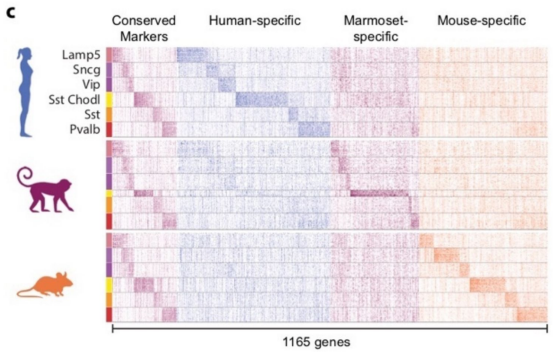
Single Cell Transcriptomics

Newsletter April 2020

Paper 1

Bakken, TE *et al.* Evolution of cellular diversity in primary motor cortex of human, marmoset monkey, and mouse, *bioRxiv, 2020.*



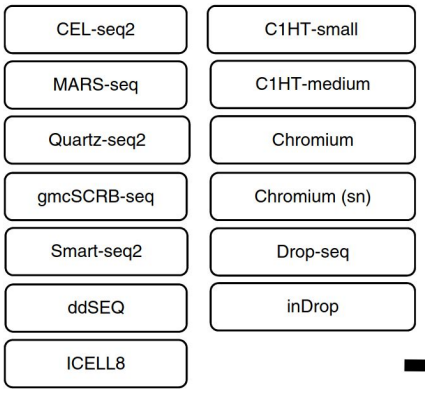
A large collaborative project headed by Ed Lein from Allen Brain Institute published the pre-print of their results on evolution of the primary motor cortex. Single-nucleus RNA-seq sequencing (SMART-Seq v4 and 10x Chromium v3) was used for comprehensive comparison of cell type composition across species. Moreover, dual-omic expression and chromatin accessibility (SNARE-seq2) assays were applied to reveal regulatory processes defining M1 cell types. A pre-print by Yao Z et al for a companion study, focusing only on the mouse brain was also uploaded. Beware, the Results section without figures alone takes 20 pages.

Papers 2,3

Ding, J *et al.* Systematic comparison of single-cell and single-nucleus RNA-sequencing methods, *Nature Biotech, 2020*

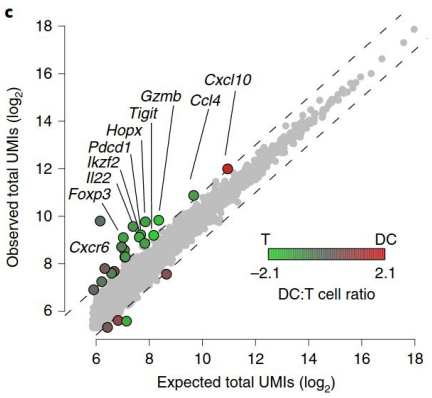
Mereu, E *et al.* Benchmarking single-cell RNA-sequencing protocols for cell atlas projects, *Nature Biotech, 2020*

Two papers on comparison of scRNA-seq protocols were published. The first paper compares 7 protocols on 3 types of samples: cell lines, peripheral blood mononuclear cells and brain tissue. Smart-Seq2 and CEL-seq2 were picked as low-throughput methods, and 10x Chromium, Drop-Seq, Seq-Well, inDrops and sci-RNA-seq represent the family of high throughput. Smart-Seq2 and inDrops were shown to have the highest fraction of exonic reads. As expected, low-throughput methods have higher sensitivity, while among high-throughput, 10x detected the most UMIs and genes per cell. The second paper compares 13 protocols (see the picture). On their benchmarks, Quartz-seq2 got the highest score even beating 10x Chromium, which took second place.



Paper 4

Giladi, A *et al.* [Dissecting cellular crosstalk by sequencing physically interacting cells](), *Nature Biotech, 2020*

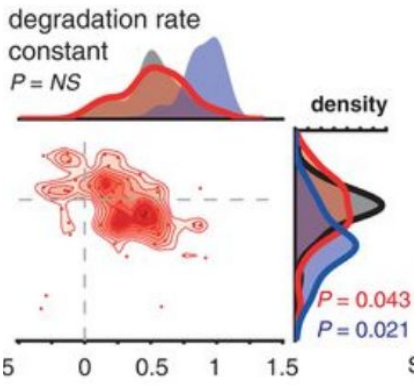


Scientists from the Weizmann Institute developed a method for sequencing of physically interacting cells (PIC-seq). To pick interacting cells of two specific cell types, the authors propose to select a pair of markers, which are mutually exclusive in these types. Then, through careful dissociation, authors collect cells without separating ones, connected in physical space. It allows a pair of interacting cells to be selected as a "doublet" inside one well, which can be distinguished as they express both of the markers selected above. Comparing expression of doublet cells (i.e. PICs) to the expression of singlets, the authors perform deconvolution of the expression to infer expression change, corresponding to the interaction.

For now, the technology is limited in its scope, and the deconvolution step reduces power dramatically. But it's a solid step forward in understanding of cell-cell interactions.

Paper 5

Battich, N, *et al.* [Sequencing metabolically labeled transcripts in single cells reveals mRNA turnover strategies](), *Science, 2020*



Battich et al developed a method that simultaneously quantifies metabolically 5-ethynyl-uridine-labeled (EU) and preexisting unlabeled transcripts in thousands of individual cells (scEU-seq). This method allows to study RNA synthesis and degradation using pulse-chase analysis. Varying either the EU incubation time or the length of a chase phase the authors were able to estimate the synthesis and the degradation rates for all detected transcripts. Furthermore, they studied how these rates change over time by placing individual cells along cell cycle or differentiation trajectories. Clustering of the expression levels, synthesis rates and degradation rate constants revealed distinct strategies of mRNAregulation during the cell cycle, showing three types of regulatory strategies: cooperative, neutral and destabilizing. Findings also suggest that both synthesis and degradation rates are changing during cell cycle. Overall, this study is a good basis to start validating models behind RNA-velocity methods.

Next Single Cell Seminar

The seminar is cancelled due to COVID19.

If you would like to announce anything single cell related, being it job announcement, event, your published paper, technology development etc, please contact us.

Contact viktor.petukhov@bric.ku.dk