Vignette Title

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22 November 2023

Abstract

Description of your vignette

Contents

This vignette shows an example of applying pathway level to infer cell-type-specific co-expression networks and extracting co-expressed gene modules that are enriched for biological functions in cell types.

1 1. Load packages and data

```
library(CSCORE)
library(Seurat)
library(ggraph)
library(gridExtra)
source("../R/functions_2.R")
```

In this vignette, we use the single cell RNA-sequencing data on Peripheral blood mononuclear cells (PBMC) from COVID patients and healthy controls from Wilk et al. (https://www.nature.com/articles/s41591-020-0944-y), which were also studied in our manuscript (https://www.biorxiv.org/content/10.1101/2022.12.13.520181v1). This data set can be downloaded via the following bash script

```
#wget https://hosted-matrices-prod.s3-us-west-2.amazonaws.com/Single_cell_atlas_c
cat("dowload")
```

```
## dowload
```

After downloading blish_covid.seu.rds, we load it into the R session

```
####Load the gene set and convert into list
geneset<-geneIds(getGmt("../data/h.all.v2023.2.Hs.symbols.gmt"))
pbmc <- readRDS('../data/blish_covid.seu.rds')
# Use the original UMI counts stored in Assay 'RNA'
DefaultAssay(pbmc) <- 'RNA'
```

2 2. Select cell types and gene sets to study

In this example, we focus on B cells and infer the B cell-specific co-expression network.

```
pbmc_B = pbmc[,pbmc$cell.type.coarse %in% 'B']
```

Depending on the biological question of interest, one may choose to study the co-expression network for any gene set. Here, we chose to infer the co-expression network for the genes with meaningful expression levels in B cells (top 5000 among 26361 genes). There are several reasons

for our choice:

1. All genes with moderate to high expression levels provides a comprehensive and unbiased set of genes that could have meaningful biological functions in a cell type.

2. If the genes have much lower expression levels, it would be statistically more challenging and biologically less interesting to infer their co-expressions, as these genes might have almost all UMI counts equal to 0.

In general, it will be up to the users's choice to select the gene sets to study. We recommend choosing the gene sets that are of interest to your application.

```
mean_exp = rowMeans(pbmc_B@assays$RNA@counts/pbmc_B$nCount_RNA)
genes_selected = names(sort.int(mean_exp, decreasing = T))[1:5000]
```

3   3. Run `Pathway Level` to infer cell-type-specific co-expression network on the specified gene set

We further subset the B cells to those from healthy control subjects in order to study B-cell specific co-expression network among healthy control B cells.

```
metaData<-pbmc_B@meta.data
metaData_Healthy<-metaData[metaData$Status=="Healthy",]
metaData_COVID<-metaData[metaData$Status=="COVID",]
set.seed(666);metaData_COVID<-metaData_COVID[sample(1:dim(metaData_COVID)[1],dim(
```

4   4. Get the Subset of two groups

```
pbmc_B.sub<-subset(pbmc_B, cells=c(rownames(metaData_Healthy), rownames(metaData_
rm(pbmc_B)
```

5   5. Calculate the network, or score of networks

```
cor_data_score<-calculate_seq_correlation(geneset,pbmc_B.sub,genes_selected,"COVI
```

```
## [1] "IRLS converged after 5 iterations."
## [1] "25 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.4981% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1726% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1260% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0758% co-expression estimates were smaller than -1 and were set to -1."
## I am here line 62
```

```
save(cor_data_score, file = "COVIDHD_cor_data_score.RData")
```

Next, based on the thresholded co-expression matrix, we apply WGCNA (https://bmcbioinformatics.biomedcentral.com/articles/10.1186/1471-2105-9-559) to extract co-expressed gene modules. In particular, we use `CS-CORE` estimates to measure co-expressions for single cell RNA-sequencing data, which replace the Pearson correlations used in traditional WGNCA workflow, that suffer from inflated false positives and attenuation bias on single cell data as demonstrated in our manuscript (https://www.biorxiv.org/content/10.1101/2022.12.13.520181v1).

6   6. Calculate the network, or score of networks for permutations

```
cor_data_perm_list<-runPermute_seq_correlation(geneset,pbmc_B.sub,genes_selected,
```

```
## ########################################1700654808   1   perm start
## covid_557.7029 HIP045.1505 covid_561.474 HIP002.2085 covid_555_2.2338HIP023.70
## [1] "16 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2287% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0799% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "13 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1825% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0686% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700655199   2   perm start
## HIP045.1746 covid_558.1097 covid_555_1.1080 HIP043.341 covid_558.1332covid_557
## [1] "15 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2196% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0842% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1614% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0477% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700655595   3   perm start
## HIP043.339 HIP044.3911 covid_558.2927 covid_557.2319 HIP023.1427HIP015.459 HIF
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1838% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0645% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "15 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2064% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0552% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700655992   4   perm start
## covid_558.251 covid_555_2.1654 HIP043.833 covid_555_2.2709 covid_557.814HIP023
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1761% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0708% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "12 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1892% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0547% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700656388   5   perm start
## covid_558.2853 HIP045.1983 HIP023.3167 HIP015.366 HIP023.3407HIP015.454 HIP043
## [1] "15 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1804% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0454% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
```

```
## [1] "0.2067% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0686% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700656785   6   perm start
## HIP043.859 covid_558.1461 covid_556.765 covid_555_2.494 HIP044.3906covid_556.1
## [1] "12 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2268% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1072% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "11 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2228% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0757% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700657180   7   perm start
## HIP044.424 covid_561.717 HIP044.1280 covid_557.6583 HIP044.3116HIP023.3152 HIP
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1861% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0527% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1962% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0678% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700657572   8   perm start
## covid_555_2.400 covid_558.1067 HIP043.5069 covid_558.201 covid_555_1.550covid_
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1799% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0640% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2262% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0725% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700657966   9   perm start
## HIP015.278 covid_561.2669 covid_555_1.1166 covid_557.6844 covid_555_2.392HIP04
## [1] "8 among 5000 genes have negative variance estimates. Their co-expressions
## [1] "0.2076% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0523% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 6 iterations."
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2362% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0850% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700658366   10   perm start
## covid_555_1.1578 HIP044.3396 HIP044.579 covid_555_2.720 covid_555_1.1717covid_
## [1] "12 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1675% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0551% co-expression estimates were smaller than -1 and were set to -1."
```

```
## [1] "IRLS converged after 4 iterations."
## [1] "13 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2304% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0955% co-expression estimates were smaller than -1 and were set to -1."
## ##########################################1700658763   11  perm start
## covid_558.3585 covid_556.690 covid_557.6543 covid_555_2.4294 covid_557.1505HIF
## [1] "11 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2104% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0881% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "7 among 5000 genes have negative variance estimates. Their co-expressions
## [1] "0.1904% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0606% co-expression estimates were smaller than -1 and were set to -1."
## ##########################################1700659162   12  perm start
## covid_556.458 covid_556.824 covid_558.682 covid_555_1.912 HIP043.1212covid_556
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2019% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0792% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "8 among 5000 genes have negative variance estimates. Their co-expressions
## [1] "0.2223% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0787% co-expression estimates were smaller than -1 and were set to -1."
## ##########################################1700659564   13  perm start
## covid_556.1573 HIP045.499 covid_558.2434 covid_557.654 covid_558.204covid_556.
## [1] "17 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1736% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0620% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1863% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0390% co-expression estimates were smaller than -1 and were set to -1."
## ##########################################1700659962   14  perm start
## covid_556.1753 covid_558.2460 covid_557.867 HIP044.980 HIP043.2117covid_557.52
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2131% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0848% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "10 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2134% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0835% co-expression estimates were smaller than -1 and were set to -1."
## ##########################################1700660365   15  perm start
## HIP023.1466 covid_556.693 covid_557.5408 covid_558.34 HIP044.2121covid_556.82
## [1] "13 among 5000 genes have negative variance estimates. Their co-expression
```

```
## [1] "0.1932% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0616% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "20 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1858% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0621% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700660772   16  perm start
## HIP045.100 HIP044.3303 covid_557.5011 HIP023.3207 HIP044.242covid_558.94 covic
## [1] "8 among 5000 genes have negative variance estimates. Their co-expressions
## [1] "0.1548% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0439% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "19 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2815% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1374% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700661169   17  perm start
## covid_555_1.2269 HIP002.258 HIP002.175 covid_561.1511 HIP002.1617HIP044.1033 H
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2361% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1032% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "13 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2352% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1011% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700661569   18  perm start
## covid_555_2.1324 covid_561.1393 covid_558.2257 covid_558.3035 HIP044.1467covic
## [1] "10 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.3014% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1653% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "15 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1728% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0530% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700661965   19  perm start
## HIP044.2154 HIP043.2906 covid_555_2.2365 covid_556.722 HIP044.1099HIP044.3511
## [1] "13 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2279% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0921% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 5 iterations."
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2149% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0764% co-expression estimates were smaller than -1 and were set to -1."
## ########################################1700662370   20  perm start
```

```
## covid_557.4552 covid_558.3414 covid_556.1788 covid_557.2194 covid_555_2.4184HI
## [1] "14 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.2076% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0734% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "16 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1734% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0681% co-expression estimates were smaller than -1 and were set to -1."
```

```
save(cor_data_perm_list, file = "COVIDHD_cor_data_hallmark_perm_list_20.RData")
```

7   7. Calculate p values

```
pvalues<-sort(getPvaluesTTest(cor_data_score, cor_data_perm_list))
save(pvalues, file = "pvaluesTtest.RData")
```

8   8. Generate the figures for top pathways

```
gglist <-list()
for(ii in 1:1){
  pathway<-names(pvalues)[ii]
  networkslist<-network_seq_correlation(geneset[[pathway]],pbmc_B.sub,genes_selec
  gglist[[ii]]<-network_plot(networkslist,name1="COVID",name2="Healthy", fileName
}
```

```
## [1] "IRLS converged after 5 iterations."
## [1] "25 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.4981% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1726% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1260% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0758% co-expression estimates were smaller than -1 and were set to -1."
```

```
## Warning: package 'dplyr' was built under R version 4.1.3
```

```
##
## Attaching package: 'dplyr'
```

```
## The following objects are masked from 'package:GSEABase':
##
##     intersect, setdiff, union

## The following object is masked from 'package:graph':
##
##     union

## The following object is masked from 'package:AnnotationDbi':
##
##     select

## The following objects are masked from 'package:IRanges':
##
##     collapse, desc, intersect, setdiff, slice, union

## The following objects are masked from 'package:S4Vectors':
##
##     first, intersect, rename, setdiff, setequal, union

## The following object is masked from 'package:Biobase':
##
##     combine

## The following objects are masked from 'package:BiocGenerics':
##
##     combine, intersect, setdiff, union

## The following object is masked from 'package:gridExtra':
##
##     combine

## The following objects are masked from 'package:stats':
##
##     filter, lag

## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union

## Warning: package 'igraph' was built under R version 4.1.3

##
## Attaching package: 'igraph'

## The following objects are masked from 'package:dplyr':
##
##     as_data_frame, groups, union
```

```
## The following object is masked from 'package:GSEABase':
##
##     union

## The following objects are masked from 'package:graph':
##
##     degree, edges, intersection, union

## The following object is masked from 'package:IRanges':
##
##     union

## The following object is masked from 'package:S4Vectors':
##
##     union

## The following objects are masked from 'package:BiocGenerics':
##
##     normalize, path, union

## The following objects are masked from 'package:stats':
##
##     decompose, spectrum

## The following object is masked from 'package:base':
##
##     union

## Using "stress" as default layout
## Using "stress" as default layout
## Using "stress" as default layout

## Warning: Using the `size` aesthetic in this geom was deprecated in ggplot2 3.4
## i Please use `linewidth` in the `default_aes` field and elsewhere instead.
## This warning is displayed once every 8 hours.
## Call `lifecycle::last_lifecycle_warnings()` to see where this warning was
## generated.
```

```
for(ii in 2:2){
  pathway<-names(pvalues)[ii]
  networkslist<-network_seq_correlation(geneset[[pathway]],pbmc_B.sub,genes_selec
  gglist[[ii]]<-network_plot(networkslist,name1="COVID",name2="Healthy", fileNames
}
```

```
## [1] "IRLS converged after 5 iterations."
## [1] "25 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.4981% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1726% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1260% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0758% co-expression estimates were smaller than -1 and were set to -1."
```

```
## Using "stress" as default layout
## Using "stress" as default layout
## Using "stress" as default layout
```

```
for(ii in 3:3){
  pathway<-names(pvalues)[ii]
  networkslist<-network_seq_correlation(geneset[[pathway]],pbmc_B.sub,genes_selec
  gglist[[ii]]<-network_plot(networkslist,name1="COVID",name2="Healthy", fileName
}
```

```
## [1] "IRLS converged after 5 iterations."
## [1] "25 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.4981% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1726% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1260% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0758% co-expression estimates were smaller than -1 and were set to -1."
```

```
## Using "stress" as default layout
## Using "stress" as default layout
## Using "stress" as default layout
```

```
for(ii in 4:4){
  pathway<-names(pvalues)[ii]
  networkslist<-network_seq_correlation(geneset[[pathway]],pbmc_B.sub,genes_selec
  gglist[[ii]]<-network_plot(networkslist,name1="COVID",name2="Healthy", fileName
}
```

```
## [1] "IRLS converged after 5 iterations."
## [1] "25 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.4981% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.1726% co-expression estimates were smaller than -1 and were set to -1."
## [1] "IRLS converged after 4 iterations."
## [1] "18 among 5000 genes have negative variance estimates. Their co-expression
## [1] "0.1260% co-expression estimates were greater than 1 and were set to 1."
## [1] "0.0758% co-expression estimates were smaller than -1 and were set to -1."
```

```
## Using "stress" as default layout
## Using "stress" as default layout
## Using "stress" as default layout
```

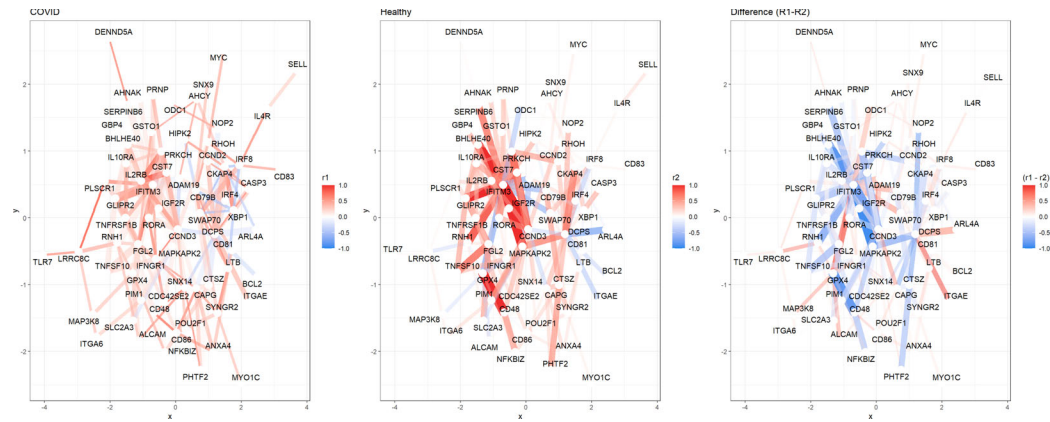# 9   9. Show plots

Plot the first pathway.

```
gridExtra::grid.arrange(gglist[[1]]$gg1, gglist[[1]]$gg2, gglist[[1]]$ggDiff, r
```
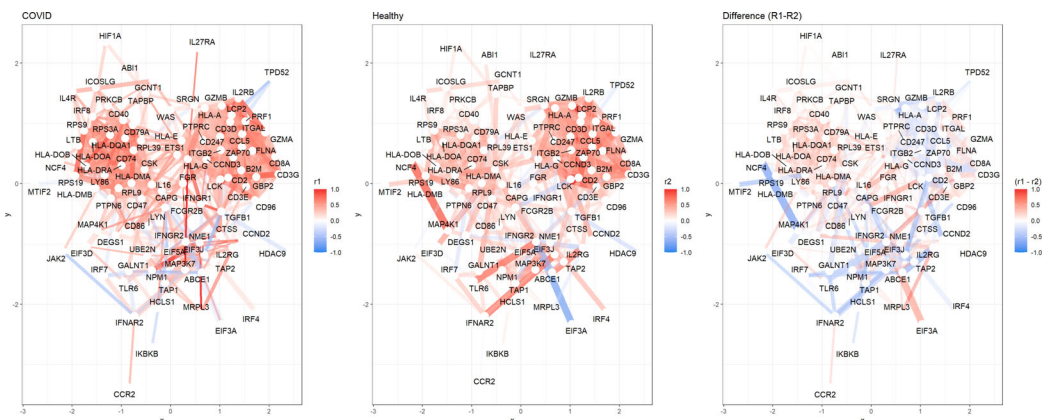

10   10. Show plots

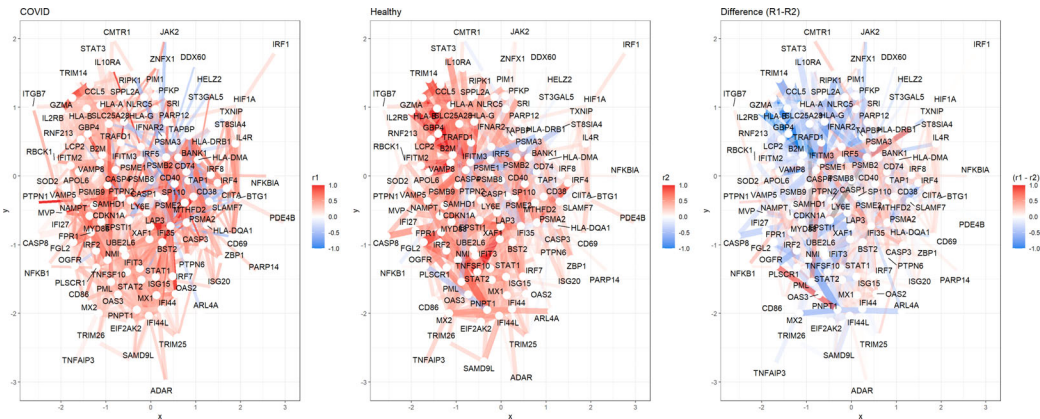Plot the second pathway.

```
library(ggraph)
gridExtra::grid.arrange(gglist[[2]]$gg1, gglist[[2]]$gg2, gglist[[2]]$ggDiff, r
```

11   11. Show plots

Plot the third pathway.

```
library(ggraph)
gridExtra::grid.arrange(gglist[[3]]$gg1, gglist[[3]]$gg2, gglist[[3]]$ggDiff, r
```
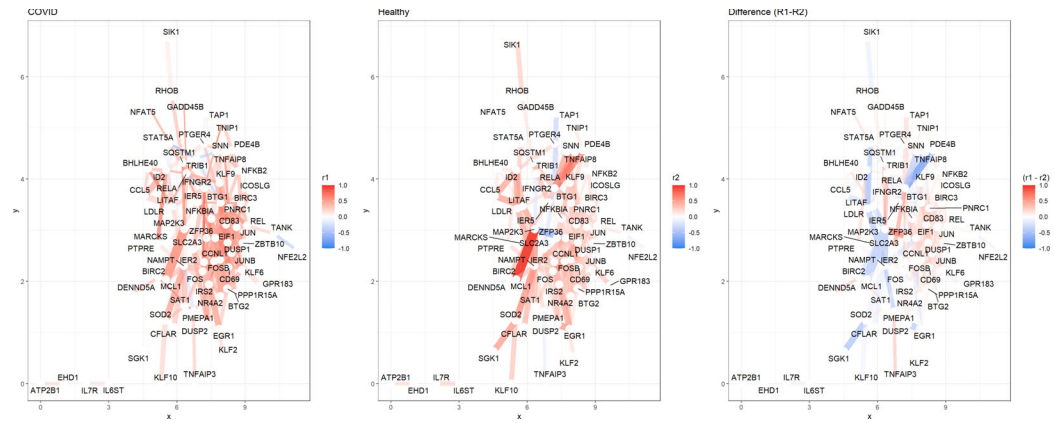

12   12. Show plots

Plot the fourth pathway.

```
library(ggraph)
gridExtra::grid.arrange(gglist[[4]]$gg1, gglist[[4]]$gg2, gglist[[4]]$ggDiff, r
```

The other Analysis is possible # Session info {.unnumbered}

```
## R version 4.1.2 (2021-11-01)
## Platform: x86_64-w64-mingw32/x64 (64-bit)
## Running under: Windows 10 x64 (build 19045)
##
## Matrix products: default
##
## locale:
## [1] LC_COLLATE=English_United States.1252
## [2] LC_CTYPE=English_United States.1252
## [3] LC_MONETARY=English_United States.1252
## [4] LC_NUMERIC=C
## [5] LC_TIME=English_United States.1252
##
## attached base packages:
## [1] stats4    parallel  stats     graphics  grDevices utils     datasets
## [8] methods   base
##
## other attached packages:
##  [1] igraph_1.3.5        dplyr_1.1.2         GSEABase_1.56.0
##  [4] graph_1.72.0        annotate_1.72.0     XML_3.99-0.13
##  [7] AnnotationDbi_1.56.2 IRanges_2.28.0     S4Vectors_0.32.4
## [10] Biobase_2.54.0      BiocGenerics_0.40.0 doParallel_1.0.17
## [13] iterators_1.0.14    foreach_1.5.2       gridExtra_2.3
## [16] ggraph_2.1.0        ggplot2_3.4.2       SeuratObject_4.1.3
## [19] Seurat_4.3.0        CSCORE_0.0.0.9000   BiocStyle_2.22.0
##
## loaded via a namespace (and not attached):
##   [1] plyr_1.8.8          lazyeval_0.2.2      sp_1.6-0
##   [4] splines_4.1.2       listenv_0.9.0       scattermore_0.8
##   [7] GenomeInfoDb_1.30.1 digest_0.6.31       htmltools_0.5.4
##  [10] magick_2.7.3        viridis_0.6.2       fansi_1.0.4
##  [13] memoise_2.0.1       magrittr_2.0.3      tensor_1.5
##  [16] cluster_2.1.4       ROCR_1.0-11         Biostrings_2.62.0
##  [19] globals_0.16.2      graphlayouts_0.8.4  matrixStats_0.63.0
##  [22] spatstat.sparse_3.0-0 colorspace_2.1-0  blob_1.2.3
##  [25] ggrepel_0.9.3       xfun_0.36           RCurl_1.98-1.9
##  [28] crayon_1.5.2        jsonlite_1.8.4      progressr_0.13.0
##  [31] spatstat.data_3.0-0 survival_3.5-0      zoo_1.8-11
##  [34] glue_1.6.2          polyclip_1.10-4     gtable_0.3.1
##  [37] zlibbioc_1.40.0     XVector_0.34.0      leiden_0.4.3
##  [40] future.apply_1.10.0 abind_1.4-5         scales_1.2.1
##  [43] DBI_1.1.3           spatstat.random_3.1-3 miniUI_0.1.1.1
##  [46] Rcpp_1.0.10         viridisLite_0.4.1   xtable_1.8-4
```

```
##  [49] reticulate_1.28       bit_4.0.5              htmlwidgets_1.6.1
##  [52] httr_1.4.5            RColorBrewer_1.1-3    ellipsis_0.3.2
##  [55] ica_1.0-3             pkgconfig_2.0.3       farver_2.1.1
##  [58] sass_0.4.5            uwot_0.1.14           deldir_1.0-6
##  [61] utf8_1.2.2            labeling_0.4.2        tidyselect_1.2.0
##  [64] rlang_1.1.0           reshape2_1.4.4        later_1.3.0
##  [67] munsell_0.5.0         tools_4.1.2           cachem_1.0.6
##  [70] cli_3.6.0             RSQLite_2.2.20        generics_0.1.3
##  [73] ggridges_0.5.4        evaluate_0.20         stringr_1.5.0
##  [76] fastmap_1.1.0         yaml_2.3.7            goftest_1.2-3
##  [79] bit64_4.0.5           knitr_1.42            fitdistrplus_1.1-8
##  [82] tidygraph_1.2.3       purrr_1.0.1           RANN_2.6.1
##  [85] KEGGREST_1.34.0       pbapply_1.7-0         future_1.30.0
##  [88] nlme_3.1-161          mime_0.12             compiler_4.1.2
##  [91] rstudioapi_0.14       plotly_4.10.1         png_0.1-8
##  [94] spatstat.utils_3.0-1  tibble_3.2.1          tweenr_2.0.2
##  [97] bslib_0.4.2           stringi_1.7.12        highr_0.10
## [100] lattice_0.20-45       Matrix_1.5-3          vctrs_0.6.1
## [103] pillar_1.9.0          lifecycle_1.0.3       BiocManager_1.30.19
## [106] spatstat.geom_3.0-6   lmtest_0.9-40         jquerylib_0.1.4
## [109] RcppAnnoy_0.0.20      bitops_1.0-7          data.table_1.14.6
## [112] cowplot_1.1.1         irlba_2.3.5.1         httpuv_1.6.8
## [115] patchwork_1.1.2       R6_2.5.1              bookdown_0.33
## [118] promises_1.2.0.1      KernSmooth_2.23-20    parallelly_1.34.0
## [121] codetools_0.2-18      MASS_7.3-58.2         withr_2.5.0
## [124] sctransform_0.3.5     GenomeInfoDbData_1.2.7 grid_4.1.2
## [127] tidyr_1.3.0           rmarkdown_2.20        Rtsne_0.16
## [130] spatstat.explore_3.0-6 ggforce_0.4.1         shiny_1.7.4
```