Spatiotempotal properties of NDD genes during brain development for biomarker discovery

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1 Aims of the project

The aims of this project are:

1) To define and explore cell type-specific expression patterns of NDD genes via a meta-analysis of brain cell type RNA-expression data

2) To characterize the developmental trajectory of gene expression for ID and CP genes and assess their expression during cellular maturation in brain organiods and assess their expression across multiple fetal developmental periods

what to review

- human brain single cell rna-seq studies

- reread papers used for PhD proposal

- number and types of samples

- method used for sequencing

- data availablity

- main conclusions of the studies

- co-expression networks and their utility in spatiotemporal studes

- this kind of analysis in other areas (particularly cancer)

- Use of single-cell analysis vs bulk rna-seq

section structure:

- Introduction

- Neurodevelopmental disorders

- RNA-sequencing studies and its use in brain

- Utility of single cell in this area

- co-expression analyses amd their application in NDDs

- Gene lists for NDD

- Lack of gene networks in NDDs

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2   Introduction

Human brain development is a complex and a tightly regulated process duroing which changes occur at both anatomical and functional levels. The processes of brain development are highly dependent on the appropriate expression of RNA and proteins, Mutatations that result in altered expression or function of these gene products can cause or contribute to neurodevelopmental disorders (NDDs).

3   Neurodevelopmental disorders

Neurodevelopmental disorders (NDDs) such as autism spectrum disorder, intellectual disability and epilipsy are characterized by abnormal brain development. High co-occurance of NDDs indicate a shared, underlying biological mechanism. The genetic heterogeneity and overlap observed in NDDs make it difficult to identify the genetic causes of specific clinical symptoms

4 Co-mobidity of NDDs

5 Expression studies

- what are the datasets available

- where am i going to get the genelists from

- what gene ontologies am I getting with my genes

- current co-expression networks that are available

- lack of ID gene networks

- benchmark potentially?

- Issues with bulk rna?

6 Thesis aims

- To comprehensively characterize the expression properties of ID and CP enes in the normal human brain

    - To determine whether ID and CP genes are expressed in a cell-type speciic mannner using single-cell RNA-seq data

    - To characterize the developmental trajectory of gene expression for ID and CP genes and assess their expression during cellular maturation in brain organiods and assess their expression across multiple fetail developmental periods

    - To characterize the spatial and temporal properties of ID and CP gene expression in the adult brain, by assessing age-dependent changes brain-region and cortical layer-specificity

- To determine whether convergent gene expression changes are observed in ID and CP in patient-derived cells with heterogenous mutations

7 Characterisation of brain diversity using single-cell

7.1 Studies that have characterized the single-cell transcriptome in the brain

Year	Cells reported	Method	Technique	Species	Cell isolation	Brain region	Developmental stag
2014							