



MOBP

PCP4

HBB

IGKC

NPY

other

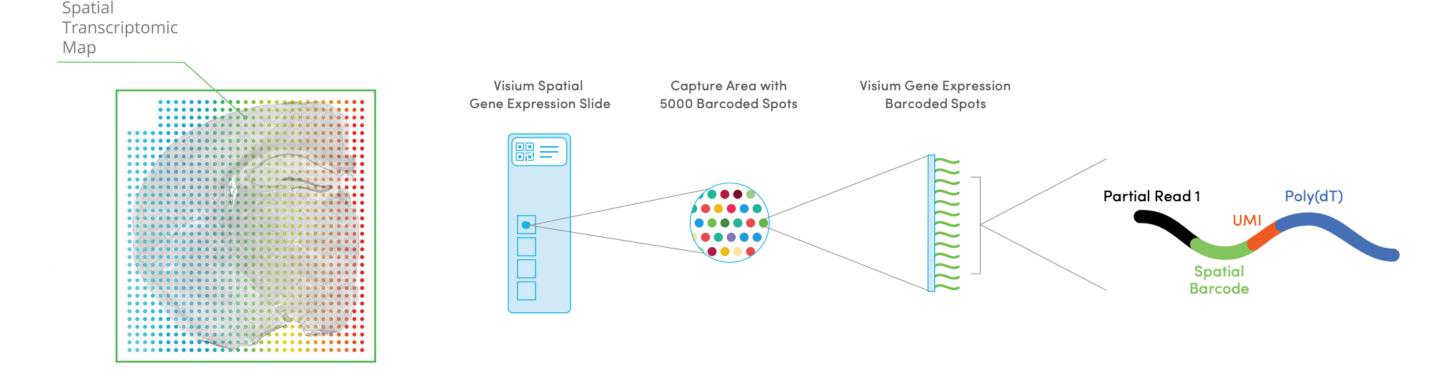
SNAP25

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# **Spatial transcriptomics**

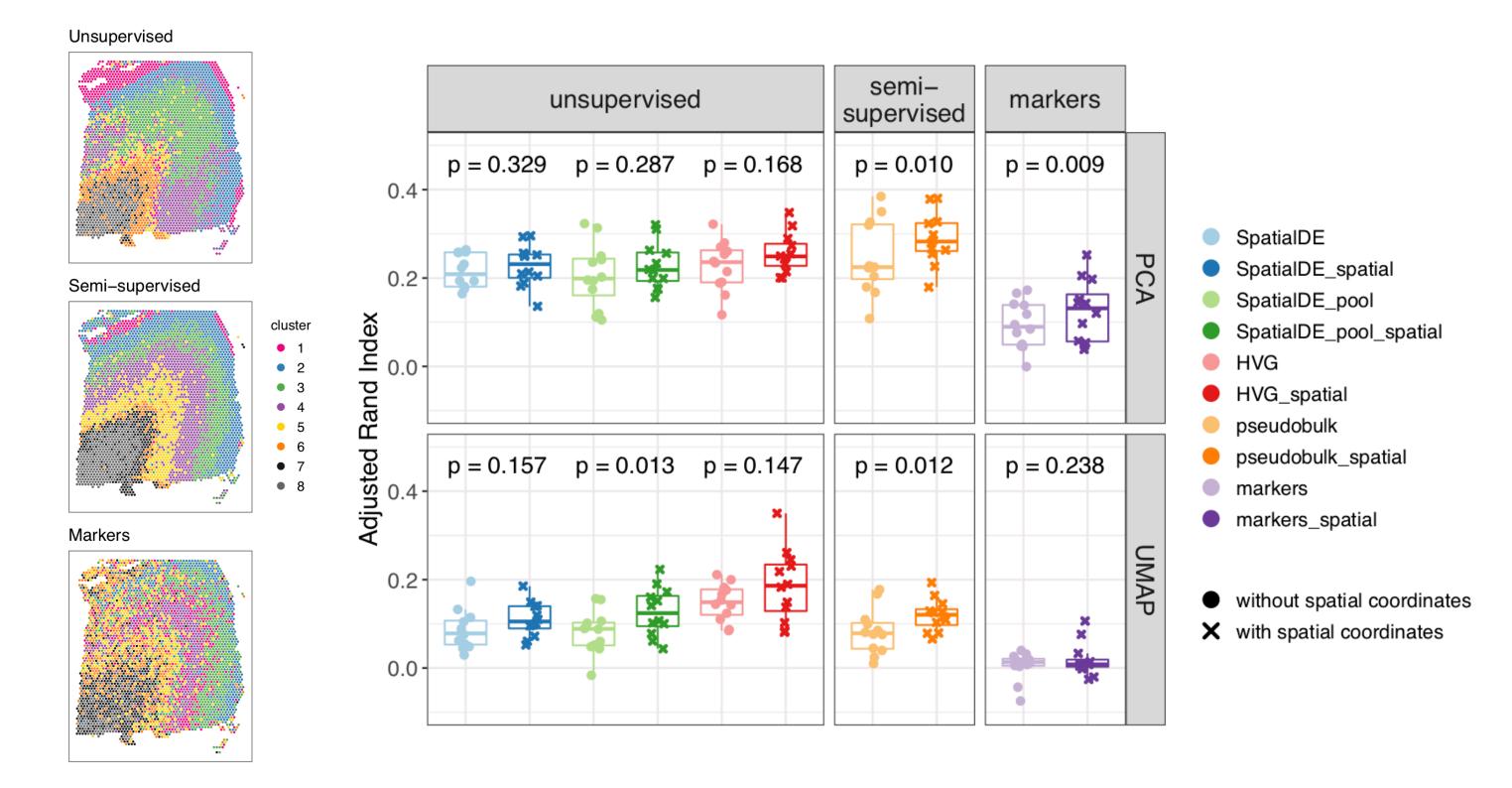
- Transcriptome-wide gene expression measured at grid of spatial coordinates (spots) on tissue slide
- Slide dimensions 6.5mm x 6.5mm, approximately 5000 spots
- Commercially available platform: 10x Genomics Visium



# Results

#### **Unsupervised clustering**

- Various implementations of clustering (with and without spatial information)
- Evaluate performance using ground truth from manual annotation

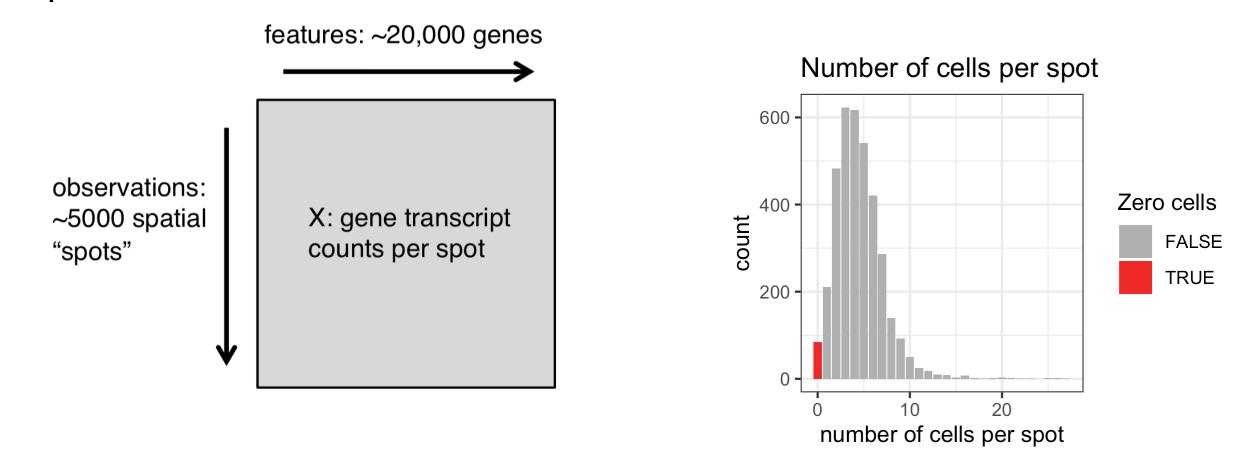


More details:

https://www.10xgenomics.com/products/spatial-gene-expression

## **Data analysis**

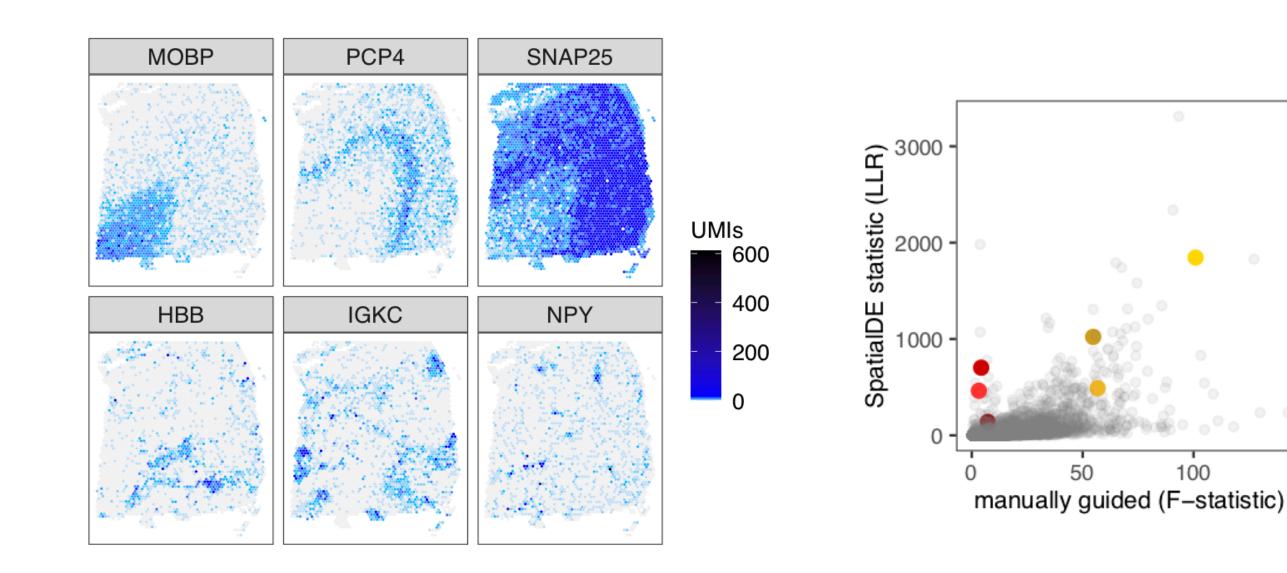
Similarities to single-cell RNA sequencing (scRNA-seq) with additional spatial resolution



- Resolution on the order of single cells, depending on tissue type
- Zero, one, or multiple cells per spot
- Interested in detecting **cell populations** (clustering, marker genes, spatially variable genes)

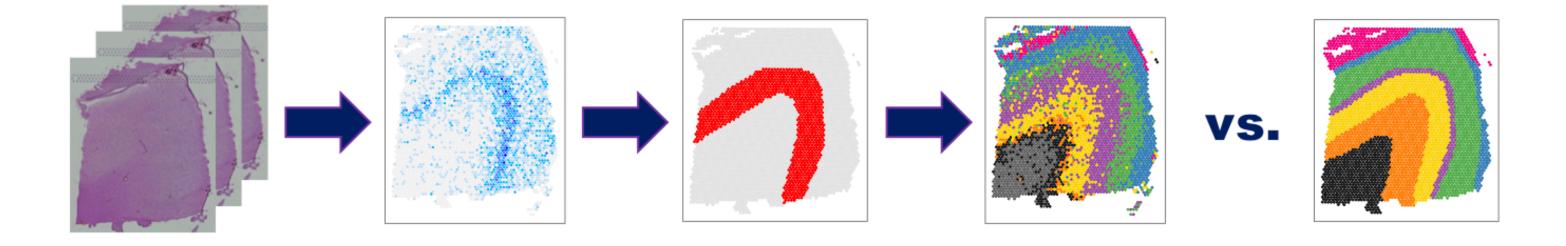
#### **Unexpected results**

- Laminar vs. non-laminar spatially variable genes  $\bullet$
- Spatially variable genes from SpatialDE (Svensson et al. 2018)



#### **Unsupervised analysis pipeline**

- Unsupervised vs. supervised analyses
- Steps in unsupervised analysis:  $\bullet$ 
  - preprocessing and normalization
  - identification of variable genes
  - clustering
  - characterization of clusters
- Example: human brain dorsolateral prefrontal cortex (DLPFC)



## **Experimental collaboration**

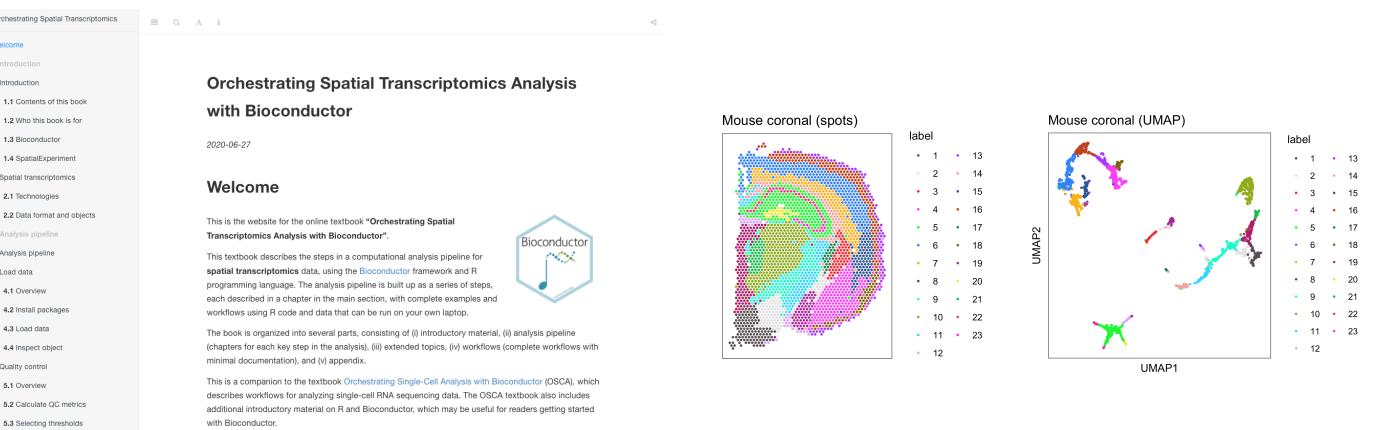
- 3 neurotypical adult donors, 12 samples (2 pairs of spatially adjacent) samples per donor)
- Define spatial landscape of gene expression in human DLPFC, e.g. cortical layer marker genes, layer-enriched gene expression signatures
- Supervised (manually guided) and unsupervised analyses

# **Future work**

- Methods: preprocessing, spatially variable genes, spatially aware clustering
- Complete pipeline for unsupervised analyses



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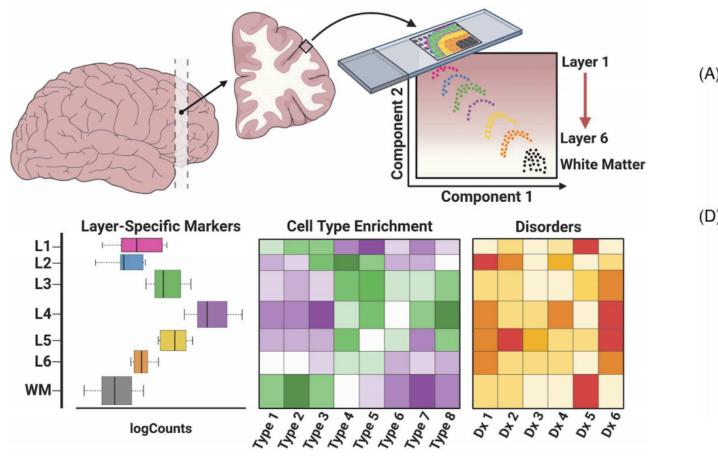


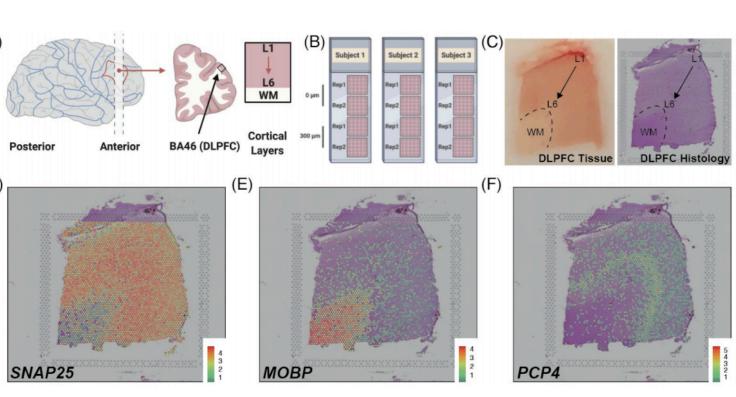
# More details

- Preprint: Maynard and Collado-Torres et al. (2020) https://www.biorxiv.org/content/10.1101/2020.02.28.969931v1
- Code and data resources (Leonardo Collado-Torres) Shiny web app: <a href="http://research.libd.org/spatialLIBD/">http://research.libd.org/spatialLIBD/</a> Bioconductor package: <u>http://bioconductor.org/packages/spatialLIBD</u> Code repository: <a href="https://github.com/LieberInstitute/HumanPilot/">https://github.com/LieberInstitute/HumanPilot/</a>



Integration with neuropsychiatric disorder gene sets and spatial registration of existing single-nucleus RNA sequencing (snRNA-seq) data





More details:

Maynard and Collado-Torres et al. (2020) https://www.biorxiv.org/content/10.1101/2020.02.28.969931v1

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ranscriptome-scale spatial gene expression in the human dorsolateral		Posted February 28, 2020.	
refrontal cortex         Kristen E Maynard, I Leonardo Collado-Torres, I Lukas M. Weber, I Cadric Uytingco,         Brianna K. Barry, Stephen R. Williams, I Joseph L. Catallini II, I Matthew N. Tran, Zachary Besich,         Madhavi Tippani, Jennifer Chew, Yifeng Yin, Joel E. Kleinman, Thomas M. Hyde, Nikhil Rao,         Stephanie C. Hicks, I Keri Martinowich, A Andrew E Jaffe         oi: https://doi.org/10.1101/2020.02.28.969931         nis article is a preprint and has not been certified by peer review [what does this mean?].         Abstract       Info/History		<ul> <li>Download PDF</li> <li>Supplementary Material</li> <li>Data/Code</li> <li>Tweet</li> <li>Like 1</li> <li>Subject Area</li> <li>Neuroscience</li> </ul>	<ul> <li>Email</li> <li>Share</li> <li>Citation Tools</li> </ul>
Abstract We used the 10x Genomics Visium platform to define the spatial topography expression in the six-layered human dorsolateral prefrontal cortex (DLPFC).	5	Subject Areas	

## Acknowledgments

Johns Hopkins Bloomberg School of Public Health Prof. Stephanie Hicks

#### JOHNS HOPKINS **BLOOMBERG SCHOOL** of PUBLIC HEALTH

· a shiny web application that we are hosting at spatial.libd.org/spatialLIBD/ that can

· and a research article with the scientific knowledge we drew from this dataset. The

 a Bioconductor package at bioconductor.org/packages/spatialLIBD (or from here) that lets you analyze the data and run a local version of our web application (with our data

Welcome to the spatialLIBD project! It is composed of

analysis code for our project is available here

handle a limited set of concurrent users

spatialLIBD

#### Lieber Institute for Brain Development

Dr. Kristen Maynard Dr. Leonardo Collado-Torres Prof. Keri Martinowich Prof. Andrew Jaffe



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