Differential network analysis (rewiring) between HTN and T2DM

Loranda_Calderon

2024-10-11

```
# Load required libraries
library(DGCA)
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```

```
library(WGCNA)
```

```
## Loading required package: dynamicTreeCut

## Loading required package: fastcluster

##
## Attaching package: 'fastcluster'

## The following object is masked from 'package:stats':
##
##     hclust

##
## Attaching package: 'WGCNA'

## The following object is masked from 'package:stats':
##
##     cor
```

```
library(dplyr)
```

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##
## Attaching package: 'dplyr'

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

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

```r
library(tidyr)
library(readr)
library(tibble)
library(clusterProfiler)
```

```
## clusterProfiler v4.13.0  For help: https://yulab-smu.top/biomedical-knowledge-mining-book/
##
## If you use clusterProfiler in published research, please cite:
## T Wu, E Hu, S Xu, M Chen, P Guo, Z Dai, T Feng, L Zhou, W Tang, L Zhan, X Fu, S Liu, X Bo, and G Yu.

##
## Attaching package: 'clusterProfiler'

## The following object is masked from 'package:stats':
##
##     filter
```

```r
library(org.Hs.eg.db)
```

```
## Loading required package: AnnotationDbi

## Loading required package: stats4

## Loading required package: BiocGenerics

##
## Attaching package: 'BiocGenerics'

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

## The following objects are masked from 'package:stats':
##
##     IQR, mad, sd, var, xtabs

## The following objects are masked from 'package:base':
##
##     anyDuplicated, aperm, append, as.data.frame, basename, cbind,
##     colnames, dirname, do.call, duplicated, eval, evalq, Filter, Find,
##     get, grep, grepl, intersect, is.unsorted, lapply, Map, mapply,
##     match, mget, order, paste, pmax, pmax.int, pmin, pmin.int,
##     Position, rank, rbind, Reduce, rownames, sapply, setdiff, sort,
##     table, tapply, union, unique, unsplit, which.max, which.min

## Loading required package: Biobase

## Welcome to Bioconductor
##
##     Vignettes contain introductory material; view with
##     'browseVignettes()'. To cite Bioconductor, see
##     'citation("Biobase")', and for packages 'citation("pkgname")'.
```

```
## Loading required package: IRanges

## Loading required package: S4Vectors

##
## Attaching package: 'S4Vectors'

## The following object is masked from 'package:clusterProfiler':
##
##     rename

## The following object is masked from 'package:tidyr':
##
##     expand

## The following objects are masked from 'package:dplyr':
##
##     first, rename

## The following object is masked from 'package:utils':
##
##     findMatches

## The following objects are masked from 'package:base':
##
##     expand.grid, I, unname

##
## Attaching package: 'IRanges'

## The following object is masked from 'package:clusterProfiler':
##
##     slice

## The following objects are masked from 'package:dplyr':
##
##     collapse, desc, slice

##
## Attaching package: 'AnnotationDbi'

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

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

##
```

```r
# Read in data
expr_htn <- read.csv(
  "/Users/lorandacalderonzamora/Downloads/Rewiring/datExpr_integrative_HTN.csv",
  row.names = 1,
  check.names = FALSE,
  stringsAsFactors = FALSE
)

expr_t2dm <- read.csv(
  "/Users/lorandacalderonzamora/Downloads/Rewiring/datExpr_integrative_T2DM.csv",
  row.names = 1,
  check.names = FALSE,
  stringsAsFactors = FALSE
)

rownames(expr_htn)  <- sub("\\.[0-9]+$", "", rownames(expr_htn))
rownames(expr_t2dm) <- sub("\\.[0-9]+$", "", rownames(expr_t2dm))

metadata  <- read.csv("/Users/lorandacalderonzamora/Downloads/Rewiring/datMeta_merge_T2DM_HTN.csv", row
annotation <- read.csv("/Users/lorandacalderonzamora/Downloads/Rewiring/annotation.csv", row.names = NU
```

```r
# align genes
common_genes <- intersect(rownames(expr_htn), rownames(expr_t2dm))
expr_htn  <- data.matrix(expr_htn)
expr_t2dm <- data.matrix(expr_t2dm)
expr_htn   <- expr_htn[common_genes, ]
expr_t2dm <- expr_t2dm[common_genes, ]
```

```r
# Compute gene-gene correlations
corr_htn  <- cor(t(expr_htn))
corr_t2dm <- cor(t(expr_t2dm))
delta_corr <- corr_t2dm - corr_htn
```

```r
# Match genes across datasets
common_genes <- intersect(rownames(expr_htn), rownames(expr_t2dm))
expr_htn <- expr_htn[common_genes, ]
expr_t2dm <- expr_t2dm[common_genes, ]
```

```r
 #Combine into a single DGCA object
# Bind expression, create design matrix for DGCA
expr_combined <- cbind(expr_htn, expr_t2dm)
group <- c(rep("HTN", ncol(expr_htn)), rep("T2DM", ncol(expr_t2dm)))
# Build design data.frame
colData <- data.frame(Sample = colnames(expr_combined), Condition = group)
```

```r
# Load your differential expression results for T2DM
de_t2dm <- read_csv("/Users/lorandacalderonzamora/Downloads/Rewiring/DE_integrative_T2DM.csv", show_col
```

```
## New names:
## * `` -> `...1`
```

```r
# 2) Filter for significant genes
sig_t2dm <- de_t2dm %>%
  dplyr::filter(adj.P.Val < 0.05, abs(logFC) > 1) %>%
  dplyr::pull(ensembl_gene_id)

sig_genes <- sig_t2dm

length(sig_genes)
```

```
## [1] 603
```

```r
# Remove version suffixes from the row names of your expression matrices
rownames(expr_htn)  <- sub("\\.[0-9]+$", "", rownames(expr_htn))
rownames(expr_t2dm) <- sub("\\.[0-9]+$", "", rownames(expr_t2dm))

# Clean the DE gene IDs of any version suffix
sig_t2dm_clean <- sub("\\.[0-9]+$", "", sig_t2dm)

# Find the intersection between your HTN genes and the cleaned DE list
common_sig <- intersect(rownames(expr_htn), sig_t2dm_clean)
length(common_sig)  # should be > 0
```

```
## [1] 576
```

```r
expr_htn  <- expr_htn[common_sig, , drop = FALSE]
expr_t2dm <- expr_t2dm[common_sig, , drop = FALSE]


dim(expr_htn)
```

```
## [1] 576  25
```

```r
dim(expr_t2dm)
```

```
## [1] 576  33
```

```r
# Define the sample grouping vector
groupVec <- c(rep("HTN",  ncol(expr_htn)),
              rep("T2DM", ncol(expr_t2dm)))
design   <- makeDesign(groupVec)

# Combine the two expression matrices
expr_combined <- cbind(expr_htn, expr_t2dm)

# 3) Run differential correlation analysis with DGCA
ddcResults <- ddcorAll(
  inputMat    = expr_combined,
  design      = design,
  compare     = c("HTN", "T2DM"),
  adjust      = "perm",
```

```
  nPerms      = 500,
  corrType    = "pearson",
  heatmapPlot = FALSE
)
```

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## Calculating permutation number 500.
## Calculating empirical p-values using the permutation sample statistics.
## Sorting the combination of the actual and permuted test statistics.
## Finding the proportion of each actual test statistic greater than the permuted test statistics.
## Calculating qvalues from the empirical p-values.
## Classifying the differential correlation calls.
```

```r
# Calculate the differential correlation (dCor) for each gene pair
ddcResults <- ddcResults %>%
  mutate(dCor = T2DM_cor - HTN_cor)

# 2) Filter for significant rewiring edges
sigEdges <- ddcResults %>%
  mutate(dCor = T2DM_cor - HTN_cor) %>%
  filter(pValDiff_adj < 0.05, abs(dCor) > 0.3) %>%
  as_tibble()

#
nodes <- sigEdges %>%
  pivot_longer(
    cols      = c(Gene1, Gene2),
    names_to  = "end",
    values_to = "gene"
  ) %>%
  group_by(gene) %>%
  summarise(
    score_mag  = sum(abs(dCor)),
    score_dir   = sum(dCor),
    degree = n(),
    .groups = "drop"
  )

nrow(nodes)
```

```
## [1] 576
```