Multi-omic Studies of the Small and Large Intestines

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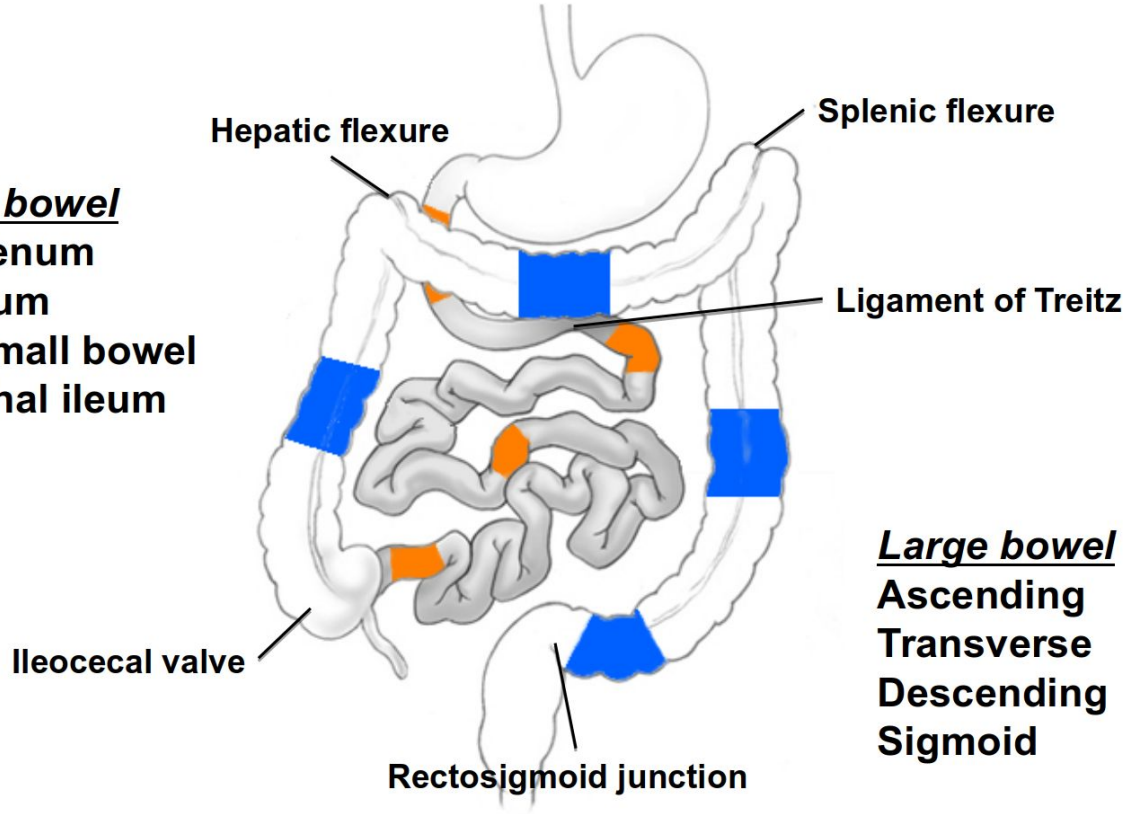
Lin, Greenleaf and Plevritis, co-PIs

2019 HuBMAP Meeting

Stanford TMC - Bowel Map

Bowel collection sites: 8 Sites

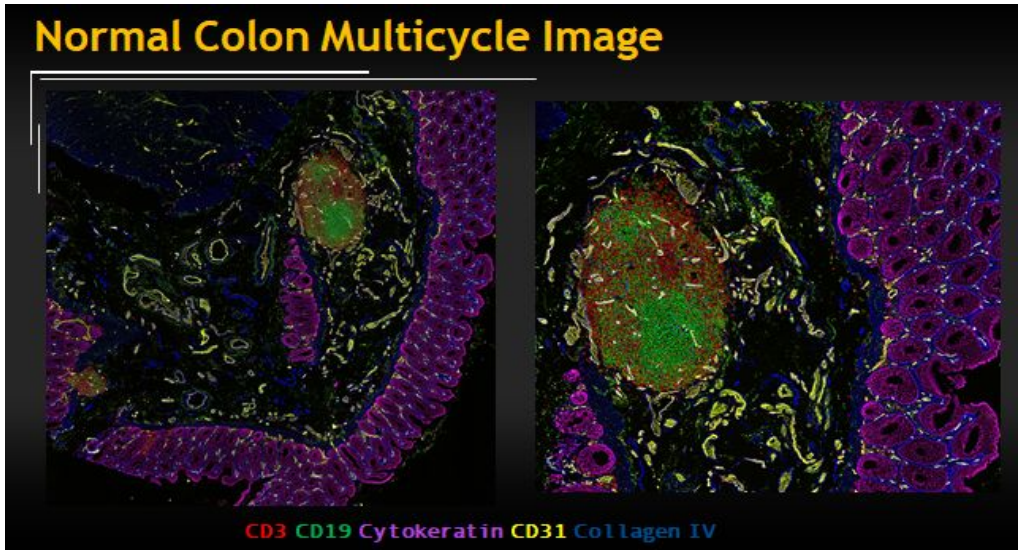
Small bowel
Duodenum
Jejunum
Mid-small bowel
Terminal ileum



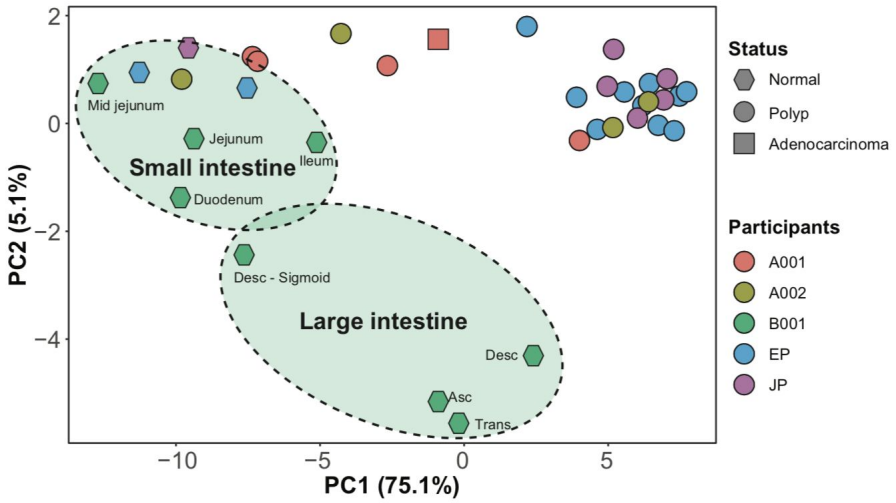
Large bowel
Ascending
Transverse
Descending
Sigmoid

2019 HuBMAP Meeting

CODEX



Lipidomics



Next Year's Deliverables

- What resources / data do you expect to make available in 2020?
- 1-2 sets of the following data for all eight regions of the bowel
  - Codex images
  - scRNA-Seq
  - scATAC-Seq
  - Bulk genome, proteome, metabolome, lipidome. Possibly methylome

- What do you need to do in order to be able to share?
  - Database ready to go.

Collaborative Projects

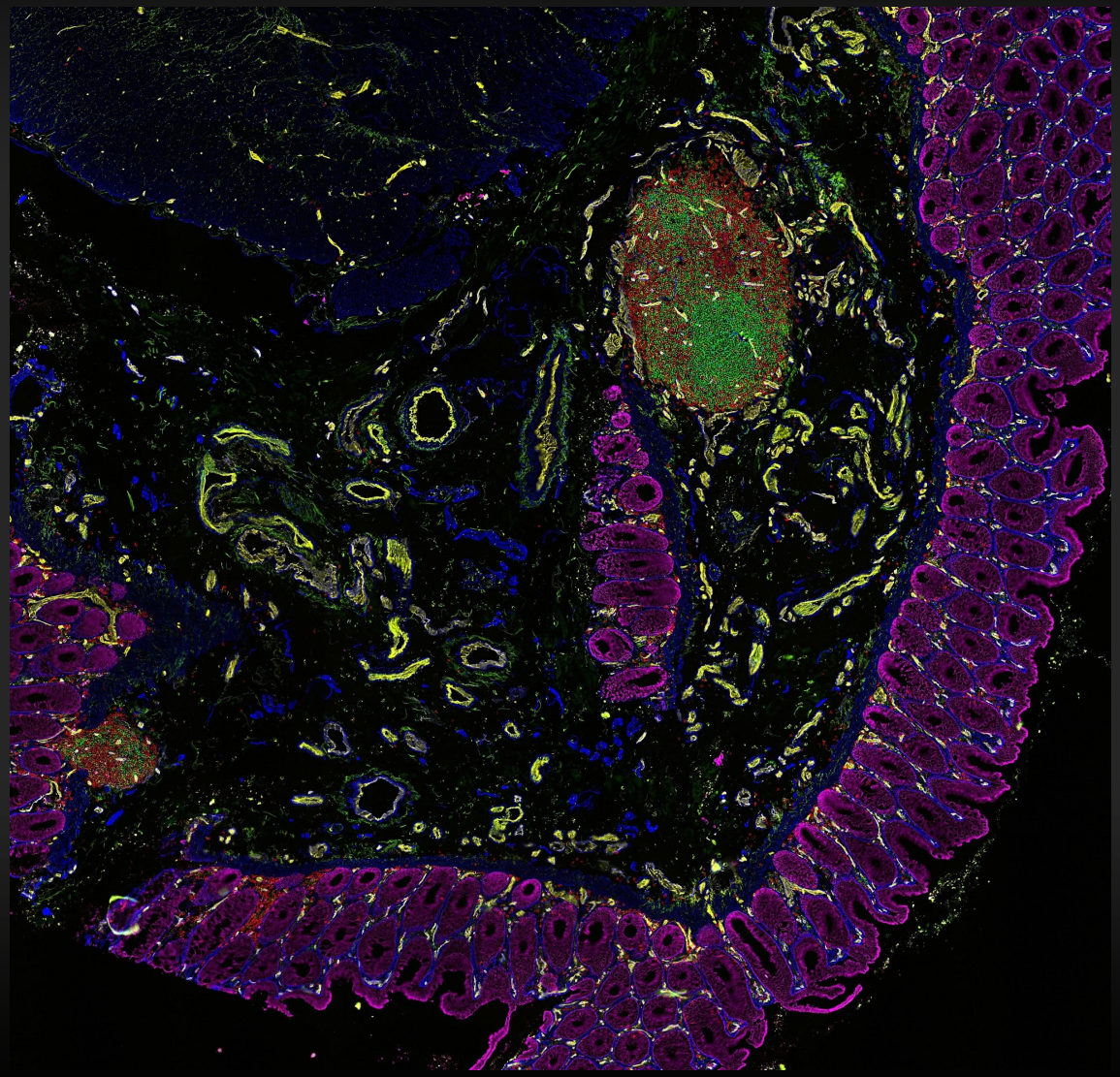
- Consortium-wide common tissue
- Specific tissue to be decided
  - Will plan to collect under open access consent
- This month, we plan collecting tissue with standard consent for a "dry-run"
  - Distribute for consortium-wide QC and protocol refinement

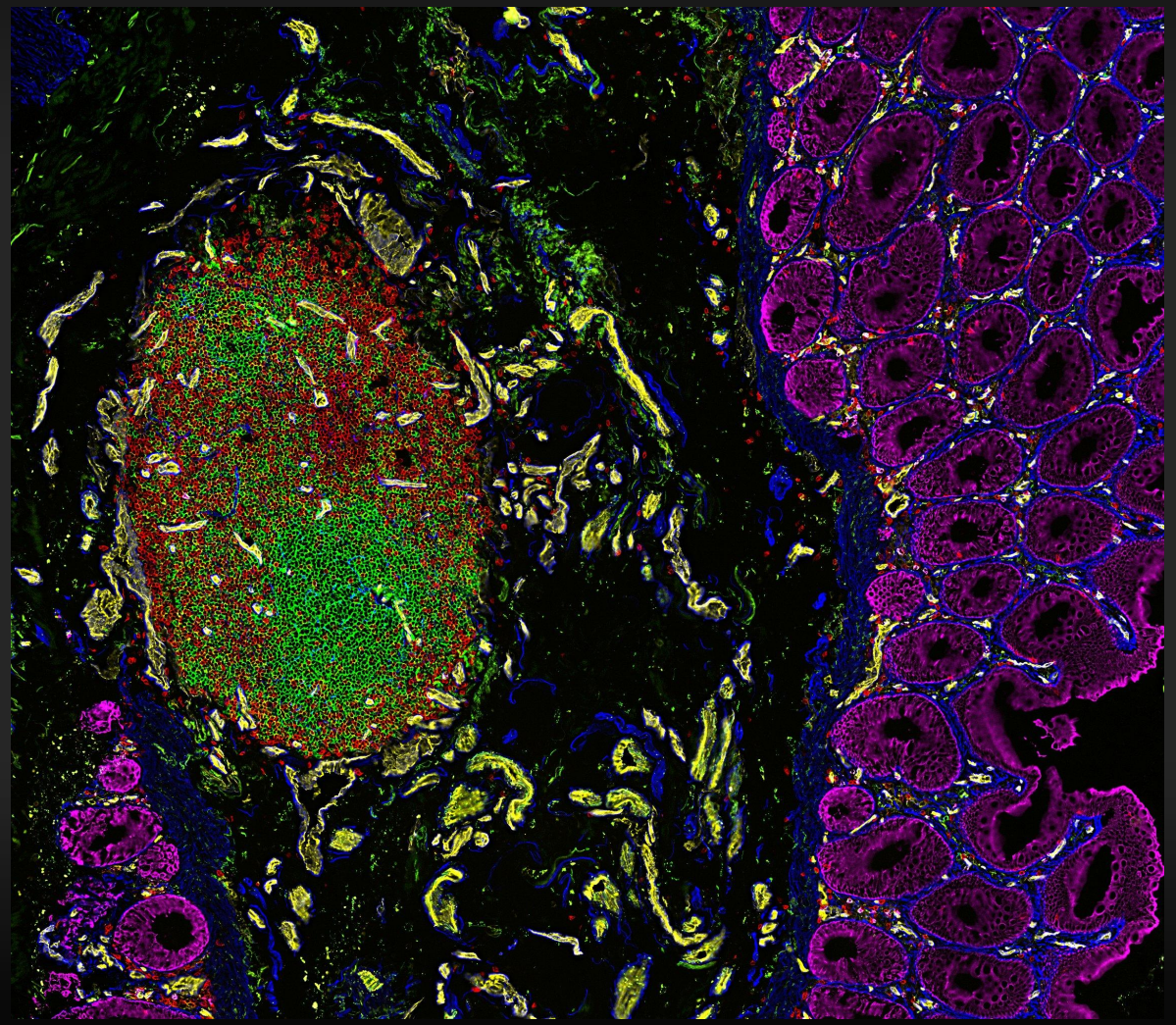
- Collaboration with CalTech / UW
- Heart tissue -- collected under standard consent for protocol testing
- Bowel tissue -- collected under standard consent and sent to CalTech/UW for protocol testing

What should HuBMAP Do ?

- What do you think the priorities for the Consortium should be?
  - Generate the best possible 2D/3D maps
  - Evaluate technologies
  - Generate new methods
  - Deliver data in a sharable format

CODEX Imaging

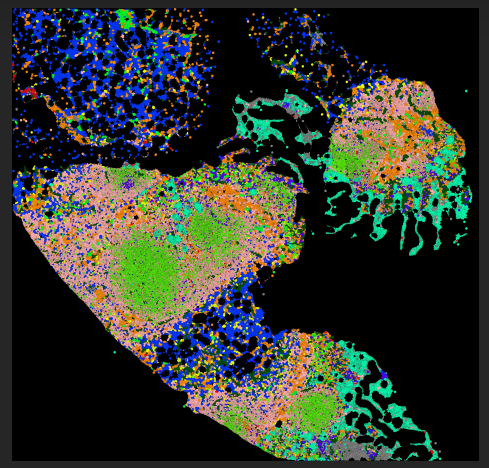
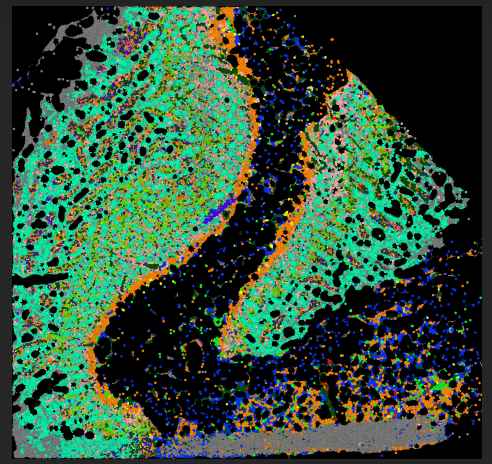
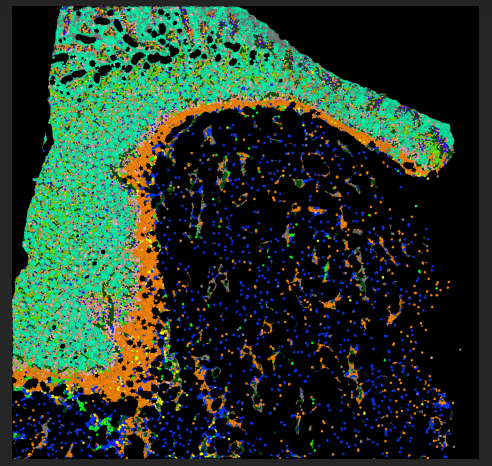
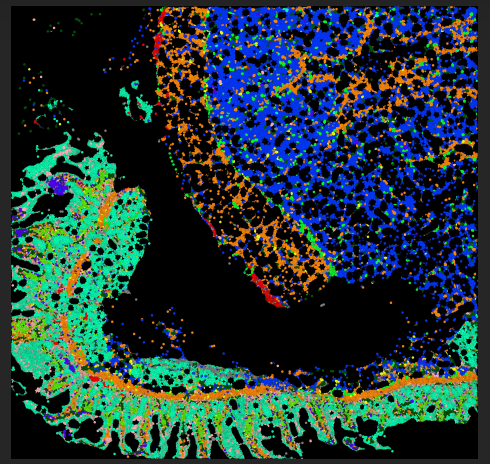
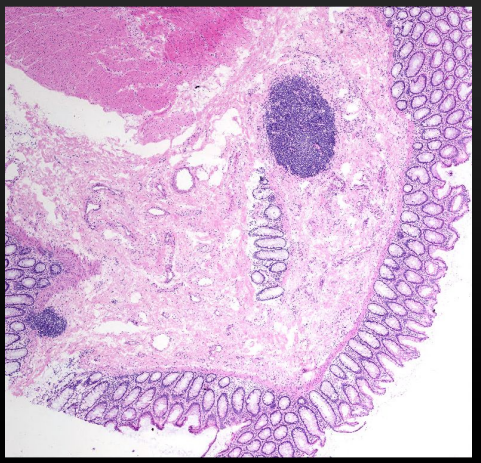
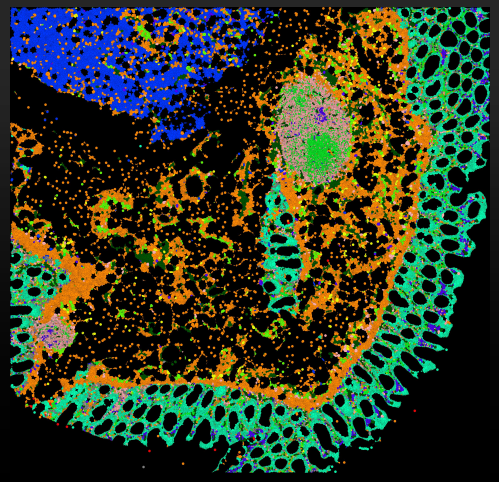
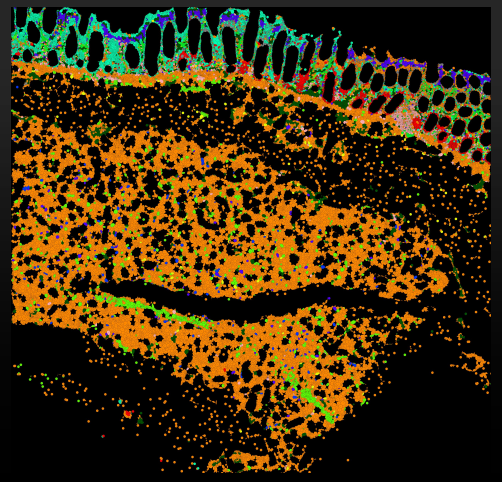
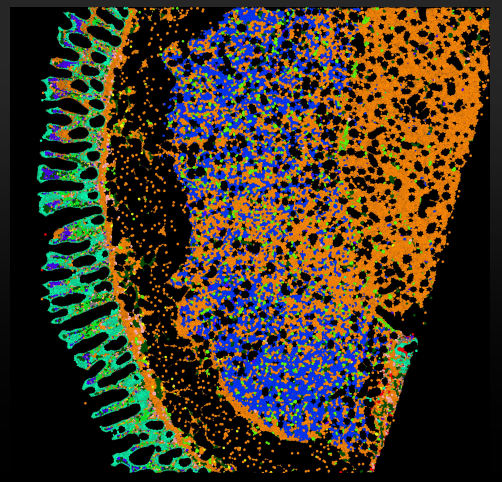
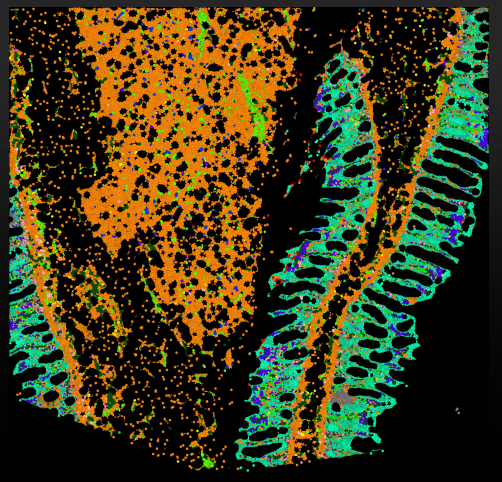




CD3 CD19 Cytokeratin CD31 Collagen IV

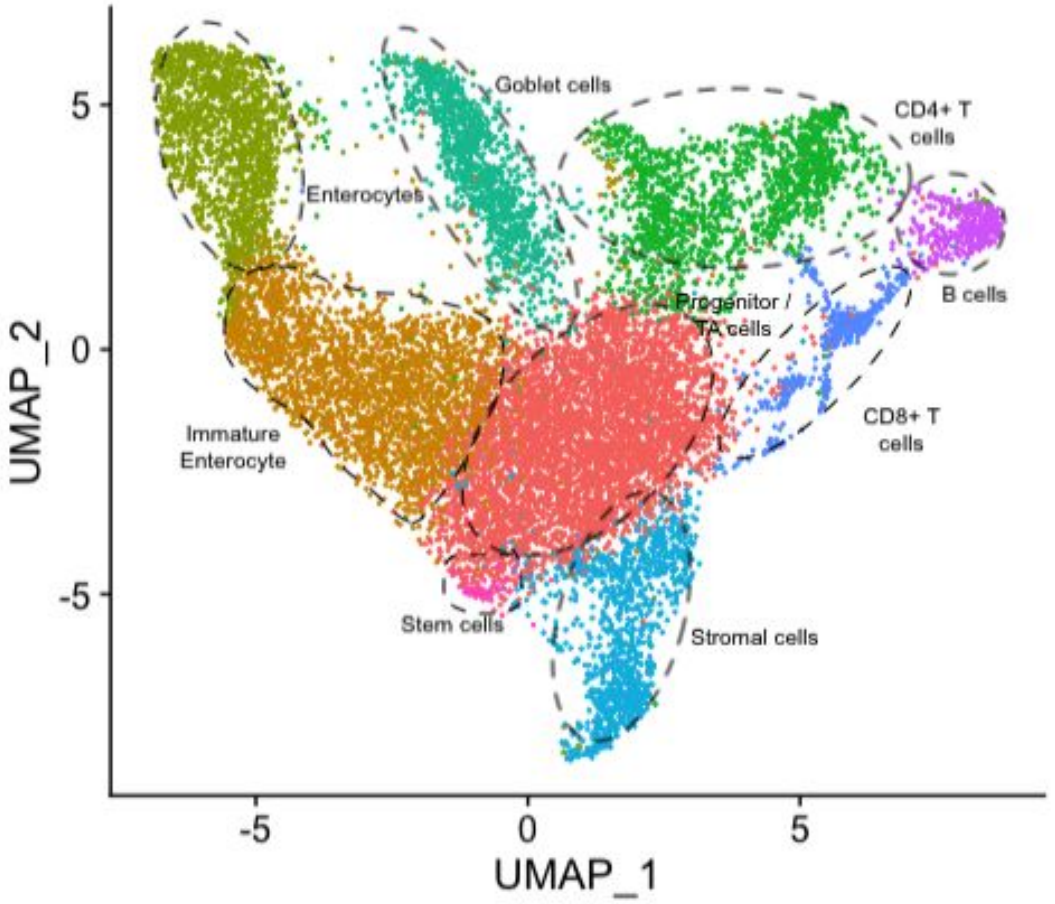
CODEX Voronoi Diagrams

A 01-Granulocytes
B 02-Stroma
C 03-Mast/ICCs
D 04-B cells
E 05-Lymphatics
F 06-Epithelium
G 07-T cells
H 08-Smooth Muscle
I 09-Macrophages
J 10-Vasculature

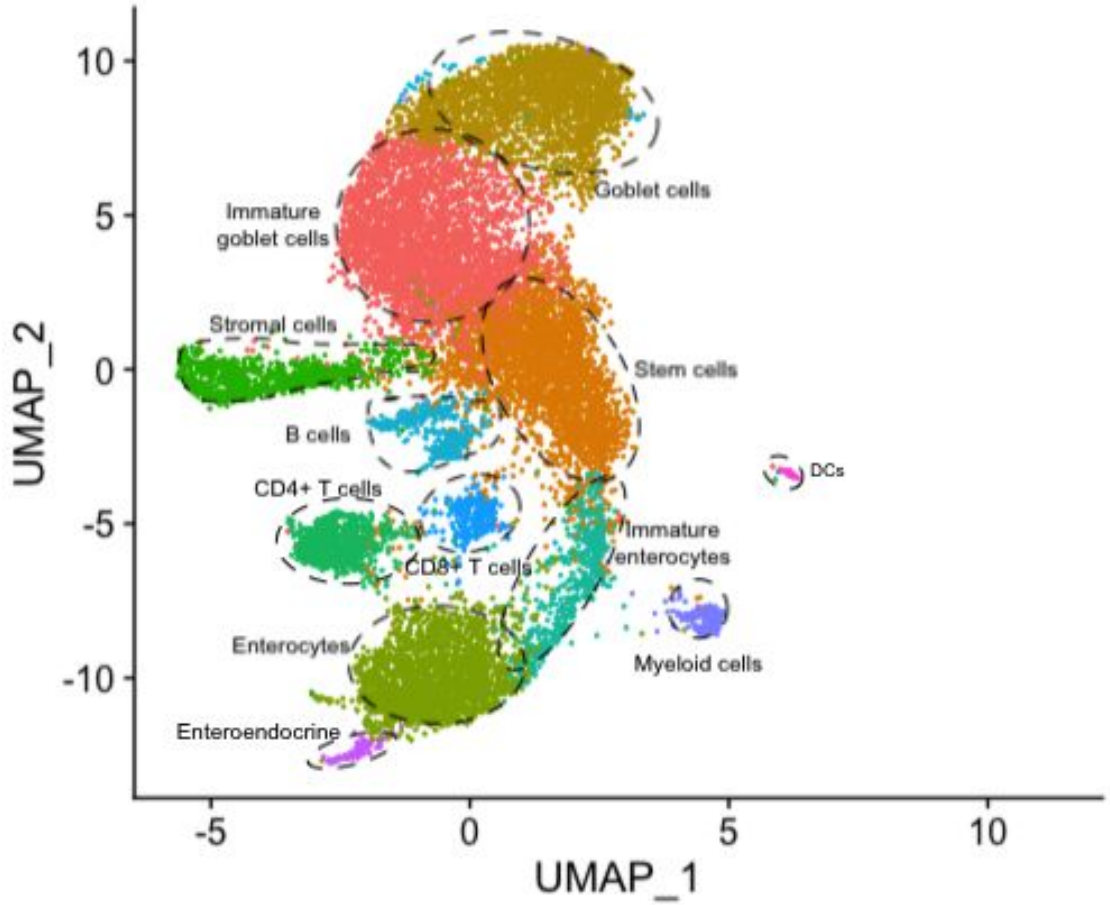










Single Cell Analysis of Colon Tissues Shows Immune and Intestinal Cell Types

scRNA seq - Small Bowel - Ileum

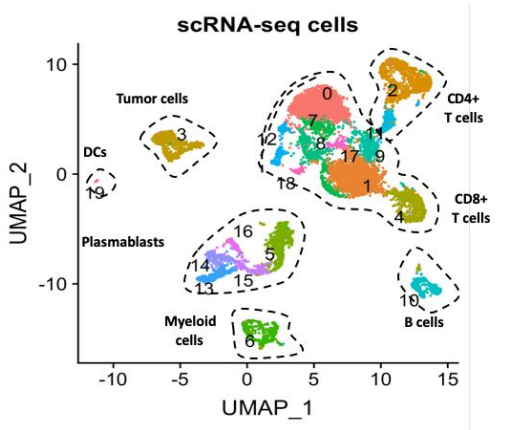


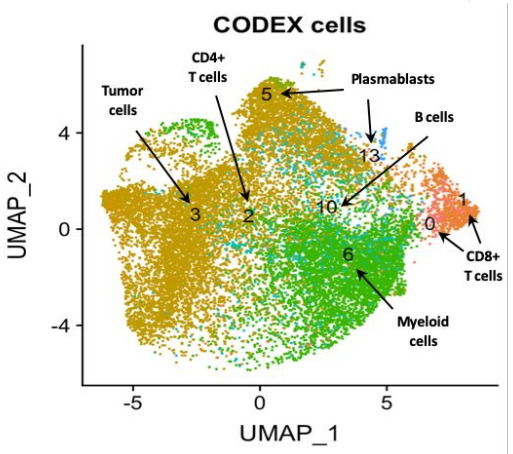
scRNA seq - Small Bowel - Mid Jejunum



Computational Tools for Building and Characterizing a Human Tissue Atlas Based on Single Cell Genomic and Spatial Data

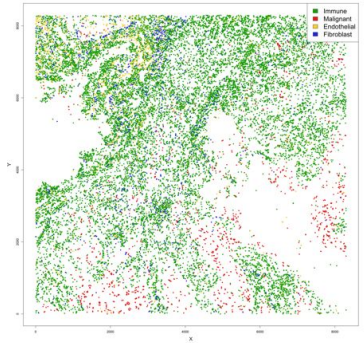
(1) Concordance Mapping of scRNA-seq and CODEX data



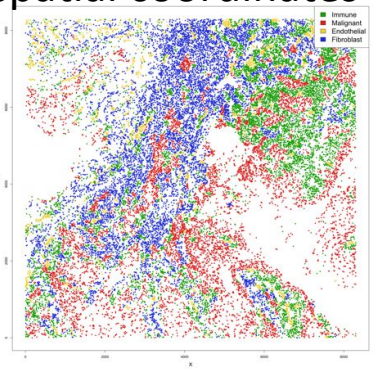


(2) Cell Type Identification on CODEX images

(A) Manual gating

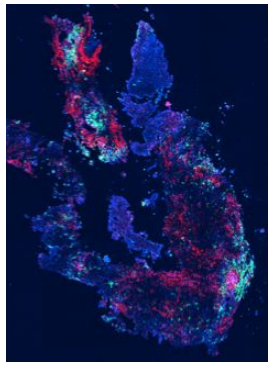


(B) Automated algorithm using spatial coordinates

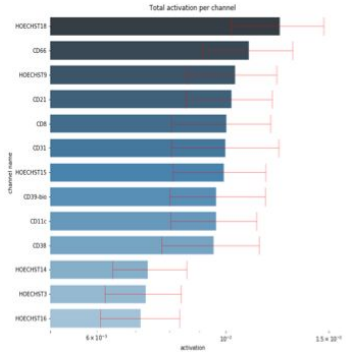


(3) Marker saliency map on using CNN on CODEX images (without cell segmentation)

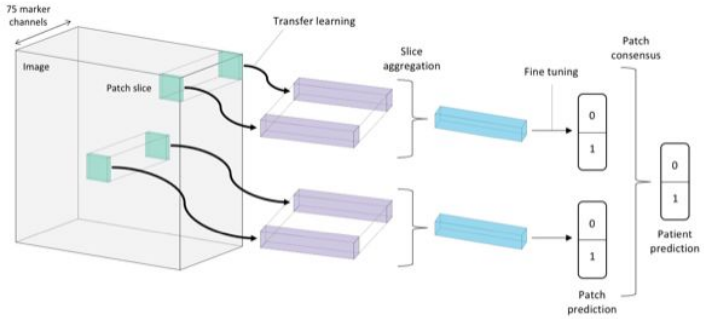
(A)



(B)



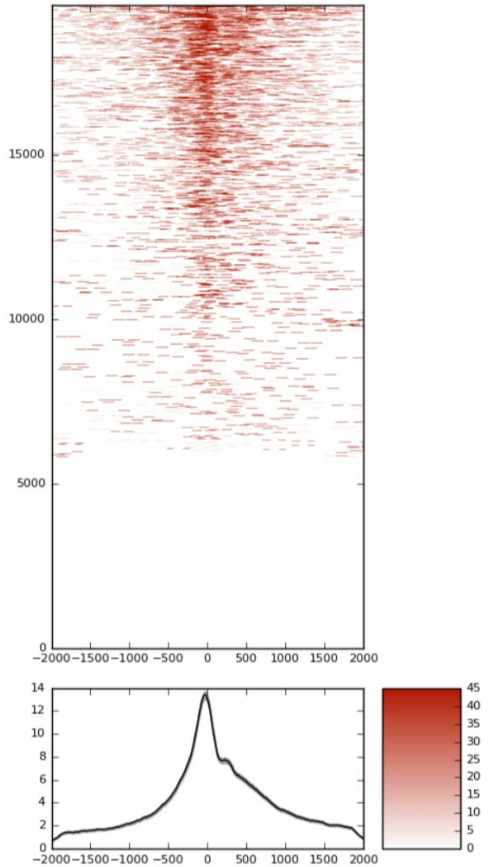
(C)



ATACseq

Initial QC of Samples (~3-5M reads/sample) looks promising. (i.e. High TSS enrichment, etc.)

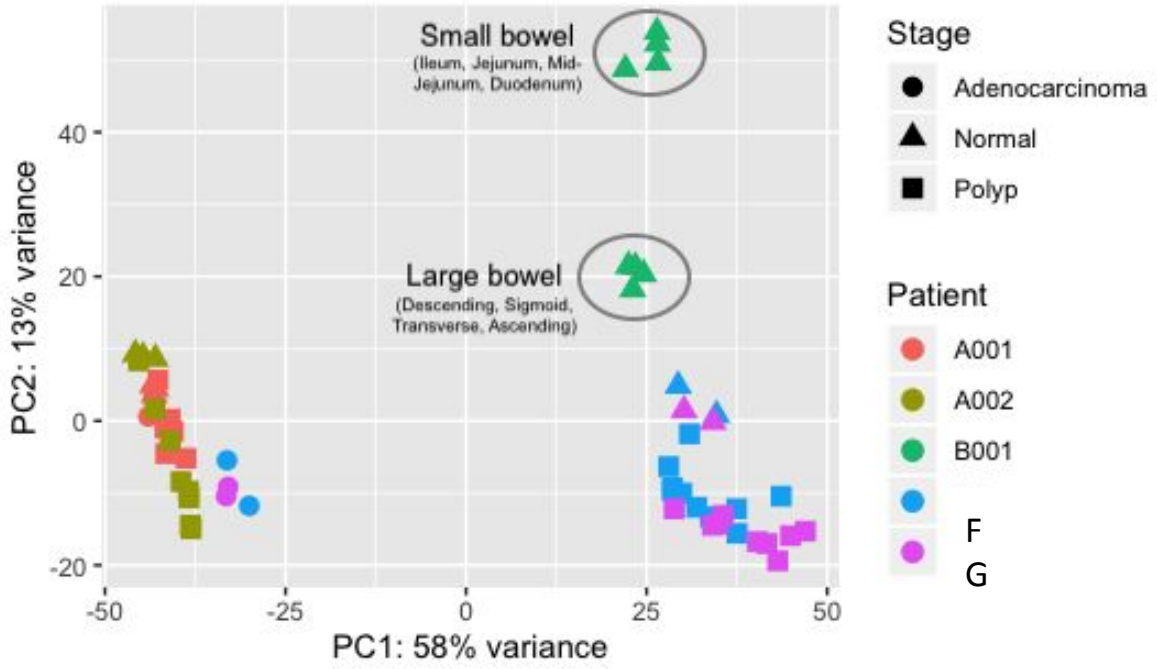
Will resequence to ~25M/reads/sample



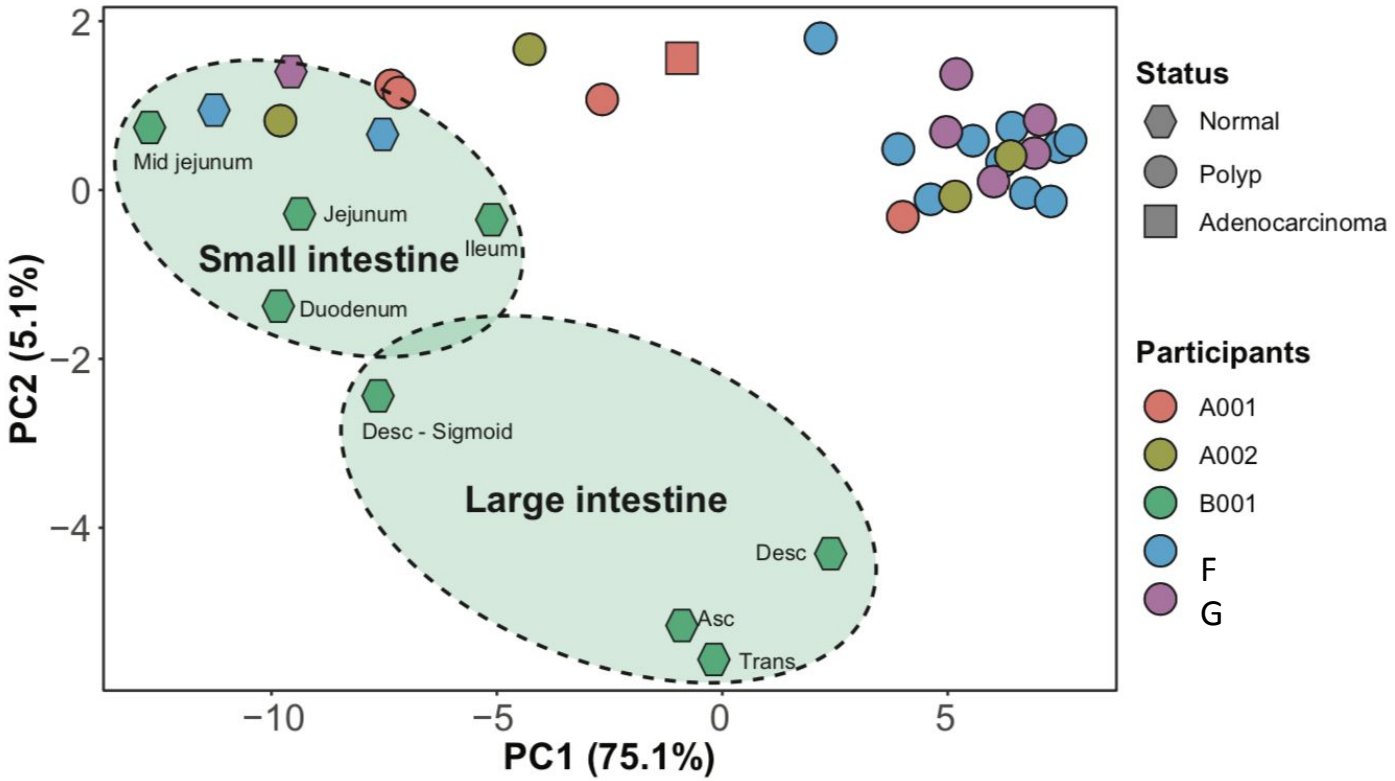
Transcriptome

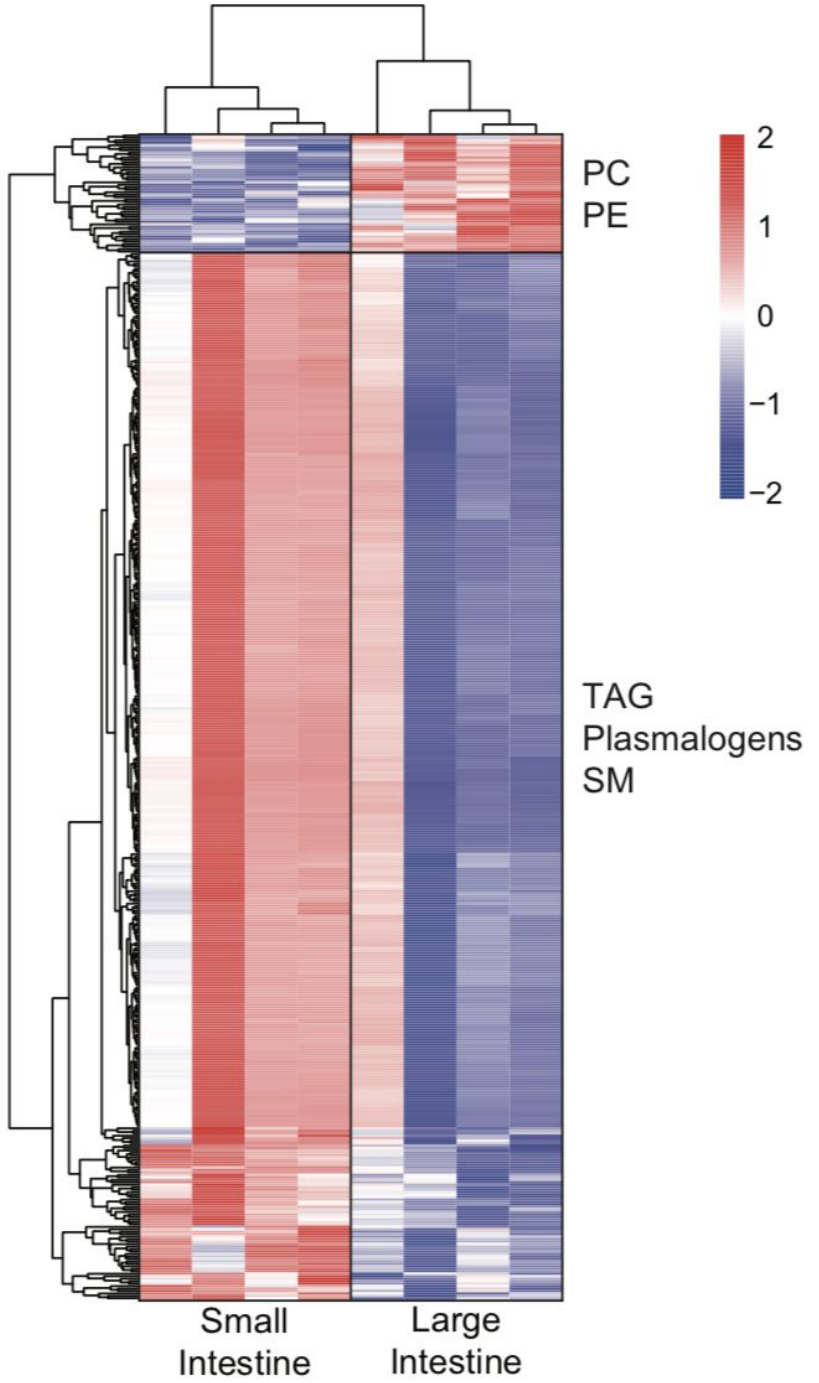
Different regions of the intestine separate (small bowel vs. large bowel)

Different stages of colon tissue separate (normal, benign polyps, adenocarcinoma)



Lipidome


Mid jejunum
Jejunum
Ileum
Small intestine
Duodenum
Desc - Sigmoid
Large intestine
Desc
Asc
Trans
PC2 (5.1%)
PC1 (75.1%)
2
0
−2
−4
−10
−5
0
5
Status
Normal
Polyp
Adenocarcinoma
Participants
A001
A002
B001
F
G


PC
PE
TAG
Plasmalogens
SM
2
1
0
−1
−2
Small Intestine
Large Intestine

Acknowledgements

Snyder Lab
Stephanie Nevins
Lihua Jiang, PhD
Kevin Contrepois, PhD
Amir Bahmani, PhD
Roxanne Chiu

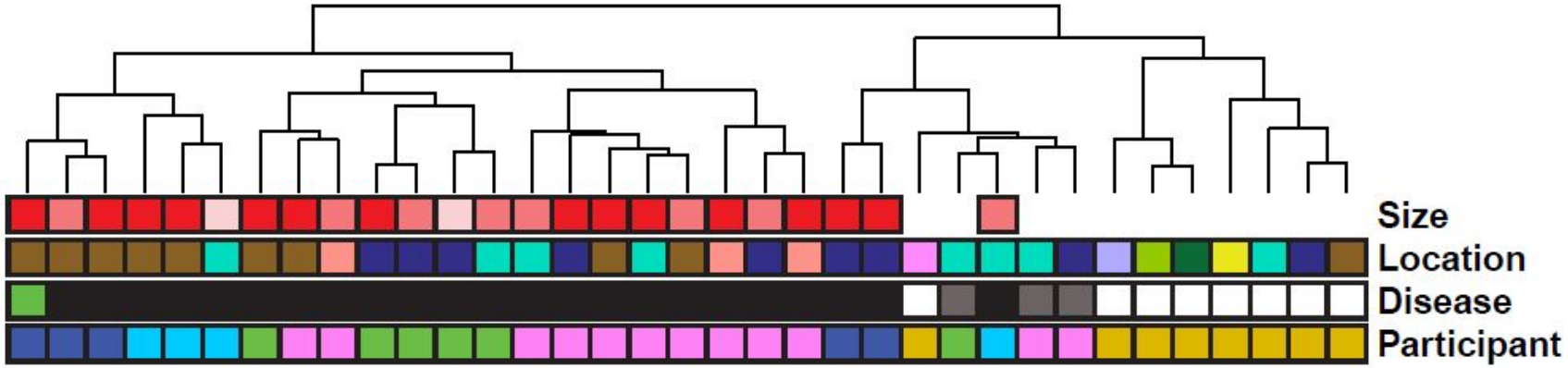
Nolan Lab
John Hickey, PhD
Christian Schuerch, MD, PhD
Sarah Black
Vishal Gautham Venkataraaman

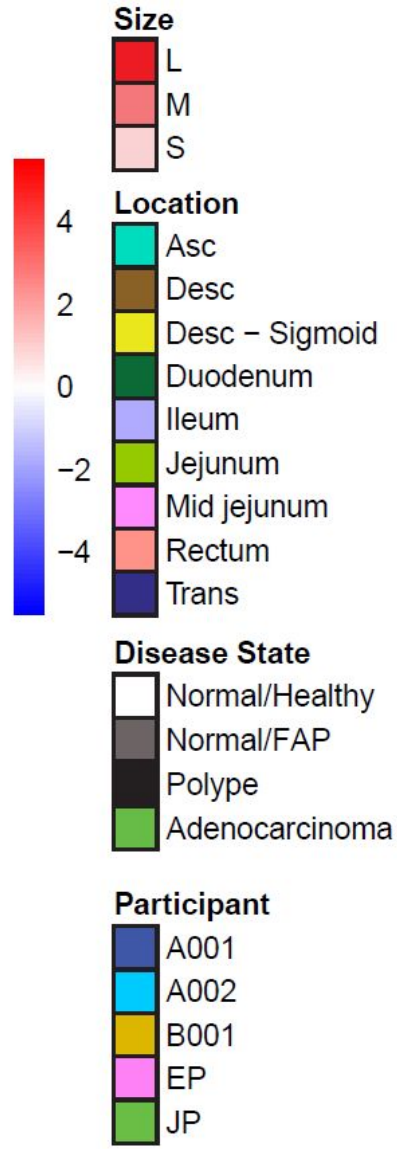
Greenleaf Lab
Winston Becker

Plevritis Lab
Zina Good, PhD

Lin Lab
Min Xu, MD
Jianwei Xing

Lipidome





- Hierarchical clustering on 745 lipid species
- Cluster of normal tissue from healthy individuals and FAP patients.
  - Lipidomic signature can differentiate tissue stage.
- Polyps are mainly clustered by participants
  - Suggests a lipid signature that is independent of polyp size

Future Direction