Implementation of Slide-seq for high-resolution, whole-transcriptome human tissue maps

Broad Institute, Cambridge MA 02142

PI – Evan Macosko

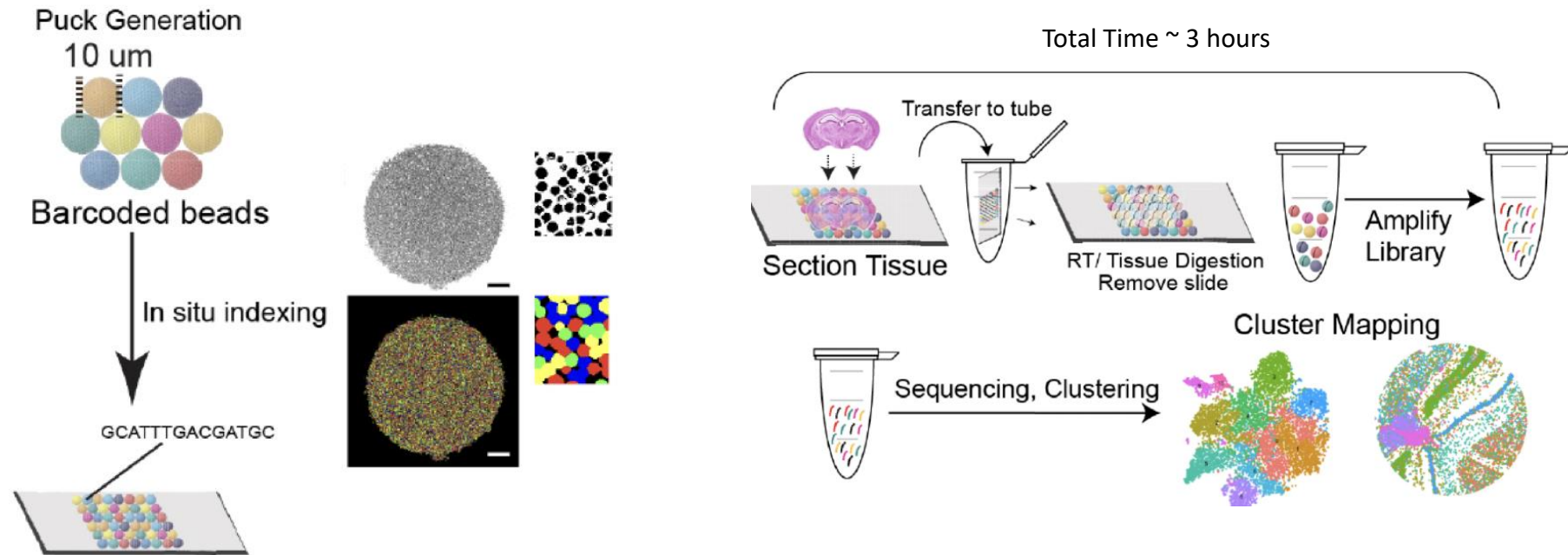Co-I – Fei Chen

Co-I – Kristin Ardlie

Co-I – Samouil Farhi

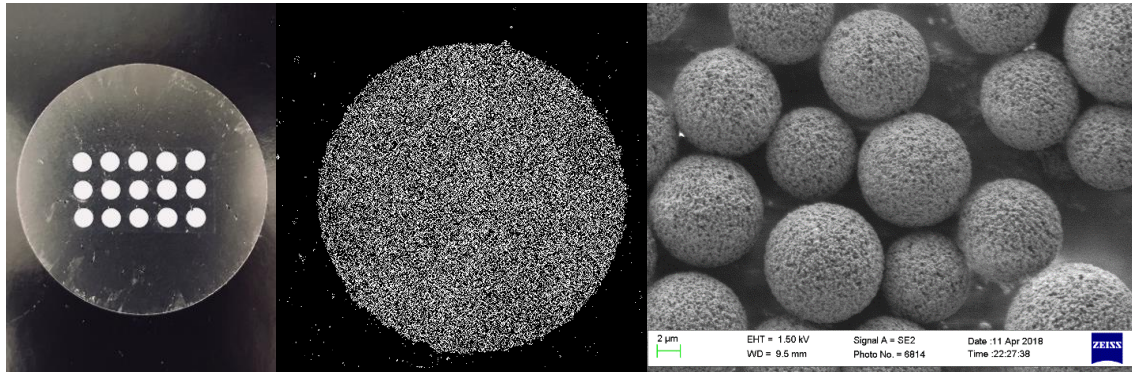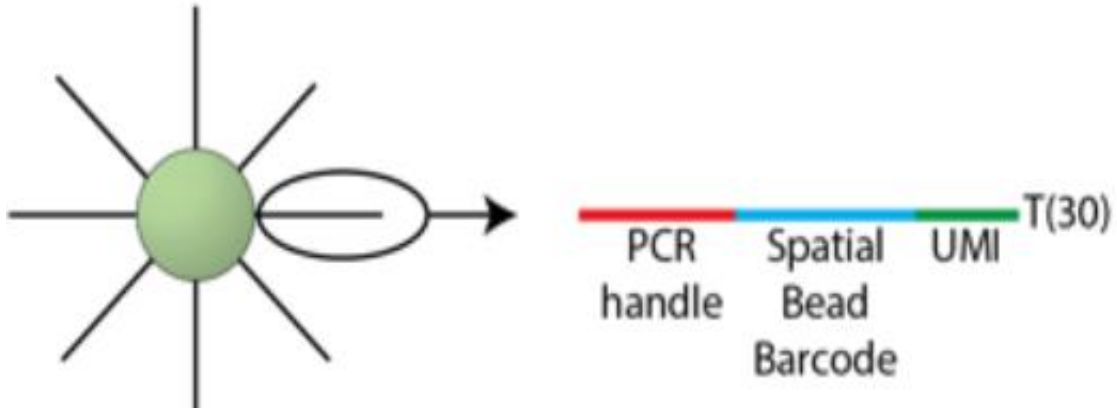Co-I – Aviv Regev

Co-I – Orit Rozenblatt-Rosen

2019 HuBMAP Meeting

Rapid Technology Summary

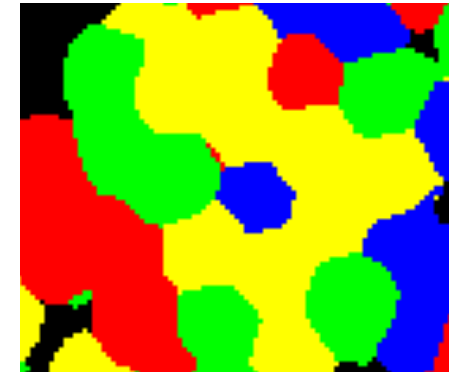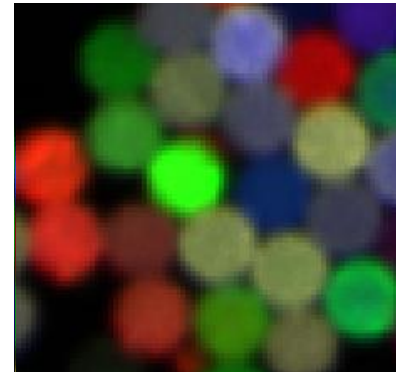**Slide-seq: Spatially resolved genome-wide RNA profiling**

Rapid Technology Summary

1 DEPOSIT BEADS INTO ARRAYS
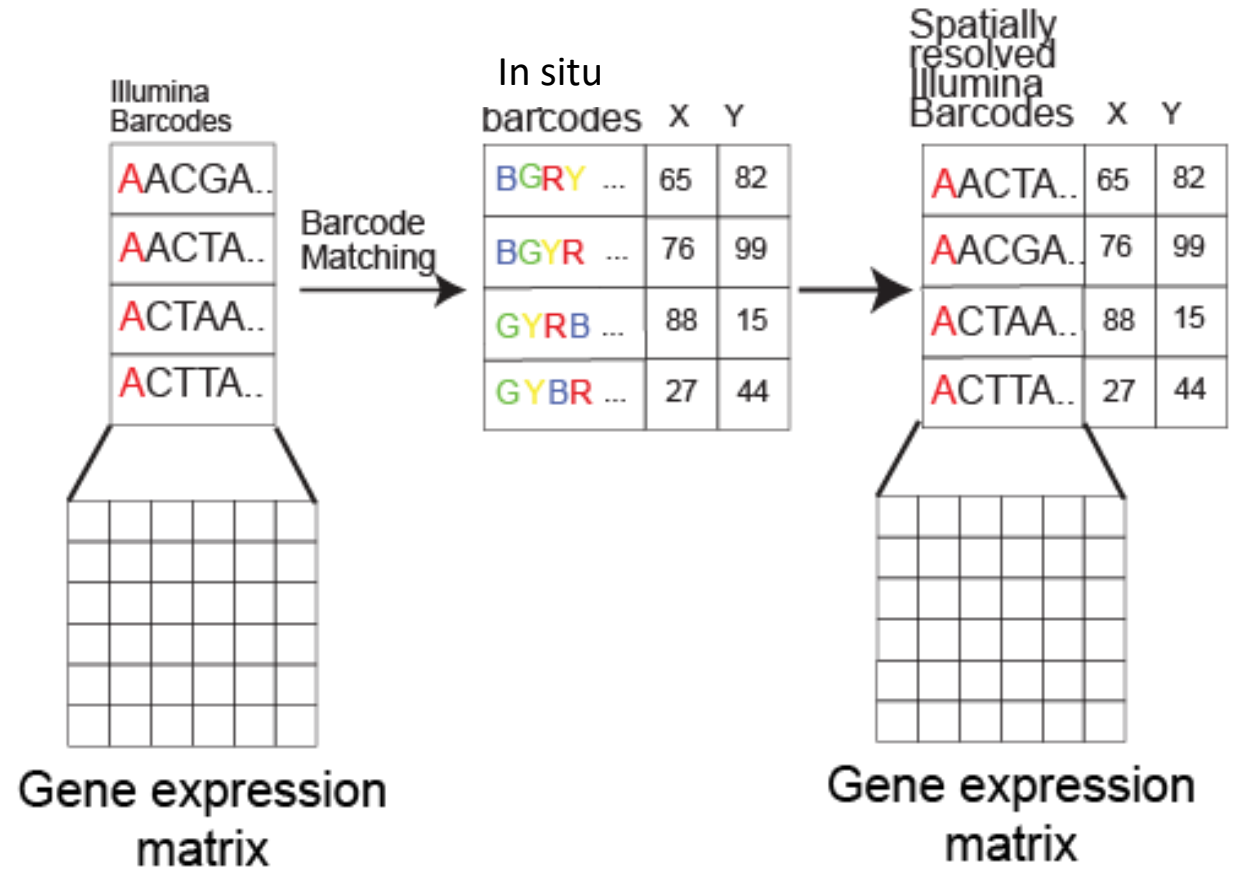

2 SEQUENCE BEAD BARCODES
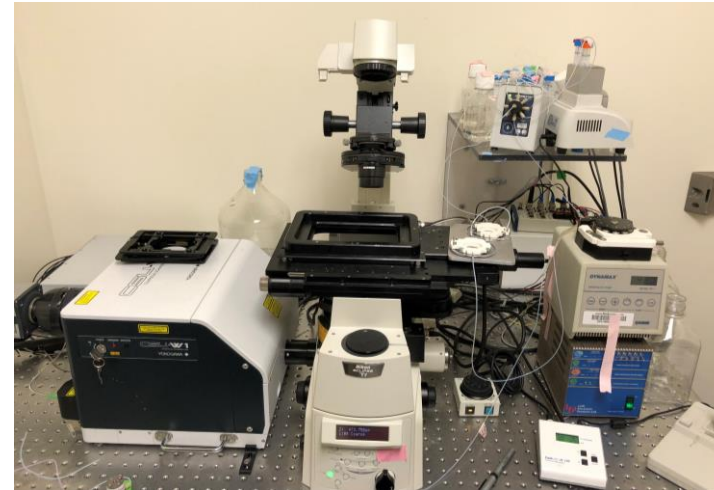
SOLiD seq barcodes	X	Y
BGYR ...	65	82
BGRY ...	76	99
GYRB ...	88	15
GYBR ...	27	44

Total Time ~ 3 hours

Transfer to tube

Section Tissue

RT/ Tissue Digestion
Remove slide

Amplify
Library

1 **DEPOSIT BEADS INTO ARRAYS**

2 **SEQUENCE BEAD BARCODES**

3 **SLICE TISSUE ONTO PUCK**

4 **SEQUENCING**

Illumina Barcodes

Illumina Barcodes
AACGA...
AACTA...
ACTAA...
ACTTA...

Barcode Matching

In situ

barcodes	X	Y
BGRY ...	65	82
BGYR ...	76	99
GYRB ...	88	15
GYBR ...	27	44

Spatially resolved Illumina Barcodes

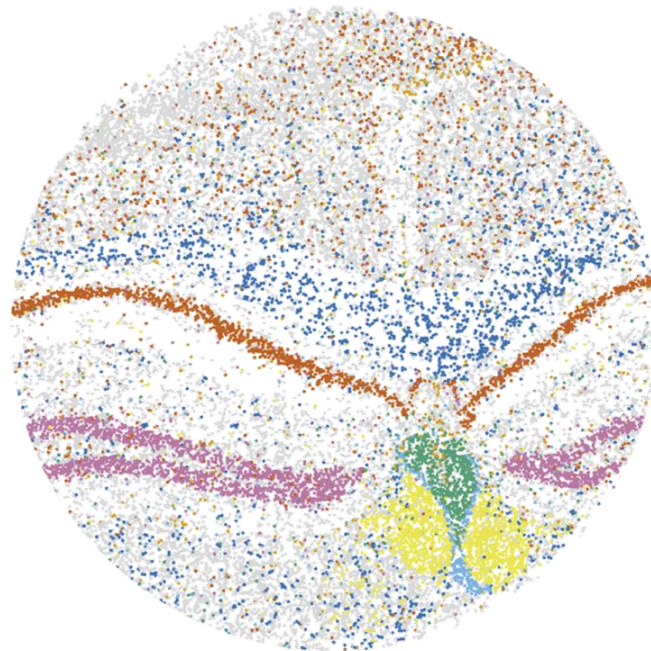| Illumina Barcodes	X	Y
AACTA..	65	82
AACGA..	76	99
ACTAA..	88	15
ACTTA..	27	44

Gene expression matrix

Gene expression matrix
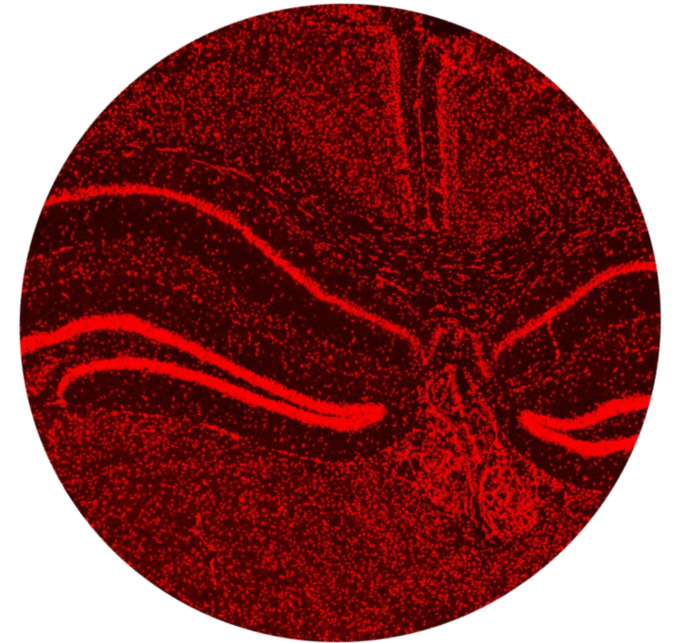
5 MAP GENE EXPRESSION INTO SPACE

tSNE embedding of Slide-seq data
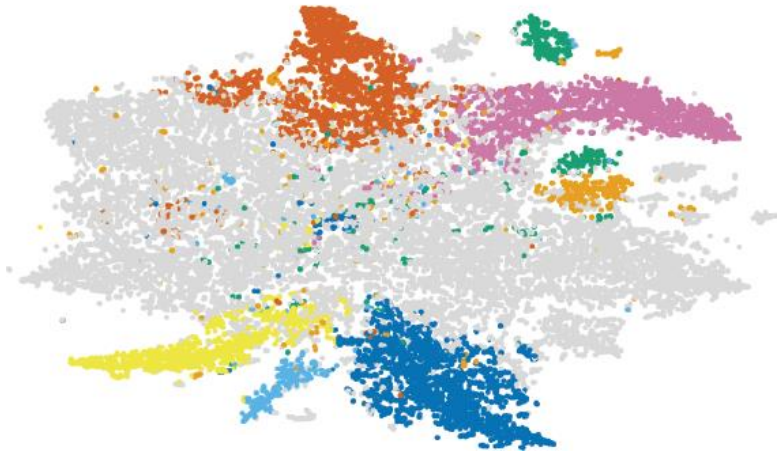
- Fibroblast
- Ependymal
- Choroid
- Habenula
- Oligo
- CA1
- DG

Slide-seq Reconstruction
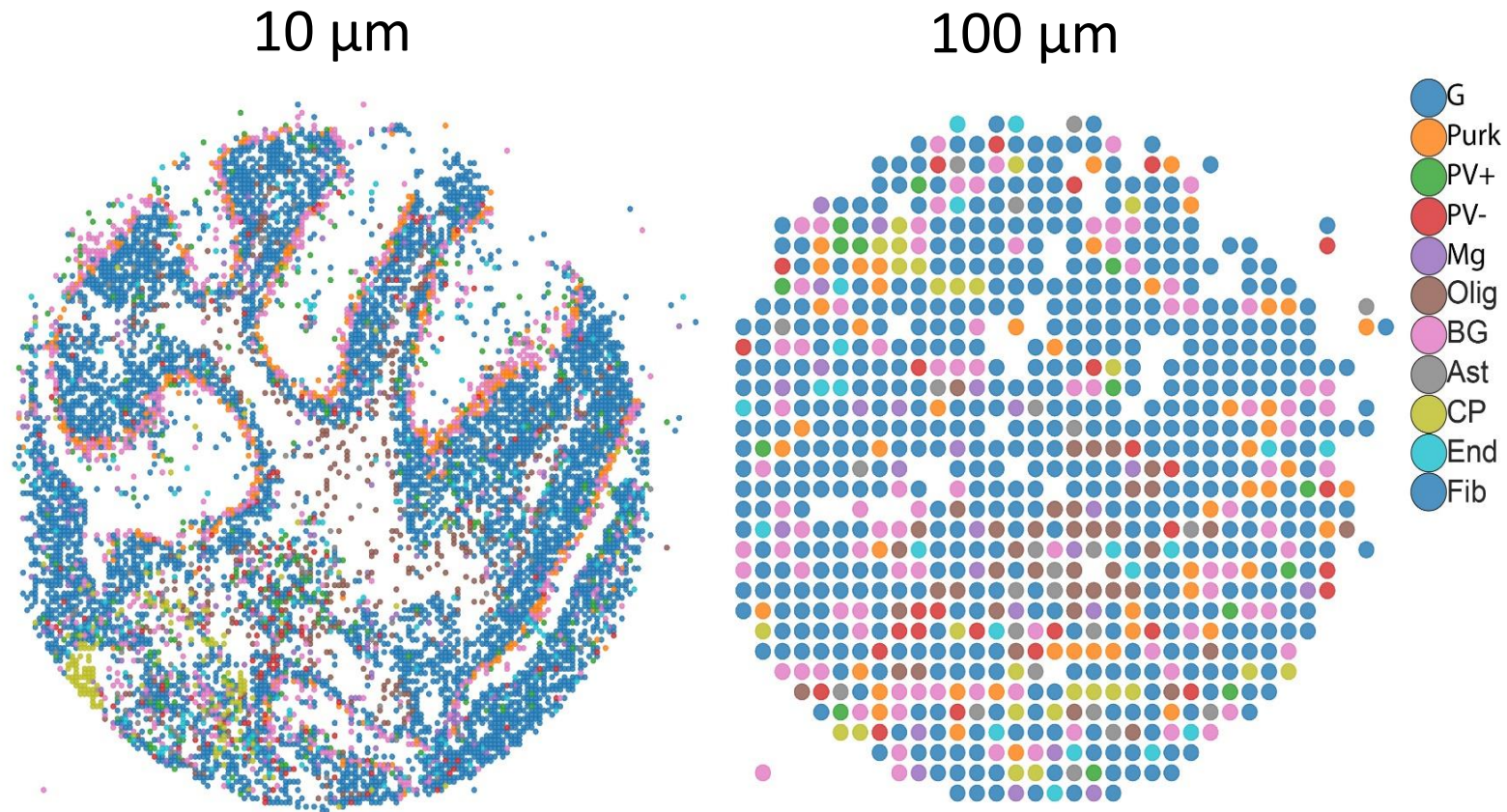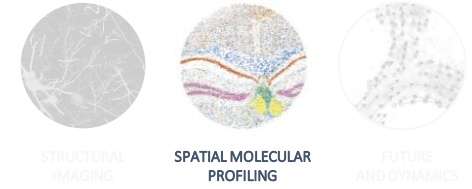No Microscopy

DAPI Stained Serial Section

The importance of spatial resolution

10 μm   100 μm

G
Purk
PV+
PV-
Mg
Olig
BG
Ast
CP
End
Fib

Slide-seq: Scalable spatial genomics

- Spatial localization of the transcriptome
  - Untargeted, genome wide gene expression

- 10 µm resolution
  - Connection to morphology and pathology

- Discovery of spatial patterns of gene expression
  - Spatial differential gene expression
  - Discovery of tissue reorganization without a priori knowledge of cell type


Liver
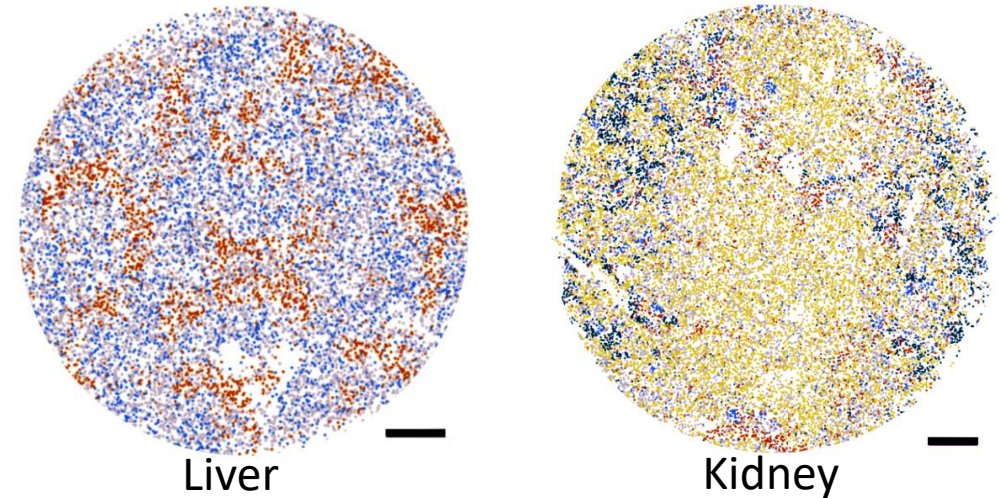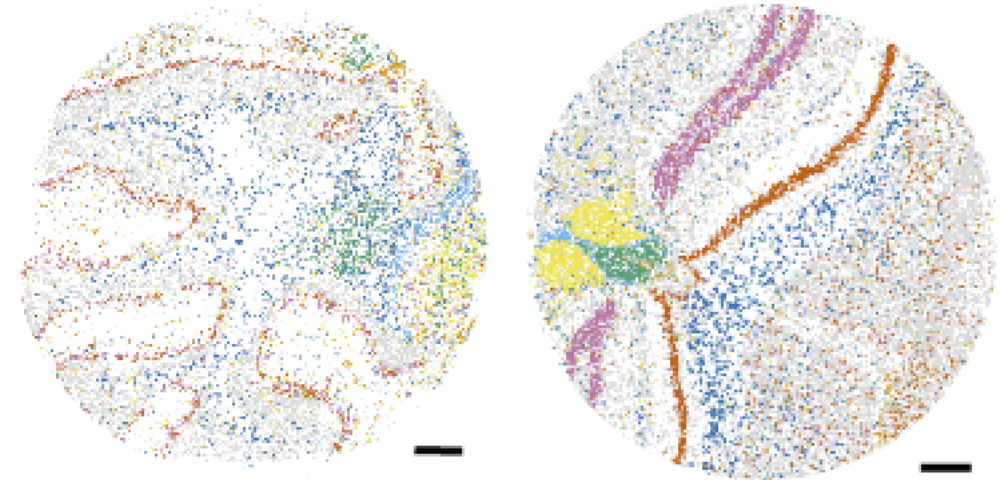
Kidney

Aims

- **1. Collection of samples and establishment of parameters that predict high-quality Slide-seq data across tissues.**

- **2. Optimization of Slide-seq for colon/small intestine and kidney.**

- **3. Generation and dissemination of scalable experimental and computational pipelines for constructing Slide-seq datasets for the HuBMAP consortium.**

Next Year's Deliverables

- ## What resources / data do you expect to make available in 2020?
  - Tissue sampling protocols harmonized with existing HuBMAP TMCs
  - Sample QC metrics predictive of Slide-seq performance (for ~7 tissues)
  - Slide-seq data (~7 tissues, 4 replicates/tissue)
  - Reference snRNAseq data for multiple replicates from initial target tissues (n=2)
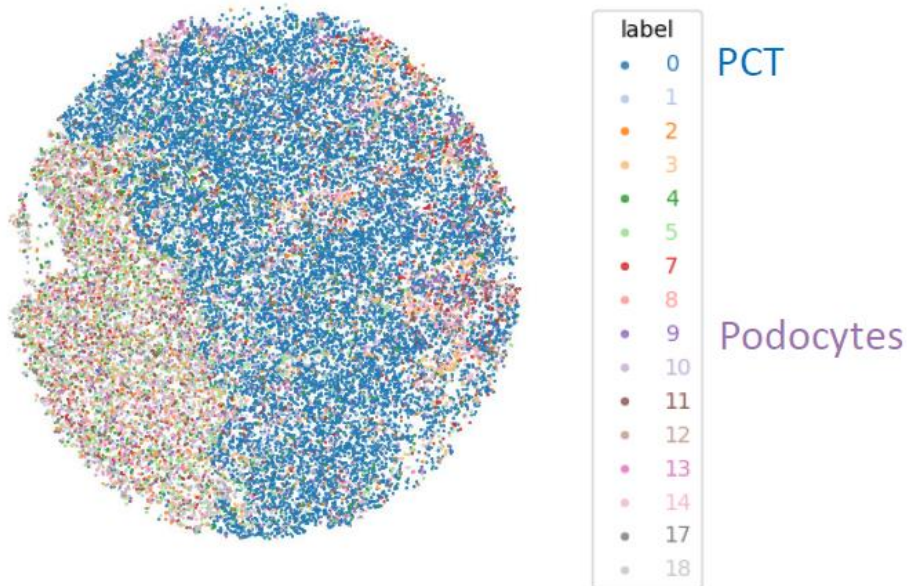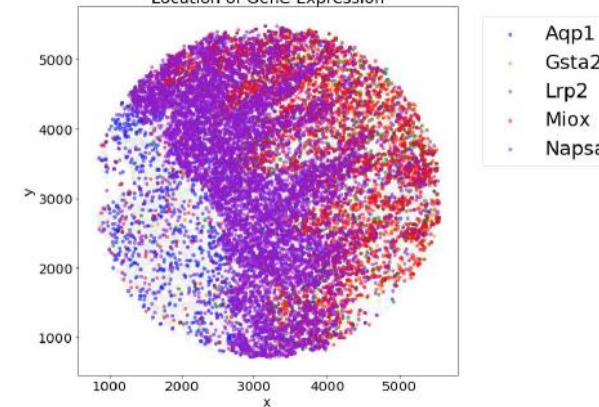
Collaborations

- Summary of collaborative projects.
  - We proposed starting with TWO initial collaborative projects, with (1) Stanford TMC (Snyder) and (2) KULMAP TMC (Zhang). We will be:
    - Harmonize tissues sampled, and sampling protocols (Kidney and Colon/small intestine) with both TMCs
    - Share samples, so as to run matched samples collected by each TMC on Slide seq in our facility
    - Transfer technology (and matched samples) to both TMCs
    - Perform training, testing and running of Slide-seq at and by both TMCs
- What are the barriers to collaboration?
  - None so far, but would like to get to know and learn more about other TMCs so as to expand the collaborations and implementation of Slide-seq with other data types being produced

What should HuBMAP Do ?

- Help foster and enable collaborations across consortium especially for implementation of new technologies
- Diversify number of tissue types, as well as donors
- Make sure diverse set of biomolecules are mapped
- Collaborate with other programs, including those with already existing rich datasets