

# Neurodevelopmental gene dysregulation score

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## **Aim**

Use genes that are casual in monogenic neurodevelopmental disorders and to see if they as a group are dysregulated in the brain of ASD patients

## **1 Paper Summary**

- In summary, single-nucleus RNA seq of the cortical tissue of patients with autism was used to identify autism associated changes in specific cell types
- Samples included prefrontal cortex and anterior cingulate cortex
- 15 ASD patients and 16 controls
- generated 104,559 single nuclei gene expression profiles (52,556 from controls and 52,003 from ASD patients)
- Identified 17 cell types
- neurons expressed more genes and transcripts than glia
- Nuclear profiles from ASD and control subjects for each cell type using a linear mixed model

- 692 differentially expression events were found which included 513 unqiue differentially expressed genes
- 79% of differentially expressed genes were coming from a single cell type
- Intersection of DEGs with the SFARI database was made and found a 13% overlap (75 genes)
- SFARI genes were most overreepresented with L2/3 and L4 excitatory neurons
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## 2 Method

- Obtain the single-cell data from Velmeshev et al
- Make a list of neurodevelopmental disease genes with subcategories
- For each gene:
  - Calculate the z-score of its expression in a given individual and cell type relative to all cells from controls in the same cell-type
  - Box-plot the z-scores and calculate a wilcoxon's rank sums test comparing NDDs and non-NDD genes for each individual

## 3 Tasks to do

- Download raw data
- make a list of NDD and non-NDD genes and divide into subcategories
- plot mean gene expression to see what the rate of expression is like

- check variance of expression
- in which cell types are NDD cells mainly expressed
- variance of expression in NDD vs non-NDD genes
- average out expression and calculate z-score for each gene in each cell type for one ASD individual vs control
- make boxplot of expression
- calculate wilcoxon ranks sums test between NDD and non-NDD genes