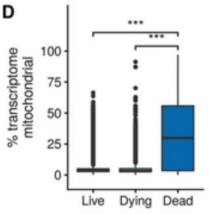
Single Cell Transcriptomics

Newsletter November 2019

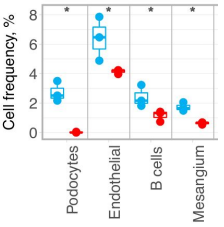
Papers 1-2: benchmarking biological workflows

O'Flanagan, CH. et al. [Dissociation of solid tumor tissues with cold active protease for single-cell RNA-seq minimizes conserved collagenase-associated stress responses] *Genome Biology, 2019.*



A rare paper evaluating different ways of tissue processing. The authors aim to determine the effects of enzymatic dissociation and temperature on gene expression artifacts in tumor tissues and cell lines. Examining 48 samples, containing 155k cells in total they investigate transcriptional response on different processing conditions.

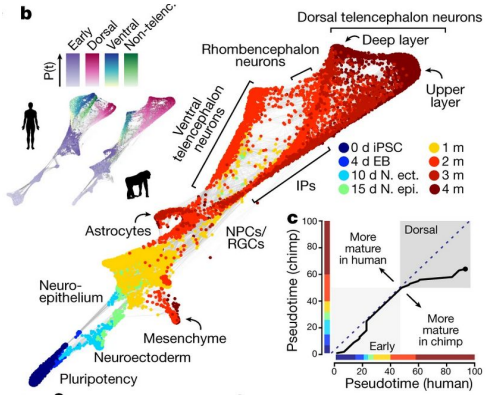
Denisenko, E. et al. [Systematic bias assessment in solid tissue 10x scRNA-seq workflows] *bioRxiv, 2019.*



Second paper on the topic compares two tissue dissociation protocols, two cell preservation methods, bulk tissue RNA sequencing, single-cell and three single-nucleus RNA sequencing workflows for the 10x Genomics Chromium platform on mouse kidneys. The authors conclude that in addition to stress response, different processing steps may greatly affect cell type composition in sample.

Paper 3

Kanton, S. et al. [Organoid single-cell genomic atlas uncovers human-specific features of brain development] *Nature, 2019.*

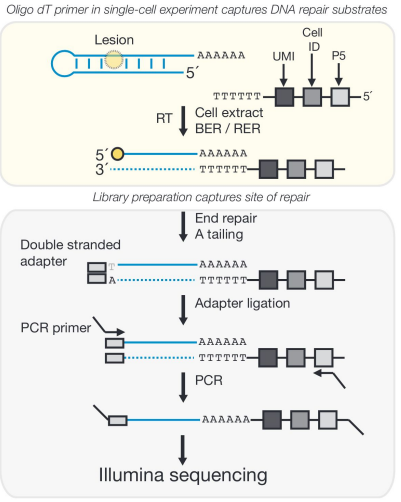


In collaboration, Camp and Treutlein labs published a large study on the development of the human brain in comparison to chimpanzee, bonobo and macaque. The authors measured single-cell expression across a time course of the organoid development and compared trajectories in different species. Single-cell ATAC-seq was also performed to identify potential regulatory mechanisms.

Papers 4-5: multimodal measurements from single cells

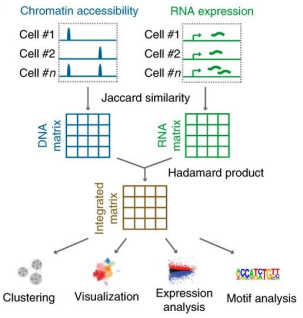
Richer, AL. et al. [Simultaneous measurement of biochemical phenotypes and gene expression in single cells] *bioRxiv 2019.*

Here, researchers from the University of Colorado developed a new method to simultaneously measure biochemical activities and mRNA levels in single cells. Investigators were able to measure simultaneous activity of several enzymatic activities (however w/o ability to unambiguously link them to specific enzymes) in sequenced blood cells altogether with the measurement of expression levels of mRNAs. Thus sc-mRNA profiles were augmented by extra modality of cell enzymatic activity. Though gene detection sensitivity dropped **twice** compared to standard 10x protocol possibly due to purification of cDNA prior to the cDNA pre-amplification step. Moreover, it is unclear how to measure prevailing majority of enzymatic activities present in the cell (e.g. glucose metabolism, etc) not based on modification of RNA/DNA. Fluorescence based readout could be another option (not mentioned in the paper), but more easily applicable to plate-based techniques and limited to a small amount of simultaneous enzymatic reactions due to spectral overlaps between fluorescent molecules/probes. Thus currently presented technique could be useful for measuring several DNA/RNA modifying activities in single cells, but not more than that.



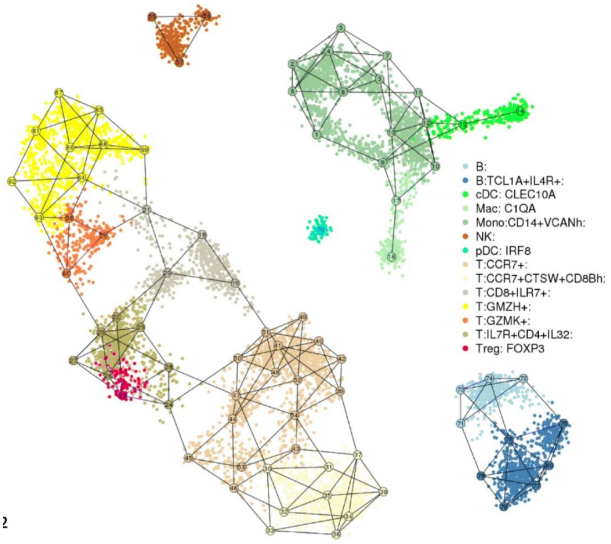
Zhu, C. et al. [An ultra high-throughput method for single-cell joint analysis of open chromatin and transcriptome] *Nature Structural & Molecular Biology 2019.*

This paper proposes a novel method for parallel analysis of transcriptome and accessible chromatin. In comparison to previous works, it greatly reduces costs and increase throughput enabling profiling of millions of single cells.



Paper 6

Baran, Y. et al. [MetaCell: analysis of single-cell RNA-seq data using K-nn graph partitions] *Genome Biology*, 2019.



Finally, here is a bioinformatic paper. Amos Tanay lab published the tool, which they already used in at least 6 top-level publications. MetaCell is an R package that searches for groups of cells with statistically "identical" expression profiles. Which means that cells within the same group can be considered as coming from exactly the same state in a way that all differences can be explained by sampling bias. Given this assumption, cells from the same group can be aggregated to meta-cells with denser expression vector. Thus, the whole dataset can be reduced to 100-200 meta-cells, removing computational limitations for the analysis and increasing the quality of the data.

The approach has a lot in common with PAGA, though different formulation of cell grouping problem (meta-cells instead of clusters) allow to expand analysis far beyond differentiation trajectories and visualization. However, if you decide to try it, be aware that usage of the method is as complex as its description!

Conferences

- Single cell profiling and analysis in neuroscience, 15 June - 3 July 2020, Bordeaux, France

Next Single Cell Seminar

Date: 29th November 2019, Location: Mærsk Tower, Top Floor

9:00 – 9:40
Mykhailo Batuik, BRIC - Investigation of schizophrenia using single cell transcriptomics

10:00 – 10:40
Amalie Kai Bentzen, DTU - Simultaneous identification of antigen-specificity and T cell receptor sequence in single cells

10:40 – 11:00 Coffee and Discussion

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