

# Uncover Key Genes Regulating Human Embryonic Prefrontal Cortex Development by Single Cell Sequencing

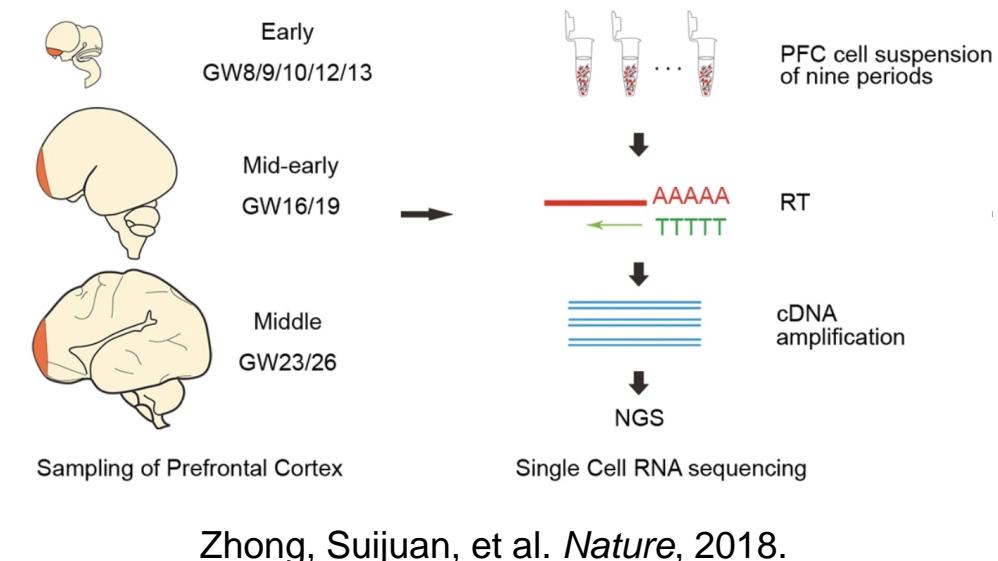
CSIC 5011 Final Project

Dong SONG, Jiabao LI, Zongchao MO, Zhihan ZHU

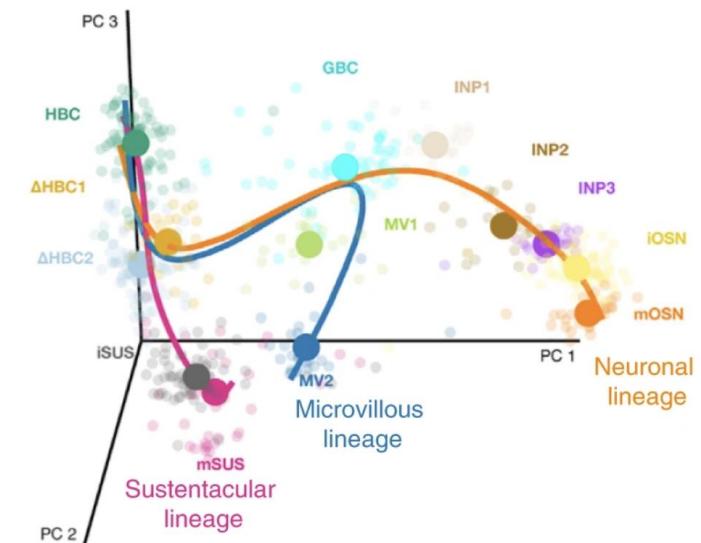
2021.05.21

# Background

- Human prefrontal cortex (PFC) has the highest-order cognitive functions
  - Still difficult to identify cell subgroups in the developing human prefrontal cortex and to distinguish their developmental properties
- Single cell sequencings and developmental trajectories enable our journey to explore PFCs
- Questions:
  - What is the developmental subgroups of PFCs?
  - What are the key genes regulating the prefrontal cortex in the developmental trajectories?
  - What are the functions of the above genes?



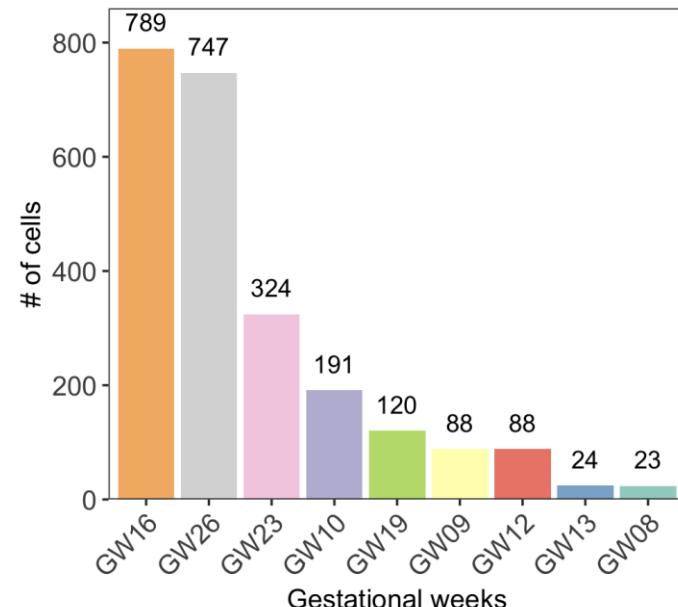
Zhong, Suijuan, et al. *Nature*, 2018.



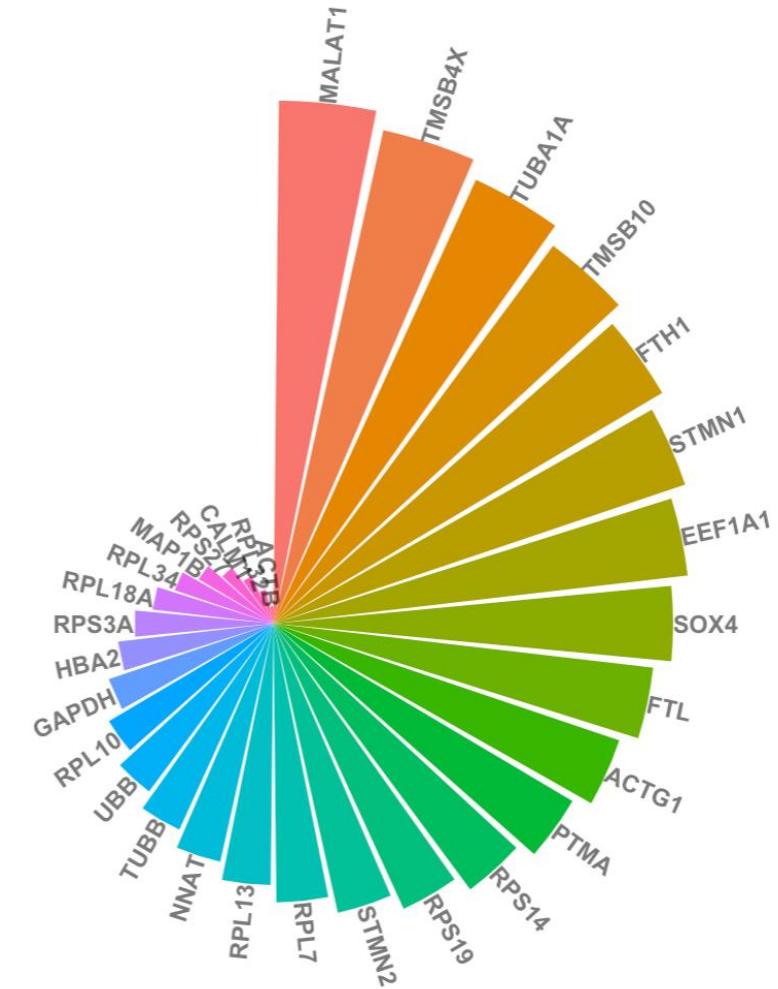
Van den Berge, Koen, et al. *Nat com*, 2020.

# Data & software

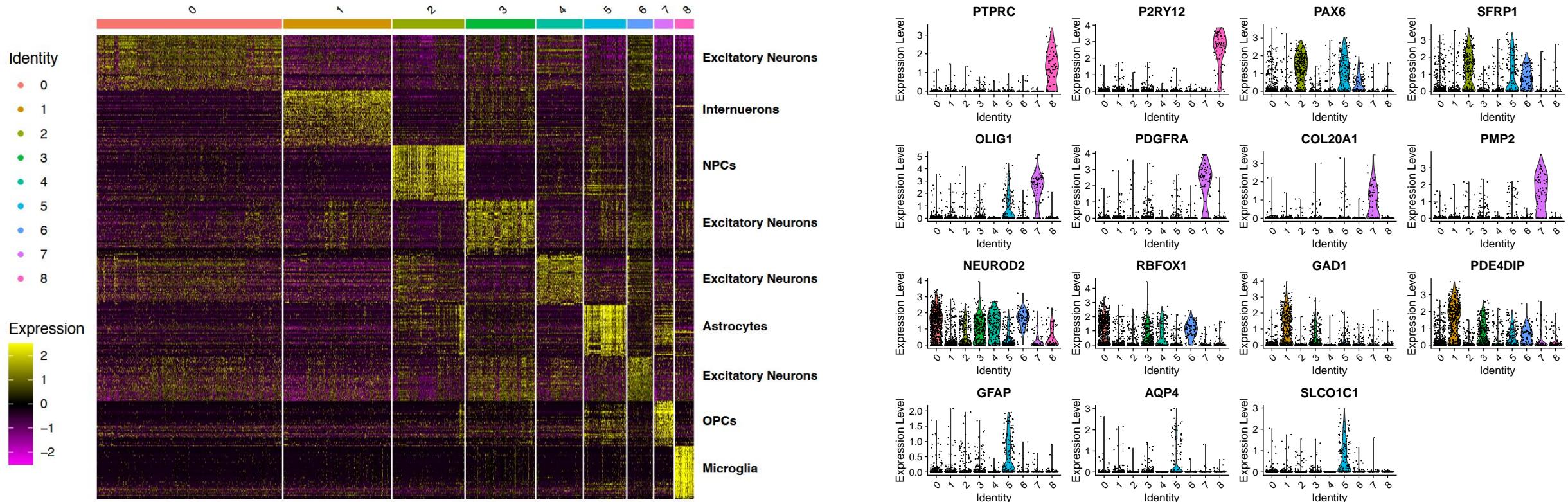
- There are 2394 single cells from gestational weeks (GW) 8 to 26
- There are 24153 transcripts per million (TPM) of genes for each cell
- Software: slingshot, TSCAN, monocle3, R, python



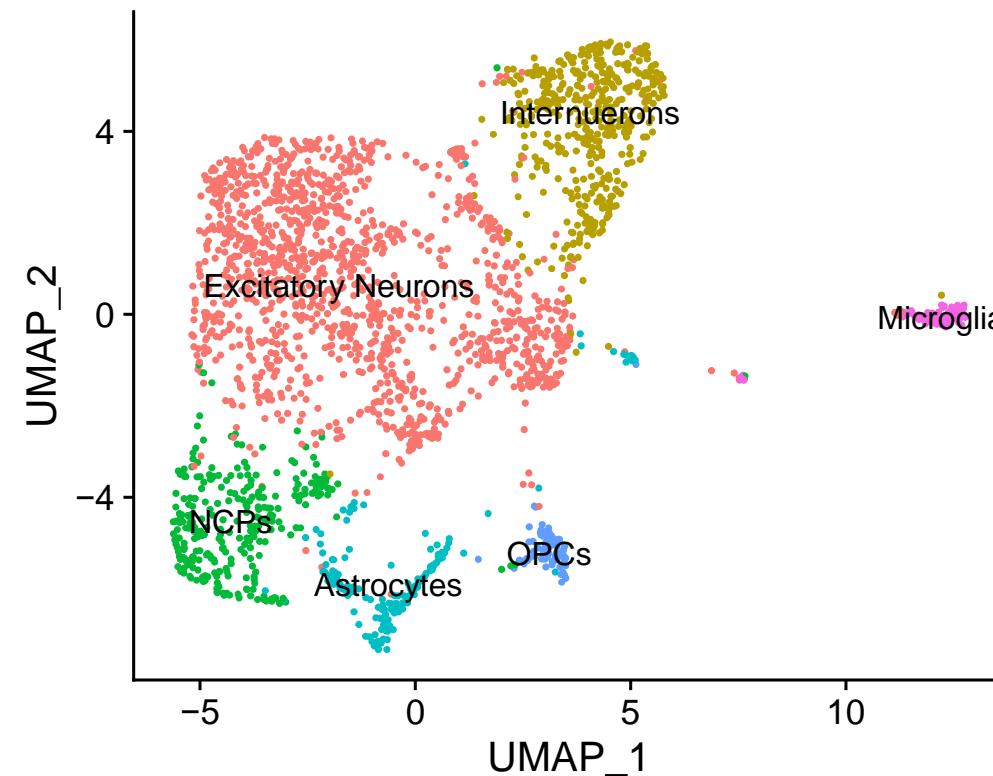
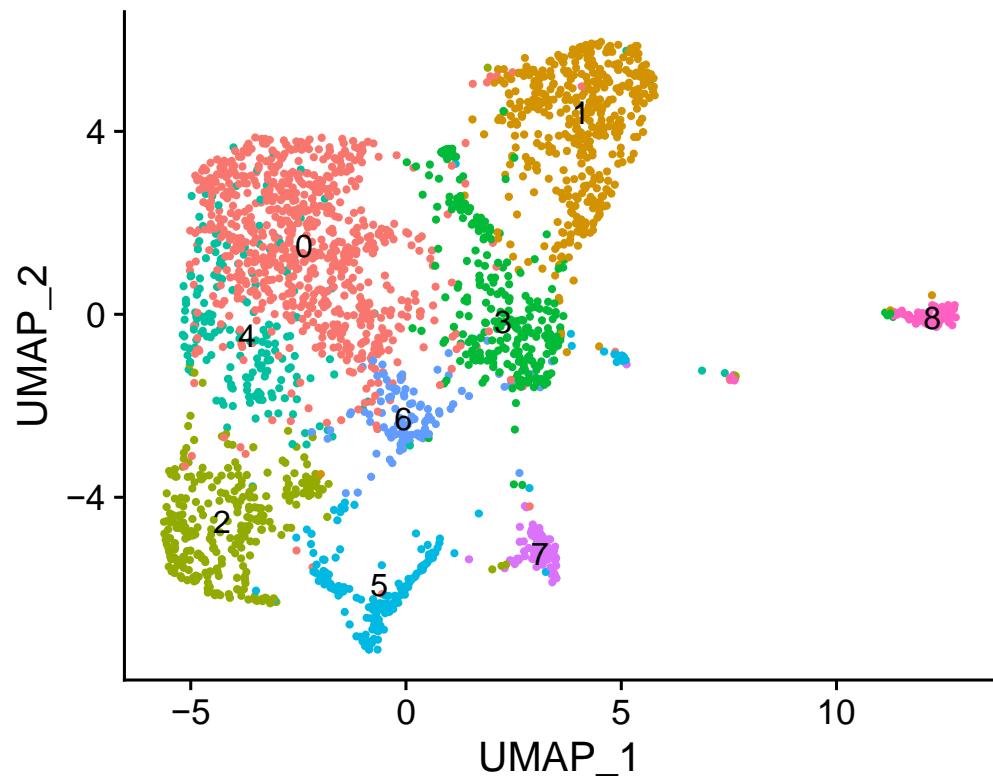
Top 30 genes in the dataset



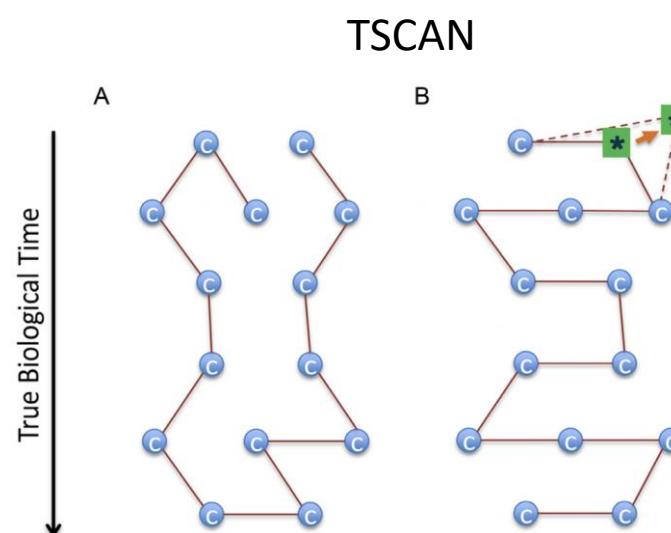
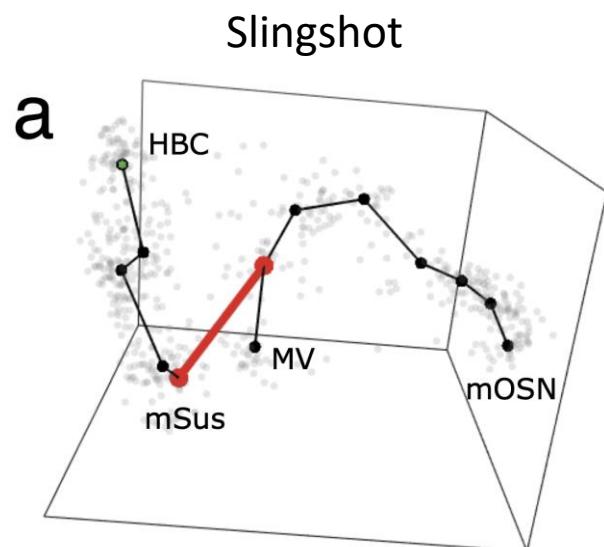
# Cell Subgrouping



# Cell Subgrouping Identification

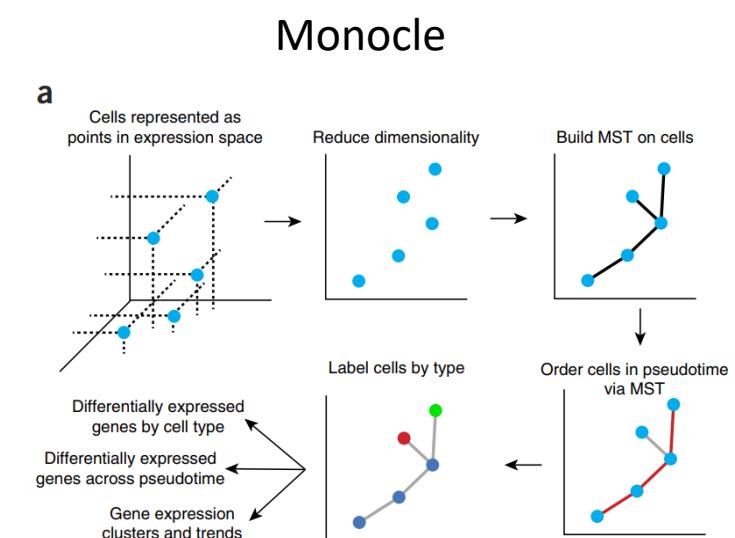


# Trajectories Inference Methods



Street, K, et al. *BMC Genomics*, 2018.

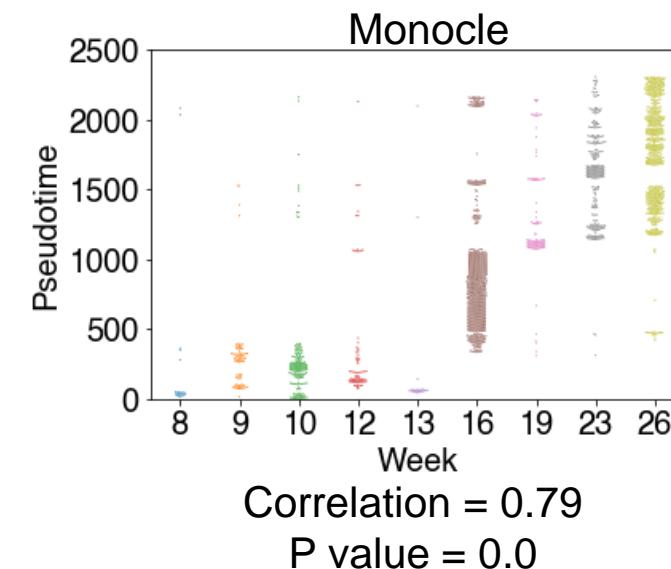
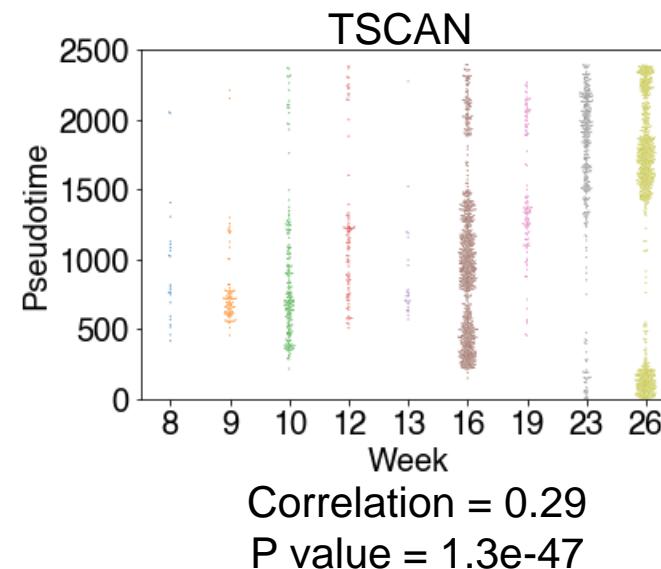
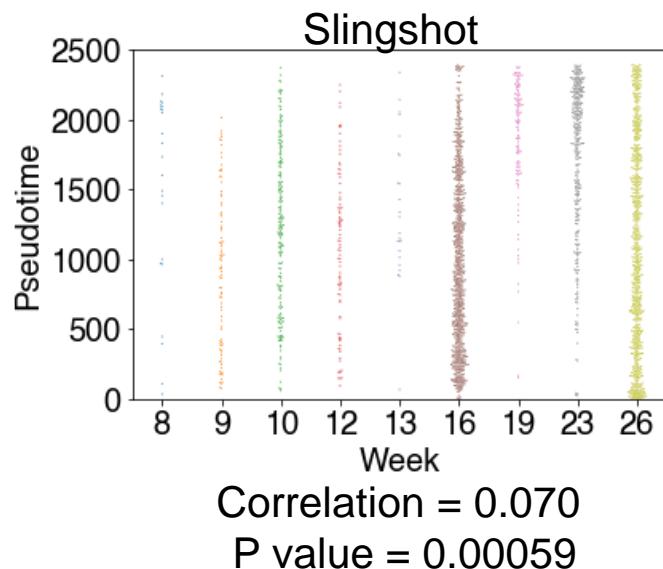
Z Ji, et al. *Nucleic acids research*, 2016.



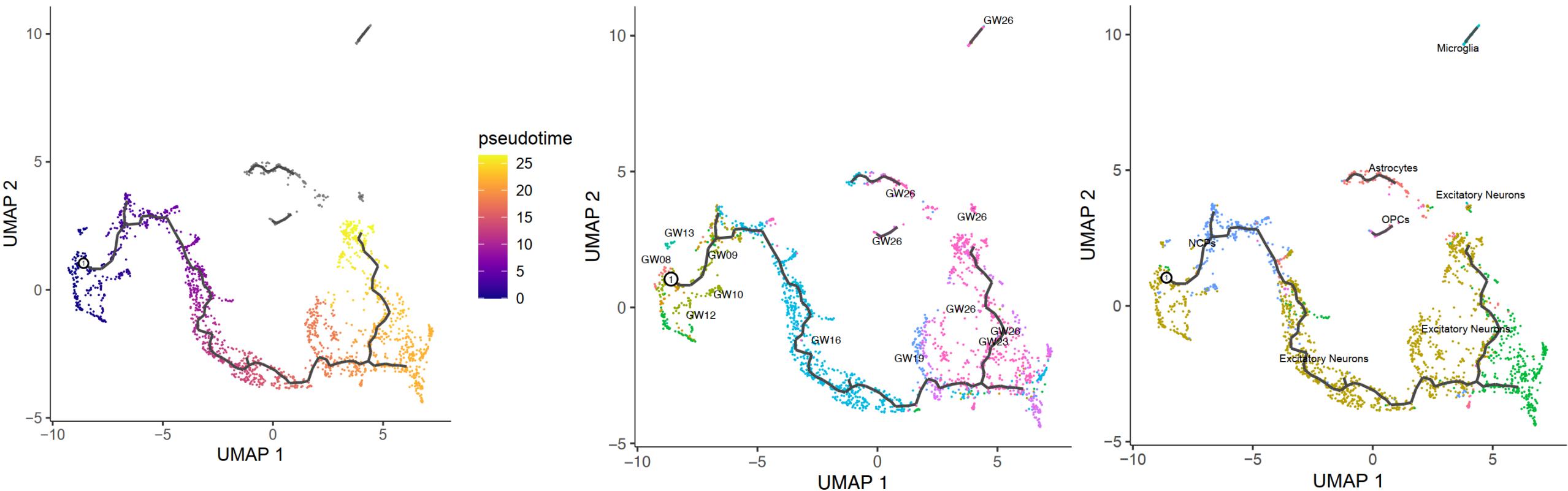
C Trapnell, et al. *Nature biotechnology*, 2014.

# Results

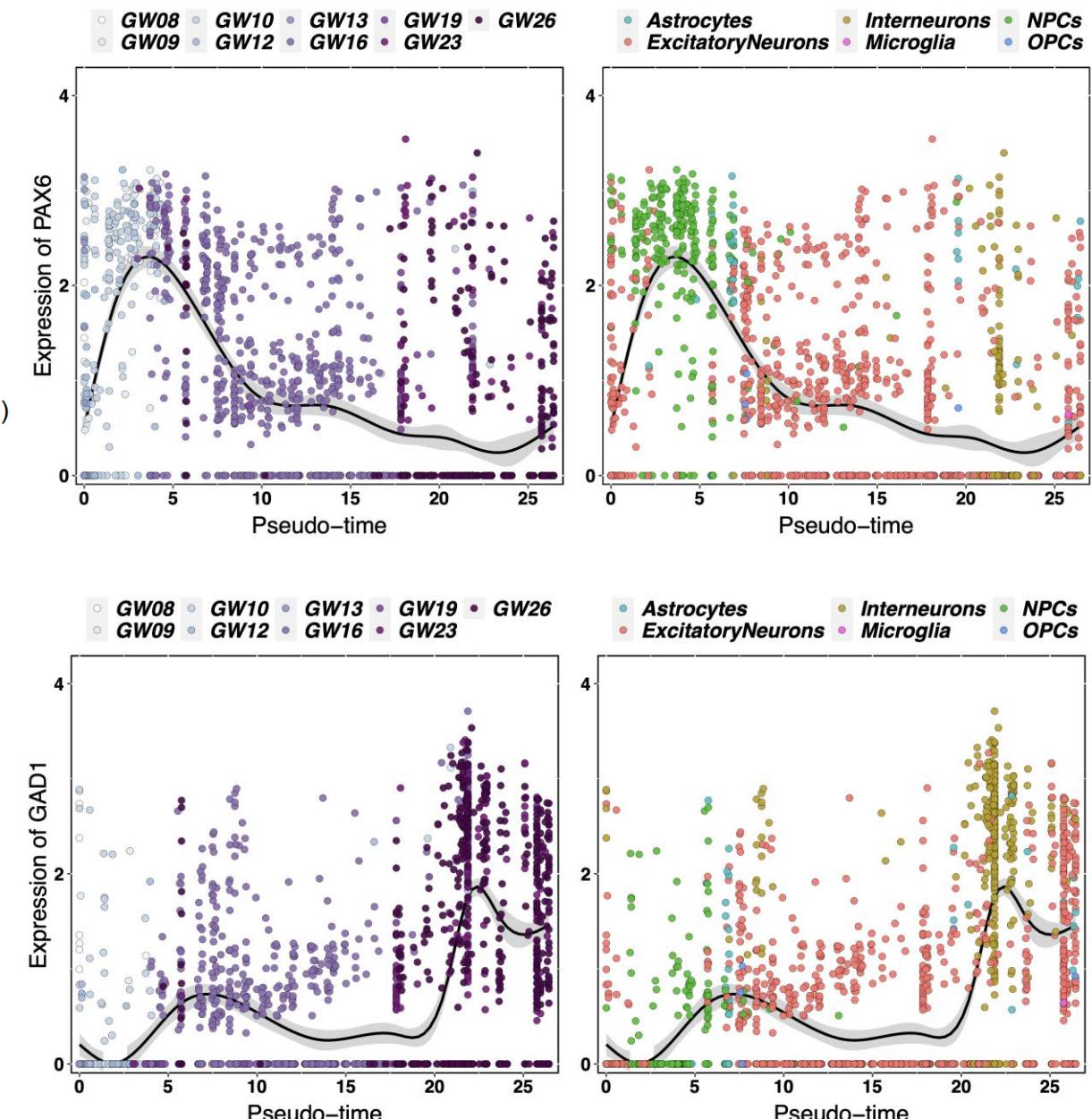
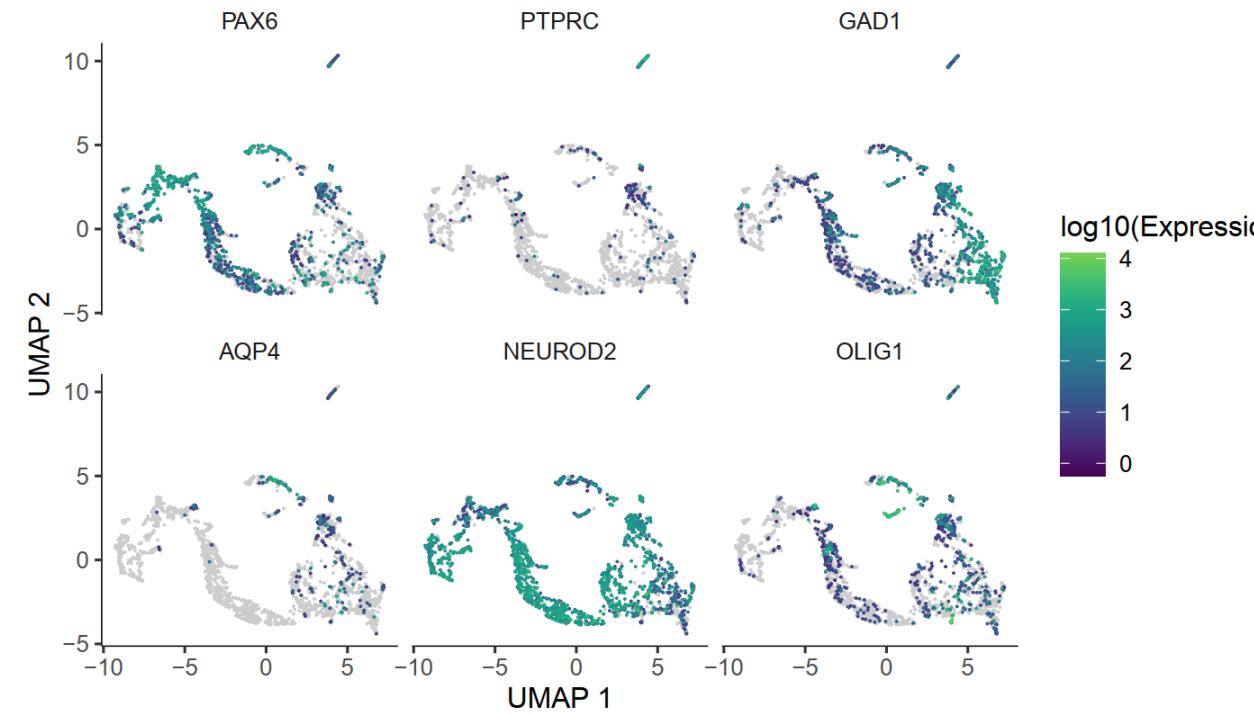
The Spearman rank-order correlation of pseudo time and week number:



# Trajectory inference via Monocle

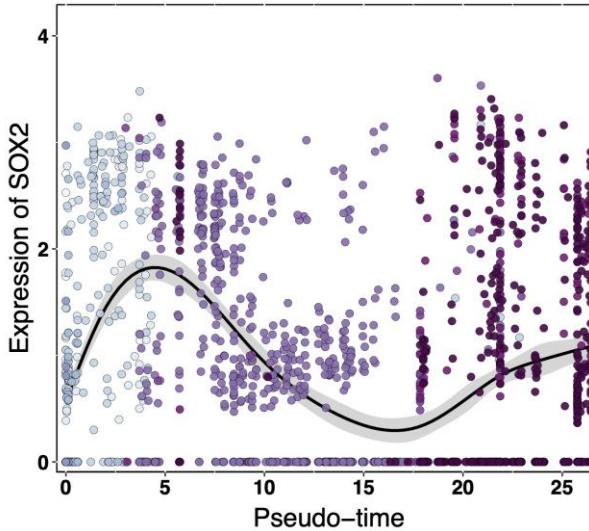


# Expression of known markers with pseudo-time

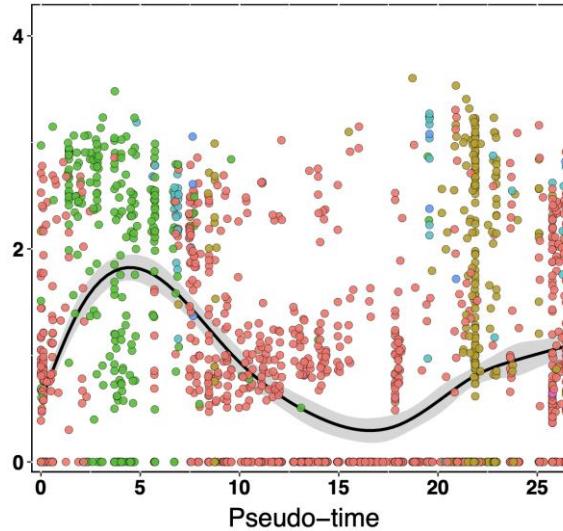


# Expression of known markers with pseudo-time

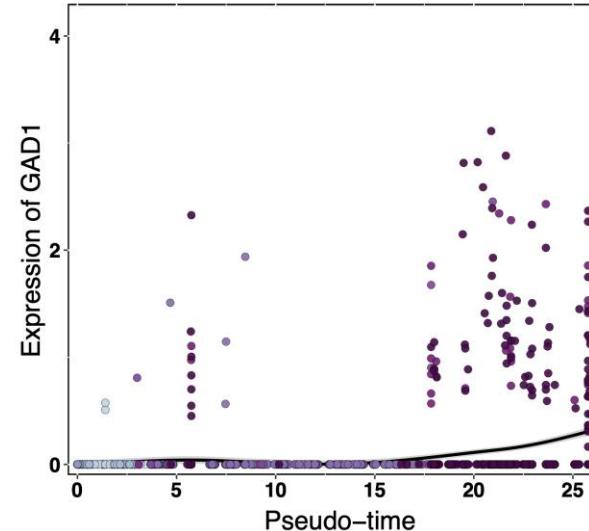
GW08 GW10 GW13 GW19 GW26  
GW09 GW12 GW16 GW23



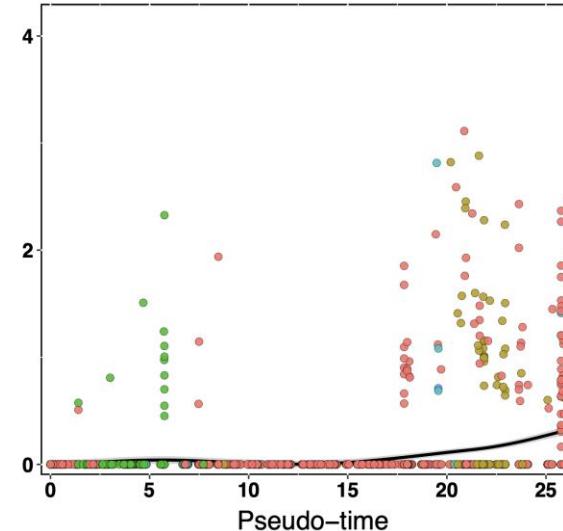
Astrocytes Interneurons NPCs  
ExcitatoryNeurons Microglia OPCs



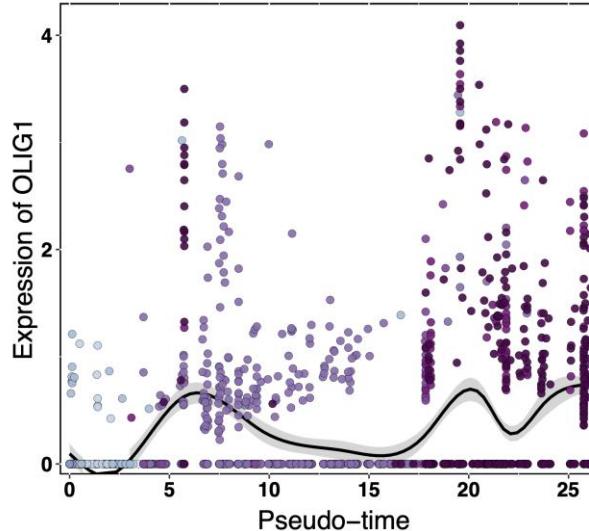
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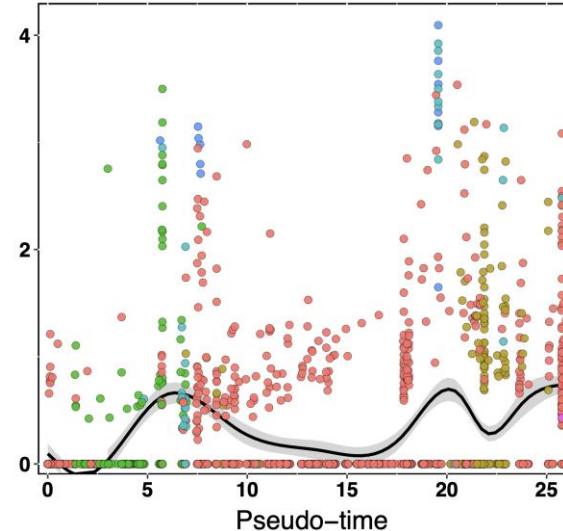
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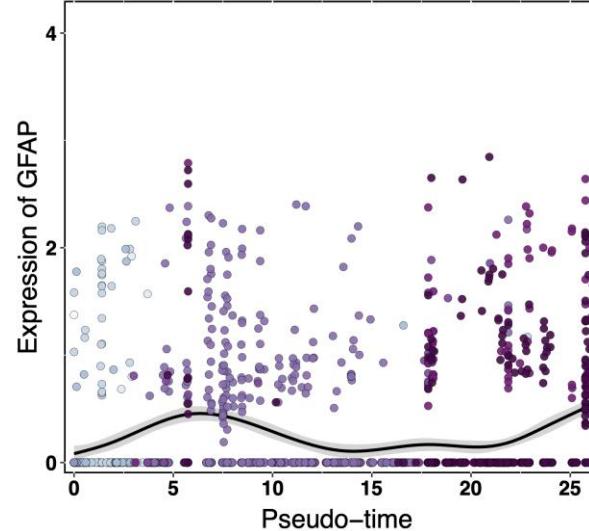
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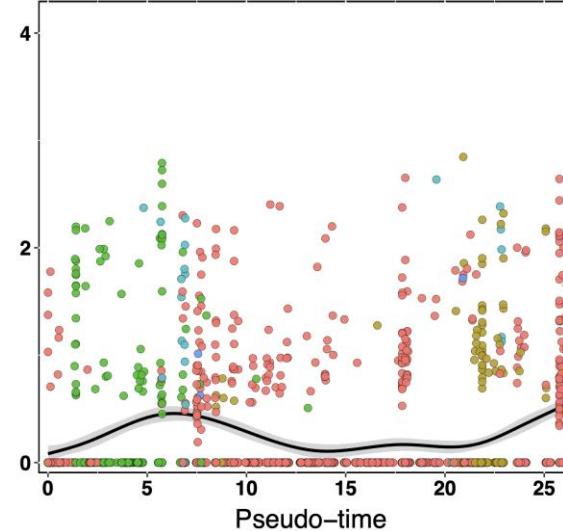
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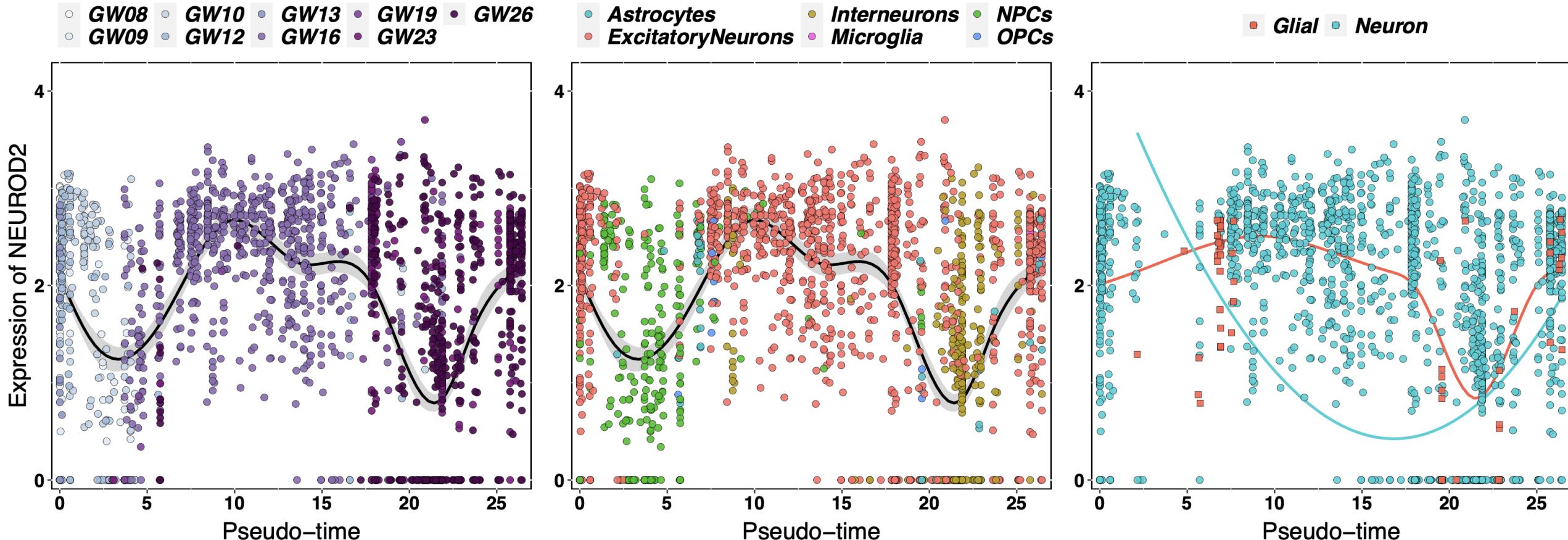
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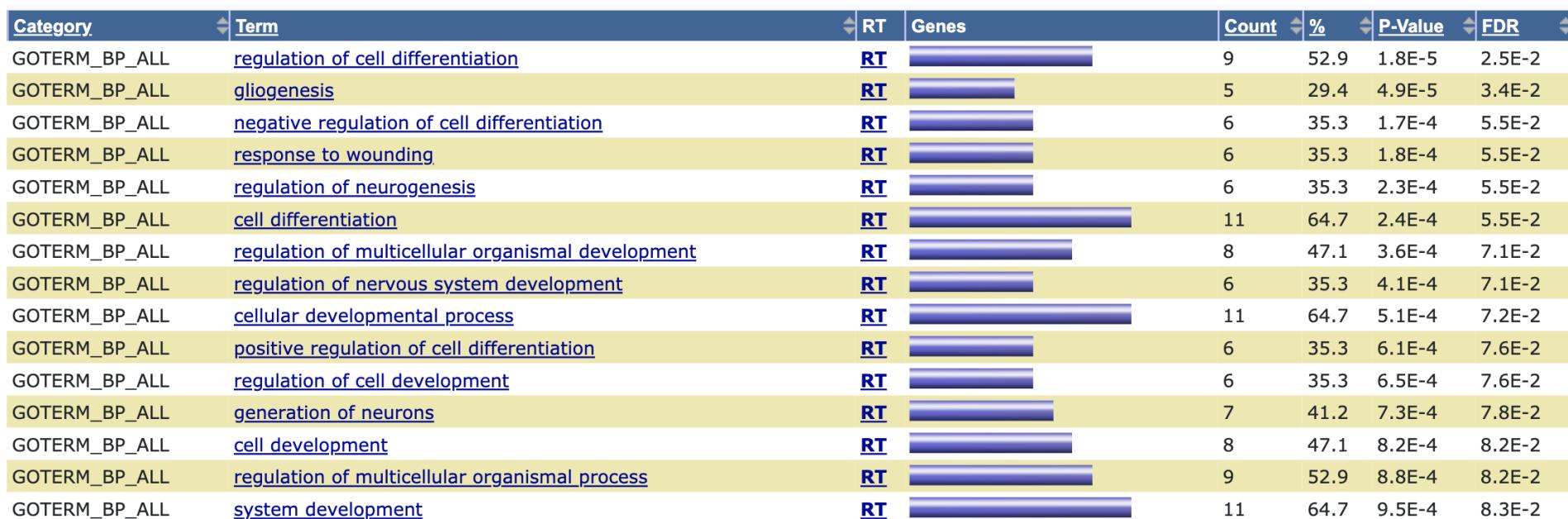
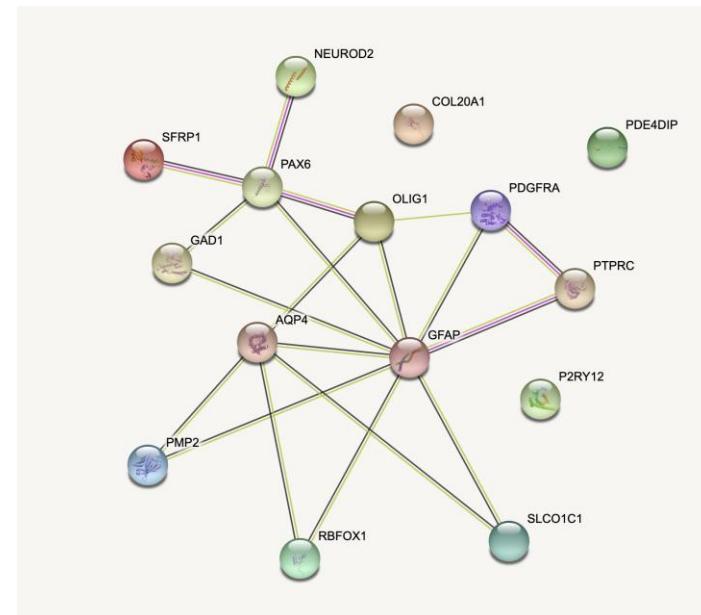


# Expression of known markers with pseudo-time



# Gene functions of found markers

Gene ID	Description
RBFOX1	RNA binding protein, fox-1 homolog 1(RBFOX1)
AQP4	aquaporin 4(AQP4)
COL20A1	collagen type XX alpha 1 chain(COL20A1)
GFAP	glial fibrillary acidic protein(GFAP)
GAD1	glutamate decarboxylase 1(GAD1)
NEUROD2	neuronal differentiation 2(NEUROD2)
OLIG1	oligodendrocyte transcription factor 1(OLIG1)
PAX6	paired box 6(PAX6)
PMP2	peripheral myelin protein 2(PMP2)
PDE4DIP	phosphodiesterase 4D interacting protein(PDE4DIP)
PDGFRA	platelet derived growth factor receptor alpha(PDGFRα)
PTPRC	protein tyrosine phosphatase, receptor type C(PTPRC)
P2RY12	purinergic receptor P2Y12(P2RY12)
SFRP1	secreted frizzled related protein 1(SFRP1)
SLCO1C1	solute carrier organic anion transporter family member 1C1(SLCO1C1)



# Summary

- Assigned 2378 cells to 6 subgroups of cell types via clustering & UMAP
- Tested 3 different trajectory inference algorithm and constructed a solid trajectory model via Monocle
- Illustrated the dynamic expression change of key genes during the development of human prefrontal cortex
- Elucidated the potential roles of these found markers

# Thank you!

- Video Link:
- <https://youtu.be/B94WFYlnl8Y>