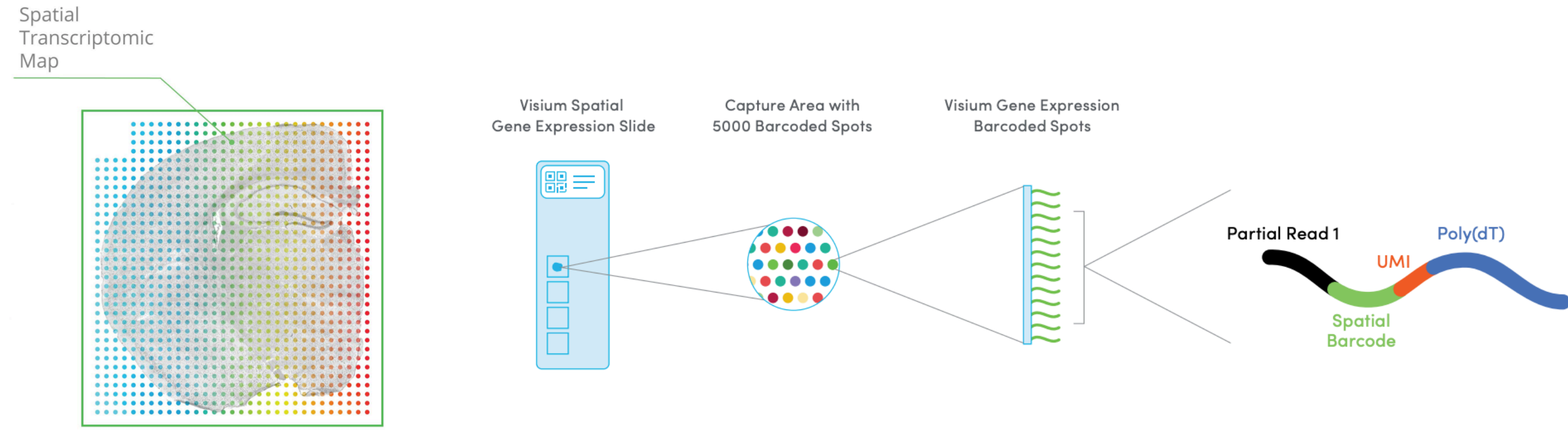


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Spatial transcriptomics

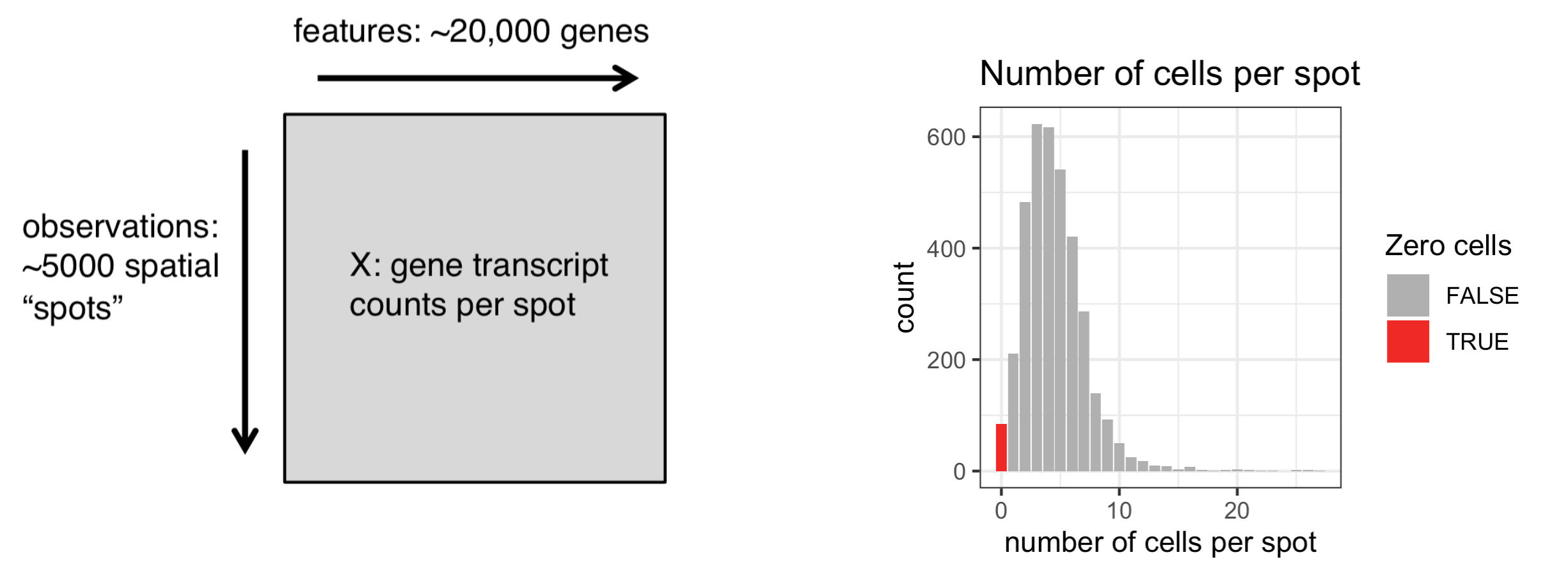
- Transcriptome-wide gene expression measured at grid of spatial coordinates (spots) on tissue slide
- Slide dimensions 6.5mm x 6.5mm, approximately 5000 spots
- Commercially available platform: 10x Genomics Visium



- More details:
<https://www.10xgenomics.com/products/spatial-gene-expression>

Data analysis

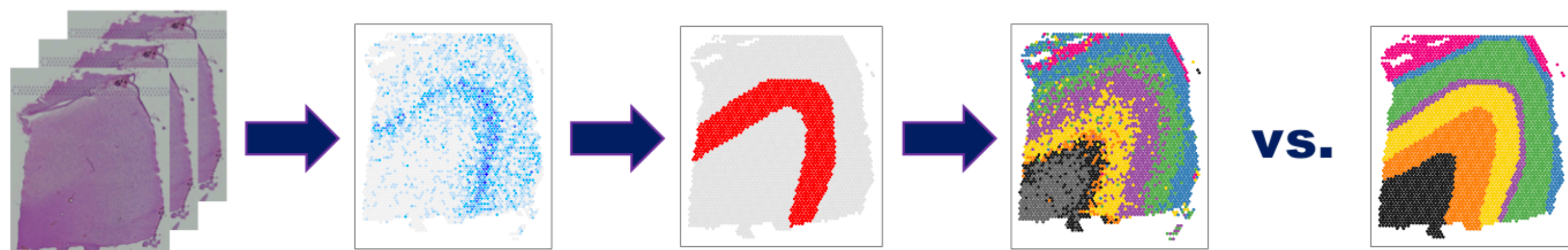
- Similarities to single-cell RNA sequencing (scRNA-seq) with additional spatial resolution



- 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)

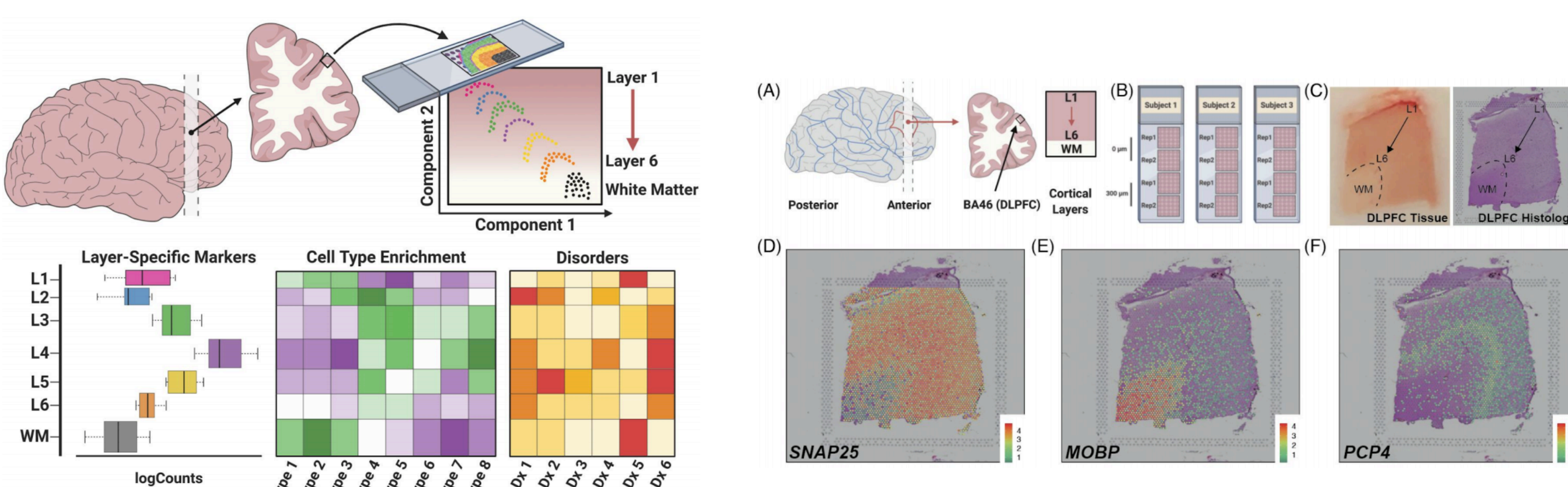
Unsupervised analysis pipeline

- Unsupervised vs. supervised analyses
- Steps in unsupervised analysis:
 - 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
- Integration with neuropsychiatric disorder gene sets and spatial registration of existing single-nucleus RNA sequencing (snRNA-seq) data

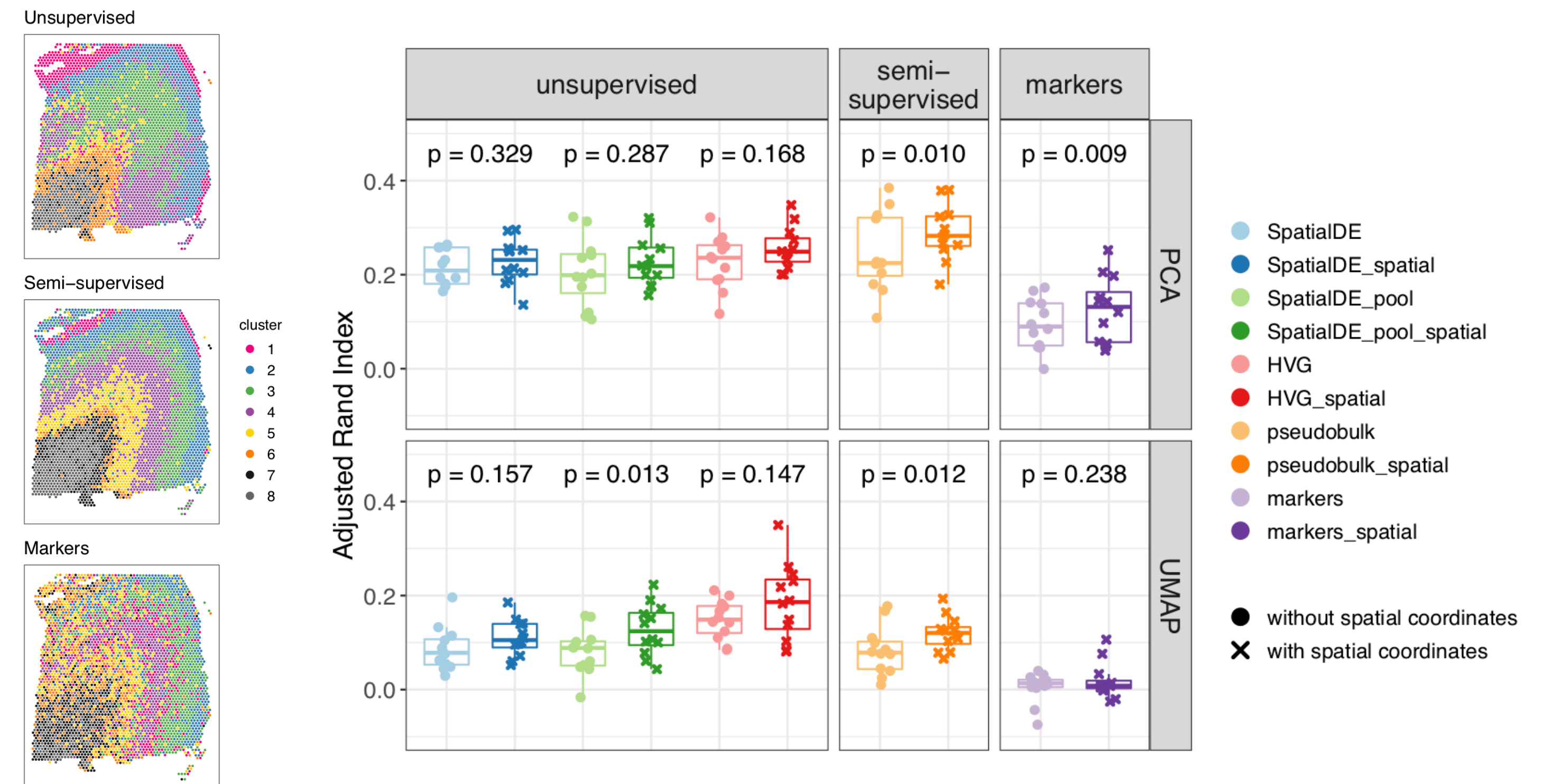


- More details:
Maynard and Collado-Torres et al. (2020)
<https://www.biorxiv.org/content/10.1101/2020.02.28.969931v1>

Results

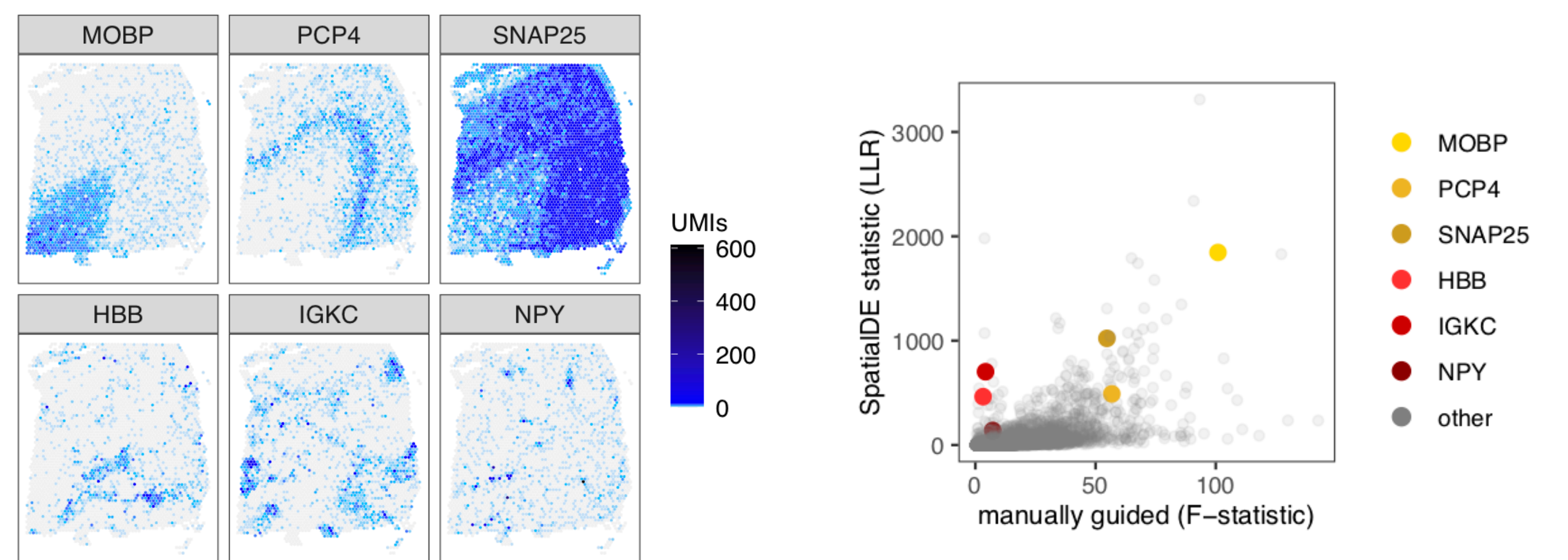
Unsupervised clustering

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



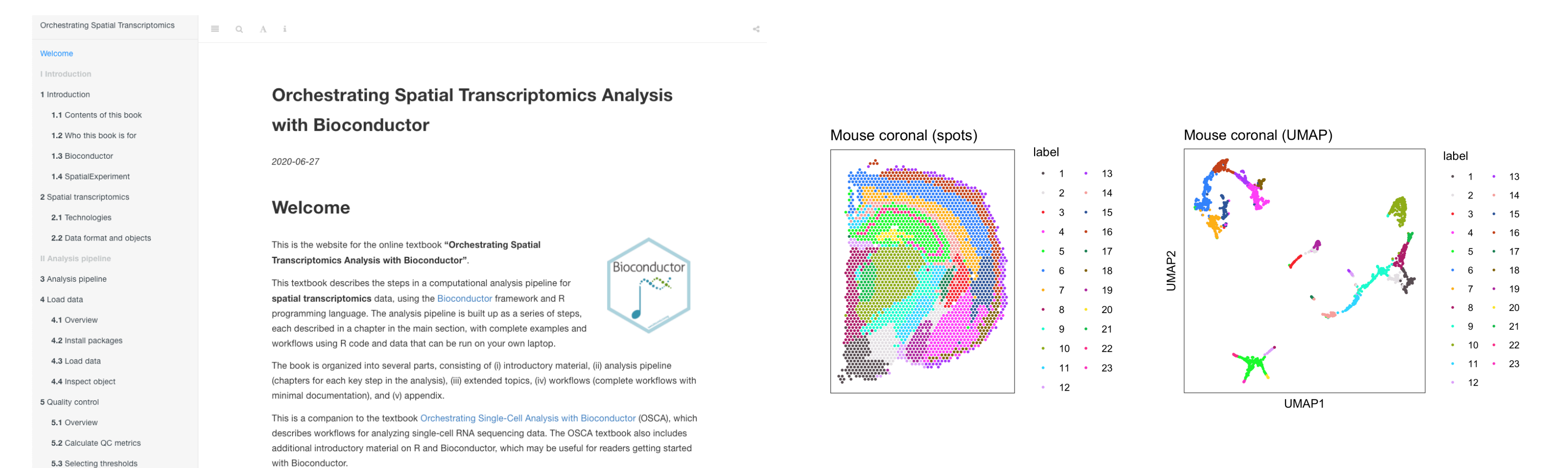
Unexpected results

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



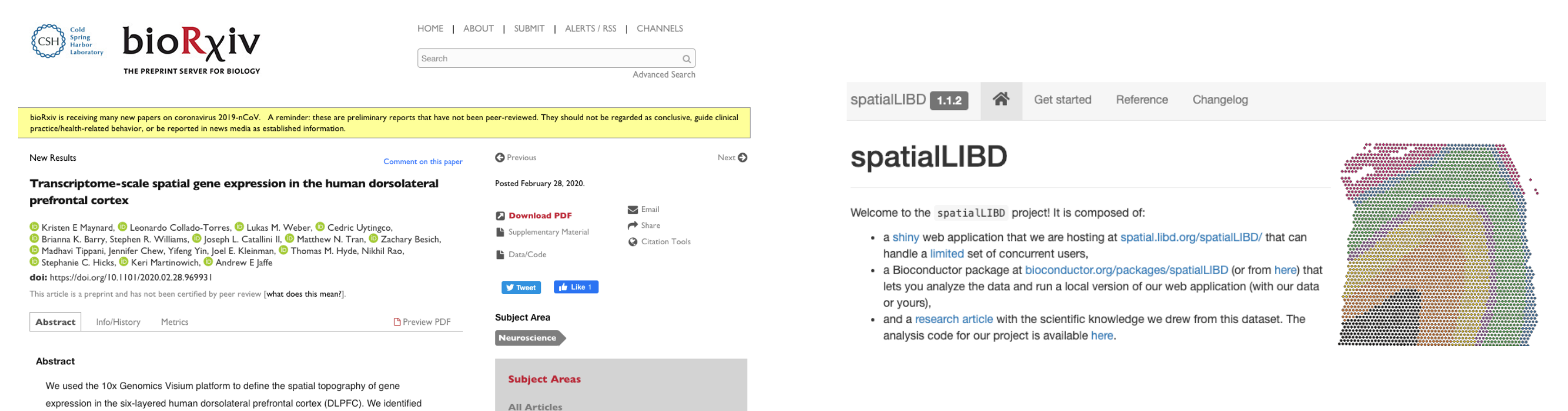
Future work

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



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: <http://research.libd.org/spatialLIBD/>
Bioconductor package: <http://bioconductor.org/packages/spatialLIBD>
Code repository: <https://github.com/LieberInstitute/HumanPilot/>



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