

main

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1 Extract unique male specific SZ-associated genes

```
[1]: import functools
import numpy as np
import pandas as pd
from os import environ
from gtfparse import read_gtf
from scipy.stats import mannwhitneyu
from statsmodels.stats.multitest import fdrcorrection

[2]: environ['NUMEXPR_MAX_THREADS'] = '16'

[3]: @functools.lru_cache()
def get_res_df(feature):
    return pd.read_csv('../interaction_model/dlpfc/_m/%s/
↳residualized_expression.tsv' %
                        feature, sep='\t').T

@functools.lru_cache()
def get_pheno_df():
    return pd.read_csv('/ceph/projects/v3_phase3_paper/inputs/phenotypes/_m/
↳dlpfc_phenotypes.csv',
                        index_col=0)

@functools.lru_cache()
def get_res_pheno_df(feature):
    return pd.merge(get_pheno_df(), get_res_df(feature), left_index=True,
↳right_index=True)

@functools.lru_cache()
def get_gtf(gtf_file):
    return read_gtf(gtf_file)
```

```

[4]: def map_features(feature):
    return {"genes": "gene", 'transcripts': 'tx',
            'exons': 'exon', 'junctions': 'jxn'}[feature]

def gene_annot(feature):
    gtf_file = '/ceph/genome/human/gencode25/gtf.CHR/_m/gencode.v25.annotation.
    ↪gtf'
    gtf0 = get_gtf(gtf_file)
    gtf = gtf0[(gtf0["feature"] == feature)]
    return gtf[["gene_id", "gene_name", "transcript_id", "exon_id", "gene_type",
                "seqname", "start", "end", "strand"]]

def get_de(feature):
    f = pd.read_csv('../.../female_analysis/_m/%s/diffExpr_szVctl_full.txt' %
    ↪feature,
                    sep='\t', index_col=0)\
        .rename(columns={'gencodeGeneID': 'gencodeID'})
    m = pd.read_csv('../.../male_analysis/_m/%s/diffExpr_szVctl_full.txt' %
    ↪feature,
                    sep='\t', index_col=0)\
        .rename(columns={'gencodeGeneID': 'gencodeID'})
    return f, m

def get_unique(x, y, thres=0.05):
    return x.merge(pd.DataFrame(index = list(set(x[(x['adj.P.Val'] <= thres)].
    ↪index) -
                                                set(y[(y['adj.P.Val'] <= thres)].
    ↪index))),
                  left_index=True, right_index=True)

def subset_sz_female(feature):
    df = get_res_pheno_df(feature)
    ctl = df[(df['Dx'] == 'Control') & (df['Sex'] == 'F')].copy()
    sz = df[(df['Dx'] == 'Schizo') & (df['Sex'] == 'F')].copy()
    return ctl, sz

def add_pvals_adjustPval(feature, df):
    ctl, sz = subset_sz_female(feature)
    f_pval = []
    for gene_id in df.Feature:
        stat, pval = mannwhitneyu(ctl[gene_id], sz[gene_id])
        f_pval.append(pval)

```

```

fdr_f = fdr correction(f_pval)
return pd.concat([df.set_index('Feature'),
                  pd.DataFrame({'Female_Pval': f_pval, 'Female_FDR':
                                fdr_f[1]}),
                  index=df.Feature)], axis=1)

```

1.1 Genes

```
[5]: gtf_annot = gene_annot('gene')
```

```
INFO:root:Extracted GTF attributes: ['gene_id', 'gene_type', 'gene_status',
'gene_name', 'level', 'havana_gene', 'transcript_id', 'transcript_type',
'transcript_status', 'transcript_name', 'transcript_support_level', 'tag',
'havana_transcript', 'exon_number', 'exon_id', 'ont', 'protein_id', 'ccdsid']
```

```
[6]: f, m = get_de('genes')
m['Feature'] = m.index
#genes = get_unique(get_unique(m, f), a)
genes = get_unique(m, f)
genes = pd.merge(gtf_annot[['gene_id', 'seqname']], genes, left_on='gene_id',
                 right_on='Feature', how='right').rename(columns={'seqname':
                                'Chrom'})
genes = genes[['Feature', 'gencodeID', 'Symbol', 'ensemblID',
                 'Chrom', 'logFC', 't', 'adj.P.Val']].sort_values('adj.P.Val')
genes = add_pvals_adjustPval('genes', genes)
genes = genes[~(genes['Female_Pval'] <= 0.05)].sort_values('adj.P.Val') ##
Stringents
genes['Type'] = 'gene'
genes.shape
```

```
[6]: (122, 10)
```

1.2 Transcripts

```
[7]: gtf_annot = gene_annot('transcript')
```

```
[8]: f, m = get_de('transcripts')
m['Feature'] = m.index
m['ensemblID'] = m.gene_id.str.replace('\\.\\d+', '', regex=True)
#trans = get_unique(get_unique(m, f), a)
trans = get_unique(m, f)
trans = pd.merge(gtf_annot[['transcript_id', 'seqname']], trans,
                 left_on='transcript_id', right_on='Feature',
                 how='right').rename(columns={'seqname': 'Chrom'})
trans = trans[['Feature', 'gene_id', 'Symbol', 'ensemblID', 'Chrom',
                 'logFC', 't', 'adj.P.Val']].rename(columns={'gene_id':
                                'gencodeID'})
```

```
trans = add_pvals_adjustPval('transcripts', trans)
trans = trans[~(trans['Female_Pval'] <= 0.05)].sort_values('adj.P.Val') ##
↳Stringents
trans['Type'] = 'transcript'
trans.shape
```

[8]: (22, 10)

1.2.1 Exons

```
[9]: gtf_annot = gene_annot('exon')
gtf_annot['ensemblID'] = gtf_annot.gene_id.str.replace('\\.\d+', '', regex=True)
```

```
[10]: f, m = get_de('exons')
m['Feature'] = m.index
#exons = get_unique(get_unique(m, f), a)
exons = get_unique(m, f)
exons = pd.merge(gtf_annot[['ensemblID', 'seqname']], exons,
                  on='ensemblID', how='right').rename(columns={'seqname':
↳'Chrom'})
exons = exons[['Feature', 'gencodeID', 'Symbol', 'ensemblID', 'Chrom',
                  'logFC', 't', 'adj.P.Val']].sort_values('adj.P.Val')\
                  .groupby('Feature').first().reset_index()
exons = add_pvals_adjustPval('exons', exons)
exons = exons[~(exons['Female_Pval'] <= 0.05)].sort_values('adj.P.Val') ##
↳Stringents
exons['Type'] = 'exon'
exons.shape
```

[10]: (116, 10)

1.2.2 Junctions

```
[11]: f, m = get_de('junctions')
m['Feature'] = m.index
#juncs = get_unique(get_unique(m, f), a)
juncs = get_unique(m, f)
juncs = pd.merge(gtf_annot[['ensemblID', 'seqname']], juncs,
                  on='ensemblID', how='right').rename(columns={'seqname':
↳'Chrom'})
juncs = juncs[['Feature', 'gencodeID', 'Symbol', 'ensemblID', 'Chrom',
                  'logFC', 't', 'adj.P.Val']].sort_values('adj.P.Val')\
                  .groupby('Feature').first().reset_index()
juncs = add_pvals_adjustPval('junctions', juncs)
juncs['Type'] = 'junction'
juncs = juncs[~(juncs['Female_Pval'] <= 0.05)].sort_values('adj.P.Val') ##
↳Stringents
```

```
juncs.shape
```

```
[11]: (49, 10)
```

1.3 DE summary

1.3.1 DE (feature)

```
[12]: gg = len(set(genes.index))
      tt = len(set(trans.index))
      ee = len(set(exons.index))
      jj = len(set(juncs.index))

      print("\nGene:\t\t%d\nTranscript:\t%d\nExon:\t\t%d\nJunction:\t%d" %
            (gg, tt, ee, jj))
```

```
Gene:          122
Transcript:    22
Exon:          116
Junction:      49
```

DE (EnsemblID)

```
[13]: gg = len(set(genes['ensemblID']))
      tt = len(set(trans['ensemblID']))
      ee = len(set(exons['ensemblID']))
      jj = len(set(juncs['ensemblID']))

      print("\nGene:\t\t%d\nTranscript:\t%d\nExon:\t\t%d\nJunction:\t%d" %
            (gg, tt, ee, jj))
```

```
Gene:          122
Transcript:    22
Exon:          80
Junction:      42
```

DE (Gene Symbol)

```
[14]: gg = len(set(genes['Symbol']))
      tt = len(set(trans['Symbol']))
      ee = len(set(exons['Symbol']))
      jj = len(set(juncs['Symbol']))

      print("\nGene:\t\t%d\nTranscript:\t%d\nExon:\t\t%d\nJunction:\t%d" %
            (gg, tt, ee, jj))
```

```
Gene:          108
```

Transcript: 22
Exon: 79
Junction: 42

1.3.2 Feature effect size summary

```
[15]: feature_list = ['Genes', 'Transcript', 'Exons', 'Junctions']  
feature_df = [genes, trans, exons, juncs]  
for ii in range(4):  
    ff = feature_df[ii]  
    half = len(set(ff[(np.abs(ff['logFC']) >= 0.5)].index))  
    one = len(set(ff[(np.abs(ff['logFC']) >= 1)].index))  
    print("\nThere are %d unique %s with abs(log2FC) >= 0.5" % (half,   
→feature_list[ii]))  
    print("There are %d unique %s with abs(log2FC) >= 1" % (one,   
→feature_list[ii]))
```

There are 9 unique Genes with abs(log2FC) >= 0.5
There are 0 unique Genes with abs(log2FC) >= 1

There are 11 unique Transcript with abs(log2FC) >= 0.5
There are 5 unique Transcript with abs(log2FC) >= 1

There are 15 unique Exons with abs(log2FC) >= 0.5
There are 0 unique Exons with abs(log2FC) >= 1

There are 4 unique Junctions with abs(log2FC) >= 0.5
There are 0 unique Junctions with abs(log2FC) >= 1

```
[16]: feature_list = ['Genes', 'Transcripts', 'Exons', 'Junctions']  
feature_df = [genes, trans, exons, juncs]  
for ii in range(4):  
    ff = feature_df[ii]  
    half = len(set(ff[(np.abs(ff['logFC']) >= 0.5)].ensemblID))  
    one = len(set(ff[(np.abs(ff['logFC']) >= 1)].ensemblID))  
    print("\nThere are %d unique %s with abs(log2FC) >= 0.5" % (half,   
→feature_list[ii]))  
    print("There are %d unique %s with abs(log2FC) >= 1" % (one,   
→feature_list[ii]))
```

There are 9 unique Genes with abs(log2FC) >= 0.5
There are 0 unique Genes with abs(log2FC) >= 1

There are 11 unique Transcripts with abs(log2FC) >= 0.5
There are 5 unique Transcripts with abs(log2FC) >= 1

There are 10 unique Exons with $\text{abs}(\log_2\text{FC}) \geq 0.5$
There are 0 unique Exons with $\text{abs}(\log_2\text{FC}) \geq 1$

There are 4 unique Junctions with $\text{abs}(\log_2\text{FC}) \geq 0.5$
There are 0 unique Junctions with $\text{abs}(\log_2\text{FC}) \geq 1$

```
[17]: df = pd.concat([genes.reset_index(), trans.reset_index(),  
                    exons.reset_index(), juncs.reset_index()], axis=0)  
df.to_csv('male_specific_DE_4features.txt', sep='\t', index=False, header=True)
```

1.4 Number of DEGs on allosomes

```
[18]: df[(df['Chrom'].isin(['chrX', 'chrY']))].groupby(['Type', 'Chrom']).size()
```

```
[18]: Type      Chrom  
exon      chrX      7  
gene      chrX      4  
junction  chrX      2  
transcript chrX      1  
dtype: int64
```

```
[ ]:
```