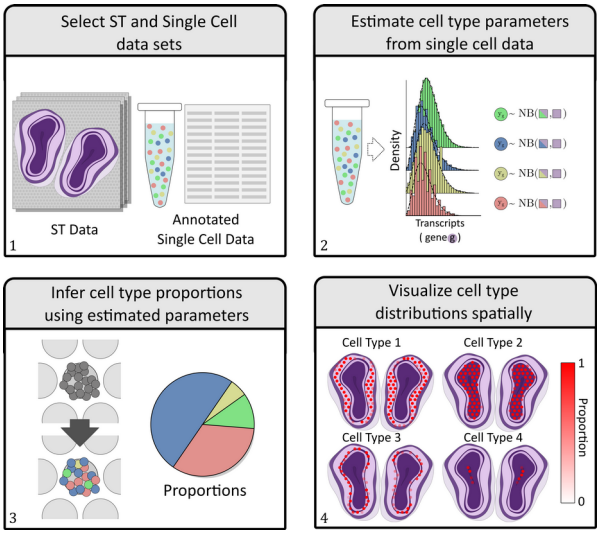
Single Cell Transcriptomics

Newsletter December 2019

Paper 1. Spatial mapping of cell types by integration of transcriptomics data

Andersson A. et al., *bioRxiv*, 2019.



Lundeberg group from SciLifeLab (Sweden) is known for the development of spot based spatial transcriptomics technology currently commercialized by 10x. It provides good sensitivity for transcript detection together with the spatial coordinates of transcripts in the tissue. However, expression data is derived from several neighboring cells that overlap with the RNA capture spot limiting the resolution to supracellular level.

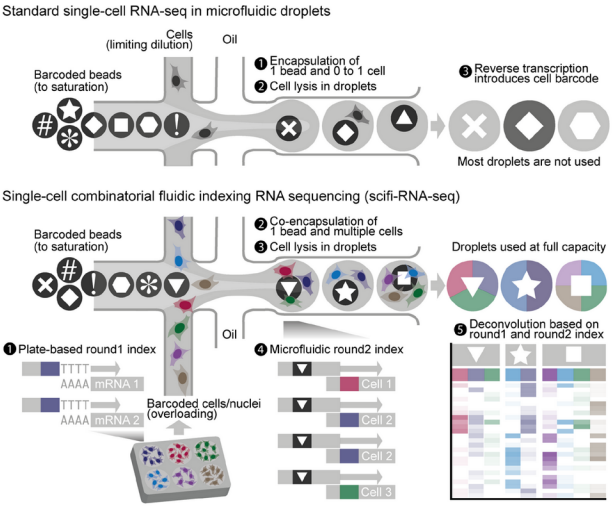
To resolve this limitation, the same lab proceeded with the development of a tool (*Stereoscope*) aimed to increase the resolution to the single cell level. *Stereoscope* is based on defining cell type identities from any available annotated single cell transcriptomic dataset. Following, profiles describing the expression from a mixture of cells, like that in a spot, can be obtained by a weighted combination of the single cell profiles. This allows spatial mapping of cell types in tissue based on supracellular spatial transcriptomic data.

Stereoscope was tested on publicly available human developing heart and mouse brain single cell transcriptomic datasets and in house spatial transcriptomic data with good results when compared to the references (Allen Brain Atlas, etc.).

Stereoscope is available at https://github.com/almaan/stereoscope for python. Due to the release of commercial spatial transcriptomics kits based on spot RNA capture, availability of such analytic tools is of high importance.

Paper 2. Ultra-high throughput single-cell RNA sequencing by combinatorial fluidic indexing

Datlinger. et al., *bioRxiv*, 2019.

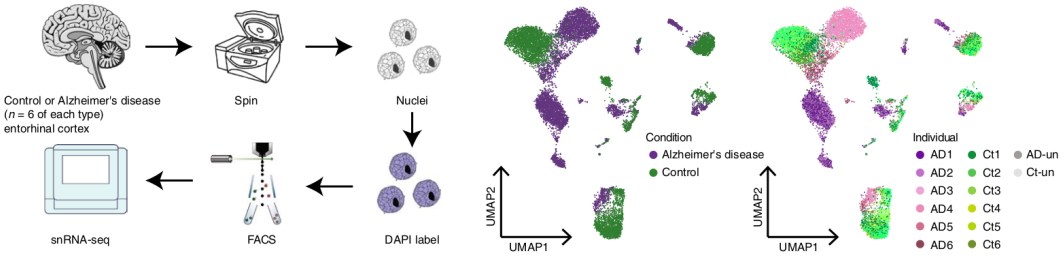


Cell atlas projects hit the limits of current technology, as they require cost-effective profiling for millions of individual cells. Thus, authors of the paper developed “single-cell combinatorial fluidic indexing” (scifi) and applied it to single-cell RNA sequencing in attempt to solve the throughput limitation. scifi-RNA-seq assay combines one-step combinatorial pre-indexing of single-cell transcriptomes during reverse transcription stage run on permeabilized cells/nuclei in the multiwell plates. This is followed by single-cell RNA-seq using 10x. Pre-indexing allowed loading of multiple cells per droplet, which increased the throughput of droplet-based single-cell RNA-seq up to 150,000 single-cell transcriptomes per channel on 10x. scifi-RNA-seq was benchmarked on various human and mouse cell lines showing its feasibility for human primary material by profiling TCR activation in T cells. In comparison, widely used cell hashing provides cell’s sample origin encoded by a single index sequence only useful for identifying and excluding doublets during data analysis or identifying origin of sample in case of single cell/drop. However, transcripts other than the index sequence cannot be assigned uniquely among multiple cells in the same droplet. In contrast, scifi-RNA-seq can resolve transcripts from overloaded droplets into the respective single-cell transcriptomes thanks to whole transcriptome pre-indexing.

However, direct comparison between standard 10x sc-RNAseq approach and current protocol is missing making hard to verify transcript detection sensitivity with custom reverse transcription and barcoding protocols.

Paper 3. A single-cell atlas of entorhinal cortex from individuals with Alzheimer's disease reveals cell-type-specific gene expression regulation

Grubman et al., *Nature Neuroscience*, 2019.



In a joint effort of Rackham Petretto and Polo labs single-nucleus RNA sequencing (DroNc-Seq) was applied to entorhinal cortex samples from 6 control and 6 Alzheimer's disease brains, yielding a total of **13,214** high-quality nuclei with **646** genes/nucleus detected. Authors detail cell-type-specific gene expression patterns, unveiling how transcriptional changes in specific cell subpopulations are associated with Alzheimer's disease. Alzheimer's disease risk gene APOE was reported specifically repressed in Alzheimer's disease oligodendrocyte progenitor cells and astrocyte subpopulations and upregulated in an Alzheimer's disease-specific microglial subopulation. Integrating transcription factor regulatory modules with Alzheimer's disease risk loci revealed drivers of cell-type-specific state transitions towards Alzheimer's disease. For example, transcription factor EB, a master regulator of lysosomal function, regulates multiple disease genes in a specific Alzheimer's disease astrocyte subpopulation. These results provide insights into the coordinated control of Alzheimer's disease risk genes and their cell-type-specific contribution to disease susceptibility.

However, limited amount of analyzed patients/sequenced cells, use of lower sensitivity approach, and apparent avoidance of batch correction algorithms leave room for further higher depth studies.

Next Single Cell Seminar

15th January 2020 9:00-10:30 Holst auditorium, Panum
Nikolai Slavov, Northeastern University, USA, will present his work on the single cell proteomics

Upcoming conferences

11-13 March 2020, Wellcome Genome Campus, UK
Single Cell Biology
Abstract deadline 15th January 2020
Bursary deadline 2nd January 2020

19-21 April 2020, San Francisco, CA, USA
The Conceptual Power of Single-Cell Biology
Abstract deadline 17th January 2020

4-8 May 2020, Firenze Fiera-Palazzo dei Congressi, Florence, Italy
Single Cell Biology: Pushing New Frontiers in the Life Sciences
Discounted Abstract Deadline 8th January 2020
Abstract Deadline 5th February 2020
Scholarship Deadline 8th January 2020

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