Epigenetically Profiling Human Brain Cell Types Utilizing ATAC-Seq

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Quynh Pham



Introduction

- The human brain contains many distinct cell types with differing morphological, electrophysiological, and connectional properties.
- We wish to identify enhancer elements that distinguish these cell types.

Aims:

- Identification of cell type-specific enhancers using ATAC-seq
- Integration of epigenetic data and transcriptomic data to identify of distinct cell class/typespecific regulators

Epigenetic Landscapes of Neuronal Classes/Type Using ATAC-seq







Vibratome sections

Each sample is:

- \rightarrow Sliced and dissected into layers (1 through 6)
- \rightarrow Dounced to isolate the nuclei
- → Stained with PE-NeuN antibody
- \rightarrow Single nuclei are sorted as NeuN⁺ and NeuN⁻ from each layer using FACS
- \rightarrow Tn5 tagmentation
- \rightarrow Indexed and amplified by PCR
- \rightarrow MiSeq

ATAC-seq data revealing the epigenetic landscape of neuronal classes/types



GABAergic

- cl1062_SCGN_Ndnf.Cxcl14
- cl1001_SOX13_Ndnf.Car4
 cl1009_CXCL14_Ndnf.Cxcl14
- cl1010_ARHGAP36_Ndnf.Cxcl14
- cl1007_CALB1_Sst.Cbin4
- d1004 CNTNAP3P2 Pvalb.Wt1
- cl1036 GCNT2 Vip.Chat
- el1006 FLT1 Vip.Chat
- cl1022 TAC3 Vip.Mybpc1

Glutamatergic

cl2001_TTC6_L5b.Cdh13
 cl2004_TRABD2A_L5a_Deptor_Pacsin2
 cl2016_PKD2L1_L5a_Deptor_Pacsin2
 cl2005_FRMD6-AS2_L2.Ngb
 cl2009_SULF1_L6a.Picxd3
 cl2002_TPBG_L4.Sparcl1
 cl2013_TNNT2_L5a.Deptor_Pacsin2
 cl2010_CARM1P1_L5b.Samd3
 cl2033_IL26_L6a.Picxd3

Glial

cl3002_GPNMB_OPC.Pdgfra
 cl3004_APBB1IP_Micro.Ctss

- Current clustered data from different cases of human brain tissues
- Reads are used to compute Jaccard distances among cells, which are used to cluster cells into like groups
- We observe major neuronal classes (excitatory and inhibitory), as well as subclass specificity in inhibitory cells

ATAC-seq results generated during internship



Comparison of single cell QC metrics with known data set → Demonstrates high quality cells **Clustering nuclei with tSNE separates distinct neuron classes**

- \rightarrow Cells cluster together (as expected)
- \rightarrow Cells cluster apart from previous cells (not as expected)
- \rightarrow Unclear whether this is sample-specific or operator-specific

Using these epigenomic elements to create viral tools for prospective marking of mouse and human cell types



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