NucleoTIDE Hackathon Project

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Introduction

Topic: Bioinformatics

- ▶ Goal: Identify mechanisms involved in neuromelanin formation by performing differential gene expression analysis between melanized and non-melanized dopaminergic brain regions
  - ▶ Melanized: Substantia nigra pars compacta (SNpc)
  - ▶ Non-melanized: Ventral tegmental area (VTA)

Why is this important?

- ▶ Process of neuromelanin formation remains a mystery - only observed in humans
- ▶ Neuromelanin is linked to Parkinson's disease
  - ▶ Provide insight into onset/progression of the disease

Volcano Plot
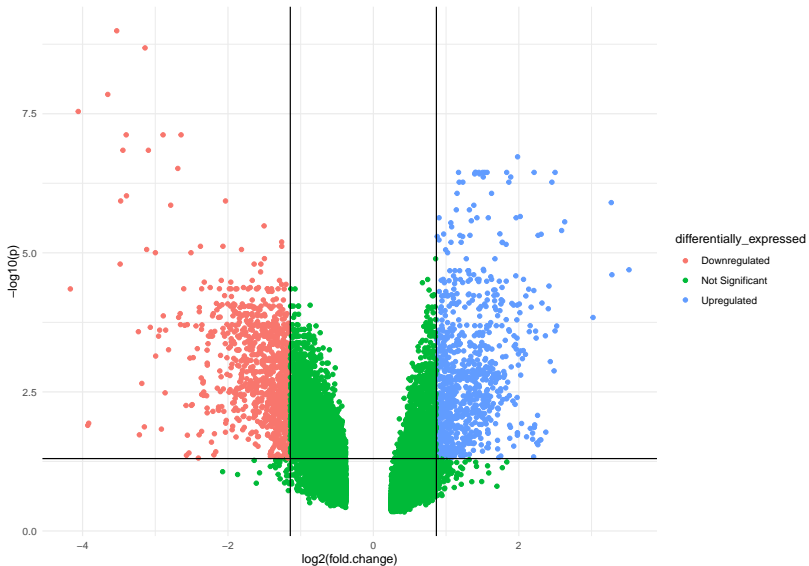
Differentially Expressed Genes

```
final_expr[,c(15, 17:18)]
```

```
##     gene.symbol           p fold.change
## 1         AGTR1 2.017857e-05 11.44100000
## 2         FEZF1 1.250000e-06  9.65900000
## 3         LMOD3 1.452381e-04  8.11800000
## 4          NPNT 2.771875e-06  6.19600000
## 5        CELSR1 3.971429e-06  6.01800000
## 6         RSPO2 2.067010e-04  5.74200000
## 7          PYGL 3.581818e-07  5.65300000
## 8        ATP2A3 9.025070e-04  5.40100000
## 9          OC90 3.955056e-05  5.33600000
## 10        SRPX2 1.012987e-04  5.30000000
## 11       SLC6A3 8.355197e-03  4.78400000
## 12        F2RL2 2.553991e-04  4.69400000
## 13      SLC18A2 1.238258e-02  4.65600000
## 14        CBLN1 3.581818e-07  4.62900000
## 15        ENPP1 4.760417e-05  4.61700000
```

Conclusions

- Dopamine active transporter (SLC6A3, BH-corrected $p = 8.355197\text{e-}03$, FC = 4.784)
- Vesicular monoamine transporter (SLC18A2, BH-corrected $p = 0.01238258$, FC = 4.656)
  - Codes for the VMAT2 enzyme, which transports dopamine into monoaminergic vesicles to prevent it from oxidizing
  - Inversely proportional to neuromelanin levels
    - Results suggest the opposite

Ideally, further analysis should be done on these 696 genes to determine which molecular pathways they are involved in. This includes gene set enrichment analysis and assigning gene ontology terms to groups of these genes. Due to time limitations, this could not be accomplished within the hackathon.