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Raphael Kubler

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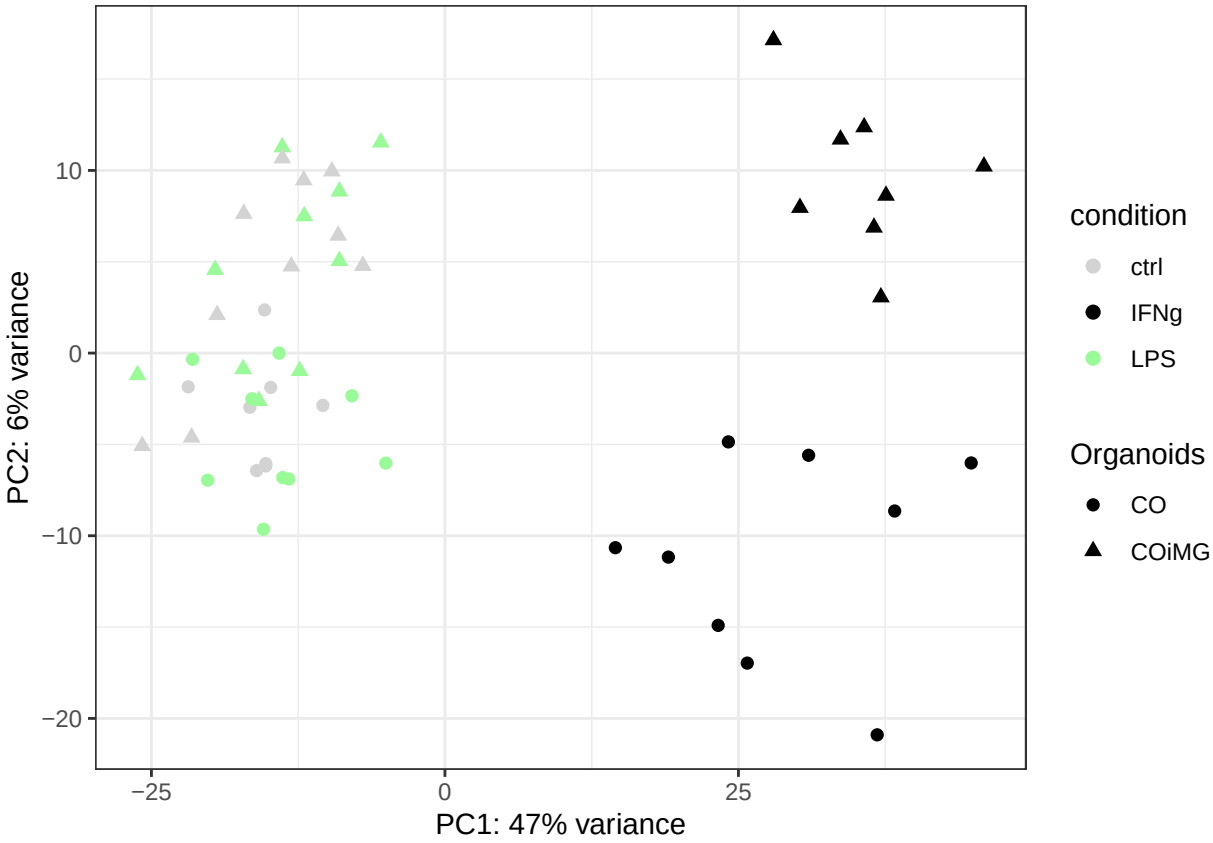
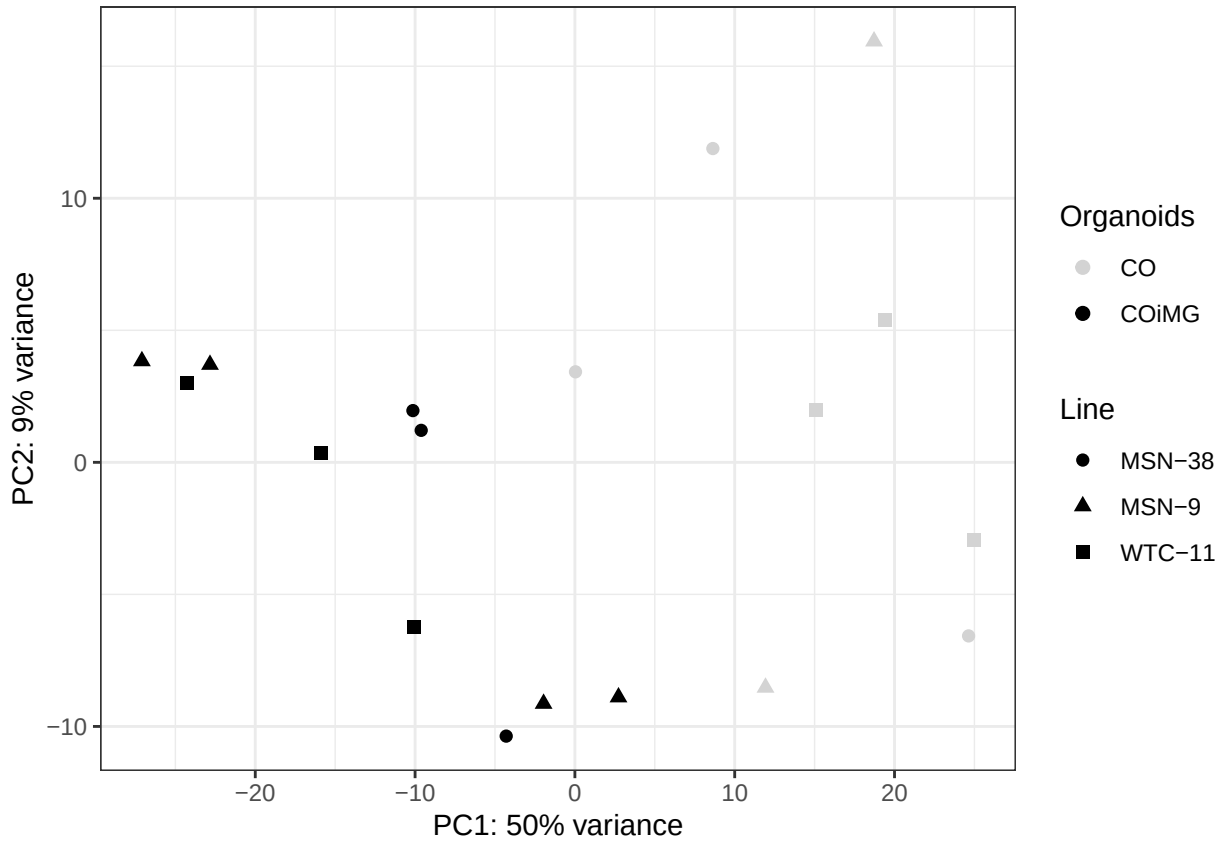
PCA IFNy, LPS, ctr

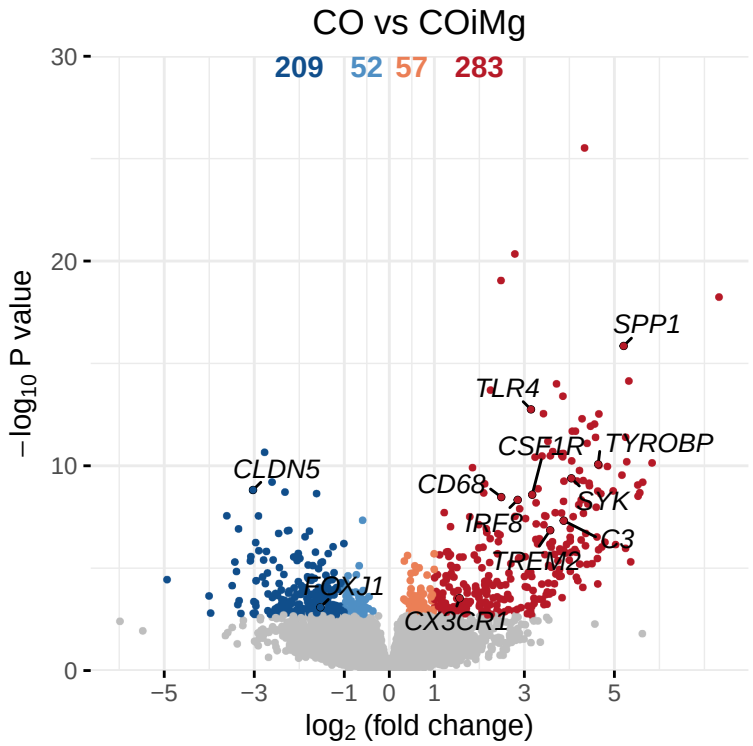


CO vs COiMG in control samples

PCA plots

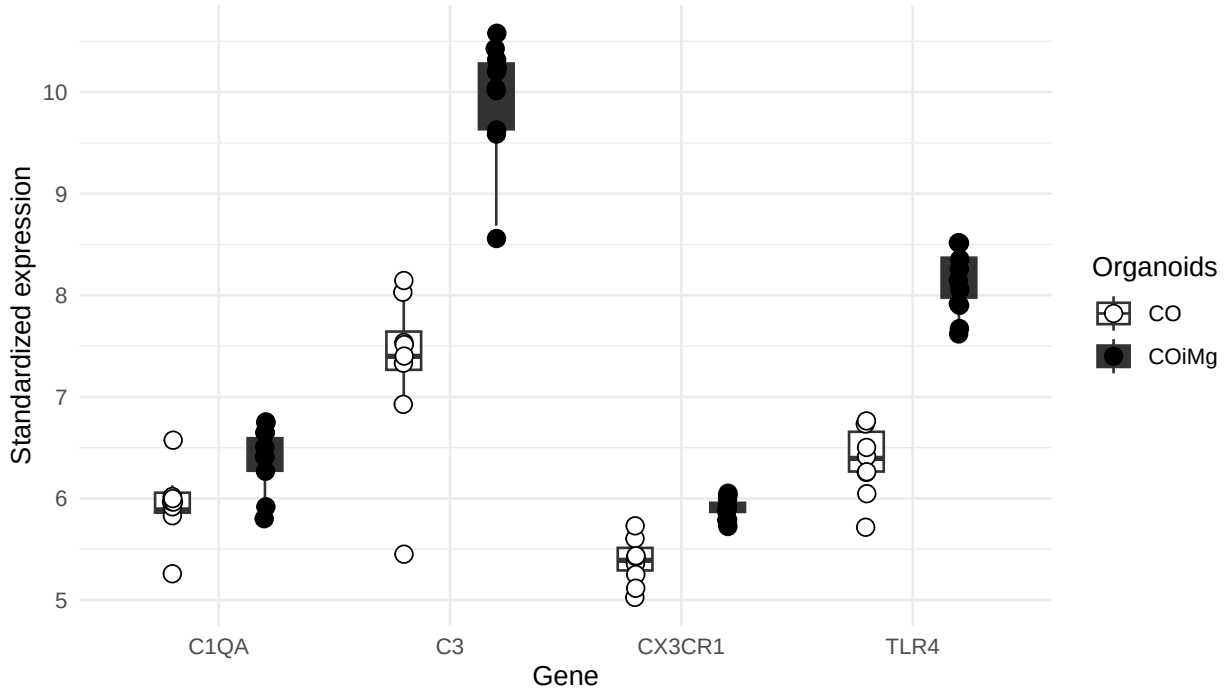


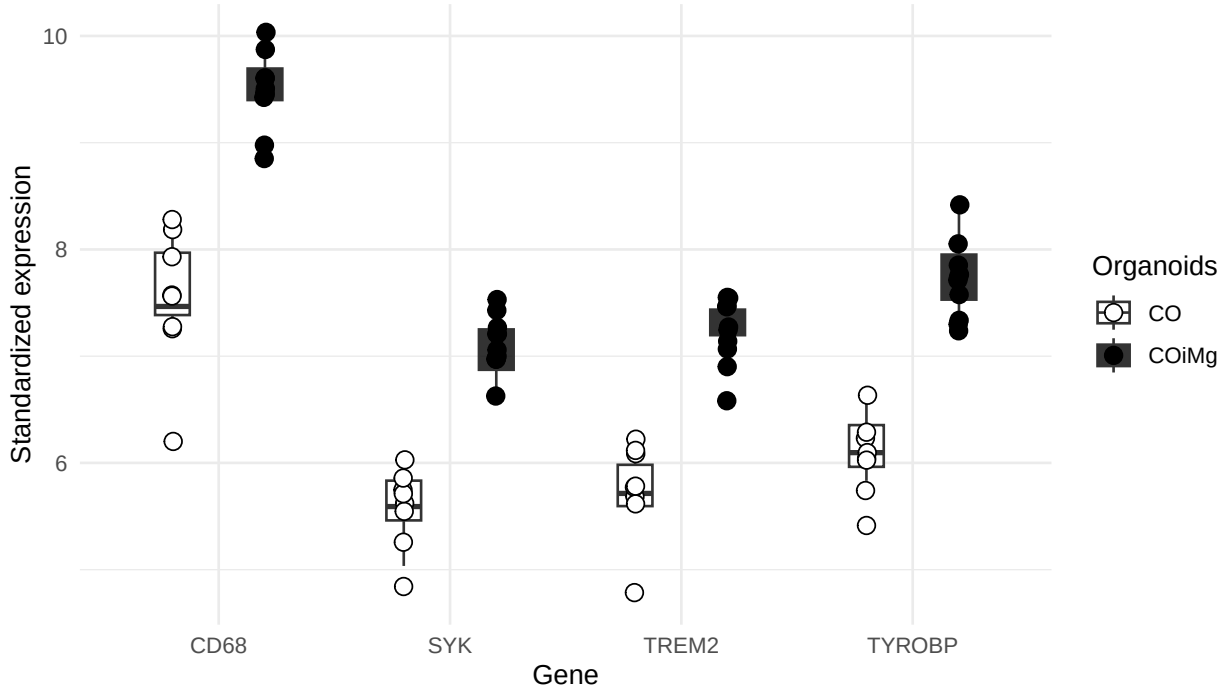
Volcano plot

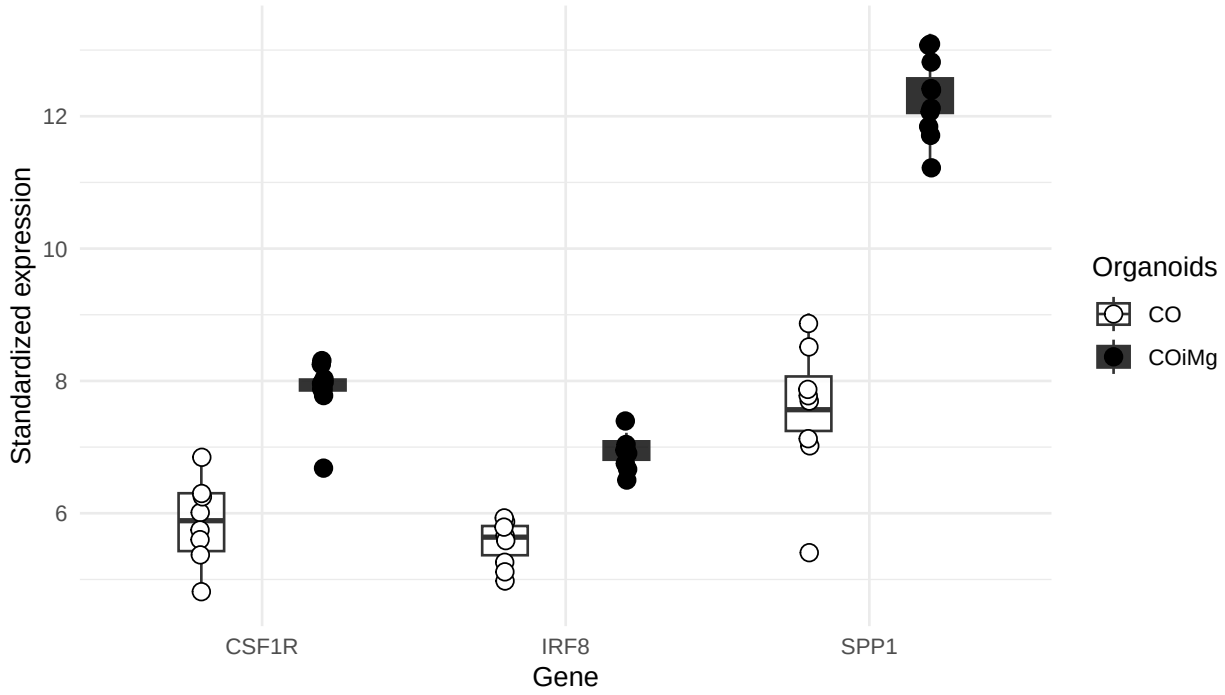


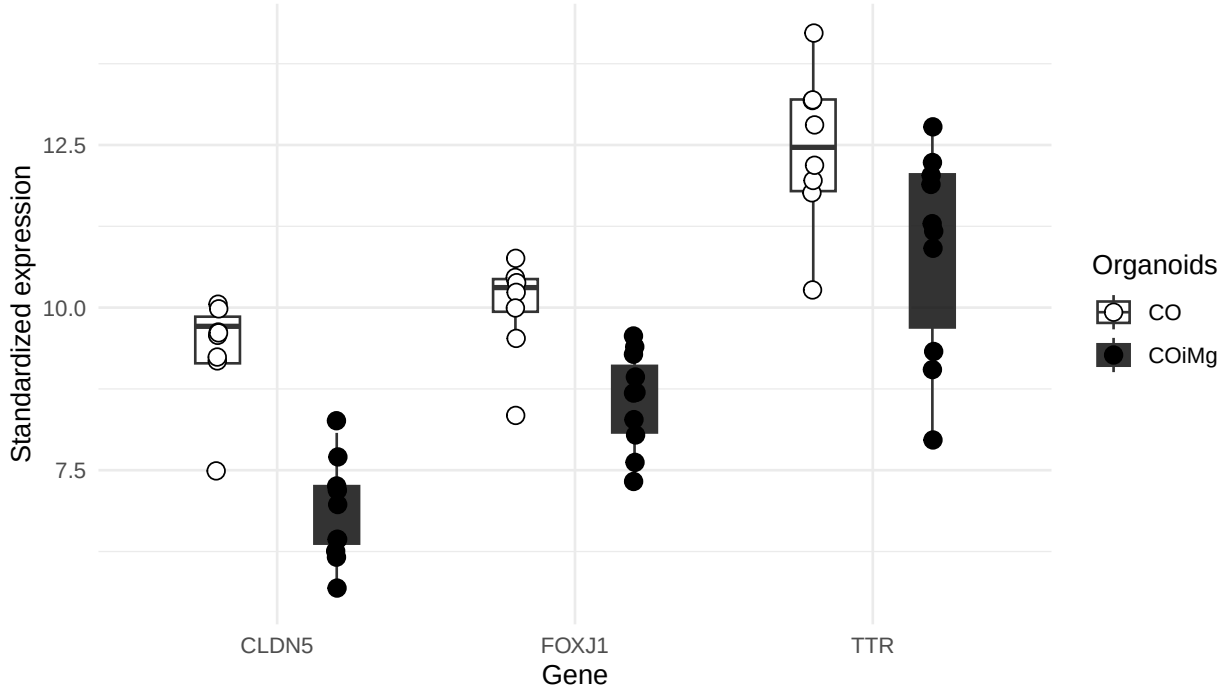
DEG table

Boxplot CO vs COiMg in CTR

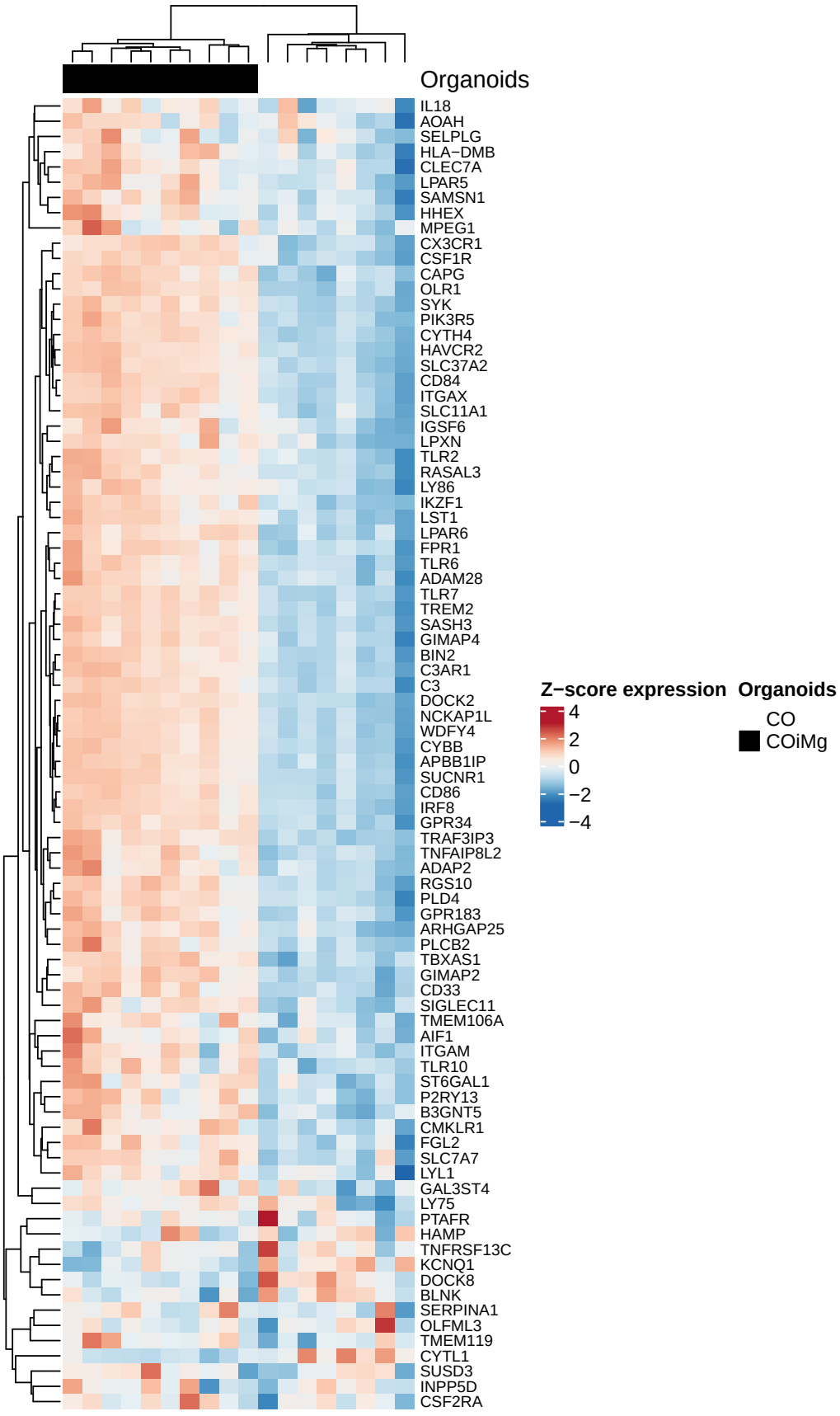




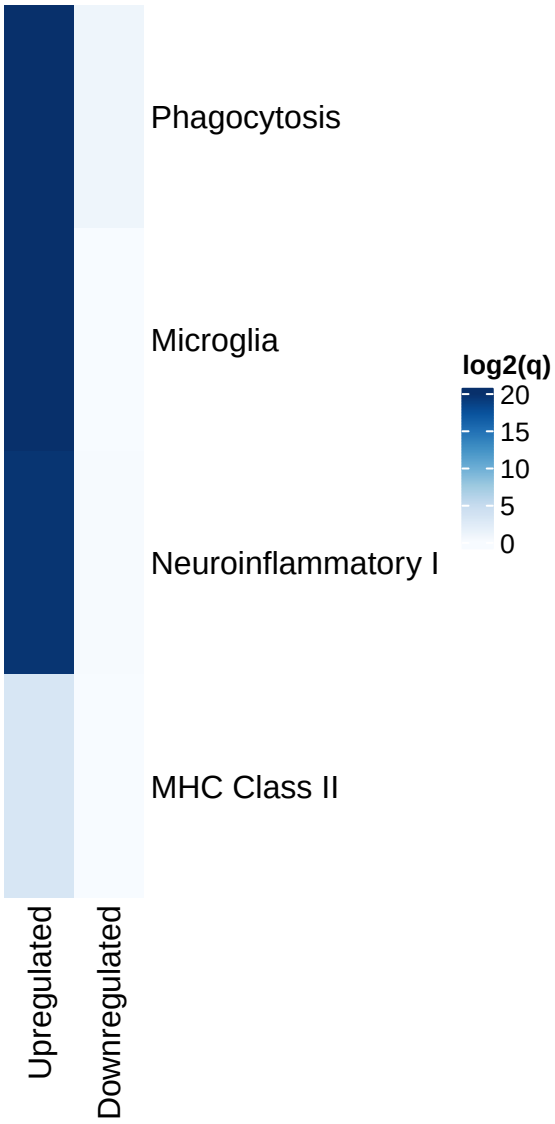

Standardized expression
12
10
8
6
CSF1R
IRF8
SPP1
Gene
Organoids
CO
COiMg


Standardized expression
12.5
10.0
7.5
CLDN5
FOXJ1
TTR
Gene
Organoids
CO
COiMg

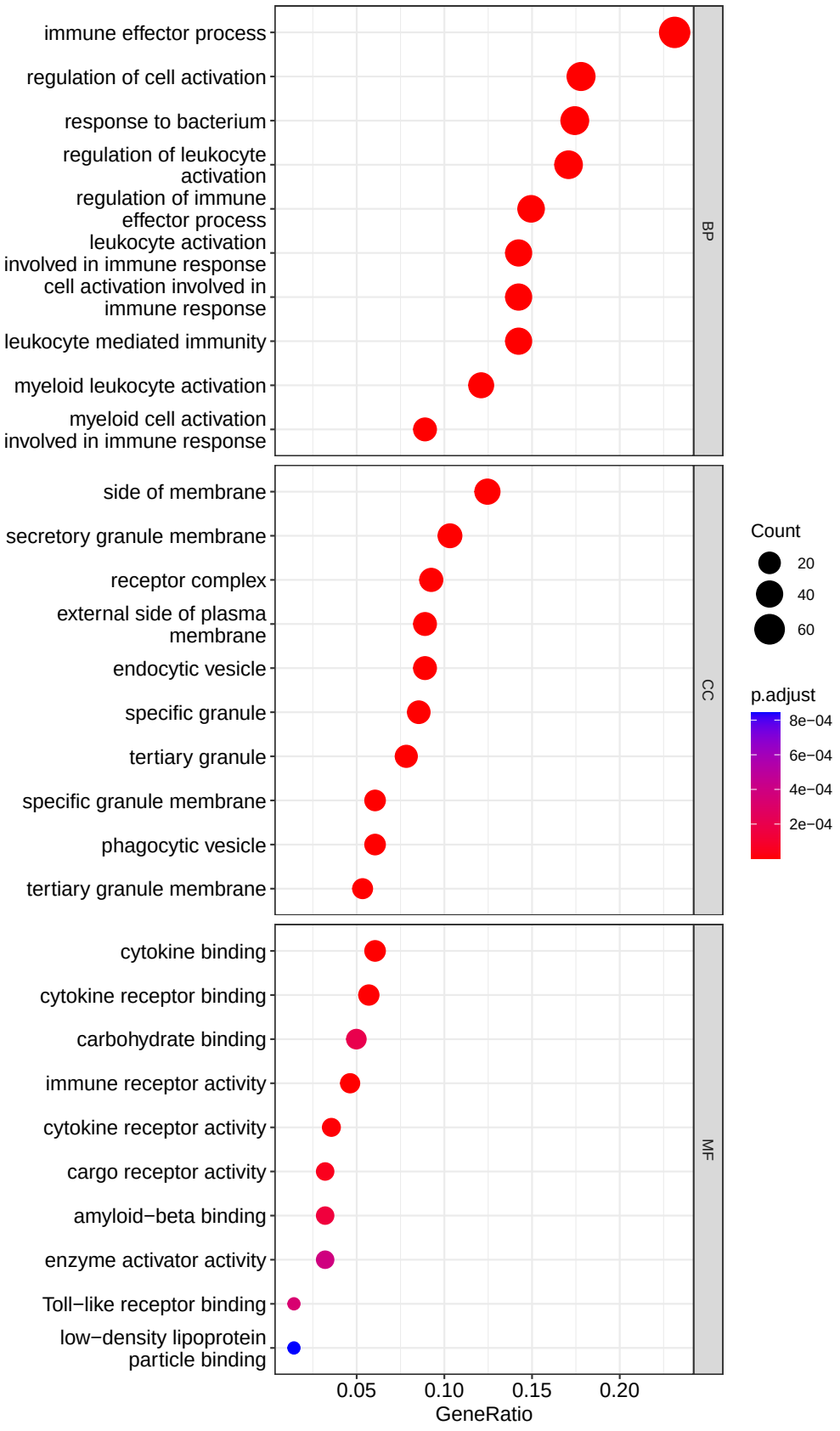
Patir microglia genes heatmap

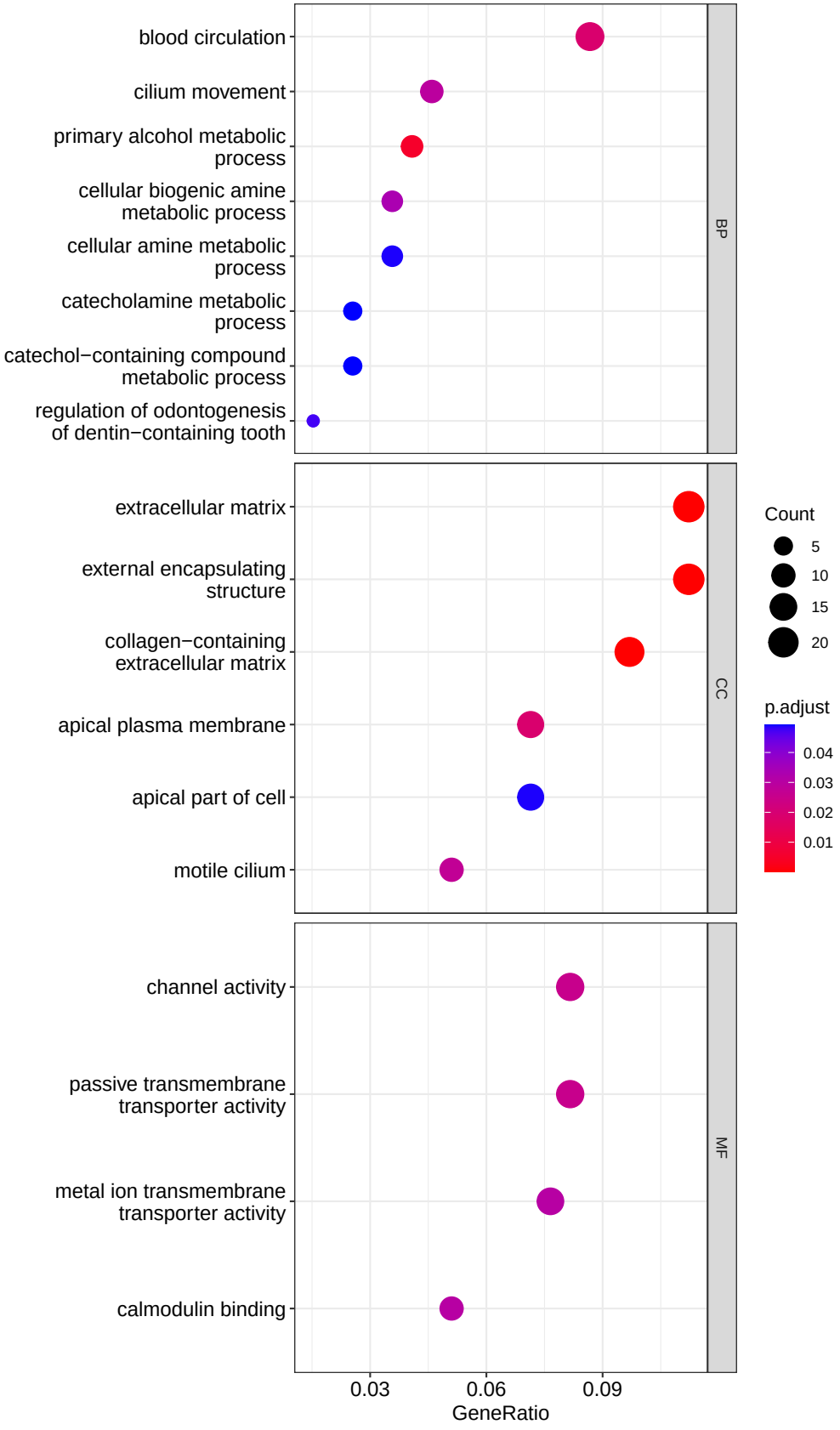


Enrichment heatmap (gene sets of interest)



GO enrichment



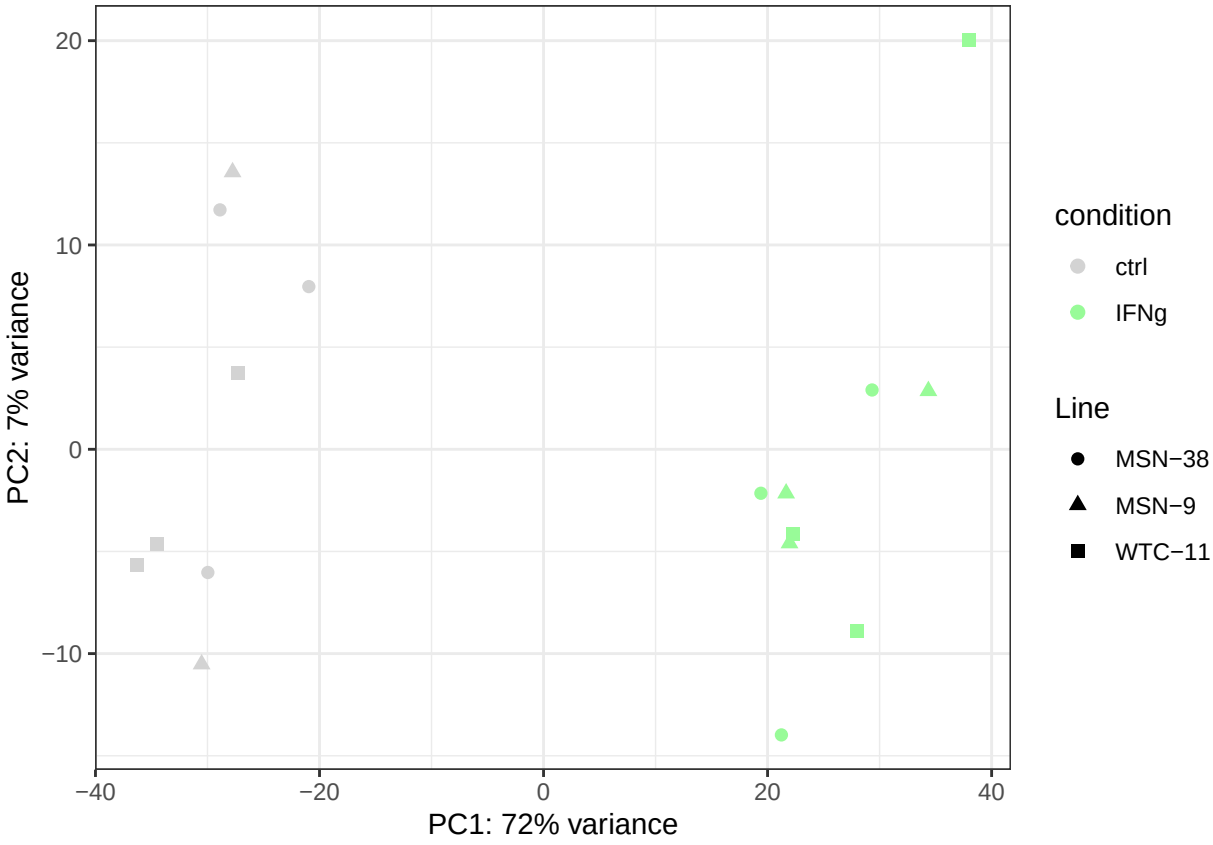

blood circulation
cilium movement
primary alcohol metabolic process
cellular biogenic amine metabolic process
cellular amine metabolic process
catecholamine metabolic process
catechol−containing compound metabolic process
regulation of odontogenesis of dentin−containing tooth
BP
extracellular matrix
external encapsulating structure
collagen−containing extracellular matrix
apical plasma membrane
apical part of cell
motile cilium
CC
channel activity
passive transmembrane transporter activity
metal ion transmembrane transporter activity
calmodulin binding
MF
0.03
0.06
0.09
GeneRatio
Count
5
10
15
20
p.adjust
0.04
0.03
0.02
0.01

Stimulation (IFNy) samples

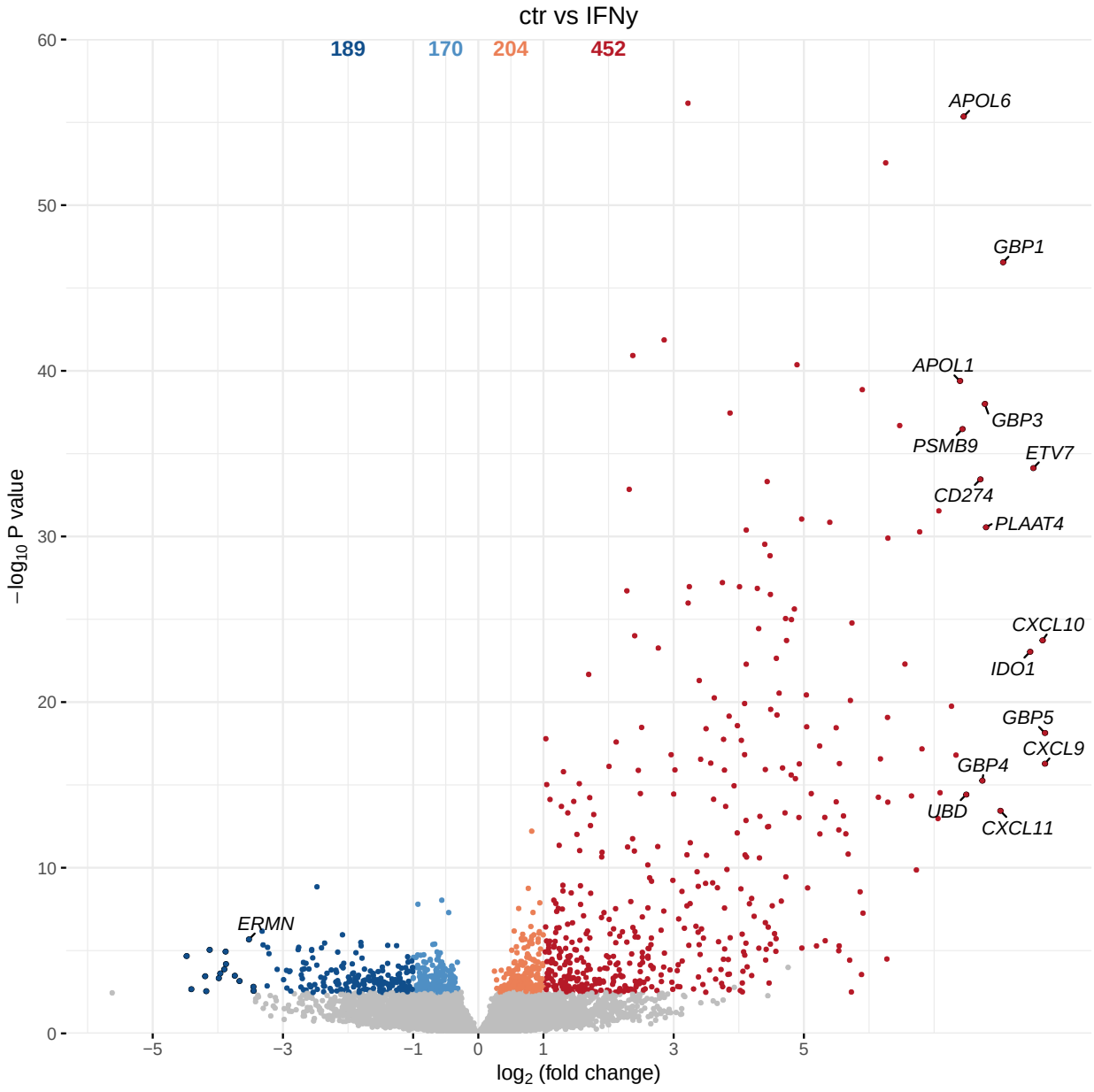
PCA plots

```
## [1] TRUE
```

```
##  [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
## [16] TRUE TRUE
```

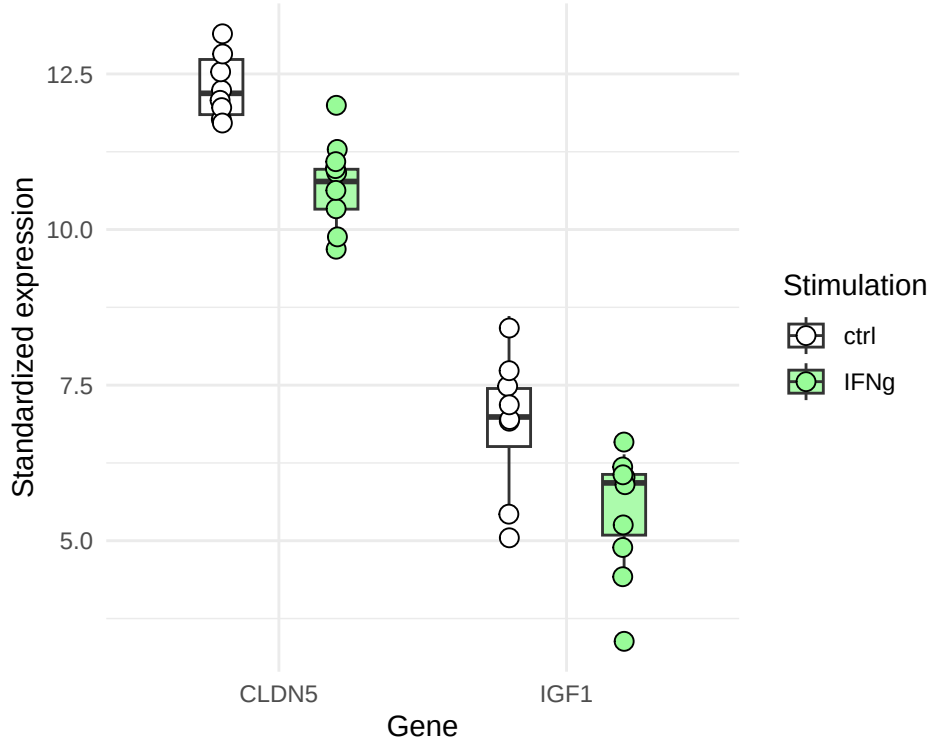


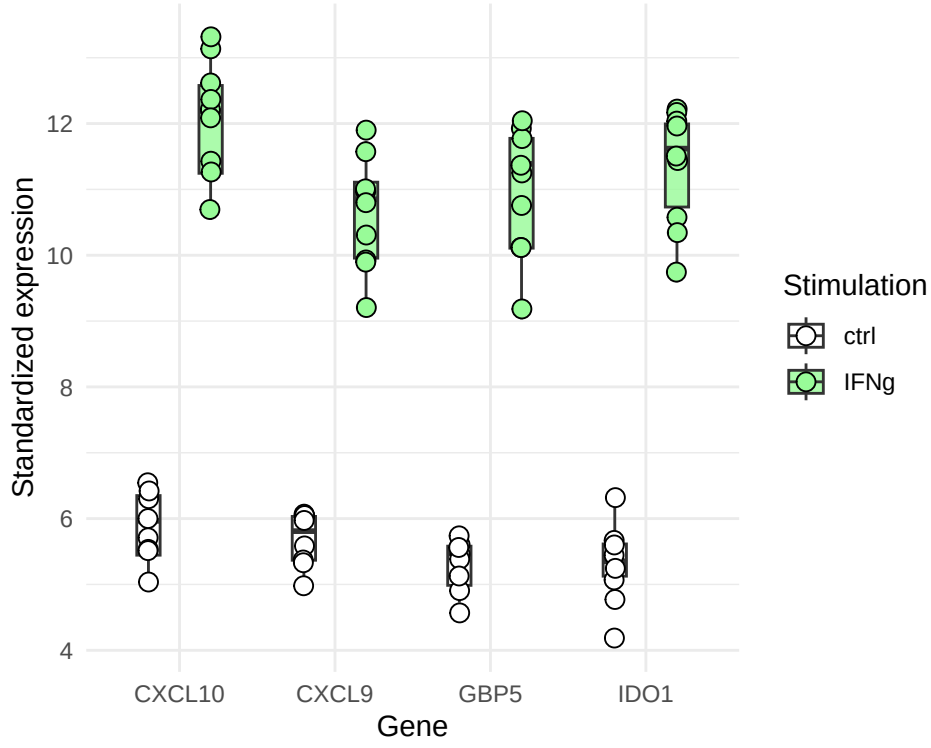
Volcano plot



DEG table

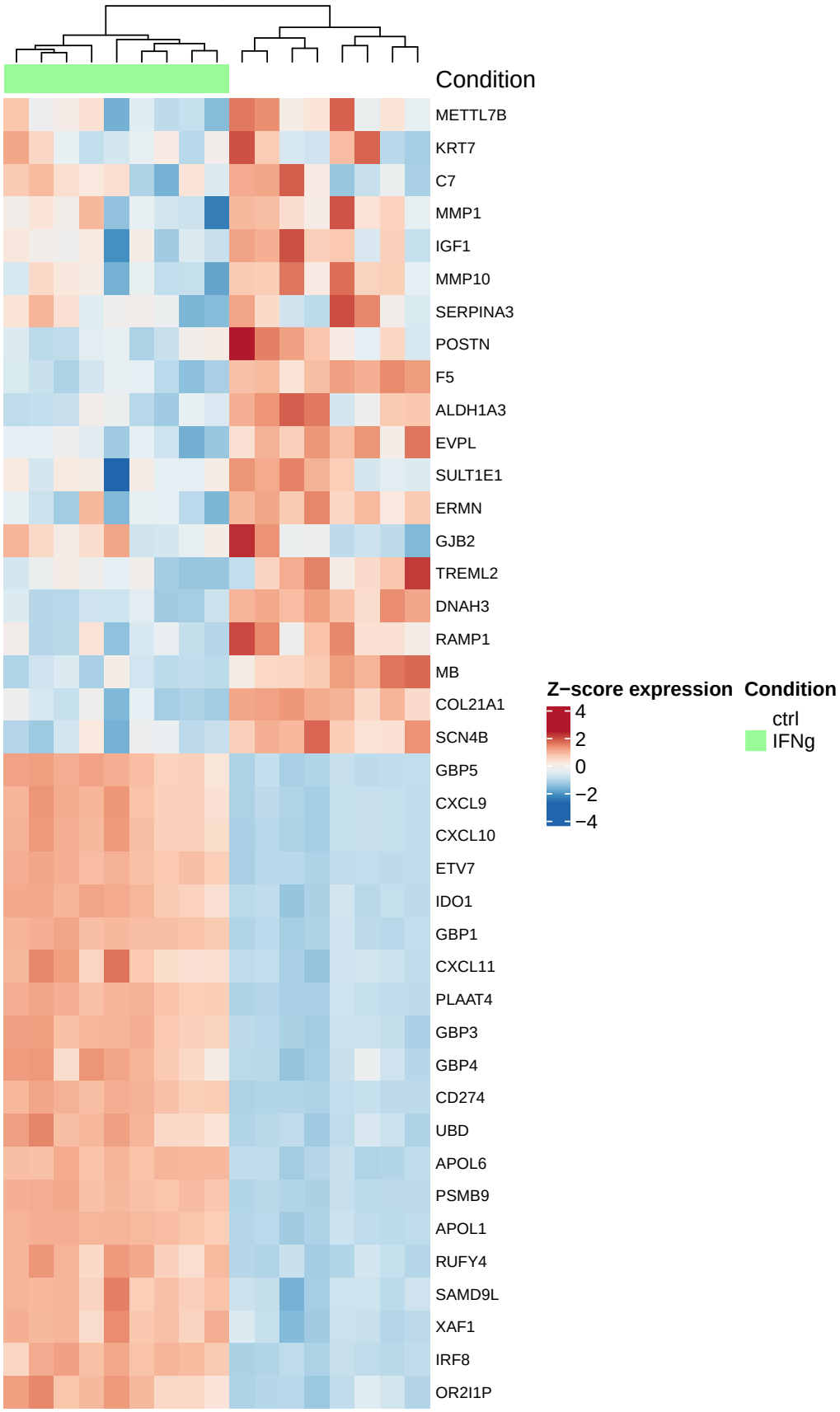
Boxplot genes of interest



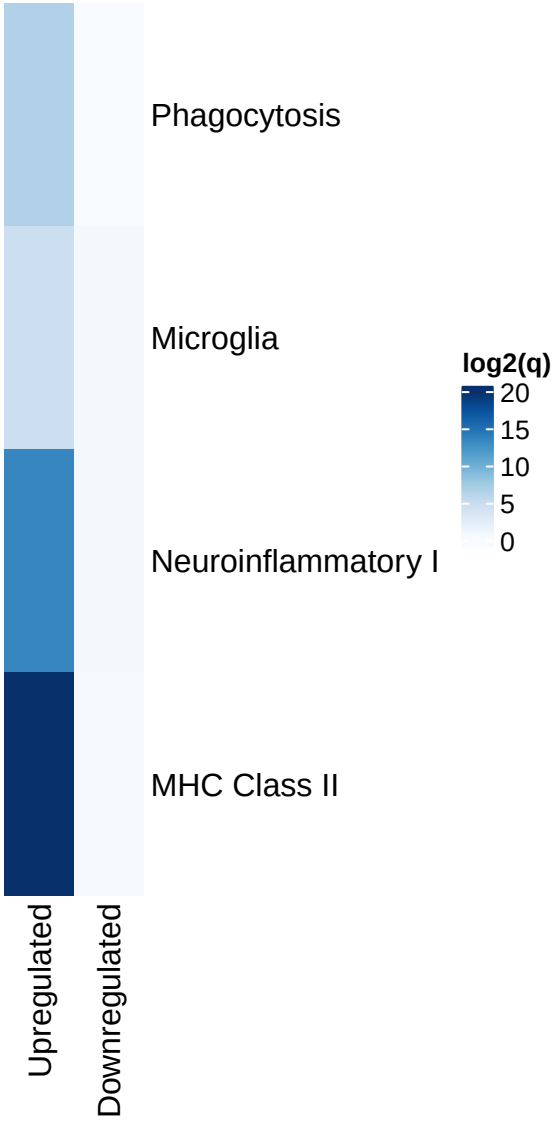


Top 40 DEGs heatmap

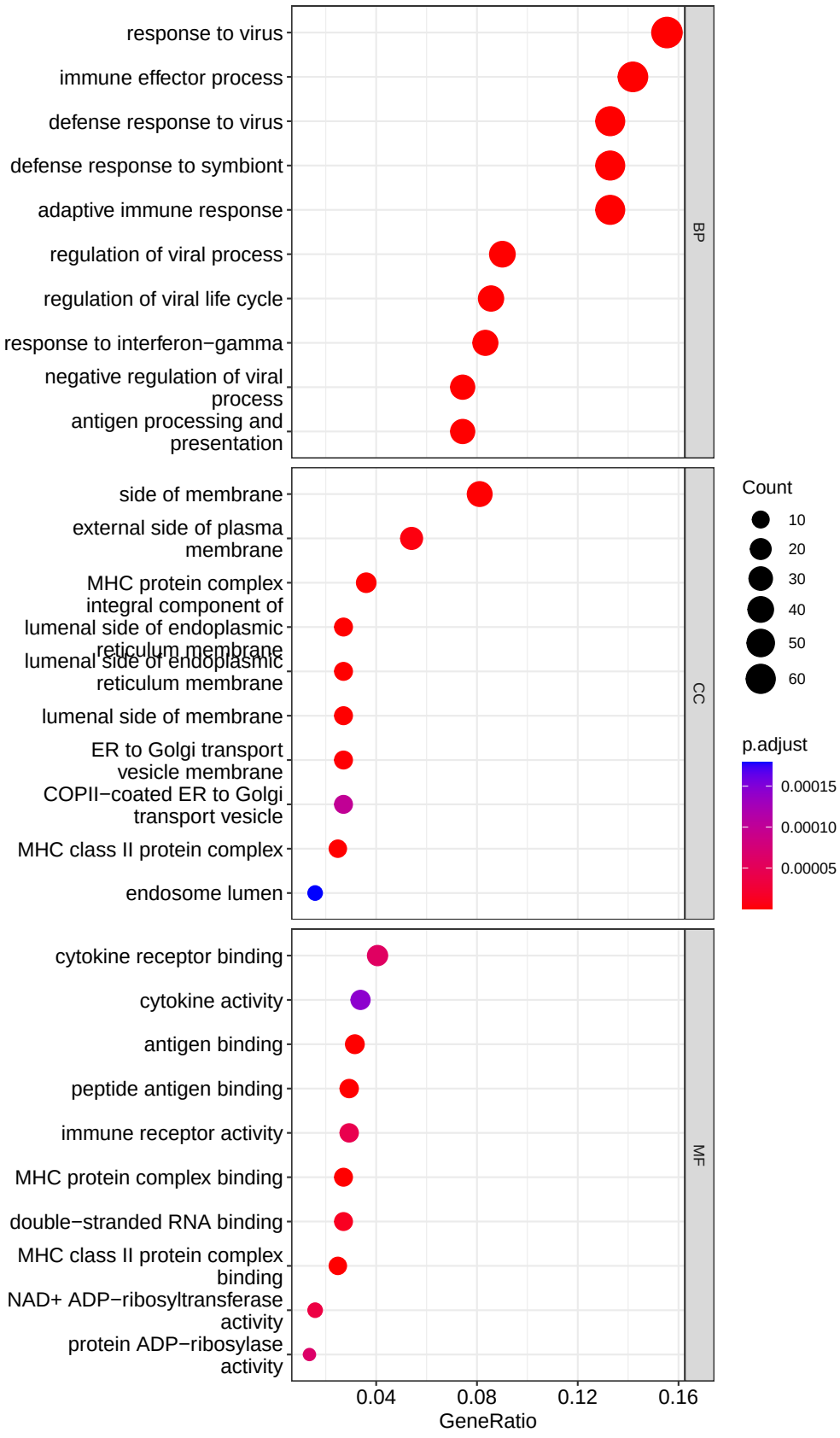
```
##  [1] FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE FALSE
## [13] FALSE FALSE FALSE FALSE FALSE
```

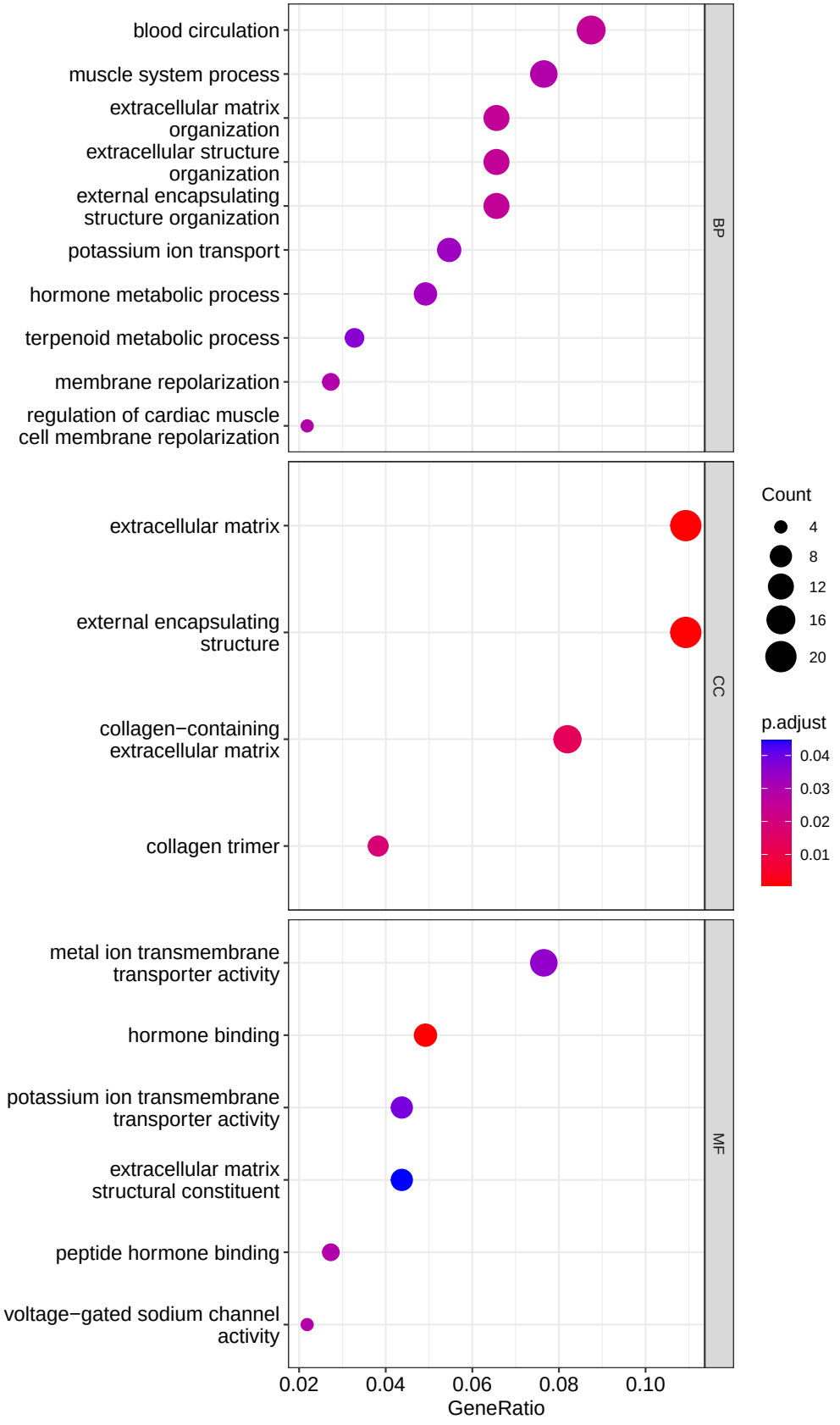

Condition
METTL7B
KRT7
C7
MMP1
IGF1
MMP10
SERPINA3
POSTN
F5
ALDH1A3
EVPL
SULT1E1
ERMN
GJB2
TREML2
DNAH3
RAMP1
MB
COL21A1
SCN4B
GBP5
CXCL9
CXCL10
ETV7
IDO1
GBP1
CXCL11
PLAAT4
GBP3
GBP4
CD274
UBD
APOL6
PSMB9
APOL1
RUFY4
SAMD9L
XAF1
IRF8
OR2I1P
Z−score expression
4
2
0
−2
−4
Condition
ctrl
IFNg

Enrichment heatmap (gene sets of interest)

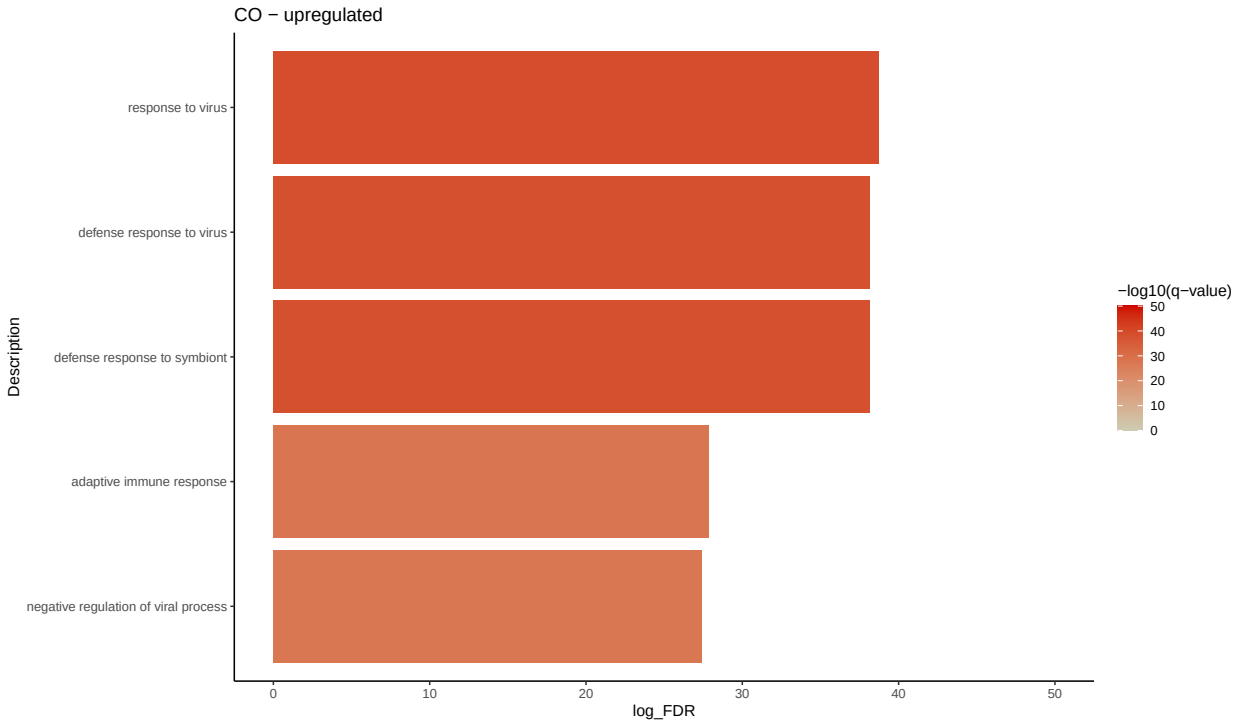


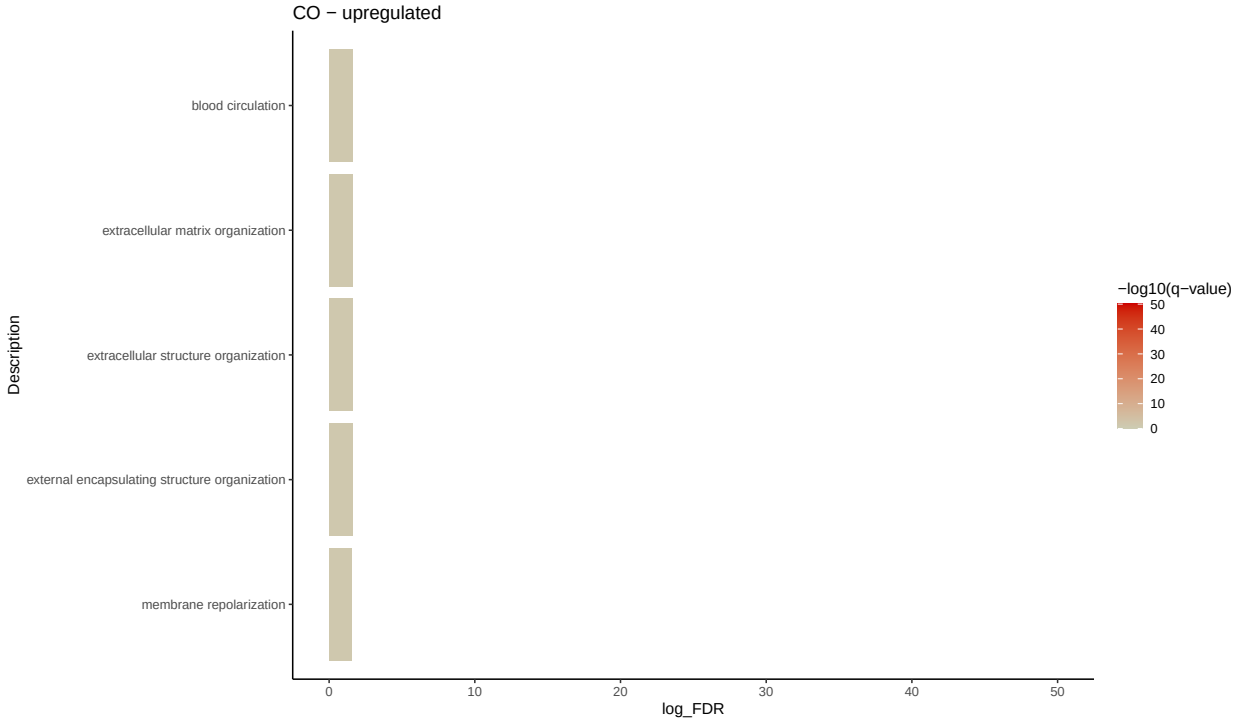
GO enrichment




blood circulation
muscle system process
extracellular matrix organization
extracellular structure organization
external encapsulating structure organization
potassium ion transport
hormone metabolic process
terpenoid metabolic process
membrane repolarization
regulation of cardiac muscle cell membrane repolarization
BP
extracellular matrix
external encapsulating structure
collagen−containing extracellular matrix
collagen trimer
CC
metal ion transmembrane transporter activity
hormone binding
potassium ion transmembrane transporter activity
extracellular matrix structural constituent
peptide hormone binding
voltage−gated sodium channel activity
MF
0.02
0.04
0.06
0.08
0.10
GeneRatio
Count
4
8
12
16
20
p.adjust
0.04
0.03
0.02
0.01

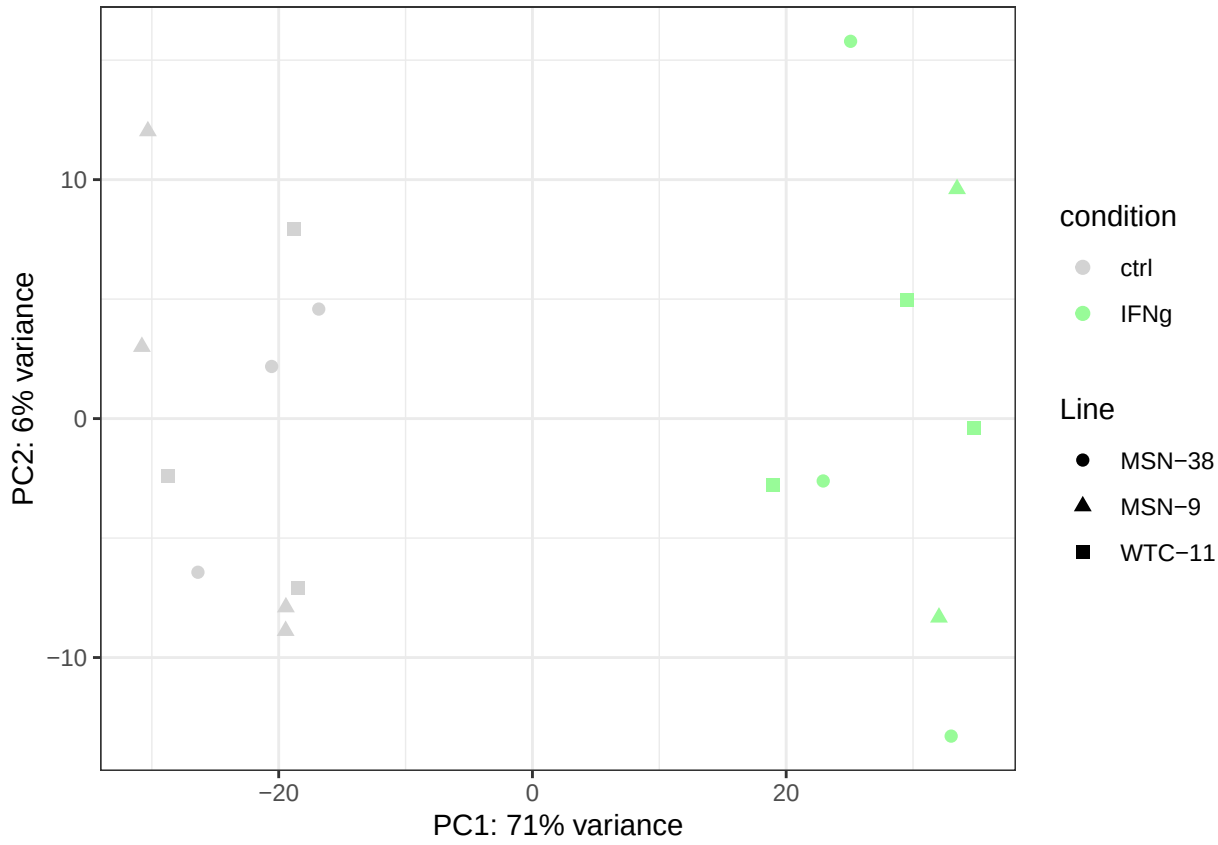
Barplots:


CO − upregulated
response to virus
defense response to virus
defense response to symbiont
adaptive immune response
negative regulation of viral process
Description
0
10
20
30
40
50
log_FDR
−log10(q−value)
50
40
30
20
10
0

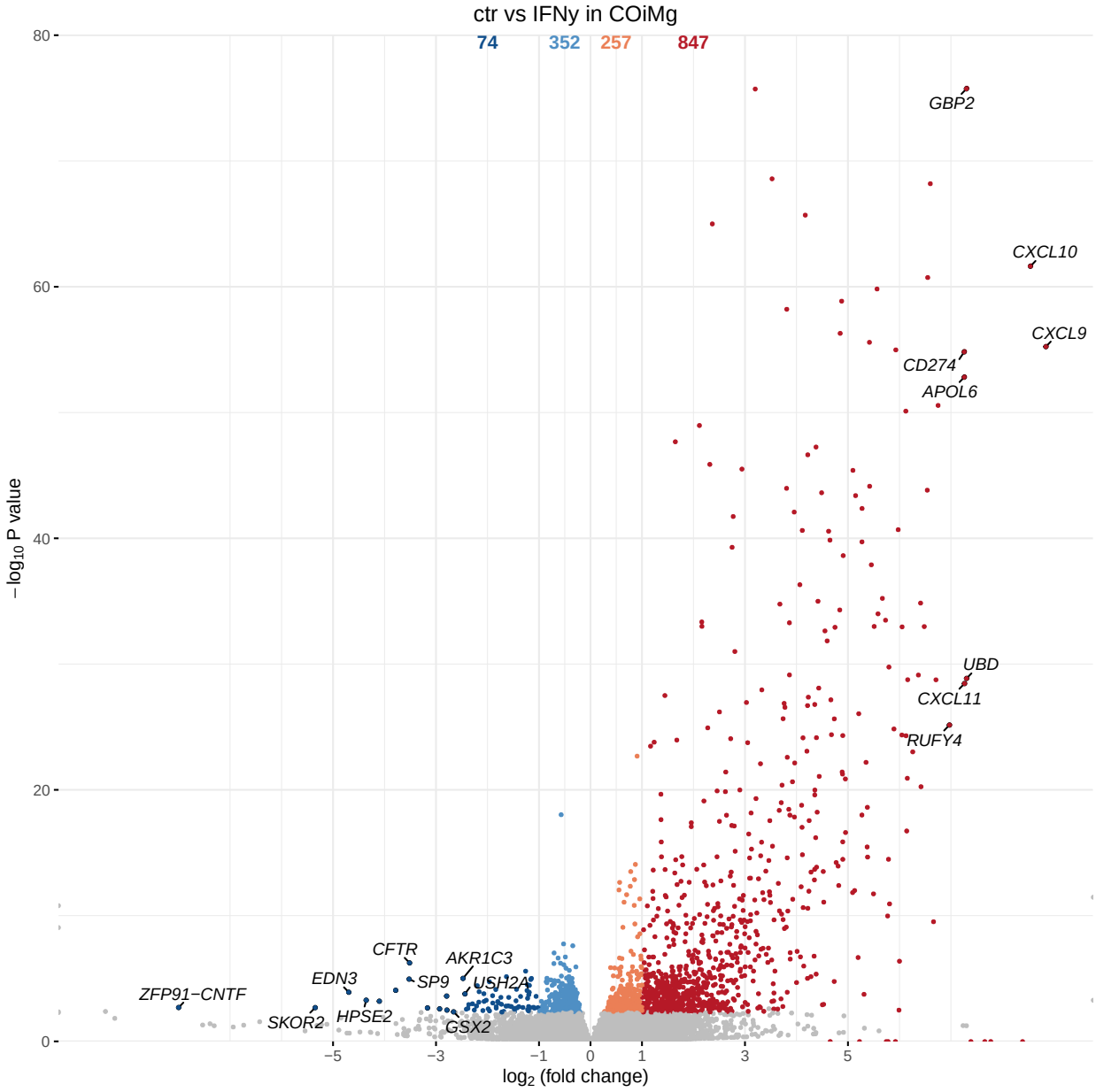

CO − upregulated
blood circulation
extracellular matrix organization
extracellular structure organization
external encapsulating structure organization
membrane repolarization
Description
0
10
20
30
40
50
log_FDR
−log10(q−value)
50
40
30
20
10
0

IFNy in COiMG

PCA plots

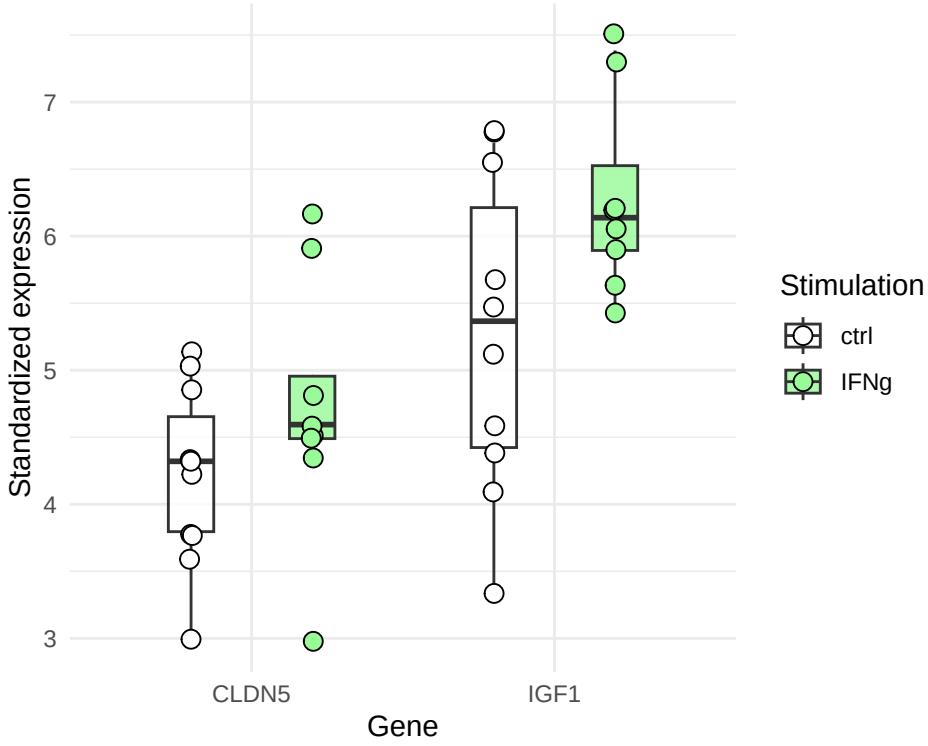


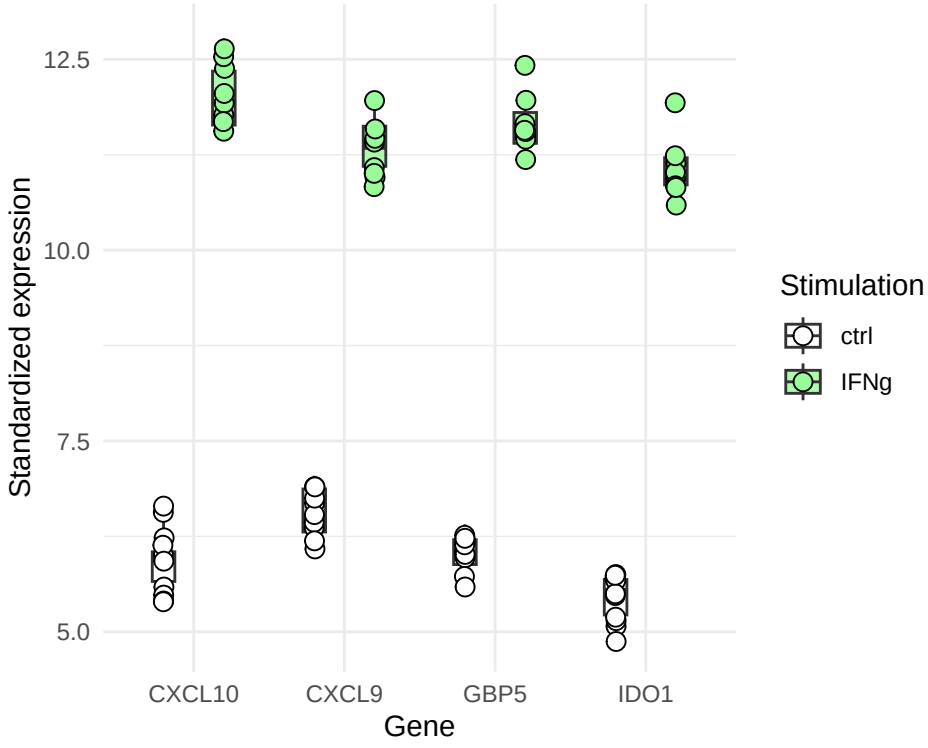
Volcano plot



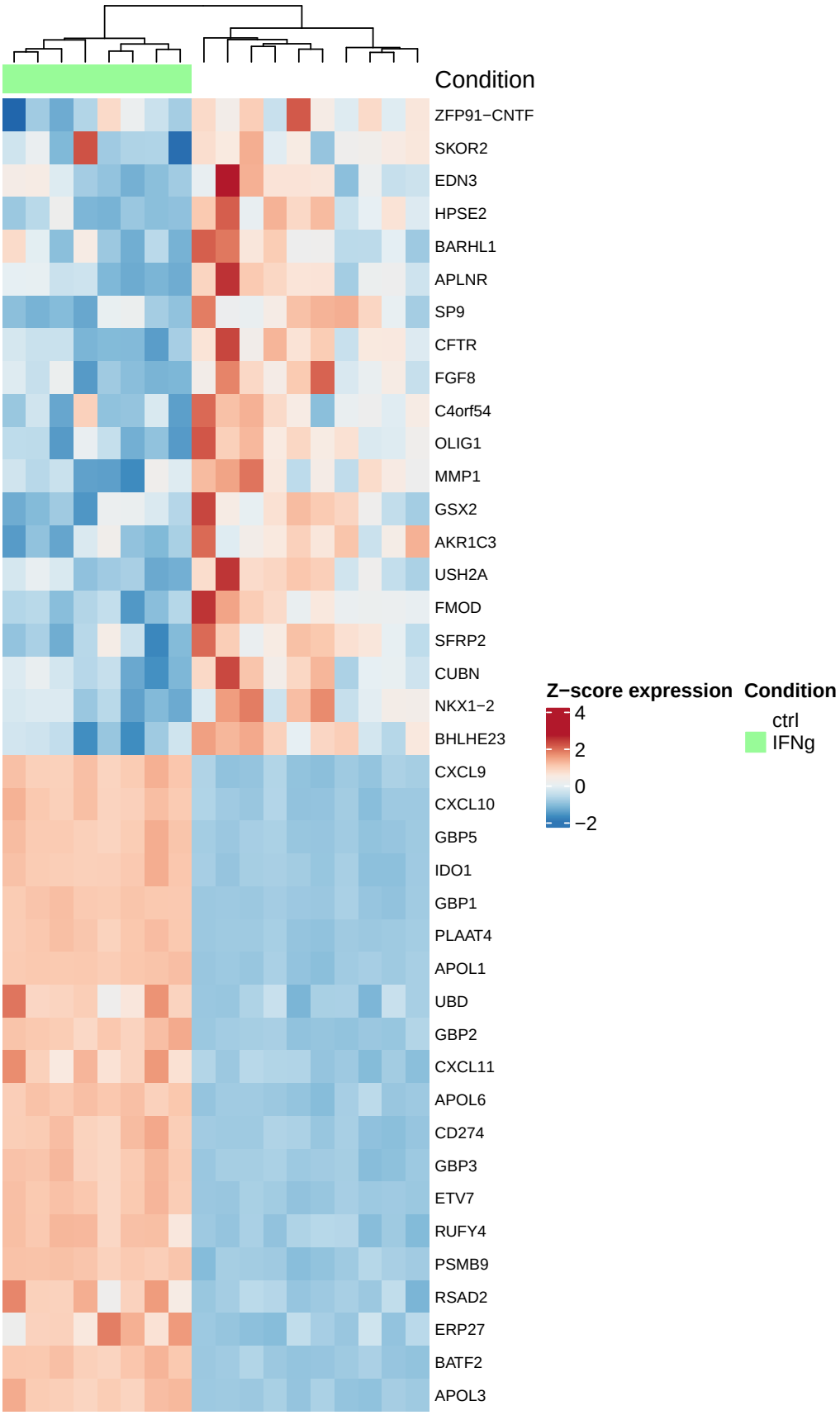
DEG table

Boxplot genes of interest

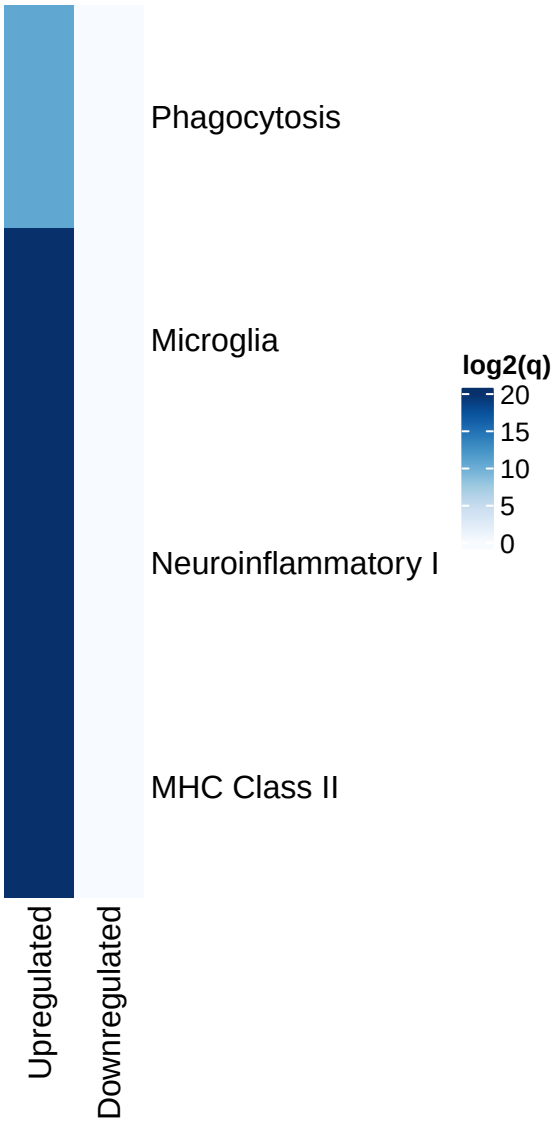




Top 40 DEGs heatmap

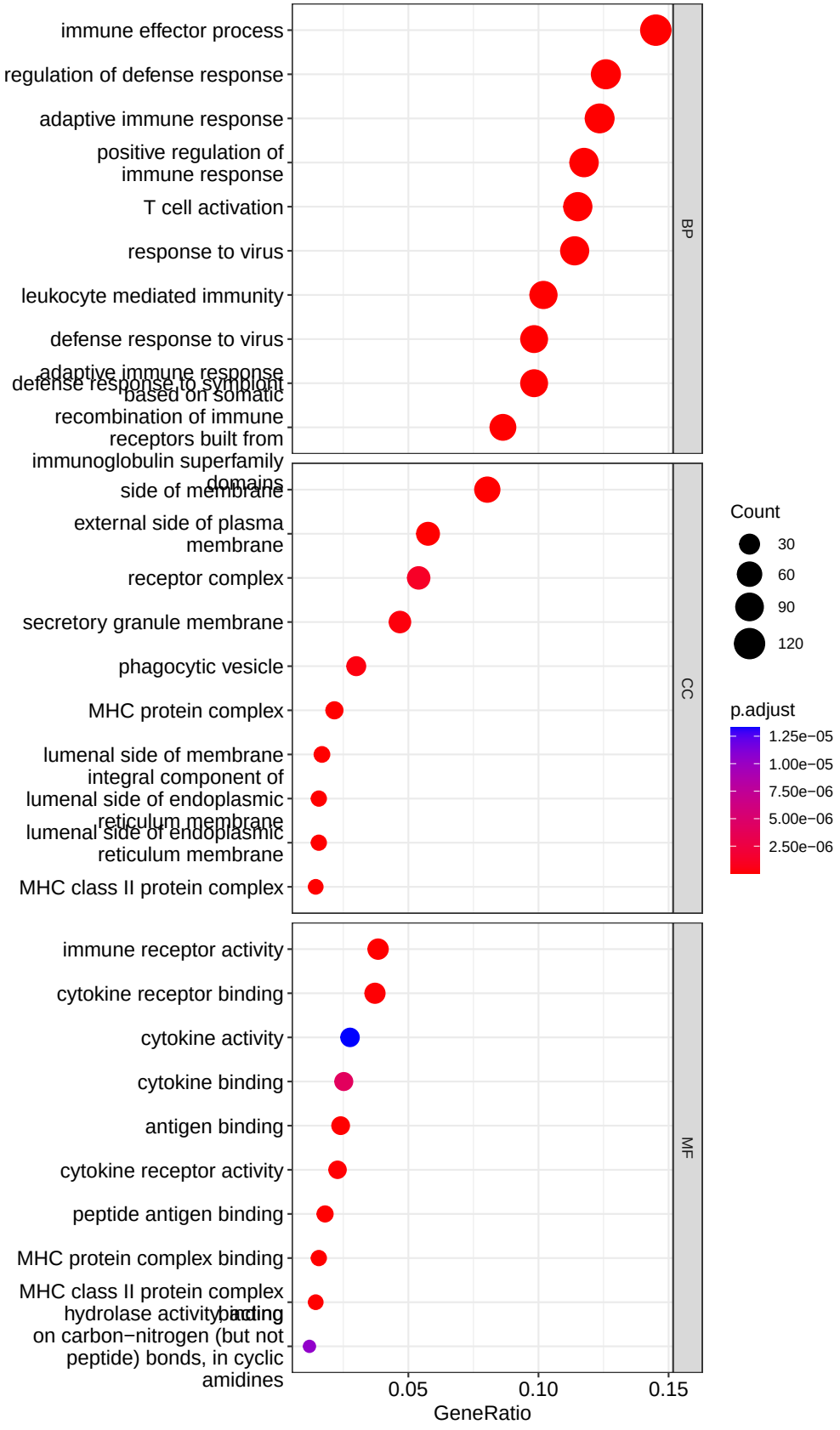


Enrichment heatmap (gene sets of interest)

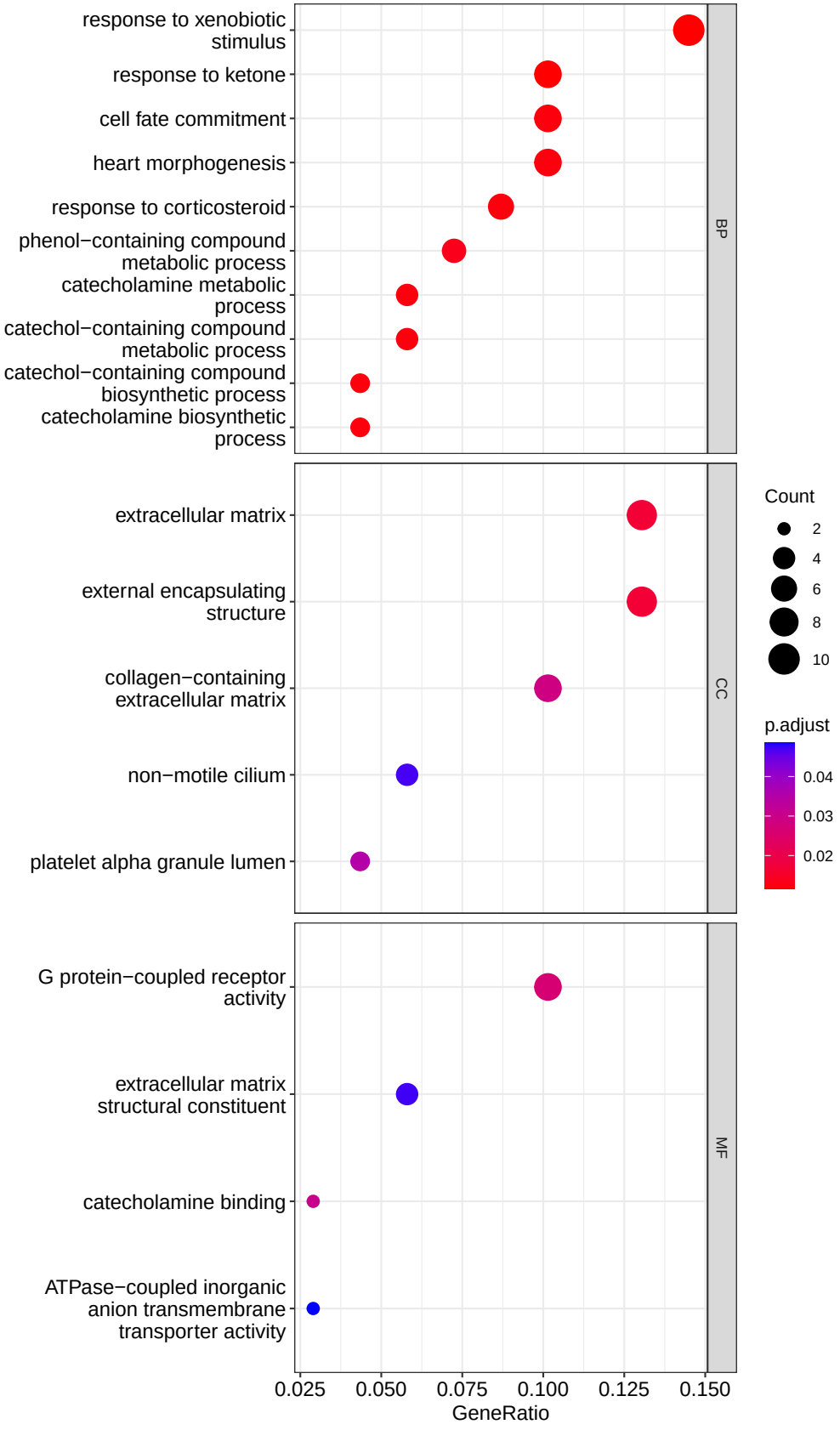


GO enrichment

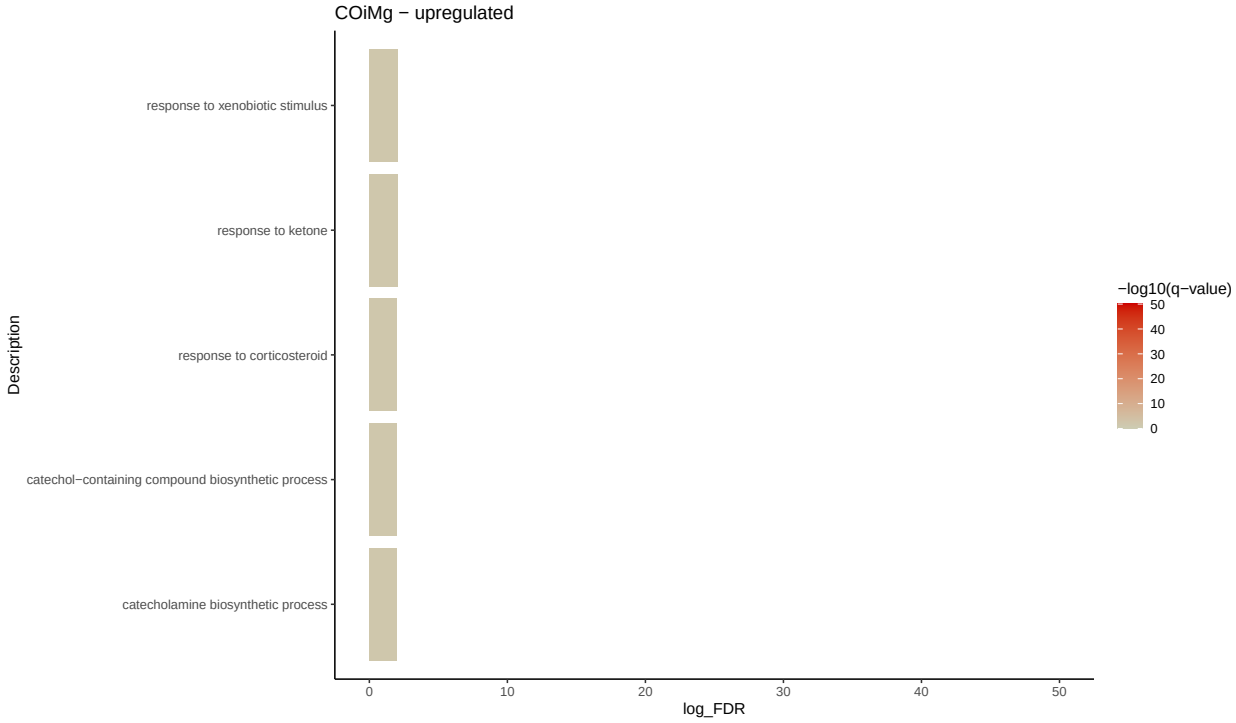
```
## [1] "Upregulated"
```

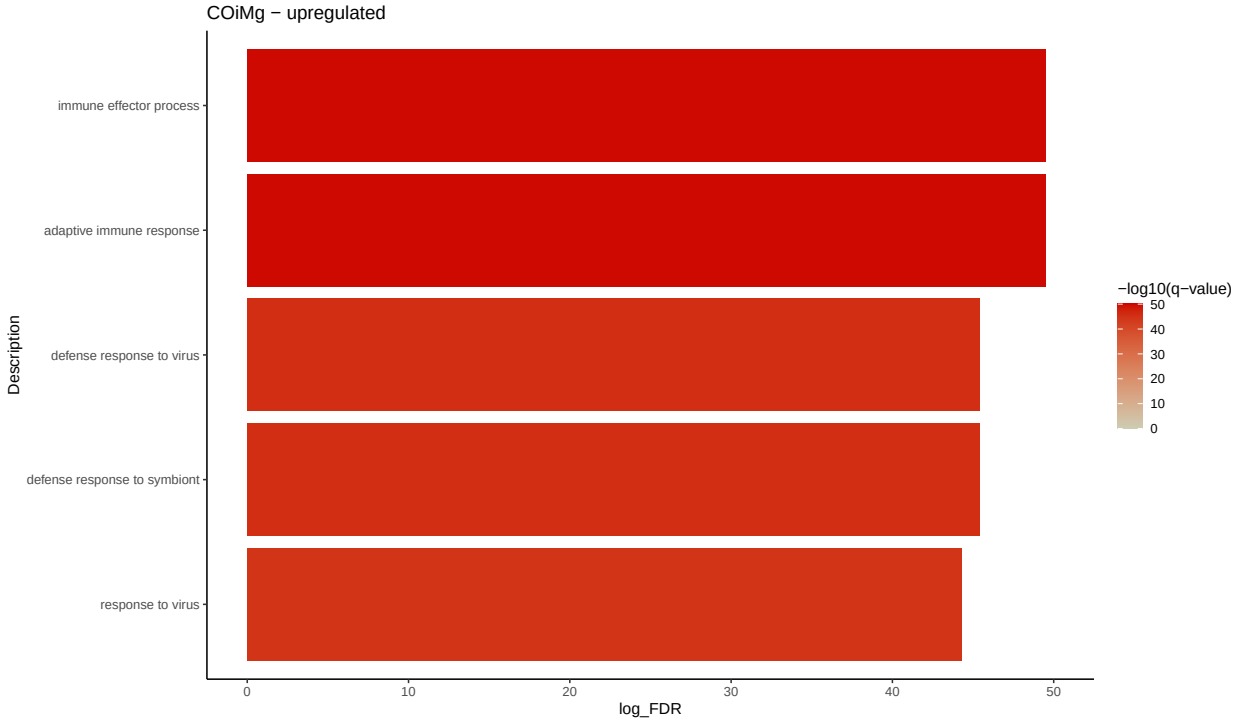

immune effector process
regulation of defense response
adaptive immune response
positive regulation of immune response
T cell activation
response to virus
leukocyte mediated immunity
defense response to virus
adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains
defense response to symbiont
BP
side of membrane
external side of plasma membrane
receptor complex
secretory granule membrane
phagocytic vesicle
MHC protein complex
lumenal side of membrane
integral component of lumenal side of endoplasmic reticulum membrane
lumenal side of endoplasmic reticulum membrane
MHC class II protein complex
CC
immune receptor activity
cytokine receptor binding
cytokine activity
cytokine binding
antigen binding
cytokine receptor activity
peptide antigen binding
MHC protein complex binding
MHC class II protein complex binding
hydrolase activity, acting on carbon−nitrogen (but not peptide) bonds, in cyclic amidines
MF
0.05
0.10
0.15
GeneRatio
Count
30
60
90
120
p.adjust
1.25e−05
1.00e−05
7.50e−06
5.00e−06
2.50e−06

```
## [1] "Downregulated"
```


response to xenobiotic stimulus
response to ketone
cell fate commitment
heart morphogenesis
response to corticosteroid
phenol−containing compound metabolic process
catecholamine metabolic process
catechol−containing compound metabolic process
catechol−containing compound biosynthetic process
catecholamine biosynthetic process
BP
extracellular matrix
external encapsulating structure
collagen−containing extracellular matrix
non−motile cilium
platelet alpha granule lumen
CC
G protein−coupled receptor activity
extracellular matrix structural constituent
catecholamine binding
ATPase−coupled inorganic anion transmembrane transporter activity
MF
0.025
0.050
0.075
0.100
0.125
0.150
GeneRatio
Count
2
4
6
8
10
p.adjust
0.04
0.03
0.02

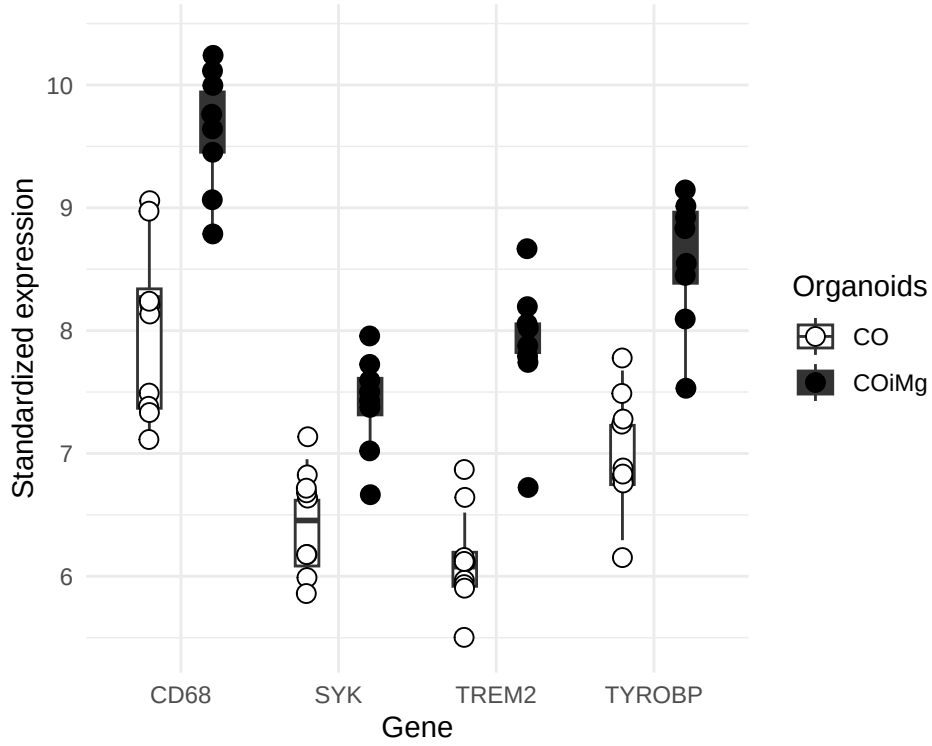
Barplots:

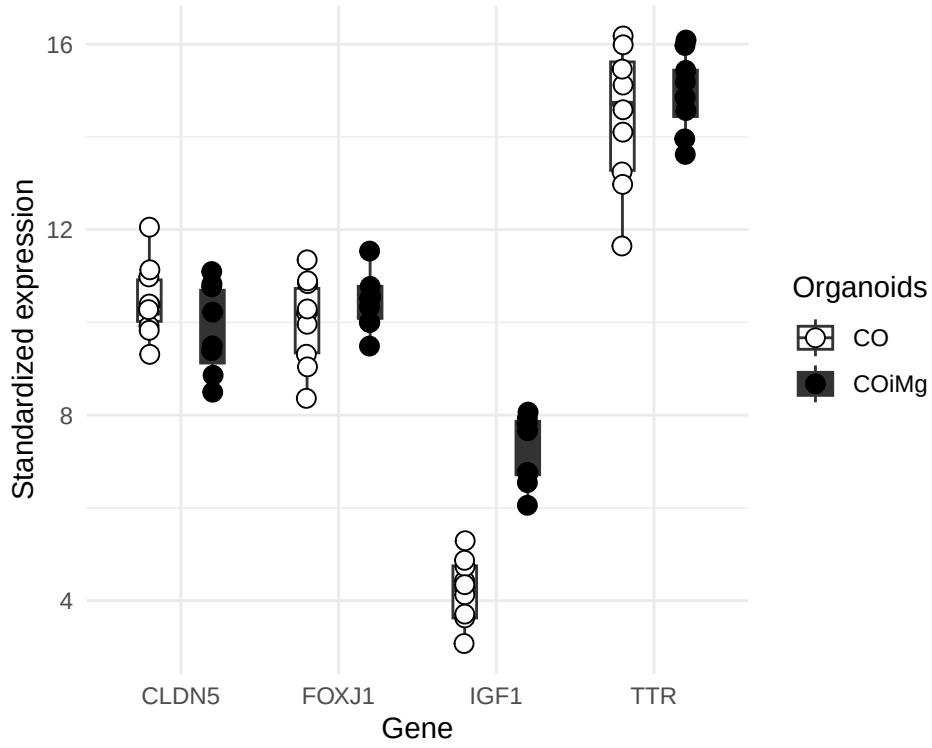

COiMg − upregulated
response to xenobiotic stimulus
response to ketone
response to corticosteroid
catechol−containing compound biosynthetic process
catecholamine biosynthetic process
Description
0
10
20
30
40
50
log_FDR
−log10(q−value)
50
40
30
20
10
0


COiMg − upregulated
immune effector process
adaptive immune response
defense response to virus
defense response to symbiont
response to virus
Description
0
10
20
30
40
50
log_FDR
−log10(q−value)
50
40
30
20
10
0

CO vs COiMg under IFNy

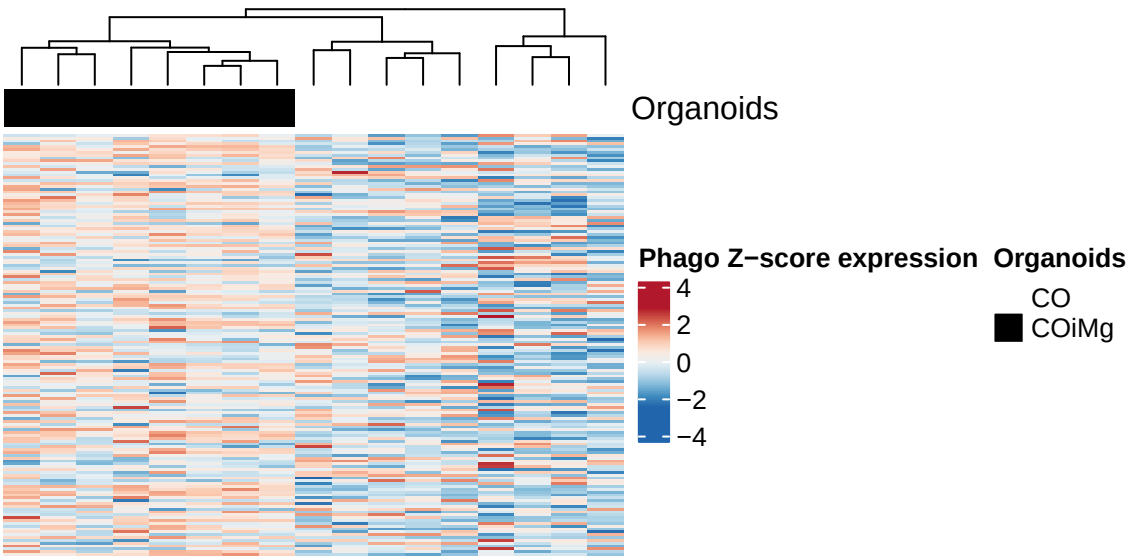
Phagocytosis: CO vs COiMg under IFNy



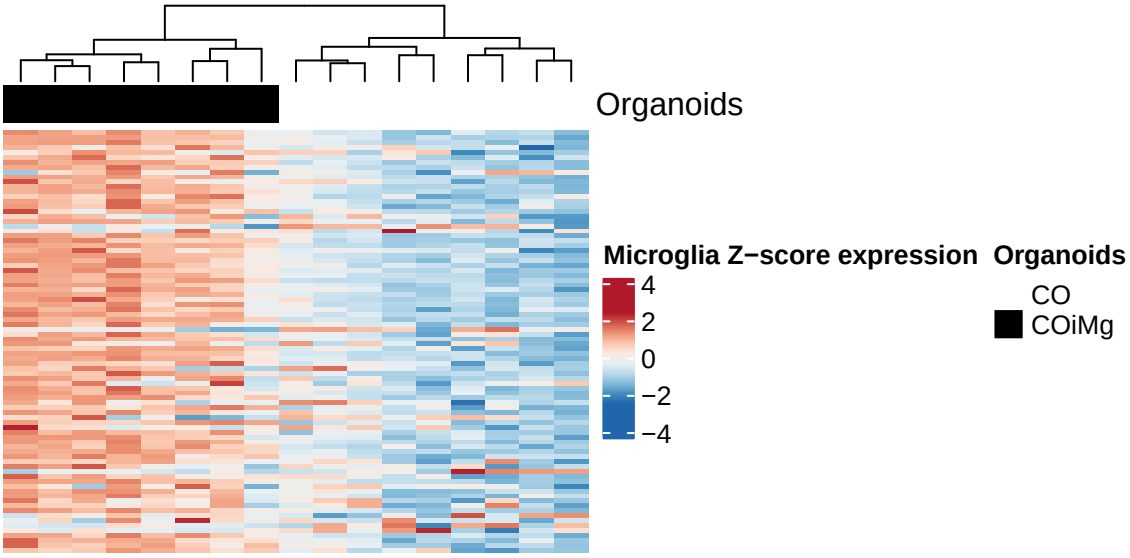


Gene set heatmap

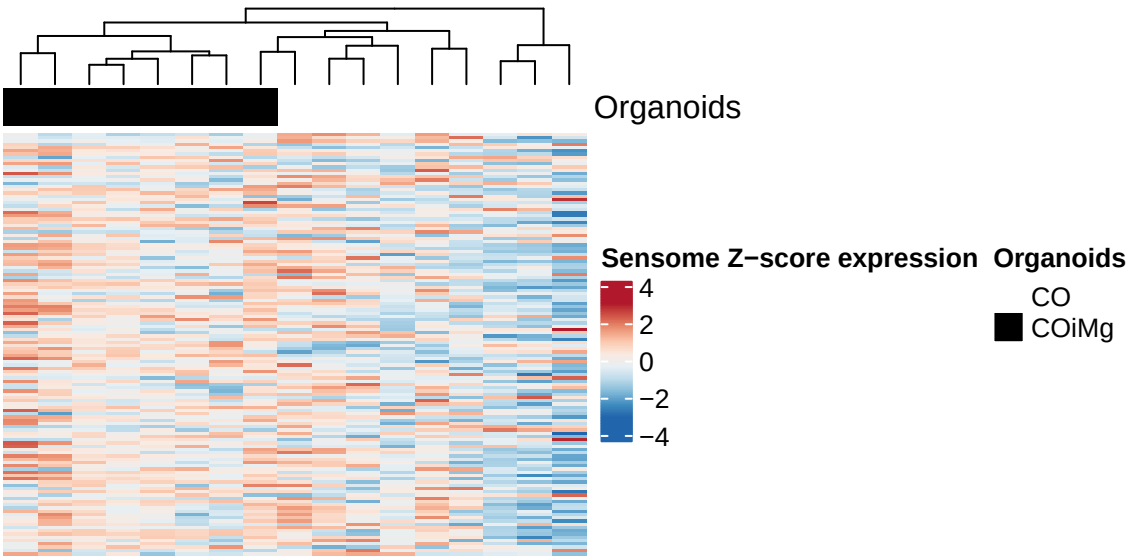
```
## [1] "Phagocytic heatmap"
```



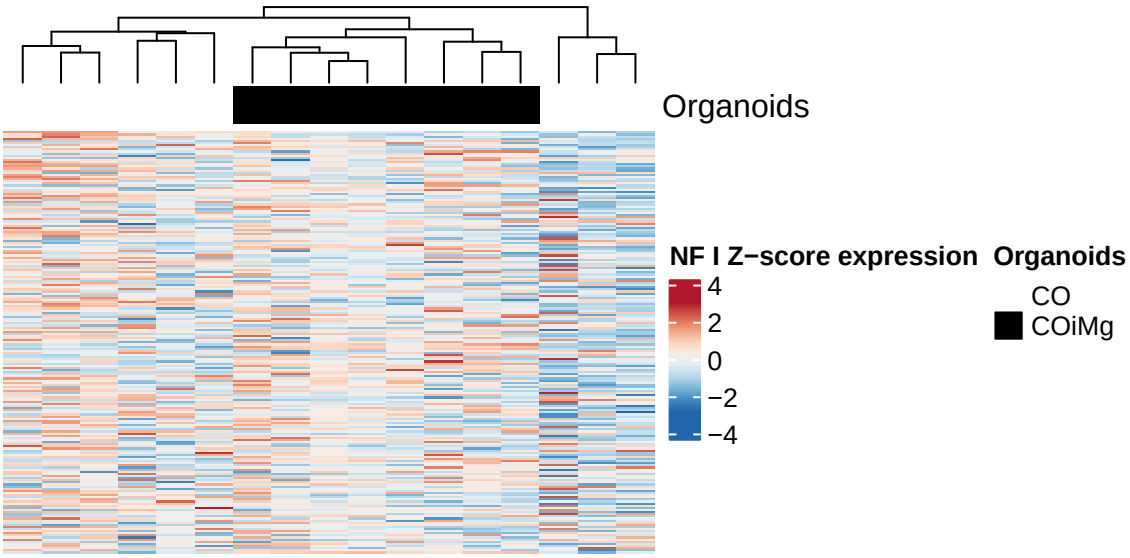

```
## [1] "Microglia heatmap"
```




```
## [1] "Sensome heatmap"
```




```
## [1] "Neuroinflammatory I heatmap"
```



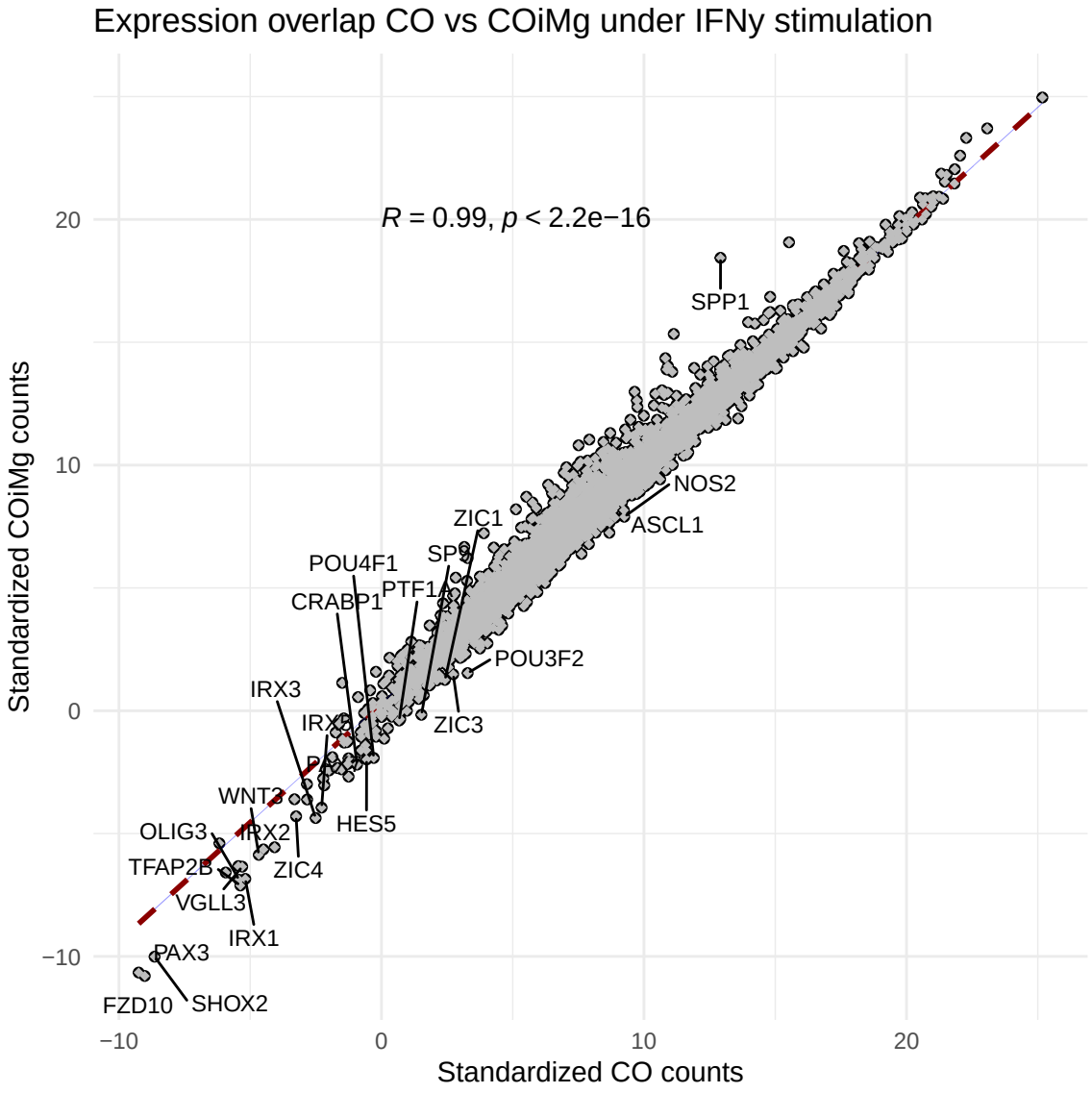
IFNy CO vs COiMG

```
##           M13       M14       M15       M21       M27       M33       F9
## M16 0.9888853 0.9750494 0.9854099 0.9860980 0.9844882 0.9665080 0.9772695
## M17 0.9882932 0.9689689 0.9821487 0.9803589 0.9830655 0.9582293 0.9703453
## M18 0.9853977 0.9796923 0.9773084 0.9801409 0.9848437 0.9628487 0.9773172
## M24 0.9893057 0.9799679 0.9870001 0.9855227 0.9831987 0.9708646 0.9793361
## M30 0.9839439 0.9849775 0.9782459 0.9812581 0.9760353 0.9881220 0.9857833
## M36 0.9808666 0.9739084 0.9819043 0.9848451 0.9726188 0.9723869 0.9735683
## F15 0.9896431 0.9848594 0.9858859 0.9880105 0.9875725 0.9839841 0.9898616
## F16 0.9736695 0.9781072 0.9730415 0.9772165 0.9707696 0.9863550 0.9842931
## F17 0.9837642 0.9760274 0.9815035 0.9841363 0.9823853 0.9590486 0.9744931
```

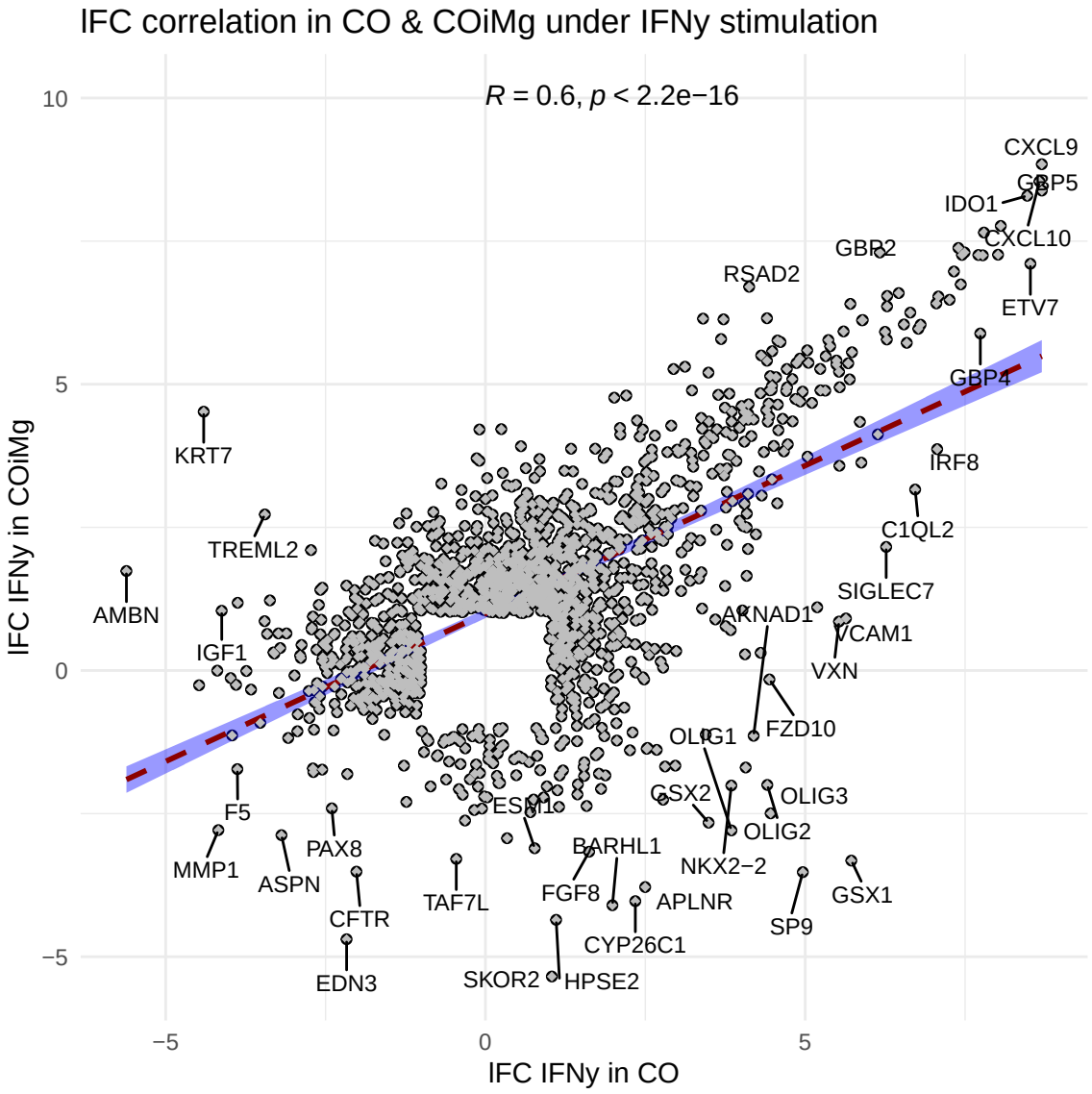
```
##           F10
## M16 0.9820133
## M17 0.9788688
## M18 0.9814824
## M24 0.9853527
## M30 0.9823925
## M36 0.9794674
## F15 0.9870064
## F16 0.9753547
## F17 0.9794916
```

```
##          0%         25%         50%         75%        100%
## -5.52300947 -0.16864063  0.01132637  0.16271150  1.86109744
```

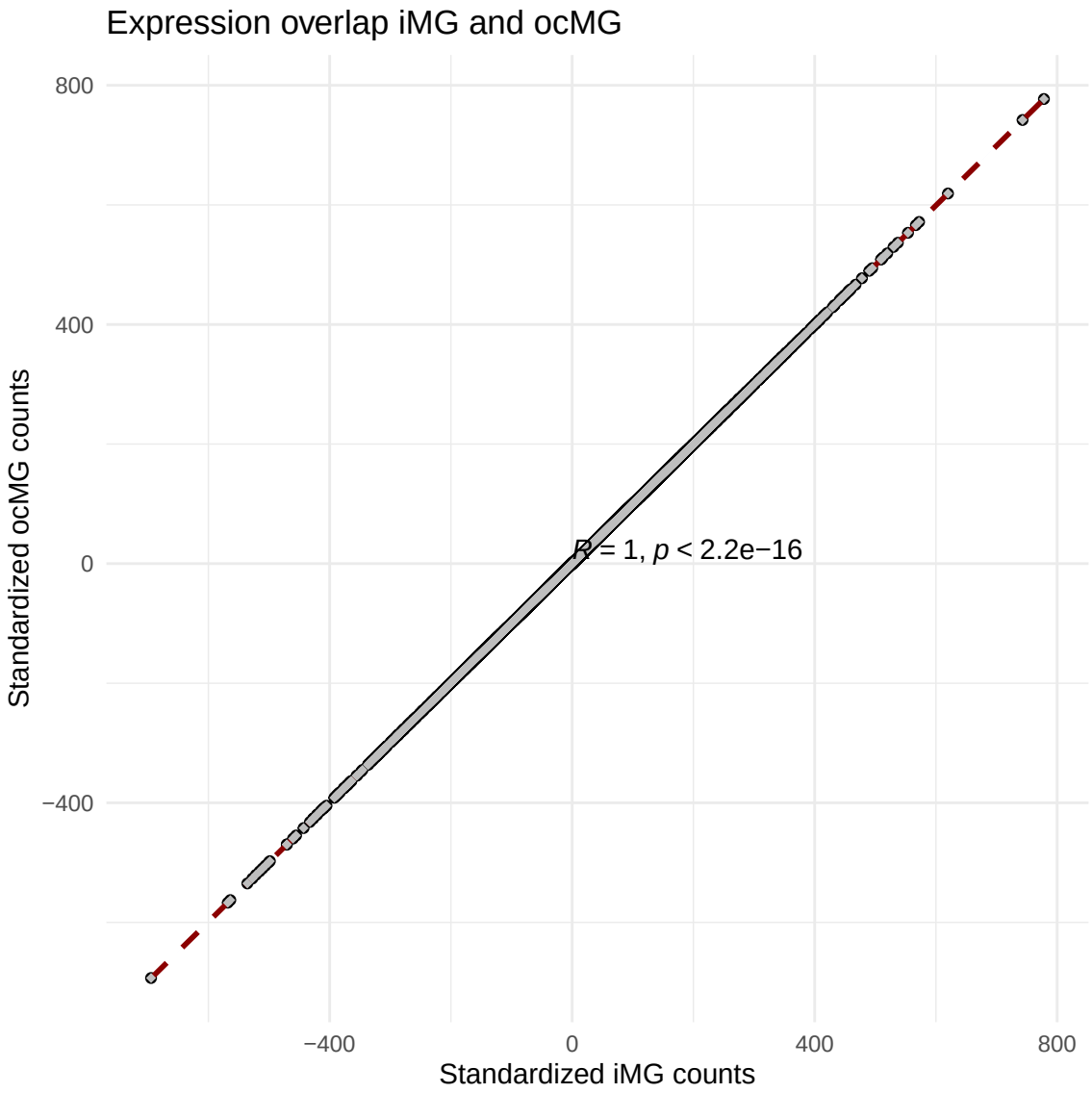
```
##  [1] "DLX6"    "NOS2"    "TFAP2B"  "MGST1"   "PAX7"    "KITLG"   "ASIC4"
##  [8] "NAALAD2" "MOXD1"   "LRP2"    "SLC32A1" "TOX3"    "WNT3"    "FZD10"
## [15] "SPP1"    "ONECUT2" "PAX3"    "GAD2"    "ASCL1"   "ZFHX3"   "GREB1L"
## [22] "C1QL2"   "DLX1"    "SFRP2"   "TENM2"   "CDH8"    "POU4F1"  "ZIC1"
## [29] "ROBO3"   "WNT7A"   "ZIC3"    "H4C8"    "VCAM1"   "NDST3"   "CRABP1"
## [36] "PTF1A"   "GBX2"    "SHOX2"   "IRX1"    "IRX2"    "HSPA6"   "LRRN3"
## [43] "WFIKKN2" "ZIC4"    "PRIMA1"  "IRX5"    "OLIG3"   "IRX3"    "GSX2"
## [50] "FIGN"    "BGN"     "SOX1"    "POU3F2"  "PCDH18"  "GREB1"   "POU3F4"
## [57] "HES5"    "TOX"     "HSPA1B"  "HSPA1A"  "VGLL3"   "TRIM71"  "UBD"
## [64] "SP9"     "OR2I1P"  "H4C14"   "H2BC8"
```


Expression overlap CO vs COiMg under IFNy stimulation
R = 0.99, p < 2.2e−16
Standardized COiMg counts
Standardized CO counts
20
10
0
−10
−10
0
10
20
SPP1
NOS2
ASCL1
ZIC1
SP9
POU4F1
PTF1A
CRABP1
POU3F2
IRX3
IRX5
ZIC3
PAX6
WNT3
HES5
OLIG3
IRX2
TFAP2B
ZIC4
VGLL3
IRX1
PAX3
FZD10
SHOX2

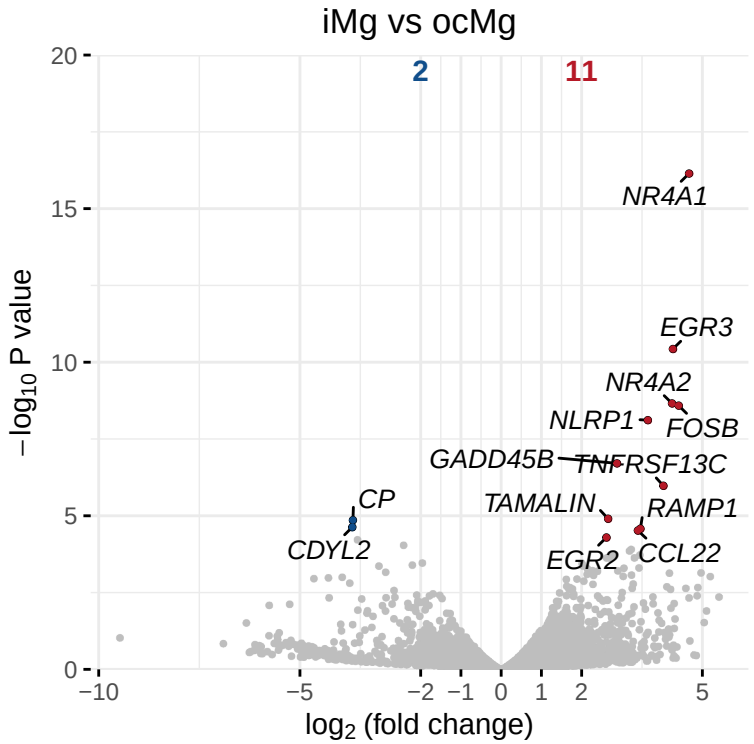
CO vs COiMg lFC correlation plot



iMG vs ocMG

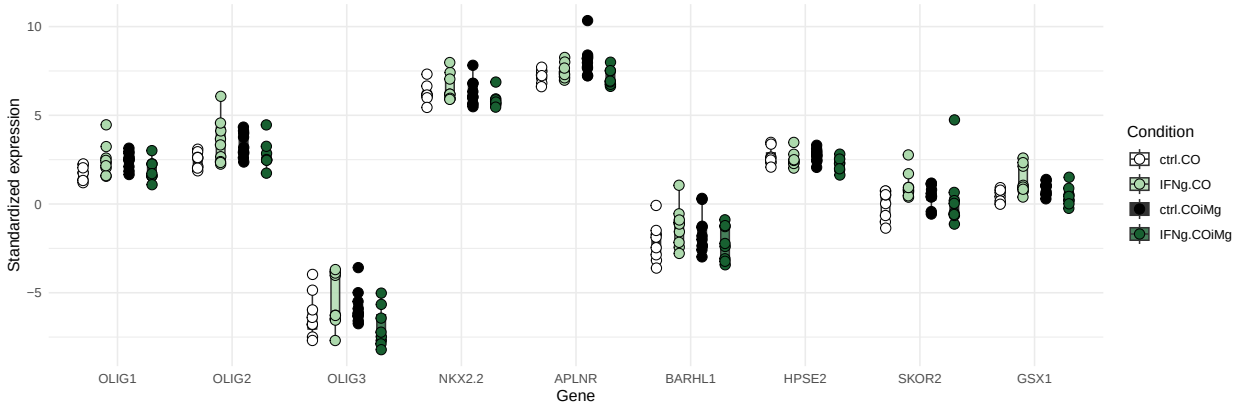

Expression overlap iMG and ocMG
800
400
0
−400
Standardized ocMG counts
R = 1, p < 2.2e−16
−400
0
400
800
Standardized iMG counts

Volcano

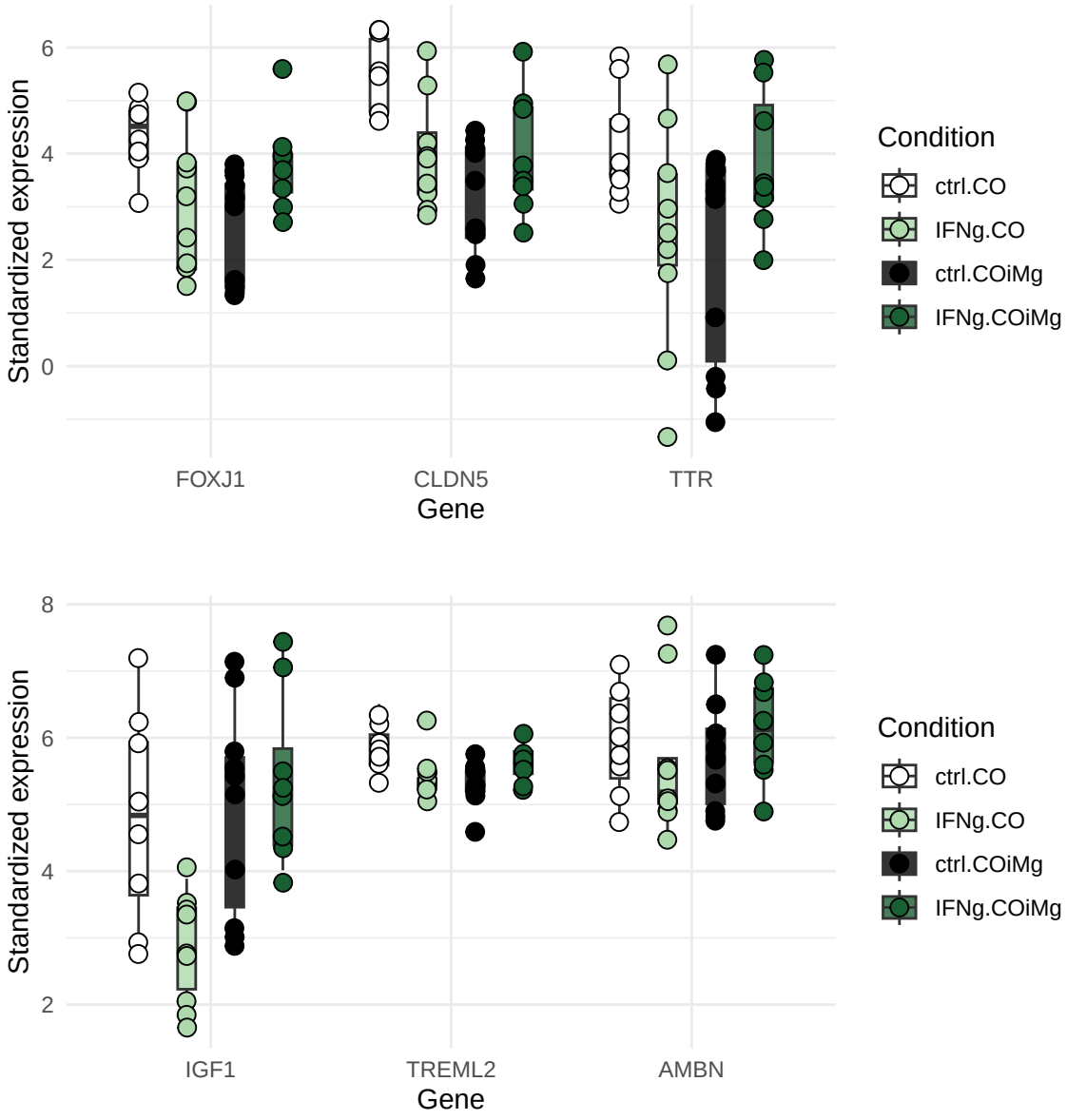


Interaction boxplots

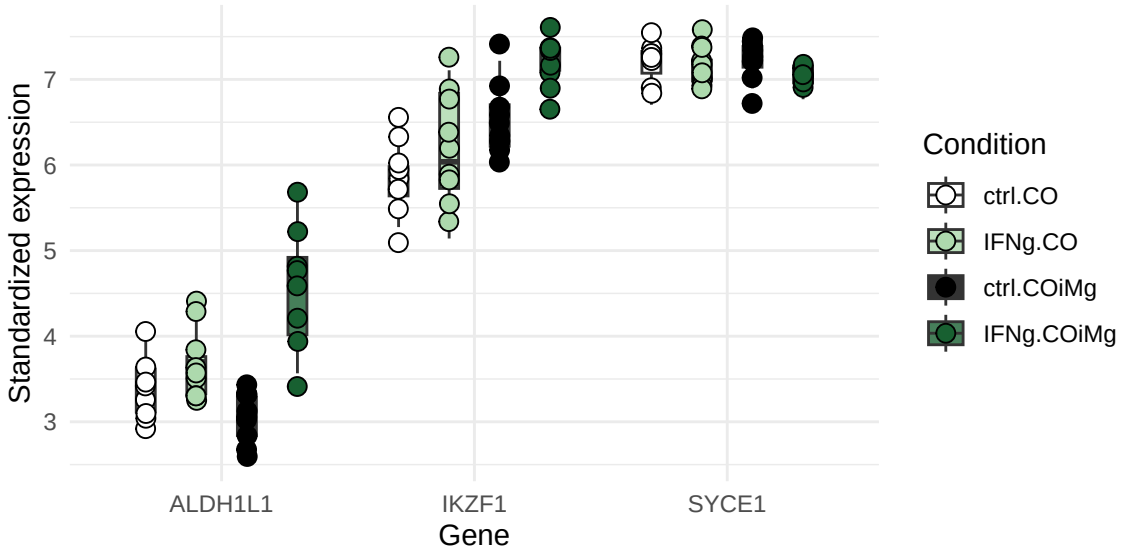
A



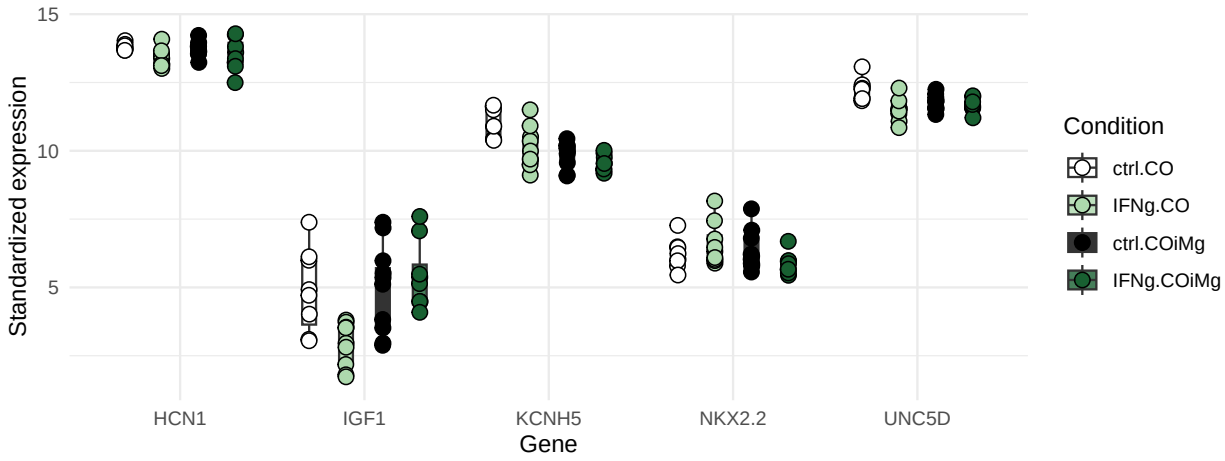
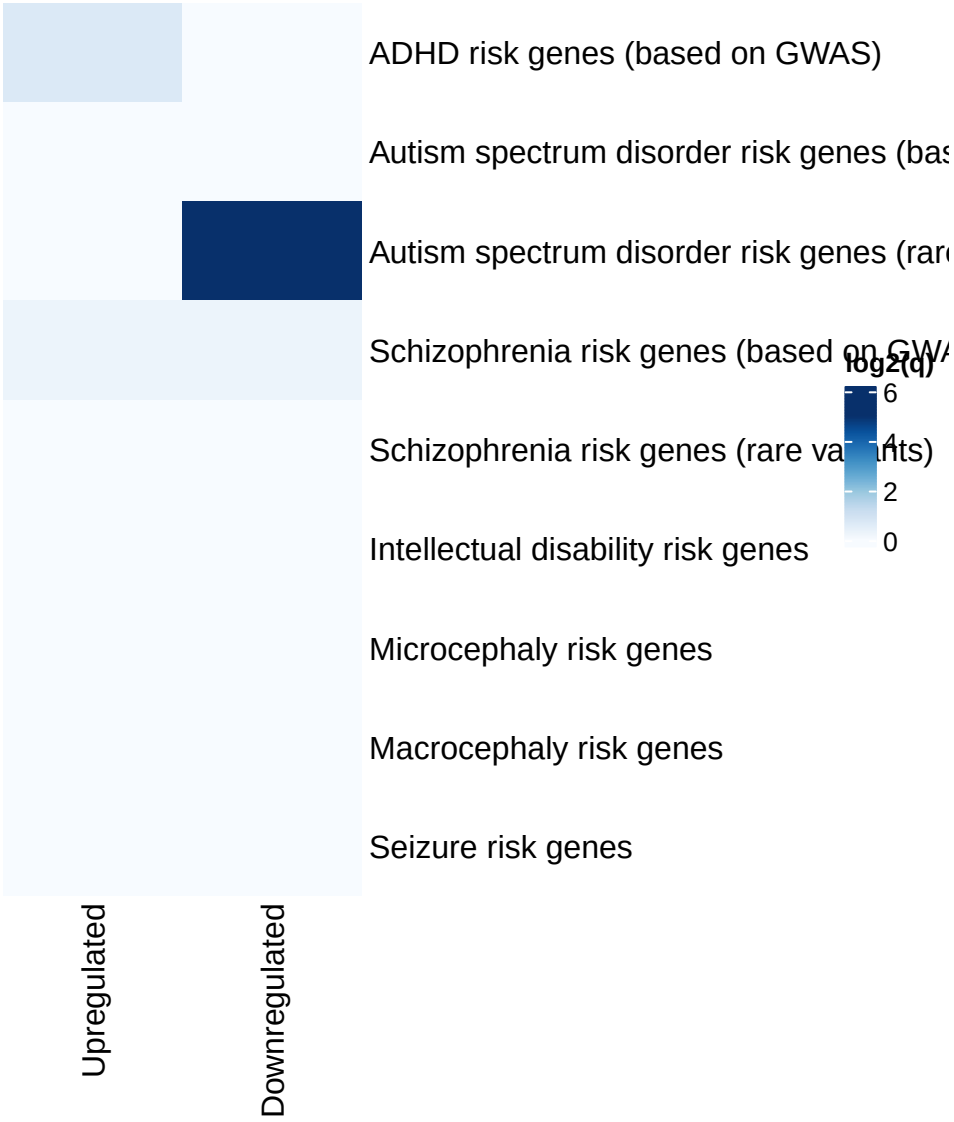
B


Standardized expression
6
4
2
0
FOXJ1
CLDN5
TTR
Gene
Condition
ctrl.CO
IFNg.CO
ctrl.COiMg
IFNg.COiMg
Standardized expression
8
6
4
2
IGF1
TREML2
AMBN
Gene
Condition
ctrl.CO
IFNg.CO
ctrl.COiMg
IFNg.COiMg

SFARI response to IFNy (COiMg genes)



SFARI response to IFNy (CO genes)



SFARI enrichment in IFNy: