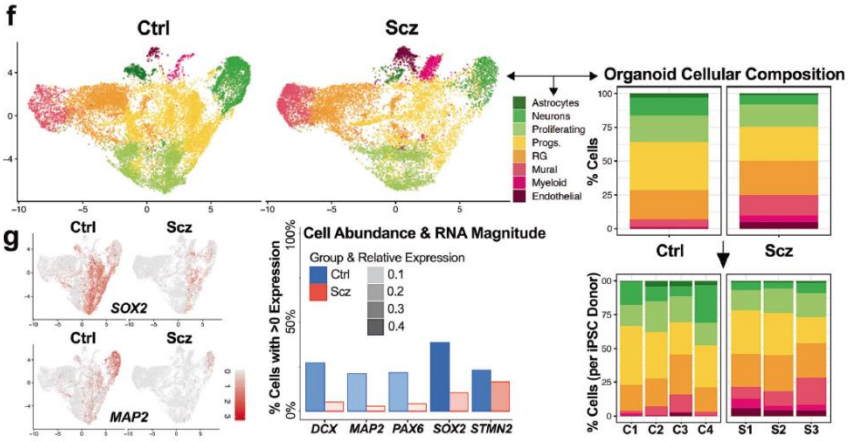
Single Cell Transcriptomics

Newsletter December 2021

Paper 1

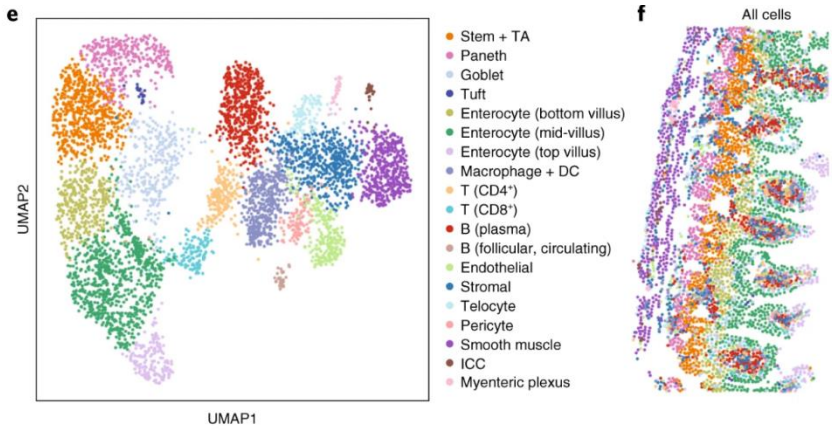
Notoras, M. et al. Schizophrenia is defined by cell-specific neuropathology and multiple neurodevelopmental mechanisms in patient-derived cerebral organoids *Molecular Psychiatry*, 2021.



Notoras *et al.* developed a patient derived schizophrenia (Scz) brain organoids for overcoming the problematic acquisition of high quality patient brain tissue. In this study, they performed both proteomics and scRNA-sequencing (10x and Illumina) to investigate the different translational and transcriptional landscapes, and compare control patient organoids with Scz patient derived organoids. Here they present results that support the paradigm of schizophrenia being a neurodevelopmental disorder. Lower amounts of differentiated neurons in Scz organoids were found compared to control, in addition, 93% of cell types were identified in control and where only 75% of cells were identified as progenitors, neurons and other glia in Scz. In Scz the remaining 25% was identified as brain-related cell-types as putative neuroendothelial cells, developing vasculature, retinal and choroid plexus specific cells. The authors found these cells were generated at the expense of neuron development from compositional analysis. Further, the Scz organoids exhibited depletion of SOX2+ and PAX6+ neuronal progenitors and mature neurons in both abundance and magnitude. Thus, this finding contributes to the notion of disrupted progenitor and neuron development in schizophrenia.

Paper 2

Petukhov, V et al. Cell segmentation in imaging-based spatial transcriptomics *Nature Biotechnology, 2021*

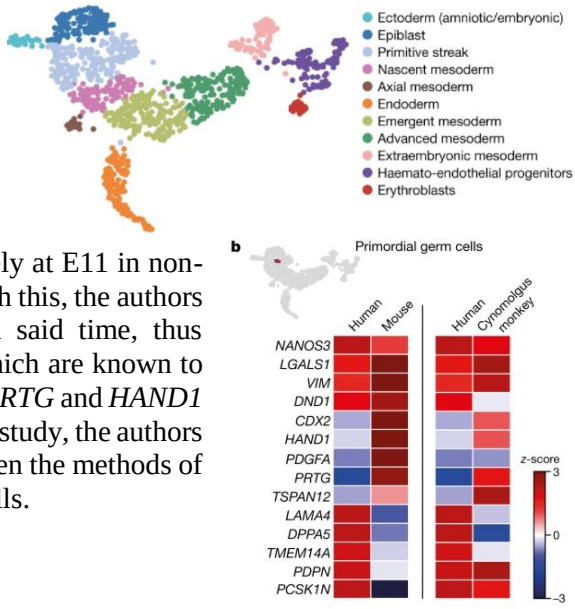


Single-cell RNA-sequencing has become a preferred and widely used technology during last decade. The higher transcriptional resolution, which these methods provides, have naturally driven the urge to combine this information with the spatial ordering of tissue. This gives higher insight into cell-cell interplay and structural relationships during development and disease. In the paper by Petukhov *et al.* they describe the segmentation method, Baysor, for analysis of image based spatial transcriptomics data from platforms as MERFISH, smFISH and osmFISH. The method optimizes two- or three-

dimensional cell boundaries considering joint likelihood of transcriptional composition and cell morphology. As in scRNA-seq studies, cell types and states can be distinguished based on the transcriptional composition of a cell. In spatial methods transcriptional composition of cells gives rise to molecular neighborhoods. With Baysor, the authors capture this structure by computing the neighborhood composition vector (NCV) for each molecule by *k* spatially nearest neighbors (NNs) and estimate the relative frequency of different genes among neighboring molecules. The segmentation and annotation of cells can be displayed as in scRNA-seq studies for clustering and annotation information in 2D and be viewed alongside the spatial composition of the tissue.

Paper 3

Tyser, R et al. Single-cell transcriptomic characterization of a gastrulating human embryo, *Nature 2021*



The authors of the paper present the first scRNA-seq data of in utero human gastrulation (Carnegie stage 7). The data is characterized morphologically, is spatially resolved and yields a total of 1,195 cells composing of 665 caudal, 340 rostral and 190 yolk sac cells. The authors contribute to the understanding of early human development and provide data for interpretation of other model systems and in vitro differentiation of human cells. By comparison with several animal models, the authors found that primordial germ cells arise approximately at E11 in non-human primates and in ex vivo cultured human embryos. Consistent with this, the authors were able to detect a small population of primordial germ cells a said time, thus confirming earlier experimental findings. Further, a range of genes, which are known to be expressed in primordial germ cells in animal models such as *CDX2*, *PRTG* and *HAND1* were found not to or to be expressed in very low amounts. Thus with this study, the authors hope to advance our understanding of human development and strengthen the methods of in-vitro differentiation of stem cells to mature and functional human cells.

Next Single Cell Seminar

Date: 1st December 2021 09:00 – 11:00,
Location: Lecture hall 7.15.92 on the 15th floor of the Mærsk Building (Blegdamsvej 3B, 2200 Kbh N)

9:00 – 9:50

Postdoc Nagendra Prasad Palani, Scheele Lab, NNF-CMBR, Copenhagen
Differentiating human adipocytes share trajectories across brown and white depots

10:10 – 11:00

Postdoc Patrick Martin, Won Lab, BRIC, Copenhagen
Vesalius: high-resolution in silico anatomization of Spatial Transcriptomic data using Image Analysis

Due to the COVID-19 landscape, the talk we be hosted in a blended format and will be available on zoom.

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: Frederik.sorensen@sund.ku.dk