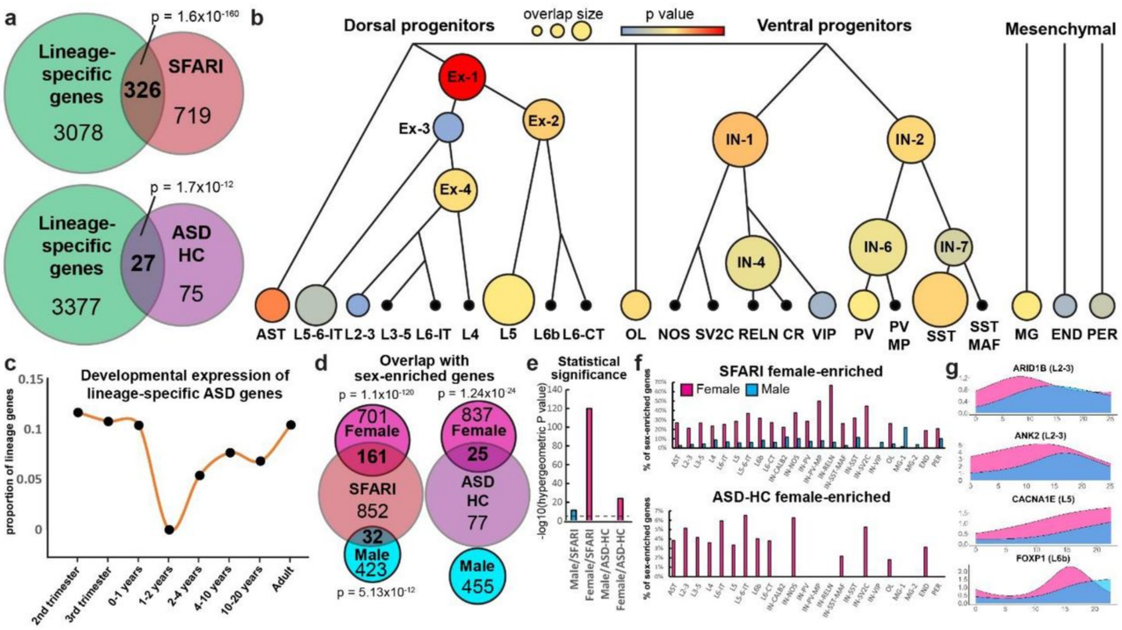
Single Cell Transcriptomics

Newsletter November 2022

Paper 1

D, Velmeshev *et al.* [Single-cell analysis of prenatal and postnatal human cortical development](#), *BioRxiv*, October 2022

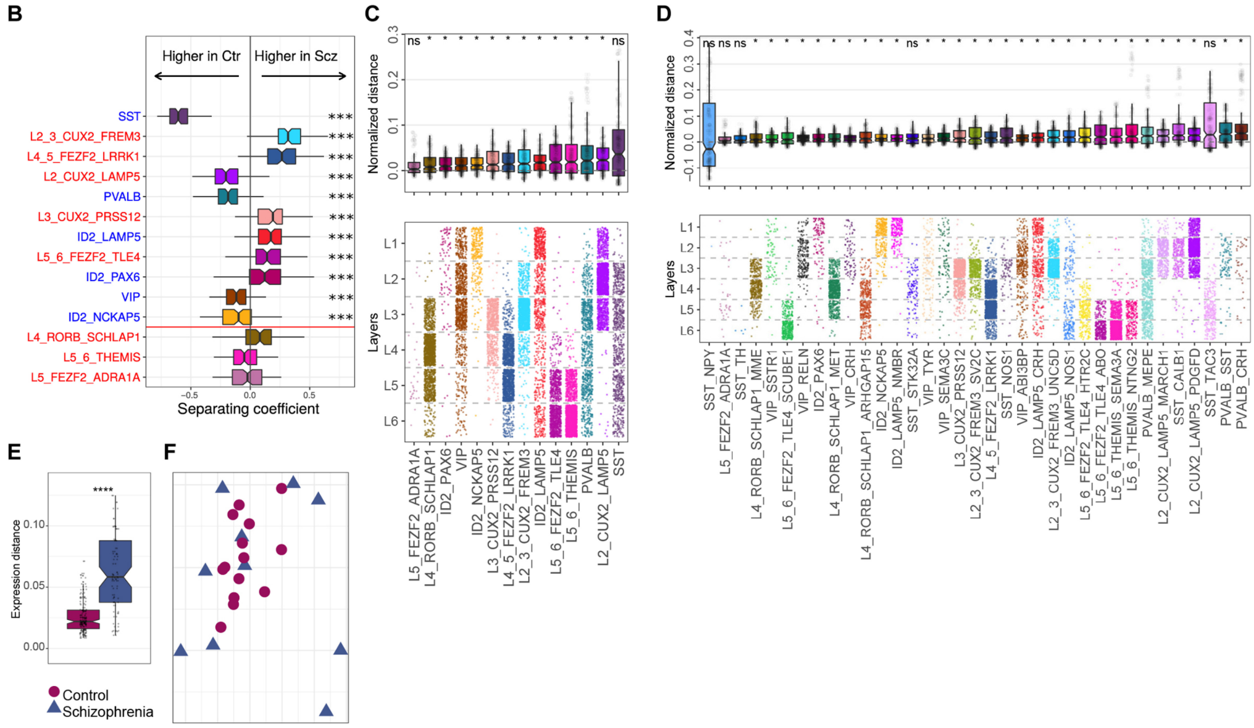
This months first paper is a preprint on early cortical development, with highlight on sex differences in neurodevelopmental disorders with particular focus on autism spectrum disorder. The study reports the analysis of single-nuclei RNA sequencing data from 108 cortical brain samples from a total of 60 donors. These span from 2nd and 3rd trimester to early postnatal all the way up to late postnatal and adult. They describe lineage-specific developmental programs in both principal and inhibitory neurons as well as glial cells, making this paper a resource for everyone studying development and disease in neonates and pediatric patients.. Further they identify sex-specific changes in developmental trajectories caused by fluctuating expression patterns. The authors infer this to have a great impact on the susceptibility to neurodevelopmental disorders such as schizophrenia and autism spectrum disorder (ASD). Certain gene-programs linked to ASD are expressed at lower levels in males during development, which might make males with heterozygous loss of function in these genes more prone to develop the disease. Ultimately the authors believe this might contribute to the explained increase in male to female ratio of autism prevalence.



Paper 2

Batiuk, M.Y. ***et al.***,[Upper cortical layer–driven network impairment in schizophrenia](#) *Science Advances*, October 2022

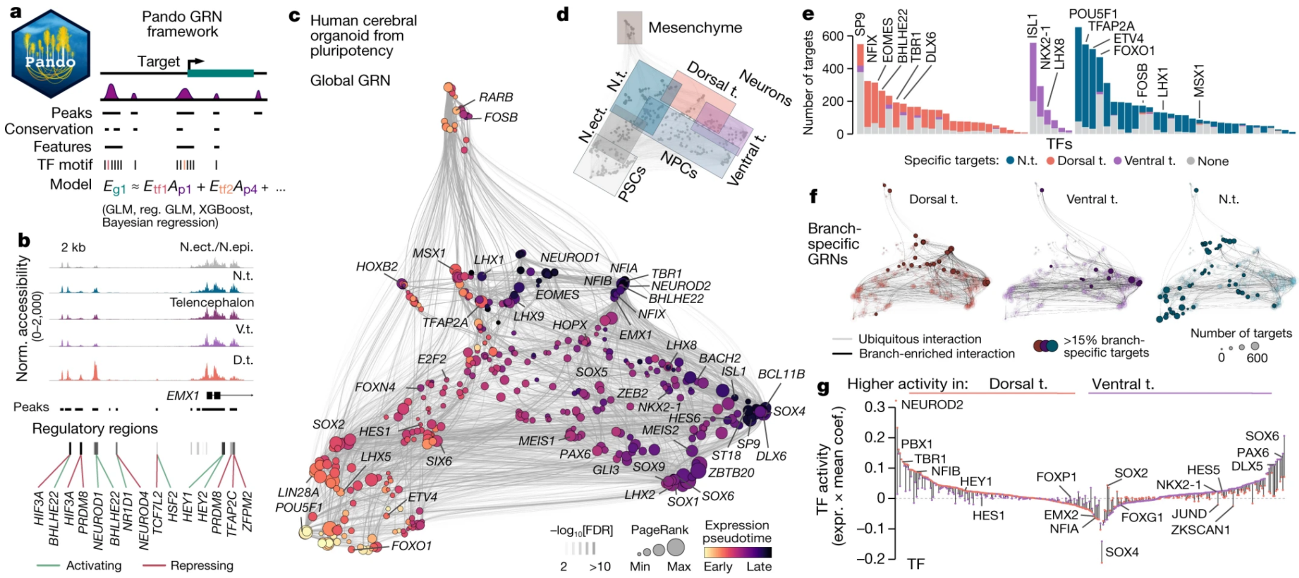
The underlying causes for schizophrenia have for many years been a black box for clinicians and scientists. Only in recent years have we begun to understand the underlying neuronal networks responsible for the devastating disease. Authors from the University of Copenhagen with M. Batiuk leading the efforts has recently uncovered the underlying genetic and compositional underpinnings of schizophrenia. They report an in depth sn-RNA-seq analysis of dorsolateral prefrontal cortex samples in a case-control matter with a cohort of 9 schizophrenia and 14 matched control subjects. >220,000 neurons were analyzed along with >115,000 neurons topographically with immunohistochemistry. The study reveals a reduction in GABAergic neuron abundance along with an increase in principal neurons compared to control. The most extensive transcriptomic changes were observed in cortical upper-layer GABAergic neurons, where neurotransmission was upregulated along with a downregulation of energy metabolism gene programs. The authors suggest that a general network impairment within upper cortical layers is responsible for symptoms and phenotypes presented in patients with schizophrenia.



Paper 3

Flek. J *et al.*, [Inferring and perturbing cell fate regulomes in human brain organoid](#) , *Nature*, October 2022

In the last paper of the month, we will focus on the method *Pando* developed by Flek. et. al. which is "a flexible framework which incorporates multi-omic data and predictions of transcription-factor-binding sites to infer a global gene regulatory network describing organoid development". Pando identifies candidate regulatory regions that show accessibility across the organoid's time course by incorporating information on several factors such as CRE annotations and evolutionary conserved gene elements. The method leverages a regression model to infer the relationship between expression of target genes, transcription factor expression and binding-site accessibility, by combining scATAC- and scRNA-seq data. Ultimately this provides information on sets of positively or negatively regulated target genes and regulatory modules for each TF. The method provides graphics and information on TF interaction strength and co-expression along with pseudotime and PageRank (algorithm ranking most important inferred data) centrality of each TF.



Next Single Cell Seminar

Date: 25th November 2022, Faculty Club, Panum, Mødelokale 16.6.16

9:00 – 10:00

Josephine Deleuran Hendriksen, postdoc, Weischenfeldt Group, BRIC

Clonal evolution of glioblastoma during therapy at single cell resolution

10:00 – 11:00

Malthe Thodberg, postdoc, Hansen Group, CBMR

Using multimodal single cell sequencing of the human liver to dissect the genetic basis of diabetes and obesity

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