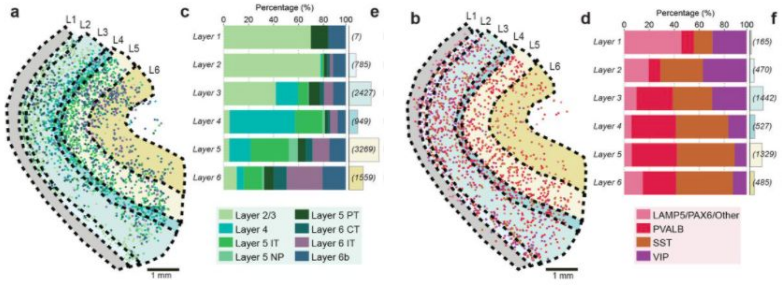
Single Cell Transcriptomics

Newsletter February 2021

Paper 1

Langseth, CM *et al.* [Comprehensive in situ mapping of human cortical transcriptomic cell types] *biorXiv, 2021.*



Here, the authors combined snRNA-seq and in situ sequencing gene expression data to spatially map cells in sections of the human cortex via probabilistic cell typing. They mapped and classified a total of 59,816 cells into all 75 previously defined subtypes by snRNA-seq to create the first spatial atlas of human cortical cells in their native position.

The presented human cortical maps include a comprehensive reference of the cells in the human temporal lobe, their spatial location, abundances and gene expression signatures. This work embodies the vision and paves the path towards a spatial Human Cell Atlas, utilizing the predefined taxonomy of cells to create maps of histological tissue structures.

Paper 2

Chazarra-Gil R *et al.* [Flexible comparison of batch correction methods for single-cell RNA-seq using BatchBench], *Nucleic Acids Res, 2021*

Batch effect is one of the biggest challenges in the single-cell RNAseq field, as an increasing number of datasets are now available and there is a need for combining them with newly generated data. Although there are already several computational methods that can remove batch effects in different ways, assessing which method performs best is still a challenge.

In this recently published paper, scientists from the Wellcome Sanger Institute present BatchBench, a modular and flexible pipeline for comparing batch correction methods for single-cell RNA-seq data.

They considered eight batch correction methods, summarized in the figure here, and they applied them to different pancreas datasets, the mouse cell atlas datasets and tabula muris dataset.

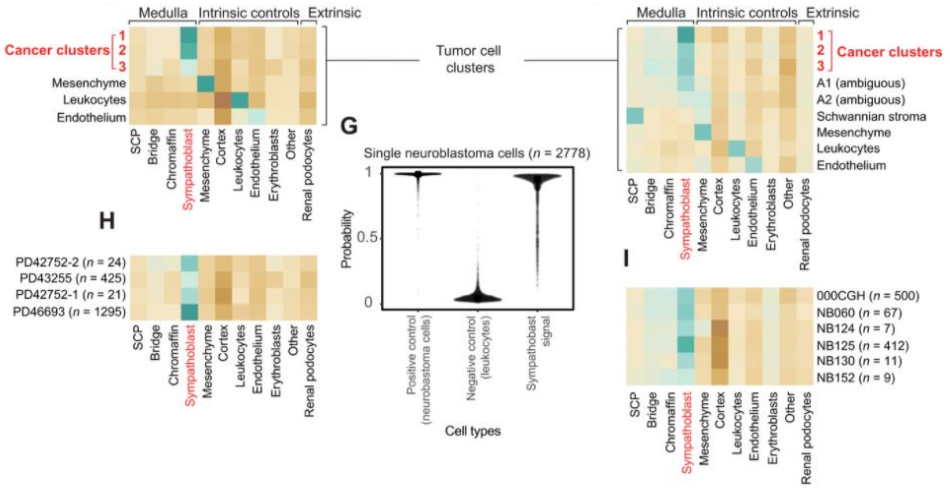
Tool	Lang.	Output	Correction principle
mnnCorrect	R	Counts matrix	Mutual nearest neighbour detection across batches.
Limma	R	Counts matrix	Fits linear model to remove batch effect components.
ComBat	R	Counts matrix	Adjusts for known batches using an empirical Bayesian framework.
Seurat	R	Counts matrix	Diagonalized CCA to reduce dimensionality and MNN detection in this space.
Scanorama	Python	Counts matrix	SVM to reduce dimensionality and mutual nearest neighbor detection and panoramic stitching.
Harmony	R	Embedding	Iterative soft k-means clustering algorithm in dimensionally reduced space.
fastMNN	R	Embedding	Mutual nearest neighbor detection after multi-sample PCA.
BBKNN	Python	Graph	Mutual nearest neighbour pair selection across batches in PCA space.

R, Bioconductor, Conda, Python.

Paper 3

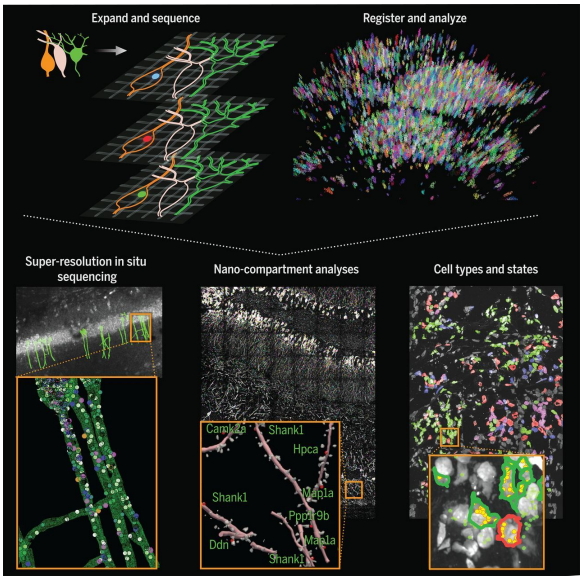
Kildisiute, G *et al.* [Tumor to normal single-cell mRNA comparisons reveal a pan-neuroblastoma cancer cell](), *Science Advances, 2021*

In this paper, scientists revealed the phenotype of neuroblastoma cancer cells by comparing cancer (n = 19,723) with normal fetal adrenal single-cell transcriptomes (n = 57,972). Neuroblastoma is a childhood cancer that resembles developmental stages of the neural crest, however, it is still not known what developmental processes neuroblastoma cancer cells represent. The principal finding of our investigation was that the neuroblastoma cancer cell represented an aberrant fetal sympathoblast, but no other fetal adrenal cell type. Therefore, their observations indicate that a pan-neuroblastoma cancer cell state exists and that there is an unexpected homogeneity in the cellular identity of neuroblastoma. Thus, this result opens the door for novel immunotherapeutic and targeted avenues.



Paper 4

Alon, S. *et al.* [Expansion sequencing: Spatially precise in situ transcriptomics in intact biological systems](), *Science, 2020*



The team showed that they could use a technique, called expansion sequencing (ExSeq), to locate and then sequence thousands of different messenger RNA molecules within the mouse brain and in human tumor samples. ExSeq combines expansion microscopy, which physically expands biological specimens, with insitu RNA sequencing. Expanding the tissue before performing RNA sequencing offers a higher-resolution look at the RNA in cells, and it makes it easier to sequence those RNA molecules. Once the tissue is expanded, the researchers can label and sequence thousands of RNA molecules in a sample, at a resolution that allows them to pinpoint the molecules' locations not only within cells but within specific compartments such as dendrites. They applied this untargeted expansion sequencing (ExSeq) to mouse brain, yielding readout of thousands of genes, including splice variants and novel transcripts and to human metastatic breast cancer biopsy, showing the organization and position-dependent states of tumor and immune cells.

Conferences

The Brain Prize Meeting 2021, 1st - 4th March 2021, Virtual conference

Keystone symposia: Single Cell Biology, 17th - 19th March 2021, Virtual conference

Next Single Cell Seminar

Date: 26th February 2021, online

9:00 – 10:00

Igor Adameyko, Karolinska Institutet/Medical University of Vienna

Evolutionary conserved and non-conserved mechanisms of a cell fate choice

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

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