of using single cell segmentation, biomarker quantification and cell classification (Neurons and Glia cells) using brain tissue images