

Spatiotemporal properties of NDD genes during brain development for biomarker discovery

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1 Aims of the project

- To comprehensively characterize the expression properties of ID and CP genes in the normal human brain
 - To determine whether ID and CP genes are expressed in a cell-type specific manner 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 organoids and assess their expression across multiple fetal 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 heterogeneous mutations

2 Introduction

Human brain development is a complex and a tightly regulated process during 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. Mutations 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) are a group of early onset neurological disorders that affect an estimated 10% to 15% of the population with prevalence rates increasing worldwide. Common NDDs include autism spectrum disorder, intellectual disability, epilepsy and motor/tic movement disorders, and are characterized by strong clinical co-morbidity which suggests common genetic etiology.

- ASD and how many genes have been identified
- ID and how many genes have been identified
- Other NDDs and how many genes have been identified

The genetic heterogeneity and overlap observed in NDDs make it difficult to identify the genetic causes of specific clinical symptoms

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

3.1 Heterogeneity of NDDs

4 Expression studies

4.1 RNA: bulk vs single-cell

4.2 Co-expression network analysis

5 Characterisation of brain diversity using single-cell

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

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 availability
- main conclusions of the studies
- co-expression networks and their utility in spatiotemporal studies

- this kind of analysis in other areas (particularly cancer)
- Use of single-cell analysis vs bulk rna-seq
- 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?