# Enrichment Analyses

### Setup

```
library(easypackages)
libraries("here")
options(stringsAsFactors = FALSE)

ndigits2use = 4

source(here("code", "genelistOverlap.R"))
fdr_thresh = 0.05

# non-zero and zero modules
nmods = 21
nonzeromods = c(1,2,6,8,10,11,13,15,17,18,21)
zeromods = c(3,4,5,7,9,12,14,16,19,20)

# Load in gene lists for enrichment analyses
load(here("data", "tidy", "enrichment_data.Rdata"))
```

### Read in data

```
# read in WGCNA results
wgcna_res = read.csv(here("WGCNAresults","wgcna_results_summary.csv"))
backgroundTotal = dim(wgcna_res)[1]
bglist = wgcna_res$geneSymbol
M0_size = dim(subset(wgcna_res, wgcna_res$moduleLabels==0))[1]
```

### Non-zero modules

Grab non-zero modules and report percentage of genes falling within those modules

```
mask = is.element(wgcna_res$moduleLabels, nonzeromods)
nonzeromod_data = subset(wgcna_res, mask)
nz_genes = nonzeromod_data$geneSymbol
# percentage of clustered genes falling within those modules
nz_prop = dim(nonzeromod_data)[1]/(backgroundTotal-M0_size)
nz_prop
```

## [1] 0.6139912

#### Zero modules

Grab zero modules and report percentage of genes falling within those modules

```
mask = is.element(wgcna_res$moduleLabels, zeromods)
zeromod_data = subset(wgcna_res, mask)
z_genes = zeromod_data$geneSymbol
```

```
# percentage of clustered genes falling within those modules
z_prop = dim(zeromod_data)[1]/(backgroundTotal-MO_size)
z_prop
## [1] 0.3860088
```

# Annotate each module by enrichment in broadly expressed, blood, brain, or lymphocyte genes

```
mod_names = c("M1_turquoise","M2_blue","M3_brown","M4_yellow",
  "M5_green", "M6_red", "M7_black", "M8_pink", "M9_magenta",
  "M10_purple", "M11_greenyellow", "M12_tan", "M13_salmon",
  "M14_cyan", "M15_midnightblue", "M16_lightcyan", "M17_grey60",
  "M18_lightgreen", "M19_lightyellow", "M20_royalblue", "M21_darkred")
geneclasses = c("BroadGenes", "BloodGenes", "BrainGenes", "LymphocyteGenes")
outcols = c("OR", "pval", "fdr")
out_mats = vector(mode = "list", length = length(geneclasses))
names(out_mats) = geneclasses
for (igc in 1:length(geneclasses)){
  out_res = data.frame(matrix(nrow = length(mod_names),
                              ncol = length(outcols)))
  colnames(out_res) = outcols
  rownames(out_res) = mod_names
  # intersect genes2 list with background
  genes2 = eval(as.name(geneclasses[igc]))
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])
  for (imod in 1:length(mod names)){
    # filename for module list
   genes1 = wgcna_res$geneSymbol[wgcna_res$moduleLabels==imod]
   overlap_res = genelistOverlap(genes1,
                                   backgroundTotal,
                                   print_result = FALSE,
                                   header = FALSE)
   out_res[imod,1] = overlap_res[[1]]$OR
   out_res[imod,2] = overlap_res[[1]]$hypergeo_p
  out_res[,3] = p.adjust(out_res[,2], method = "fdr")
  out_mats[[igc]] = out_res
}
```

### Modules enriched for broadly expressed genes

```
out_mats[[1]]
##
                           OR
                                                    fdr
                                      pval
## M1 turquoise
                    1.4754869 7.384191e-05 2.215257e-04
## M2_blue
                    4.3473823 2.843457e-59 5.971260e-58
## M3_brown
                    0.4028520 1.000000e+00 1.000000e+00
## M4_yellow
                    1.0127503 5.891632e-01 1.000000e+00
## M5_green
                    0.8250661 9.591967e-01 1.000000e+00
## M6_red
                    0.6841978 9.982855e-01 1.000000e+00
## M7_black
                    0.6557372 9.990008e-01 1.000000e+00
## M8_pink
                    3.4594286 5.151937e-23 5.409534e-22
## M9_magenta
                    0.9673481 6.687839e-01 1.000000e+00
## M10_purple
                    1.7558107 6.361290e-05 2.215257e-04
## M11_greenyellow 2.8354308 5.456839e-14 2.864840e-13
## M12 tan
                    0.9602873 6.756651e-01 1.000000e+00
## M13_salmon
                    3.2416943 6.186578e-17 4.330604e-16
## M14 cyan
                    0.8460565 8.385310e-01 1.000000e+00
## M15_midnightblue 2.9259899 8.821725e-10 3.705125e-09
## M16_lightcyan
                    0.2184977 1.000000e+00 1.000000e+00
## M17_grey60
                    0.3078006 9.999977e-01 1.000000e+00
## M18_lightgreen
                    2.0544133 1.640082e-04 4.305215e-04
## M19_lightyellow 0.1180096 1.000000e+00 1.000000e+00
## M20_royalblue
                    0.8797679 7.608833e-01 1.000000e+00
## M21_darkred
                    1.8493827 2.375546e-03 5.542940e-03
```

# Modules enriched for whole-blood-specific genes

```
out_mats[[2]]
                                       pval
## M1_turquoise
                    11.5273292 4.658437e-56 9.782719e-55
## M2_blue
                     0.0000000 1.000000e+00 1.000000e+00
## M3_brown
                     0.4055741 9.808647e-01 1.000000e+00
## M4_yellow
                     0.0000000 1.000000e+00 1.000000e+00
## M5_green
                     0.0000000 1.000000e+00 1.000000e+00
## M6_red
                     0.0000000 1.000000e+00 1.000000e+00
## M7_black
                     4.7788779 8.944644e-08 9.391876e-07
                     0.0000000 1.000000e+00 1.000000e+00
## M8_pink
## M9_magenta
                     2.1295290 4.617022e-02 1.615958e-01
## M10_purple
                     0.0000000 1.000000e+00 1.000000e+00
## M11_greenyellow
                     0.2711242 9.758859e-01 1.000000e+00
## M12_tan
                     2.3397400 2.934126e-02 1.232333e-01
## M13_salmon
                     0.8751862 6.778683e-01 1.000000e+00
## M14 cyan
                     0.4169821 9.110777e-01 1.000000e+00
## M15_midnightblue 0.0000000 1.000000e+00 1.000000e+00
## M16_lightcyan
                     5.8975148 8.474162e-06 5.931914e-05
## M17_grey60
                     0.0000000 1.000000e+00 1.000000e+00
## M18_lightgreen
                     0.0000000 1.000000e+00 1.000000e+00
## M19_lightyellow
                     5.9327166 2.006122e-05 1.053214e-04
## M20_royalblue
                     0.0000000 1.000000e+00 1.000000e+00
```

# Modules enriched for brain-specific genes

```
out_mats[[3]]
                           OR
                                     pval
                                                  fdr
## M1_turquoise
                    0.6372773 0.993733802 1.00000000
## M2_blue
                    0.1048834 0.999939871 1.00000000
## M3_brown
                    0.9104730 0.682859810 1.00000000
## M4_yellow
                    0.3257368 0.985882512 1.00000000
## M5_green
                    0.8687475 0.702908371 1.00000000
## M6 red
                    0.7366275 0.804434834 1.00000000
## M7 black
                    2.7368728 0.002137245 0.04488215
## M8_pink
                    0.0000000 1.000000000 1.00000000
## M9_magenta
## M10_purple
## M9 magenta
                    0.2348909 0.986403449 1.00000000
                    0.0000000 1.000000000 1.00000000
## M11 greenyellow 0.2542235 0.981117101 1.00000000
## M12 tan
                    1.0567651 0.540726528 1.00000000
## M13 salmon
                    0.0000000 1.000000000 1.00000000
## M14_cyan
                    0.7904823 0.725793834 1.00000000
## M15_midnightblue 0.0000000 1.00000000 1.00000000
## M16_lightcyan
                    1.3649312 0.388779322 1.00000000
## M17_grey60
                    0.4444339 0.896601020 1.00000000
## M18_lightgreen
                    0.0000000 1.000000000 1.00000000
## M19_lightyellow 2.5990629 0.051837402 0.54429272
## M20_royalblue
                    0.0000000 1.000000000 1.00000000
## M21_darkred
                    0.5515742 0.839551585 1.00000000
```

# Modules enriched for lymphocyte-specific genes

```
out_mats[[4]]
                            OR
                                       pval
                                                     fdr
## M1_turquoise
                     0.1838656 1.000000e+00 1.000000e+00
## M2_blue
                     0.2589684 9.994031e-01 1.000000e+00
## M3_brown
                     0.9595463 6.359708e-01 1.000000e+00
## M4_yellow
                     1.3943998 2.186229e-01 7.651803e-01
## M5_green
                     0.5604264 9.315386e-01 1.000000e+00
## M6_red
                    18.3563827 1.246918e-55 2.618528e-54
## M7_black
                    0.3145521 9.880536e-01 1.000000e+00
## M8 pink
                     2.0437365 2.899534e-02 1.522256e-01
## M9_magenta
                     4.1752756 1.103923e-06 7.727462e-06
## M10_purple
                     0.7885069 7.575422e-01 1.000000e+00
## M11_greenyellow
                     0.2070003 9.922681e-01 1.000000e+00
## M12_tan
                     1.0815100 5.104906e-01 1.000000e+00
## M13_salmon
                     0.0000000 1.000000e+00 1.000000e+00
                     1.3124825 3.778501e-01 1.000000e+00
## M14 cyan
## M15 midnightblue 1.0556558 5.514536e-01 1.000000e+00
## M16_lightcyan
                     0.7316755 7.628255e-01 1.000000e+00
```

```
## M17_grey60 6.8665689 1.456634e-08 1.529466e-07
## M18_lightgreen 2.5198636 3.990386e-02 1.675962e-01
## M19_lightyellow 0.8142841 7.097983e-01 1.000000e+00
## M20_royalblue 1.2667870 4.333959e-01 1.000000e+00
## M21 darkred 0.9096507 6.520517e-01 1.000000e+00
```

At the level of modules, test non-zero and zero modules for enrichment in broadly expressed, blood, brain, or lymphocyte modules

```
fname = "Subgrp_STRUCTresultMEfMRIcorr_bootlim_data4plotting_LV1_ci95.csv"
fname = here("PLSresults",fname)
plsbootdata = read.csv(fname)
var2use = "nonzero"
td_tmp = subset(plsbootdata, plsbootdata$Grp=="TD")
rownames(td_tmp) = 1:nmods
poor_tmp = subset(plsbootdata, plsbootdata$Grp=="Poor")
rownames(poor_tmp) = 1:nmods
good_tmp = subset(plsbootdata, plsbootdata$Grp=="Good")
rownames(good_tmp) = 1:nmods
td mods = as.numeric(rownames(td tmp)[td tmp[,var2use]==1])
asd_poor_mods = as.numeric(rownames(poor_tmp)[poor_tmp[,var2use]==1])
asd_good_mods = as.numeric(rownames(good_tmp)[good_tmp[,var2use]==1])
if (identical(td_mods,numeric(0))){
 td mods = NA
} else if (identical(asd_poor_mods,numeric(0))){
 asd poor mods = NA
} else if (identical(asd_good_mods,numeric(0))){
  asd_good_mods = NA
}
mask = logical(length = nmods)
nonzero_mods = sort(unique(c(td_mods, asd_poor_mods, asd_good_mods)))
mask[nonzero_mods] = TRUE
zero_mods = 1:nrow(td_tmp)
zero_mods = zero_mods[!mask]
nz_mods = mod_names[nonzero_mods]
z_mods = mod_names[zero_mods]
# broadly expressed modules
broadmods = mod_names[out_mats$BroadGenes$fdr<=fdr_thresh]; broadmods</pre>
## [1] "M1_turquoise"
                          "M2 blue"
                                              "M8 pink"
                          "M11_greenyellow"
## [4] "M10_purple"
                                             "M13 salmon"
## [7] "M15 midnightblue" "M18 lightgreen"
                                             "M21 darkred"
# test enrichment between non-zero modules and broadly expressed modules
overlap_res = genelistOverlap(nz_mods,
                              broadmods,
```

```
length(mod_names),
                              print_result = TRUE)
## [1] "OR = 184.500000, p = 0.000187"
# test enrichment between zero modules and broadly expressed modules
overlap res = genelistOverlap(z mods,
                              broadmods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 0.000000, p = 1.000000"
# blood modules
bloodmods = mod_names[out_mats$BloodGenes$fdr<=fdr_thresh]</pre>
# test enrichment between non-zero modules and blood modules
overlap_res = genelistOverlap(nz_mods,
                              bloodmods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 0.600000, p = 0.964912"
# test enrichment between zero modules and blood modules
overlap_res = genelistOverlap(z_mods,
                              bloodmods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 8.571429, p = 0.255639"
# brain expressed modules
brainmods = mod_names[out_mats$BrainGenes$fdr<=fdr_thresh]</pre>
# test enrichment between non-zero modules and brain modules
overlap_res = genelistOverlap(nz_mods,
                              brainmods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 0.000000, p = 1.000000"
# test enrichment between zero modules and brain modules
overlap_res = genelistOverlap(z_mods,
                              brainmods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 4.555556, p = 0.476190"
# lymphocyte modules
lymphocytemods = mod_names[out_mats$LymphocyteGenes$fdr<=fdr_thresh]
# test enrichment between non-zero modules and lymphocyte modules
overlap_res = genelistOverlap(nz_mods,
                              lymphocytemods,
                              length(mod_names),
```

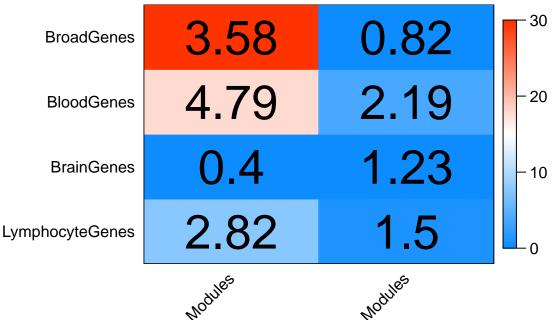
# At the level of modules, test for overlap between non-zero modules across groups

```
# show the ASD Poor modules
asd_poor_mods = mod_names[asd_poor_mods]
# show the ASD Good modules
asd_good_mods = mod_names[asd_good_mods]
# show the TD modules
td_mods = mod_names[td_mods]
# test overlap between ASD Poor and ASD Good
overlap_res = genelistOverlap(asd_poor_mods,
                              asd_good_mods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 0.000000, p = 1.000000"
# test overlap between TD and ASD Good
overlap_res = genelistOverlap(td_mods,
                              asd_good_mods,
                              length(mod_names),
                              print_result = TRUE)
## [1] "OR = 0.000000, p = 1.000000"
# test overlap between TD and ASD Poor
overlap_res = genelistOverlap(td_mods,
                              asd_poor_mods,
                              length(mod_names),
                              print result = TRUE)
## [1] "OR = 1.666667, p = 0.655659"
```

Examine enrichment at the gene-level between gene classes and non-zero or zero modules

```
geneclasses = c("BroadGenes","BloodGenes","BrainGenes","LymphocyteGenes")
res_colnames = c("Non-Zero Modules", "Zero Modules")
ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                            ncol = length(res colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
                           ncol = length(res_colnames)))
colnames(ORmat) = res colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res_colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclasses
rownames(logPmat) = geneclasses
rownames(Pmat) = geneclasses
rownames(FDRmat) = geneclasses
for (i in 1:length(geneclasses)){
  # intersect genes2 with background list
  genes2 = eval(as.name(geneclasses[i]))
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])
  overlap_res = genelistOverlap(nz_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,1] = overlap_res[[1]]$OR
  logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,1] = overlap_res[[1]]$hypergeo_p
  overlap_res = genelistOverlap(z_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,2] = overlap_res[[1]]$OR
  logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,2] = overlap_res[[1]]$hypergeo_p
}
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}
```

```
zLIM = c(0,30)
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
                      ySymbols = NULL,
                      colorLabels = FALSE,
                      colors = WGCNA::blueWhiteRed(100),
                      textMatrix = round(ORmat, digits = 2),
                      setStdMargins = FALSE,
                      cex.text = 3,
                      zlim = zLIM)
```



Lero Modules

### # Enrichment Odds Ratios

ORmat

```
##
                   Non-Zero Modules Zero Modules
## BroadGenes
                          3.5847421
                                       0.8168439
## BloodGenes
                          4.7909589
                                       2.1907949
## BrainGenes
                          0.3984724
                                       1.2301995
## LymphocyteGenes
                          2.8233783
                                        1.5007987
```

### # P-values

Pmat

##		Non-Zero Modules	Zero Modules
##	BroadGenes	1.480874e-93	1.0000000000
##	BloodGenes	1.573773e-18	0.0001826812
##	BrainGenes	1.000000e+00	0.5228156458
##	LymphocyteGenes	1.944252e-08	0.1012197835

```
## FDR

## Non-Zero Modules Zero Modules

## BroadGenes 5.923497e-93 1.0000000000

## BloodGenes 3.147546e-18 0.0007307249

## BrainGenes 1.000000e+00 0.6970875277

## LymphocyteGenes 2.592336e-08 0.2024395670
```

Examine enrichment between non-zero or zero modules and song bird DE, Human Specific, ASD Prenatal, ASD CTX Dysregulated Modules, ASD PTVs, ASD SFARI, and FMRP and CHD8 targets

```
geneclasses = list(SongBirdDE,
                   HumanSpecific1,
                   HumanSpecific2,
                   ASDPrenatal1,
                   ASDPrenatal2,
                   ASDCTXDownreg,
                   ASDCTXUpreg,
                   ASDPTVs,
                   ASDPTVs_pLI,
                   SFARIASD,
                   FMRP1,
                   FMRP2,
                   CHD81,
                   CHD82)
geneclassnames = c("Song Bird DE",
                   "Human-Specific1",
                   "Human-Specific2",
                   "ASD Prenatal1",
                   "ASD Prenatal2",
                   "ASD CTX Downreg",
                   "ASD CTX Upreg",
                   "ASD dnPTVs",
                   "ASD dnPTVs + pLI \geq 0.9",
                   "SFARI ASD",
                   "FMRP Targets1",
                   "FMRP Targets2",
                   "CHD8 Targets1",
                   "CHD8 Targets2")
res_colnames = c("Broadly Expressed", "Non-Zero Modules", "Zero Modules")
ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                             ncol = length(res_colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res_colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
```

```
ncol = length(res_colnames)))
colnames(ORmat) = res_colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res_colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclassnames
rownames(logPmat) = geneclassnames
rownames(Pmat) = geneclassnames
rownames(FDRmat) = geneclassnames
for (i in 1:length(geneclasses)){
  # intersect with background list
  genes2 = geneclasses[[i]]
 mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])
  overlap_res = genelistOverlap(BroadGenes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,1] = overlap_res[[1]]$OR
  logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,1] = overlap_res[[1]]$hypergeo_p
  overlap_res = genelistOverlap(nz_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,2] = overlap_res[[1]]$OR
  logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,2] = overlap_res[[1]]$hypergeo_p
  overlap_res = genelistOverlap(z_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,3] = overlap_res[[1]]$OR
  logPmat[i,3] = -log10(overlap_res[[1]]$hypergeo_p)
 Pmat[i,3] = overlap_res[[1]]$hypergeo_p
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
zLIM = c(0, -log10(0.005))
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
```

```
ySymbols = NULL,
colorLabels = FALSE,
colors = WGCNA::blueWhiteRed(50),
textMatrix = round(ORmat, digits = 2),
setStdMargins = FALSE,
cex.text = 1,
zlim = zLIM)
```



Broady Expressed Non-Zero modules

Lero modules

# # Enrichment Odds Ratios ORmat

##		Broadly	Expressed	Non-Zero Modules	Zero Modules
##	Song Bird DE		2.313688	1.766018	1.367557
##	Human-Specific1		1.631961	1.849270	1.098895
##	Human-Specific2		1.838675	1.737814	1.110486
##	ASD Prenatal1		0.926925	1.703069	1.188698
##	ASD Prenatal2		1.670964	1.723063	1.026814
##	ASD CTX Downreg		2.680746	1.698674	1.146462
##	ASD CTX Upreg		1.285018	1.643444	1.792725
##	ASD dnPTVs		1.518109	2.579444	1.822494
##	ASD dnPTVs + pLI >= 0.9		2.224350	2.010678	1.369595
##	SFARI ASD		1.280636	1.357698	1.263160
##	FMRP Targets1		1.797595	1.988684	1.164068
##	FMRP Targets2		1.967917	1.891329	1.637426
##	CHD8 Targets1		3.270380	2.052746	1.233921
##	CHD8 Targets2		4.519513	2.543460	1.167394

# P-values
Pmat

##

Broadly Expressed Non-Zero Modules Zero Modules

```
## Song Bird DE
                                1.207256e-12
                                                  2.931725e-03 0.1368211698
## Human-Specific1
                                1.121700e-02
                                                  1.454892e-04 0.9326513736
## Human-Specific2
                                3.930965e-04
                                                  1.157684e-02 0.8584468499
## ASD Prenatal1
                                1.000000e+00
                                                  5.633423e-03 0.7471413303
## ASD Prenatal2
                                3.797020e-03
                                                  4.664096e-03 0.9902083264
## ASD CTX Downreg
                                                  3.556493e-02 0.7510873768
                                2.357339e-13
## ASD CTX Upreg
                                                  5.025116e-02 0.0000280431
                                8.001010e-01
                                                  8.499079e-02 0.2420677095
## ASD dnPTVs
                                4.664012e-01
## ASD dnPTVs + pLI >= 0.9
                                2.704798e-03
                                                  2.351178e-02 0.3230860055
## SFARI ASD
                                7.123606e-01
                                                  6.624826e-01 0.4480139650
## FMRP Targets1
                                3.146039e-03
                                                  2.511948e-04 0.7045078476
## FMRP Targets2
                                7.574835e-03
                                                  2.692390e-02 0.0483558183
## CHD8 Targets1
                                2.526525e-66
                                                  1.922342e-11 0.6731317925
                                                  5.203285e-35 0.9979914178
## CHD8 Targets2
                               3.046940e-176
# FDR
FDRmat
##
                           Broadly Expressed Non-Zero Modules Zero Modules
## Song Bird DE
                                4.225398e-12
                                                  8.208830e-03 0.6384987923
## Human-Specific1
                                1.570380e-02
                                                  6.789495e-04 0.9979914178
## Human-Specific2
                                1.100670e-03
                                                  2.025946e-02 0.9979914178
## ASD Prenatal1
                                1.000000e+00
                                                  1.126685e-02 0.9979914178
## ASD Prenatal2
                                6.644784e-03
                                                  1.088289e-02 0.9979914178
## ASD CTX Downreg
                                1.100092e-12
                                                  4.526446e-02 0.9979914178
                                                  5.862636e-02 0.0003926034
## ASD CTX Upreg
                                8.616473e-01
## ASD dnPTVs
                                5.936015e-01
                                                  9.152854e-02 0.8472369833
```

## Assess enrichments with individual modules

6.292077e-03

8.310873e-01

6.292077e-03

1.178308e-02

1.768568e-65

4.265716e-175

3.657388e-02 0.9046408153 6.624826e-01 0.9979914178

8.791818e-04 0.9979914178

3.769346e-02 0.3384907284

1.345639e-10 0.9979914178

7.284599e-34 0.9979914178

## ASD dnPTVs + pLI >= 0.9

## SFARI ASD

## FMRP Targets1

## FMRP Targets2

## CHD8 Targets1

## CHD8 Targets2

```
geneclasses = list(SongBirdDE,
                    HumanSpecific1,
                    HumanSpecific2,
                    ASDPrenatal1,
                    ASDPrenatal2,
                    ASDCTXDownreg,
                    ASDCTXUpreg,
                    ASDPTVs,
                    ASDPTVs_pLI,
                    SFARIASD,
                    FMRP1,
                    FMRP2,
                    CHD81,
                    CHD82)
geneclassnames = c("Song Bird DE",
                    "Human-Specific1",
```

```
"Human-Specific2",
                   "ASD Prenatal1",
                   "ASD Prenatal2",
                   "ASD CTX Downreg",
                   "ASD CTX Upreg",
                   "ASD dnPTVs",
                   "ASD dnPTVs + pLI \geq 0.9",
                   "SFARI ASD",
                   "FMRP Targets1",
                   "FMRP Targets2",
                   "CHD8 Targets1",
                   "CHD8 Targets2")
ORmat = data.frame(matrix(nrow = length(mod_names),
                          ncol = length(geneclasses)))
colnames(ORmat) = geneclassnames
rownames(ORmat) = mod_names
Pmat = data.frame(matrix(nrow = length(mod_names),
                         ncol = length(geneclasses)))
colnames(Pmat) = geneclassnames
rownames(Pmat) = mod_names
FDRmat = data.frame(matrix(nrow = length(mod_names),
                           ncol = length(geneclasses)))
colnames(FDRmat) = geneclassnames
rownames(FDRmat) = mod_names
for (imod in 1:length(mod_names)){
  for (igc in 1:length(geneclasses)){
    # intersect geneclass list with background
   genes2 = geneclasses[[igc]]
   mask = is.element(genes2,bglist)
   genes2 = data.frame(genes2[mask])
   modulegenes = wgcna_res$geneSymbol[wgcna_res$moduleLabels==imod]
   overlap_res = genelistOverlap(modulegenes,
                                  genes2,
                                  backgroundTotal,
                                  print_result = FALSE,
                                  header = FALSE)
    ORmat[imod,igc] = overlap_res[[1]]$OR
    Pmat[imod,igc] = overlap_res[[1]]$hypergeo_p
  }
}
for (i in 1:dim(Pmat)[2]){
 FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
}
# Enrichment Odds Ratios
ORmat
```

Song Bird DE Human-Specific1 Human-Specific2

##

```
## M1_turquoise
                                         1.3602330
                                                          1.3827322
                        1.4445211
## M2 blue
                        0.7958297
                                         1.4650369
                                                          1.2453501
                        0.8860220
## M3 brown
                                         0.6767508
                                                          0.5936064
## M4_yellow
                        1.5090185
                                         1.2511181
                                                          0.8326079
## M5 green
                        0.9253541
                                         0.6903564
                                                          0.1652351
## M6 red
                                                          0.4810582
                        0.6901101
                                         0.6560055
## M7 black
                        1.1156977
                                         1.0673586
                                                          1.2112116
## M8_pink
                        1.6308335
                                         1.2989832
                                                          0.6435447
## M9_magenta
                        0.5923608
                                         1.1530506
                                                          1.5941173
## M10_purple
                        2.4734411
                                         0.7101442
                                                          1.0631122
## M11_greenyellow
                        0.8497899
                                         1.0677513
                                                          0.5077765
## M12_tan
                        0.7903243
                                         1.4725596
                                                          1.9683535
## M13_salmon
                        1.0511399
                                         2.2164479
                                                          2.1740584
## M14_cyan
                        1.5767099
                                         0.9321128
                                                          0.9290233
## M15_midnightblue
                        1.3406242
                                         1.6501061
                                                          1.8071866
## M16_lightcyan
                        0.9097010
                                         0.9637196
                                                          1.3902530
## M17_grey60
                        0.6704924
                                         0.3662373
                                                          1.0617409
## M18_lightgreen
                                                          1.3469630
                        1.4162710
                                         1.6715831
                                         0.6238701
                                                          0.6583452
## M19_lightyellow
                        1.5875813
## M20 royalblue
                        2.4333866
                                         0.1017561
                                                          0.8521449
## M21_darkred
                        0.9900495
                                         1.7789470
                                                          2.8840875
##
                     ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
                                                                        2.6647637
## M1 turquoise
                                       1.21649298
                         1.3381209
                                                         1.1577181
## M2 blue
                         0.1370147
                                       0.67341820
                                                         1.4019170
                                                                        0.3555503
## M3 brown
                         1.2149589
                                       1.01679360
                                                         0.5383083
                                                                        0.4253381
## M4_yellow
                         0.6147053
                                       1.18654720
                                                         0.9227490
                                                                        1.1016428
## M5_green
                         0.7392235
                                       0.69232381
                                                         0.8860065
                                                                        0.3617998
## M6_red
                         0.3301020
                                       0.62262775
                                                         0.5391205
                                                                        0.6774242
## M7_black
                         0.2859428
                                       0.45985351
                                                         0.9222863
                                                                        1.9704467
## M8_pink
                         0.1732171
                                       0.46607986
                                                         1.0240332
                                                                        0.1920415
## M9_magenta
                         0.3930965
                                       0.56751762
                                                         0.7069401
                                                                        4.3941300
## M10_purple
                         8.2872987
                                       3.79826082
                                                         1.7183441
                                                                        1.2261200
## M11_greenyellow
                         0.3378921
                                       1.07248377
                                                         0.7665975
                                                                        0.3881439
## M12_tan
                         0.5707456
                                                         0.6613822
                                                                        2.4172766
                                       0.35478149
## M13_salmon
                         0.7978864
                                                                        0.4104708
                                       1.33216464
                                                         1.4362206
## M14_cyan
                         2.6667225
                                       2.36212561
                                                         2.5407476
                                                                        0.9872183
## M15_midnightblue
                         3.8293530
                                       3.80990783
                                                         2.1158332
                                                                        0.6532845
## M16_lightcyan
                                       0.25869606
                         0.5241799
                                                         0.9575429
                                                                        2.4324639
## M17_grey60
                         1.1131640
                                       1.01525923
                                                         0.9575429
                                                                        0.9793079
## M18_lightgreen
                         2.3316823
                                       1.34855662
                                                         1.7337107
                                                                        0.1452521
## M19_lightyellow
                         0.4108537
                                       0.09432708
                                                         1.2952068
                                                                        0.9290014
## M20 royalblue
                         8.6813664
                                       2.92346826
                                                         2.0571087
                                                                        0.6227430
                                                         1.4525683
## M21 darkred
                         0.8633273
                                       0.54799867
                                                                        0.5045455
                     ASD dnPTVs ASD dnPTVs + pLI >= 0.9 SFARI ASD
##
## M1_turquoise
                       2.331068
                                               1.8123249 1.0941257
## M2_blue
                       0.000000
                                               0.0000000 0.5267210
## M3_brown
                       1.071075
                                               0.9634694 1.2063686
## M4_yellow
                       1.385108
                                                1.5128977 1.0624673
## M5_green
                       0.000000
                                               0.5071179 0.6020550
## M6_red
                       0.000000
                                               0.0000000 0.7762389
## M7_black
                                               0.8734169 0.8276617
                       1.643202
## M8_pink
                       1.818251
                                               0.6382691 0.4496127
## M9_magenta
                       0.000000
                                               1.0708560 0.4978471
## M10 purple
                      12.087633
                                               9.2202576 4.0020135
```

```
## M11_greenyellow
                       0.000000
                                               0.0000000 0.3568258
                       4.598326
## M12_tan
                                               1.1743421 0.7333386
## M13 salmon
                       0.00000
                                               1.2258483 0.1871304
## M14_cyan
                       3.348805
                                               2.4203375 2.6490852
## M15_midnightblue
                       0.000000
                                               0.6297367 2.5329171
                       0.00000
## M16 lightcyan
                                               0.0000000 1.2779503
## M17 grey60
                       0.000000
                                               0.6614501 1.6143994
## M18_lightgreen
                       0.00000
                                               1.4690321 0.6853322
## M19_lightyellow
                       0.000000
                                               0.0000000 1.0564072
## M20_royalblue
                       4.336976
                                               4.0008475 1.8469824
## M21_darkred
                       0.000000
                                               0.0000000 0.0000000
                    FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
                        1.77837177
                                        1.4218235
                                                      1.4026976
                                                                     1.0273298
## M1_turquoise
## M2_blue
                        0.09058257
                                        0.4497145
                                                      0.9584927
                                                                     2.2386635
## M3_brown
                        0.97644260
                                        1.5487484
                                                      0.7002422
                                                                     0.6495313
## M4_yellow
                        0.28219918
                                        0.5176744
                                                      1.9441924
                                                                     2.3620897
## M5_green
                        0.60067026
                                        1.2995524
                                                      1.1431016
                                                                     1.5181749
## M6 red
                        0.07748698
                                                      0.6686003
                                        1.3882459
                                                                     1.4838831
## M7_black
                        1.04856065
                                                      0.6734572
                                        2.1665335
                                                                     0.4274248
## M8 pink
                        0.18366396
                                        0.2232252
                                                      1.3907819
                                                                     4.0816199
## M9_magenta
                        0.10105717
                                                      0.6816482
                                                                     0.5346531
                                        1.2779379
## M10_purple
                        6.57738001
                                        5.2056148
                                                      3.2020846
                                                                     2.5922017
## M11 greenyellow
                        0.10937463
                                        0.0000000
                                                      0.9915956
                                                                     2.0356069
## M12 tan
                        1.29703596
                                        1.4024827
                                                      0.5250000
                                                                     0.4607735
## M13_salmon
                        1.89878988
                                        0.5699903
                                                      1.7081370
                                                                     1.5627897
## M14_cyan
                        1.23884272
                                        1.7002110
                                                      2.2693241
                                                                     2.4702393
## M15_midnightblue
                        4.61389446
                                        3.8651593
                                                      2.3011600
                                                                     2.0559087
                                                      0.3754422
## M16_lightcyan
                        0.78642271
                                        0.9458535
                                                                     0.2151048
## M17_grey60
                        0.78642271
                                        0.0000000
                                                      0.8627102
                                                                     0.2908104
## M18_lightgreen
                        0.86252813
                                        1.5737302
                                                      1.5458041
                                                                     2.0696739
## M19_lightyellow
                        0.65084682
                                        1.0526434
                                                      0.4203669
                                                                     0.3281622
## M20_royalblue
                        6.75317693
                                        0.5324469
                                                      2.3867476
                                                                     2.0317321
## M21_darkred
                        0.47984278
                                        1.7883298
                                                      1.5658605
                                                                     1.2546882
# P-values
Pmat.
##
                    Song Bird DE Human-Specific1 Human-Specific2
                                     0.0370449781
                                                      0.0531442710
## M1_turquoise
                     1.135926e-02
```

```
## M2 blue
                    9.377147e-01
                                     0.0126259601
                                                      0.1935379709
## M3_brown
                    8.102005e-01
                                     0.9883005346
                                                      0.9896875497
## M4 yellow
                    2.728203e-02
                                     0.1653906610
                                                      0.8194122762
## M5_green
                    7.092930e-01
                                     0.9685538226
                                                      0.9999974945
## M6 red
                    9.528888e-01
                                     0.9769653059
                                                      0.9937242112
## M7_black
                    3.840173e-01
                                     0.4545384863
                                                      0.2818489779
## M8_pink
                     1.758832e-02
                                     0.1449957535
                                                      0.9421794458
## M9_magenta
                    9.733735e-01
                                     0.3256260624
                                                      0.0490572469
## M10_purple
                    8.148640e-06
                                     0.9302965559
                                                      0.4831616424
## M11_greenyellow
                    7.730565e-01
                                     0.4579170004
                                                      0.9778899554
## M12_tan
                    8.381252e-01
                                     0.0586074419
                                                      0.0057577949
## M13_salmon
                    4.907752e-01
                                     0.0001038944
                                                      0.0016049040
## M14_cyan
                    7.659553e-02
                                                      0.6400846002
                                     0.6472804680
## M15_midnightblue 2.164513e-01
                                     0.0469912857
                                                      0.0487215926
## M16_lightcyan
                     6.632690e-01
                                     0.6040681500
                                                      0.2254255378
## M17_grey60
                    8.823591e-01
                                     0.9941921806
                                                      0.5047795745
```

```
## M18_lightgreen
                    1.834003e-01
                                     0.0540509708
                                                     0.2672967510
                                                     0.8575415339
## M19_lightyellow
                    9.966779e-02
                                     0.9159692459
## M20 royalblue
                    1.805791e-03
                                     0.9999309678
                                                     0.7045897102
## M21_darkred
                    5.741872e-01
                                     0.0415247676
                                                      0.0009591607
                    ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
                                    2.722458e-01
## M1_turquoise
                     4.066360e-02
                                                     0.470344698
                                                                   5.389578e-18
## M2 blue
                     1.000000e+00
                                    9.949803e-01
                                                     0.084889985
                                                                   9.999913e-01
## M3 brown
                     1.667206e-01
                                    5.748241e-01
                                                     0.990974520
                                                                   9.997226e-01
## M4 yellow
                     9.951909e-01
                                    2.436432e-01
                                                     0.686673625
                                                                   4.150673e-01
## M5_green
                     9.581872e-01
                                    9.704682e-01
                                                     0.730193394
                                                                   9.996131e-01
## M6_red
                     9.999970e-01
                                    9.872932e-01
                                                     0.976308498
                                                                   9.445452e-01
## M7_black
                     9.999990e-01
                                    9.992359e-01
                                                     0.674084136
                                                                   1.306131e-03
## M8_pink
                     1.000000e+00
                                    9.985516e-01
                                                     0.540636871
                                                                   9.999752e-01
## M9_magenta
                     9.997949e-01
                                    9.880782e-01
                                                     0.872129944
                                                                   1.299903e-14
## M10_purple
                     4.015611e-49
                                    4.904733e-15
                                                     0.039073174
                                                                   2.761094e-01
## M11_greenyellow
                     9.999203e-01
                                    4.481913e-01
                                                     0.815924947
                                                                   9.958920e-01
## M12_tan
                                                                   1.211472e-04
                     9.893399e-01
                                    9.996371e-01
                                                     0.894379052
## M13 salmon
                     8.610099e-01
                                    1.381745e-01
                                                     0.161605388
                                                                   9.932632e-01
## M14_cyan
                     6.180530e-06
                                    2.535122e-04
                                                     0.002704974
                                                                   5.780211e-01
## M15 midnightblue
                     1.866337e-10
                                    1.788732e-09
                                                     0.022910114
                                                                   8.807543e-01
## M16_lightcyan
                     9.771761e-01
                                   9.991133e-01
                                                     0.609303240
                                                                   2.277237e-03
## M17_grey60
                     4.086077e-01
                                    5.399646e-01
                                                     0.609303240
                                                                   5.863878e-01
## M18_lightgreen
                     5.444295e-04
                                    2.012199e-01
                                                                   9.988837e-01
                                                     0.109400839
## M19 lightyellow
                     9.922097e-01
                                    9.999668e-01
                                                     0.336696478
                                                                   6.359043e-01
                                    2.469850e-05
## M20 royalblue
                     2.902982e-26
                                                     0.042274031
                                                                   8.837559e-01
## M21 darkred
                     7.197188e-01
                                    9.471181e-01
                                                     0.251699190
                                                                   9.351176e-01
##
                      ASD dnPTVs ASD dnPTVs + pLI >= 0.9
                                                              SFARI ASD
## M1_turquoise
                    0.1017431544
                                             2.250048e-02 6.101846e-01
## M2_blue
                    1.0000000000
                                             1.000000e+00 9.827665e-01
## M3_brown
                    0.6270976927
                                             6.254016e-01 3.392103e-01
## M4_yellow
                    0.5324191633
                                             2.356721e-01 5.098157e-01
## M5_green
                    1.000000000
                                             9.105677e-01 9.241632e-01
## M6_red
                    1.000000000
                                             1.000000e+00 7.996989e-01
## M7_black
                    0.4725612191
                                             6.834226e-01 7.487100e-01
## M8 pink
                                             8.283296e-01 9.643412e-01
                    0.4388050788
## M9_magenta
                    1.000000000
                                             5.474334e-01 9.422390e-01
## M10 purple
                    0.0001377041
                                             7.743579e-13 6.135478e-07
## M11_greenyellow
                                             1.000000e+00 9.766108e-01
                    1.000000000
## M12_tan
                                             4.861569e-01 8.027132e-01
                    0.0801795280
## M13_salmon
                                             4.583188e-01 9.953270e-01
                    1.0000000000
## M14 cyan
                    0.2688111675
                                             9.433107e-02 1.067048e-02
## M15 midnightblue 1.0000000000
                                             7.998837e-01 1.936296e-02
## M16_lightcyan
                    1.000000000
                                             1.000000e+00 3.956264e-01
## M17_grey60
                    1.0000000000
                                             7.838677e-01 2.149659e-01
## M18_lightgreen
                    1.000000000
                                             4.046924e-01 7.926736e-01
## M19_lightyellow
                    1.0000000000
                                             1.000000e+00 5.502525e-01
## M20_royalblue
                    0.2148570594
                                             1.085325e-02 1.495658e-01
## M21_darkred
                    1.0000000000
                                             1.000000e+00 1.000000e+00
                    FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
## M1_turquoise
                     2.226484e-04
                                    1.474974e-01
                                                  2.984251e-03
                                                                9.969544e-01
## M2_blue
                     1.000000e+00
                                    9.810569e-01
                                                  7.951487e-01
                                                                1.781877e-18
## M3 brown
                     6.298647e-01
                                   1.357062e-01
                                                  9.983422e-01
                                                                 9.999986e-01
## M4 yellow
                     9.996186e-01 9.341598e-01
                                                  3.453303e-07
                                                                 3.641500e-15
## M5 green
                     9.593074e-01 3.267190e-01 2.527031e-01 3.054372e-04
```

```
## M6 red
                      9.999975e-01
                                    2.712390e-01
                                                   9.960769e-01
                                                                  8.703035e-04
                      5.102954e-01
                                    2.641720e-02
                                                   9.943618e-01
## M7_black
                                                                  1.000000e+00
## M8 pink
                      9.997783e-01
                                    9.891998e-01
                                                   2.638276e-02
                                                                  2.276259e-30
## M9_magenta
                      9.999479e-01
                                    3.752907e-01
                                                   9.869745e-01
                                                                  9.999973e-01
## M10_purple
                      7.335198e-21
                                    1.061350e-07
                                                   2.968418e-16
                                                                  1.466074e-13
## M11 greenyellow
                      9.998893e-01
                                    1.000000e+00
                                                   5.910126e-01
                                                                  1.147537e-07
## M12 tan
                      2.615079e-01
                                    3.060536e-01
                                                   9.994199e-01
                                                                  9.99999e-01
## M13 salmon
                      2.171335e-02
                                    8.701578e-01
                                                   1.066555e-03
                                                                  1.199621e-03
## M14_cyan
                      3.569345e-01
                                    2.241826e-01
                                                   1.218388e-05
                                                                  2.597814e-08
## M15_midnightblue
                     7.855050e-08
                                    1.857350e-03
                                                   1.717384e-05
                                                                  1.864293e-05
## M16_lightcyan
                      7.534806e-01
                                    6.322221e-01
                                                   9.997070e-01
                                                                  1.000000e+00
## M17_grey60
                      7.534806e-01
                                    1.000000e+00
                                                   7.731854e-01
                                                                  1.000000e+00
                                                                  5.017636e-05
## M18_lightgreen
                      6.884989e-01
                                    3.094799e-01
                                                   3.509229e-02
## M19_lightyellow
                      8.412809e-01
                                                   9.986039e-01
                                    5.747735e-01
                                                                  9.999997e-01
## M20_royalblue
                      1.216023e-11
                                    8.498274e-01
                                                   3.321972e-05
                                                                  1.035651e-04
## M21_darkred
                      9.204829e-01
                                    2.474667e-01
                                                   3.948243e-02
                                                                  1.581403e-01
```

# # FDR

FDRmat

```
##
                     Song Bird DE Human-Specific1 Human-Specific2
## M1_turquoise
                     0.0795148525
                                       0.175822326
                                                         0.18600495
## M2 blue
                                                         0.58061391
                     0.9733735451
                                       0.132572581
## M3_brown
                     0.9733735451
                                       0.999930968
                                                         0.99999749
## M4 yellow
                     0.1145845372
                                       0.385911542
                                                         0.99999749
## M5 green
                     0.9733735451
                                       0.999930968
                                                         0.99999749
## M6 red
                     0.9733735451
                                       0.999930968
                                                         0.99999749
## M7_black
                     0.8064362451
                                       0.801354751
                                                         0.59188285
## M8_pink
                     0.0923387045
                                       0.380613853
                                                         0.99999749
## M9_magenta
                     0.9733735451
                                       0.683814731
                                                         0.18600495
## M10_purple
                                                         0.88336426
                     0.0001711214
                                       0.999930968
## M11_greenyellow
                     0.9733735451
                                       0.801354751
                                                         0.99999749
## M12_tan
                                                         0.04030456
                     0.9733735451
                                       0.175822326
## M13_salmon
                     0.9369344138
                                       0.002181782
                                                         0.01685149
## M14_cyan
                                       0.970920702
                                                         0.99999749
                     0.2680843478
## M15 midnightblue 0.5050529741
                                       0.175822326
                                                         0.18600495
                                       0.970920702
## M16_lightcyan
                     0.9733735451
                                                         0.59174204
## M17 grey60
                     0.9733735451
                                       0.999930968
                                                         0.88336426
## M18_lightgreen
                     0.4814257997
                                       0.175822326
                                                         0.59188285
## M19_lightyellow
                     0.2990033553
                                       0.999930968
                                                         0.99999749
## M20_royalblue
                                                         0.99999749
                     0.0189608037
                                       0.999930968
## M21 darkred
                     0.9733735451
                                       0.175822326
                                                         0.01685149
##
                     ASD Prenatal1 ASD Prenatal2 ASD CTX Downreg ASD CTX Upreg
## M1_turquoise
                      1.423226e-01
                                    7.146452e-01
                                                        0.95837883
                                                                    1.131811e-16
## M2_blue
                      1.000000e+00
                                    9.999668e-01
                                                        0.35653794
                                                                    9.999913e-01
## M3_brown
                      5.001619e-01
                                    9.999668e-01
                                                        0.99097452
                                                                    9.999913e-01
## M4_yellow
                      1.000000e+00
                                    7.146452e-01
                                                        0.95837883
                                                                    9.999913e-01
                                                                    9.999913e-01
## M5_green
                      1.000000e+00
                                    9.999668e-01
                                                        0.95837883
## M6_red
                      1.000000e+00
                                    9.999668e-01
                                                        0.99097452
                                                                    9.999913e-01
## M7_black
                      1.000000e+00
                                    9.999668e-01
                                                        0.95837883
                                                                    6.857185e-03
## M8_pink
                      1.000000e+00
                                    9.999668e-01
                                                        0.95837883
                                                                    9.999913e-01
## M9_magenta
                      1.000000e+00
                                    9.999668e-01
                                                        0.98852422
                                                                    1.364898e-13
## M10 purple
                      8.432784e-48
                                    1.029994e-13
                                                        0.22193867
                                                                    9.663829e-01
## M11_greenyellow
                      1.000000e+00
                                    9.999668e-01
                                                        0.98852422
                                                                    9.999913e-01
## M12 tan
                      1.000000e+00
                                    9.999668e-01
                                                        0.98852422
                                                                    8.480307e-04
```

```
## M13 salmon
                      1.000000e+00
                                    5.803327e-01
                                                       0.48481616
                                                                    9.999913e-01
                      3.244778e-05
                                                                   9.999913e-01
## M14_cyan
                                    1.330939e-03
                                                       0.05680446
## M15 midnightblue
                      1.306436e-09
                                    1.878168e-08
                                                       0.22193867
                                                                    9.999913e-01
## M16_lightcyan
                      1.000000e+00
                                    9.999668e-01
                                                       0.95837883
                                                                   9.564394e-03
## M17 grey60
                      1.000000e+00
                                    9.999668e-01
                                                       0.95837883
                                                                    9.999913e-01
## M18 lightgreen
                      2.286604e-03
                                    7.042696e-01
                                                       0.38290294
                                                                   9.999913e-01
## M19 lightyellow
                      1.000000e+00
                                    9.999668e-01
                                                       0.78562512
                                                                    9.999913e-01
## M20 royalblue
                      3.048131e-25
                                    1.728895e-04
                                                       0.22193867
                                                                    9.999913e-01
## M21 darkred
                      1.000000e+00
                                    9.999668e-01
                                                       0.66071037
                                                                    9.999913e-01
##
                      ASD dnPTVs ASD dnPTVs + pLI >= 0.9
                                                             SFARI ASD
  M1_turquoise
                    0.712202081
                                             1.575033e-01 1.0000000000
## M2_blue
                     1.000000000
                                             1.000000e+00 1.000000000
## M3_brown
                     1.00000000
                                             1.000000e+00 1.0000000000
## M4_yellow
                     1.00000000
                                            9.898230e-01 1.0000000000
## M5_green
                    1.00000000
                                             1.000000e+00 1.0000000000
## M6_red
                     1.00000000
                                             1.000000e+00 1.000000000
## M7_black
                                             1.000000e+00 1.0000000000
                     1.000000000
## M8 pink
                    1.00000000
                                             1.000000e+00 1.000000000
## M9_magenta
                                             1.000000e+00 1.000000000
                     1.000000000
## M10 purple
                    0.002891785
                                             1.626152e-11 0.0000128845
## M11_greenyellow
                    1.000000000
                                             1.000000e+00 1.0000000000
## M12 tan
                    0.712202081
                                             1.000000e+00 1.000000000
## M13_salmon
                                             1.000000e+00 1.0000000000
                    1.00000000
## M14 cyan
                    1.00000000
                                             4.952381e-01 0.1120399904
## M15 midnightblue 1.000000000
                                             1.000000e+00 0.1355407283
## M16_lightcyan
                    1.000000000
                                             1.000000e+00 1.000000000
## M17_grey60
                     1.000000000
                                             1.000000e+00 0.9028567788
## M18_lightgreen
                    1.00000000
                                             1.000000e+00 1.000000000
## M19_lightyellow
                    1.000000000
                                             1.000000e+00 1.000000000
## M20_royalblue
                     1.00000000
                                            1.139592e-01 0.7852201971
## M21_darkred
                     1.000000000
                                             1.000000e+00 1.0000000000
##
                    FMRP Targets1 FMRP Targets2 CHD8 Targets1 CHD8 Targets2
## M1_turquoise
                      1.168904e-03
                                    6.194891e-01
                                                   8.952754e-03
                                                                 1.000000e+00
                                                   9.997070e-01
## M2_blue
                      1.000000e+00
                                    1.000000e+00
                                                                 1.870970e-17
## M3 brown
                      1.000000e+00
                                                   9.997070e-01
                                                                 1.000000e+00
                                    6.194891e-01
                                                   3.625968e-06
## M4_yellow
                      1.000000e+00
                                    1.000000e+00
                                                                 2.549050e-14
## M5 green
                      1.000000e+00
                                    6.237362e-01
                                                   4.824332e-01
                                                                 6.414182e-04
## M6_red
                      1.000000e+00
                                    6.237362e-01
                                                   9.997070e-01
                                                                 1.661489e-03
## M7 black
                                                   9.997070e-01
                      1.000000e+00
                                    1.849204e-01
                                                                 1.000000e+00
## M8_pink
                                    1.000000e+00
                                                   6.925475e-02
                                                                 4.780143e-29
                      1.000000e+00
## M9 magenta
                      1.000000e+00
                                    6.567587e-01
                                                   9.997070e-01
                                                                 1.000000e+00
  M10_purple
                      1.540392e-19
                                    2.228834e-06
                                                   6.233677e-15
                                                                 7.696889e-13
## M11_greenyellow
                      1.000000e+00
                                    1.000000e+00
                                                   9.997070e-01
                                                                 4.016379e-07
## M12_tan
                      9.152778e-01
                                    6.237362e-01
                                                   9.997070e-01
                                                                 1.000000e+00
## M13_salmon
                      9.119606e-02
                                    1.000000e+00
                                                   3.732942e-03
                                                                 2.099336e-03
## M14_cyan
                      1.000000e+00
                                    6.237362e-01
                                                   8.528716e-05
                                                                 1.091082e-07
## M15_midnightblue
                     5.498535e-07
                                    1.950218e-02
                                                   9.016265e-05
                                                                 5.592878e-05
## M16_lightcyan
                      1.000000e+00
                                    9.483331e-01
                                                   9.997070e-01
                                                                 1.000000e+00
## M17_grey60
                      1.000000e+00
                                    1.000000e+00
                                                   9.997070e-01
                                                                 1.000000e+00
## M18_lightgreen
                      1.000000e+00
                                    6.237362e-01
                                                   8.188200e-02
                                                                 1.317129e-04
## M19_lightyellow
                      1.000000e+00
                                    9.284803e-01
                                                   9.997070e-01
                                                                 1.000000e+00
## M20_royalblue
                      1.276825e-10
                                    1.000000e+00
                                                   1.395228e-04
                                                                 2.416519e-04
## M21 darkred
                      1.000000e+00
                                    6.237362e-01
                                                   8.291310e-02
                                                                 2.554575e-01
```

Examine enrichment between non-zero or zero modules after broadly expressed genes are removed and song bird DE, Human Specific, ASD Prenatal, ASD CTX Dysregulated Modules, ASD PTVs, ASD SFARI, and FMRP and CHD8 targets

```
geneclasses = list(SongBirdDE_notBE,
                   HumanSpecific1_notBE,
                   HumanSpecific2 notBE,
                   ASDPrenatal1 notBE,
                   ASDPrenatal2 notBE,
                   ASDCTXDownreg notBE,
                   ASDCTXUpreg_notBE,
                   ASDPTVs_pLI_notBE,
                   SFARIASD notBE,
                   FMRP1 notBE,
                   FMRP2_notBE,
                   CHD81 notBE,
                   CHD82_notBE)
geneclassnames = c("Song Bird DE",
                   "Human-Specific1",
                   "Human-Specific2",
                   "ASD Prenatal1",
                   "ASD Prenatal2",
                   "ASD CTX Downreg",
                   "ASD CTX Upreg",
                   "ASD dnPTVs + pLI \geq 0.9",
                   "SFARI ASD",
                   "FMRP Targets1",
                   "FMRP Targets2",
                   "CHD8 Targets1",
                   "CHD8 Targets2")
res_colnames = c("Non-Zero Modules","Zero Modules")
ORmat = data.frame(matrix(nrow = length(geneclasses),
                          ncol = length(res_colnames)))
logPmat = data.frame(matrix(nrow = length(geneclasses),
                            ncol = length(res_colnames)))
Pmat = data.frame(matrix(nrow = length(geneclasses),
                         ncol = length(res_colnames)))
FDRmat = data.frame(matrix(nrow = length(geneclasses),
                           ncol = length(res_colnames)))
colnames(ORmat) = res colnames
colnames(logPmat) = res_colnames
colnames(Pmat) = res colnames
colnames(FDRmat) = res_colnames
rownames(ORmat) = geneclassnames
rownames(logPmat) = geneclassnames
rownames(Pmat) = geneclassnames
rownames(FDRmat) = geneclassnames
```

```
for (i in 1:length(geneclasses)){
  # intersect with background list
  genes2 = geneclasses[[i]]
  mask = is.element(genes2,bglist)
  genes2 = data.frame(genes2[mask])
  overlap_res = genelistOverlap(nz_genes,
                                genes2,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,1] = overlap_res[[1]]$OR
  logPmat[i,1] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,1] = overlap_res[[1]]$hypergeo_p
  overlap_res = genelistOverlap(z_genes,
                                backgroundTotal,
                                print_result = FALSE,
                                header = FALSE)
  ORmat[i,2] = overlap_res[[1]]$OR
  logPmat[i,2] = -log10(overlap_res[[1]]$hypergeo_p)
  Pmat[i,2] = overlap_res[[1]]$hypergeo_p
for (i in 1:dim(Pmat)[2]){
  FDRmat[,i] = p.adjust(Pmat[,i], method = "fdr")
zLIM = c(0, -log10(0.005))
par(mar = c(6, 8.5, 3, 3))
WGCNA::labeledHeatmap(Matrix = logPmat,
                      xLabels = colnames(ORmat),
                      yLabels = rownames(ORmat),
                      ySymbols = NULL,
                      colorLabels = FALSE,
                      colors = WGCNA::blueWhiteRed(50),
                      textMatrix = round(ORmat, digits = 2),
                      setStdMargins = FALSE,
                      cex.text = 1,
                      zlim = zLIM)
```

Song Bird DE	1.38	1.65	
Human-Specific1	1.55	1.27	
Human-Specific2	1.32	1.27	-2
ASD Prenatal1	1.45	1.22	
ASD Prenatal2	1.43	1.15	- 1.5
ASD CTX Downreg	1.03	1.32	
ASD CTX Upreg	1.43	1.85	
0  dnPTVs + pLI >= 0.9	1.67	1.32	1
SFARI ASD	1.12	1.34	
FMRP Targets1	1.51	1.3	- 0.5
FMRP Targets2	1.65	1.68	
CHD8 Targets1	1.63	1.4	
CHD8 Targets2	1.61	1.42	0
	on Zero Modules	Lero modules	
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7	· ·		

# # Enrichment Odds Ratios ORmat

##		Non-Zero Modules	Zero Modules
##	Song Bird DE	1.379753	1.651039
##	Human-Specific1	1.546674	1.270655
##	Human-Specific2	1.317637	1.269140
##	ASD Prenatal1	1.450761	1.216592
##	ASD Prenatal2	1.432734	1.148539
##	ASD CTX Downreg	1.033342	1.319874
##	ASD CTX Upreg	1.430286	1.847027
##	ASD dnPTVs + pLI $>= 0.9$	1.669721	1.315668
##	SFARI ASD	1.121266	1.343655
##	FMRP Targets1	1.514483	1.301697
##	FMRP Targets2	1.653905	1.681547
##	CHD8 Targets1	1.631681	1.402352
##	CHD8 Targets2	1.614453	1.423758

### # P-values

Pmat

```
##
                           Non-Zero Modules Zero Modules
## Song Bird DE
                                 0.65830774 2.955475e-03
## Human-Specific1
                                 0.18486378 4.038351e-01
## Human-Specific2
                                 0.78588124 4.213025e-01
## ASD Prenatal1
                                 0.48435786 6.115897e-01
## ASD Prenatal2
                                 0.52157849 7.921408e-01
## ASD CTX Downreg
                                 0.99378945 3.313699e-01
## ASD CTX Upreg
                                 0.50833829 6.246612e-05
## ASD dnPTVs + pLI >= 0.9
                                 0.25215918 4.317354e-01
## SFARI ASD
                                 0.95180870 3.142967e-01
```

```
## FMRP Targets1 0.31184208 3.599767e-01
## FMRP Targets2 0.21524562 7.003694e-02
## CHD8 Targets1 0.03346473 5.806758e-02
## CHD8 Targets2 0.06733423 2.272613e-02
```

## # FDR

#### FDRmat

## Non-Zero Modules Zero Modules ## Song Bird DE 0.8558001 0.0192105875 ## Human-Specific1 0.6556139 0.5102327791 ## Human-Specific2 0.9287687 0.5102327791 ## ASD Prenatal1 0.7533912 0.6625555508 0.7533912 0.7921408257 0.9937895 0.5102327791 ## ASD Prenatal2 ## ASD CTX Downreg ## ASD CTX Upreg 0.7533912 0.0008120595 ## ASD dnPTVs + pLI >= 0.9 0.6556139 0.5102327791 0.9937895 0.5102327791 0.6756578 0.5102327791 0.6556139 0.1820960499 0.4350414 0.1820960499 ## SFARI ASD ## FMRP Targets1 ## FMRP Targets2 ## CHD8 Targets1 ## CHD8 Targets2 0.4376725 0.0984798866