

# Package ‘DRviaSPCN’

December 8, 2021

**Type** Package

**Title** Drug Repurposing in Cancer via a Subpathway Crosstalk Network

**Version** 0.1.0

**Maintainer** Junwei Han <hanjunwei1981@163.com>

**Description** A systematic biology tool was developed to repurpose drugs via a subpathway crosstalk network. The operation modes include 1) evaluating the eigenvector centrality (centrality score) of subpathways and identifying dysregulated subpathways in the subpathway-subpathway network, 2) evaluating the activity of subpathways by GSEA and weighting them with corresponding centrality score, 3) identifying optimal drugs for specific disease through constructing disease-drug reverse association based on the weighted activity of subpathways. There are also several functions used to visualize the results.

**License** GPL (>= 2)

**Encoding** UTF-8

**LazyData** true

**RoxygenNote** 7.1.1

**Imports** ChemmineR,  
GSVA,  
clusterProfiler,  
graphics,  
igraph,  
pheatmap,  
rvest,  
xml2,  
stats

**Depends** R (>= 3.6)

**Suggests** rmarkdown,  
knitr

**VignetteBuilder** knitr

## R topics documented:

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DRviaSPCN-package	<i>The DRviaSPCN package</i>
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## Description

DRviaSPCN is a R package for repurposing drugs via subpathway crosstalk network.

## Details

### DRviaSPCN

The main goals of the DRviaSPCN package is to provide main functions and some data.

The main functions includes: 1) DE2SubPath 2) getSubpathscore 3) optimaldrugs and four visualization functions: 1) plotSPW 2) getMolecularFM 3) Disease2SPWheatmap 4) Drug2SPWheatmap.

For more details, please see browseVignettes("DRviaSPCN")

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DE2SubPath	<i>Calculating eigenvector centrality of subpathways</i>
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## Description

The function "DE2SubPath" is used to calculate the eigenvector centrality of subpathways. According to our method, in this function, the user needs to input 6 variables. All six variables can obtain from our example data, those data from KEGG and GO, and the user can also change at will.

## Usage

```
DE2SubPath(inexpData,Label,Subpathway,Go,Jaccard,Go_SubPath_gene,perm=FALSE,nperm=1000)
```

## Arguments

inexpData	A gene expression profile of interest (rows are genes, columns are samples).The data in the expression profile is best not be log2 converted.
Label	A character vector consist of "0" and "1" which represent sample class in gene expression profile. "0" means normal sample and "1" means disease sample.
Subpathway	Subpathway information from SubpathwayMiner.
Go	Biological Process data from Gene Ontology.
Jaccard	Jaccard score shared by a subpathway with Biological Process.
Go_SubPath_gene	Genes symble shared by a subpathway with Biological Process.
perm	A boolean value. If perm=TRUE, the permutations will be implemented.
nperm	Number of random permutations (default: 1000).

**Value**

A dataframe with seven columns those are subpath ID, subpath name, subpath size, genes in subpath, centralscore (eigenvector centrality), Pvalue and FDR.

**Examples**

```
library(igraph)
#Obtain input data
GEP<-GetExample('GEP')
label<-GetExample('label')
SubPathwayInfo<-GetExample('SubPathwayInfo')
GoInfo<-GetExample('GoInfo')
Jaccardscore<-GetExample('Jaccardscore')
GoSubPconGene<-GetExample('GoSubPconGene')
#Run the function
DE2SubPathresult<-DE2SubPath(inexpData=GEP,Label=label,Subpathway=SubPathwayInfo,
                             Go=GoInfo,Jaccard=Jaccardscore,Go_SubPath_gene=GoSubPconGene,
                             perm=FALSE)

DE2SubPathresult_P<-DE2SubPath(inexpData=GEP,Label=label,Subpathway=SubPathwayInfo,
                              Go=GoInfo,Jaccard=Jaccardscore,Go_SubPath_gene=GoSubPconGene,
                              perm=TRUE)
```

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Disease2SPWheatmap	<i>Plot a heat map of the subpathways activity regulated by disease</i>
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**Description**

The "Disease2SPWheatmap" function plots a heat map of the subpathways that are regulated by disease.

**Usage**

```
Disease2SPWheatmap(
  DE2SubPathresult,
  exp,
  Label,
  pcut = 0.05,
  bk = c(-2, 2),
  cluster.rows = FALSE,
  cluster.cols = FALSE,
  show.rownames = TRUE,
  show.colnames = FALSE,
  col = c("navy", "firebrick3"),
  cell.width = NA,
  cell.height = NA,
  scale = "row",
  fontsize = 7,
  fontsize.row = 9,
  fontsize.col = 10
)
```

**Arguments**

DE2SubPathresult	A dataframe with seven columns those are subpath ID, subpath name, subpath size, genes in subpath, centralscore (eigenvector centrality), Pvalue and FDR.
exp	A gene expression profile of interest.
Label	A character vector consist of "0" and "1" which represent sample class in gene expression profile. "0" means normal sample and "1" means disease sample.
pcut	A numeric value which represent threshold. Subpathways with p-value less than this threshold will be screened out and visualized.
bk	A numeric vector that covers the range of values. Users could adjust color depth through this parameter.
cluster.rows	Boolean values determining if rows should be clustered or hclust object.
cluster.cols	Boolean values determining if columns should be clustered or hclust object.
show.rownames	Boolean specifying if row names are be shown.
show.colnames	Boolean specifying if column names are be shown.
col	Vector of colors used in heatmap.
cell.width	Individual cell width in points. If left as NA, then the values depend on the size of plotting window.
cell.height	Individual cell height in points. If left as NA, then the values depend on the size of plotting window.
scale	Character indicating if the values should be centered and scaled in either the row direction or the column direction, or none. Corresponding values are "row", "column" and "none".
fontsize	Base fontsize for the plot (default: 10).
fontsize.row	Fontsize for rownames (default: 10).
fontsize.col	Fontsize for colnames (default: 10).

**Value**

A heat map

**Examples**

```
#Load depend package
library(GSVA)
library(pheatmap)
#Obtain input data (The "DE2SubPathresult_P" is the result of function "DE2SubPath")
GEP<-GetExample('GEP')
label<-GetExample('label')
DE2SubPathresult_P<-GetExample('DE2SubPathresult_P')
#Run the function
Disease2SPWheatmap(DE2SubPathresult_P,exp=GEP,Label=label,pcut=0.05,bk=c(-2,2),
  cluster.rows=FALSE,cluster.cols=FALSE,show.rownames=TRUE,
  show.colnames=FALSE,col=c("navy","firebrick3"),
  cell.width=NA,cell.height=NA,scale="row",fontsize=7,
  fontsize.row=9,fontsize.col=10)
```

Drug2SPWheatmap

*Plot a heat map of the subpathways activity regulated by drugs***Description**

The "Drug2SPWheatmap" function plots a heat map of the subpathways that are regulated by a specific drug.

**Usage**

```
Drug2SPWheatmap(drugname="", Drug_Pvalue_matrix, exp, Label, pcut=0.05,
                bk=c(-2,2), cluster.rows=FALSE, cluster.cols=FALSE, show.rownames=TRUE,
                show.colnames=FALSE, col=c("navy", "firebrick3"),
                cell.width=NA, cell.height=NA, scale="row", fontsize=7,
                fontsize.row=9, fontsize.col=10)
```

**Arguments**

drugname	A character which represent interest drug name.
Drug_Pvalue_matrix	A matrix which columns represent drugs and rows represent subpathways. Values in this matrix is the pvalue of subpathways centrality score regulated by drugs.
exp	A gene expression profile of interest.
Label	A character vector consist of "0" and "1" which represent sample class in gene expression profile. "0" means normal sample and "1" means disease sample.
pcut	A numeric value which represent threshold. Subpathways with p-value less than this threshold will be screened out and visualized.
bk	A numeric vector that covers the range of values. Users could adjust color depth through this parameter.
cluster.rows	Boolean values determining if rows should be clustered or hclust object.
cluster.cols	Boolean values determining if columns should be clustered or hclust object.
show.rownames	Boolean specifying if row names are be shown.
show.colnames	Boolean specifying if column names are be shown.
col	Vector of colors used in heatmap.
cell.width	Individual cell width in points. If left as NA, then the values depend on the size of plotting window.
cell.height	Individual cell height in points. If left as NA, then the values depend on the size of plotting window.
scale	Character indicating if the values should be centered and scaled in either the row direction or the column direction, or none. Corresponding values are "row", "column" and "none".
fontsize	Base fontsize for the plot (default: 10).
fontsize.row	Fontsize for rownames (default: 10).
fontsize.col	Fontsize for colnames (default: 10).

## Value

A list where the elements are heat maps of drugs acting on different cell lines,duration and concentrations.

## Examples

```
#Load depend package
library(GSVA)
library(pheatmap)
##Obtain input data
#Statistic significance of subpathways centrality score
#this function need were stored in packet "DRviaSPCNDData".
#"DRviaSPCNDData" has been uploaded to the github repository.
#Users can download and install through "install_github" function and
#set parameter url="hanjunwei-lab/DRviaSPCNDData".
#After installing and loading package "DRviaSPCNDData",
#users can use the following command to get the data:
#DrugPvalueMatrix<-Getlist('DrugPvalueMatrix')
GEP<-GetExample('GEP')
label<-GetExample('label')

#Run the function
heatmap.list<-Drug2SPWheatmap(drugname = "methotrexate",
                             Drug_Pvalue_matrix=DrugPvalueMatrix,
                             exp=GEP,Label=label,pcut=0.05,bk=c(-2,2),
                             cluster.rows=FALSE,cluster.cols=FALSE,show.rownames=TRUE,
                             show.colnames=FALSE,col=c("navy","firebrick3"),
                             cell.width=NA,cell.height=NA,scale="row",fontsize=7,
                             fontsize.row=9,fontsize.col=10)

#view the result
heatmap.list[[1]]
dev.off()
heatmap.list[[2]]
dev.off()
heatmap.list[[3]]
dev.off()
```

---

envData

*An environment variable which includes some example data*


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## Description

An environment variable which includes some example data. DE2SubPathresult: The result of function "DE2SubPath" with "perm = FALSE". DE2SubPathresult\_P: The result of function "DE2SubPath" with "perm = TRUE". Drugs\_CID: PubCham Database ID of drugs. GEP: An example gene expression profile. GOInfo: Biological Process data from Gene Ontology. GoSubPconGene: Genes symble shared by a subpathway with Biological Process. heatmap.list: The result of function "Drug2SPWheatmap". Jaccardscore: Jaccard score shared by a subpathway with Biological Process. label: A character vector consist of "0" and "1" which represent sample class in gene expression profile. Opdrugresult: The result of function "optimaldrugs". SubPathwayInfo: Subpathway information from SubpathwayMiner. SubPathwaymapdata: Subpathway structure data.

**Usage**

```
envData
```

**Format**

An environment variable

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getDEscore	<i>Calculating Log2 Fold Change of genes</i>
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**Description**

Function "getDEscore" uses gene expression profile to calculate Log2 Fold Change of genes.

**Usage**

```
getDEscore(inexpData, Label)
```

**Arguments**

inexpData	A gene expression profile of interest (rows are genes, columns are samples).The data in the expression profile is best not be log2 converted.
Label	A character vector consist of "0" and "1" which represent sample class in gene expression profile. "0" means normal sample and "1" means disease sample.

**Value**

A one-column matrix of Log2 Fold Change which rownames is gene.

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GetExample	<i>Get example data</i>
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**Description**

This function is used to achieve exxample data.

**Usage**

```
GetExample(exampleData)
```

**Arguments**

exampleData	A character, should be one of"GEP", "label", "SubPathwayInfo", "GoInfo", "GoSubPconGene", "Jaccardscore", "SubPathwaymapdata", "Drugs_CID", "DE2SubPathresult", "DE2SubPathresult_P", "Opdrugresult" and "heatmap.list".
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**Value**

example data

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getMolecularFm	<i>Plot chemical molecular formula of drugs</i>
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### Description

The function "getMolecularFm" outputs the chemical molecular formula of a drug or compound . The results can be visualized by the "plot" function.

### Usage

```
getMolecularFm(drugname = "", main = "", sub = "")
```

### Arguments

drugname	A character string of drug name.
main	An overall title for the chemical structure graph.
sub	A sub title for the chemical structure graph.

### Value

Chemical molecular formula of the drug or compound.

### Examples

```
##Load depend package
library(ChemmineR)
library(rvest)
# Obtain molecular formula and visualize it.
Mole_formula<-getMolecularFm(drugname ="methotrexate")
plot(Mole_formula)
```

---

getSubpathscore	<i>Calculating weighted enrichmentscore of subpathways</i>
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### Description

Function "getSubpathscore" used to calculate enrichmentscore weighted by centrality score of sub-pathways.

### Usage

```
getSubpathscore(DE2SubPathresult, inexpData, Label)
```

**Arguments**

DE2SubPathresult	A dataframe with seven columns those are subpath ID, subpath name, subpath size, genes in subpath, centralscore (eigenvector centrality), Pvalue and FDR (The result of function "DE2SubPath").
inexpData	A gene expression profile of interest (rows are genes, columns are samples).The data in the expression profile is best not be log2 converted.
Label	A character vector consist of "0" and "1" which represent sample class in gene expression profile. "0" means normal sample and "1" means disease sample.

**Value**

A dataframe with three columns which are "SubPathID", "Weighted-ES", "Pvalue".

**Examples**

```
#Load depend package
library(clusterProfiler)
#Get input data (The "DE2SubPathresult" is the result of function "DE2SubPath")
DE2SubPathresult<-GetExample('DE2SubPathresult')
GEP<-GetExample('GEP')
label<-GetExample('label')
#Run the function
SubPathscore<-getSubpathscore(DE2SubPathresult=DE2SubPathresult,inexpData=GEP,Label=label)
```

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optimaldrugs	<i>Identifying the optimal drugs</i>
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**Description**

Function "optimaldrugs" used to identify the optimal drugs for specific disease.

**Usage**

```
optimaldrugs(SubPathscore,Drug_Pscore_matrix,nperm=1000,cut='top',
             topcut=20,pcut=0.05,weight=FALSE)
```

**Arguments**

SubPathscore	A dataframe with three columns which are "SubPathID", "Weighted-ES", "Pvalue" (The result of function "getSubPathscore").
Drug_Pscore_matrix	A matrix with n rows and m columns. n is the number of subpathways and m is the number of all drugs. The values in this matrix is weighted enrichmentscore of subpathways in every drug. The users could obtain this matrix from our example data.
nperm	Number of random permutations (default: 1000).
cut	There are two ways to select up-regulated and down-regulated subpathways. The up-regulated subpathways (down-regulated subpathways) is the top (bottom) subpathways of list in descending order of weighted enrichmentscore (weighted-ES) when cut="top". When cut="p", up-regulated subpathways and down-regulated subpathways is screened based on ES and pvalue in the results of GSEA.

topcut	When cut="top", topcut represents the number of selected up-regulated subpathways or down-regulated subpathways. The topcut defaults to 20.
pcut	When cut="p", pcut represents the threshold of statistical significance level for screen subpathways. The pcut defaults to 0.05.
weight	A boolean value determines the method for calculating the drug-disease association score of the drug. "weight=FALSE"(default): Similar to "CMap" (Lamb et al., 2006), no weight is needed. "weight=TRUE": KS random walk statistic with individualized subpathway activity score as weight was used to calculate the drug-disease reverse association score.

### Value

A dataframe with four columns which are "Drug"(drug names),"KS"(final drug-disease association score),"pvalue"(statistical significance),"FDR"(statistical significance after adjust).

### Examples

```
##Obtain input data
#Weighted enrichment score of subpathways this function need were stored
#in packet "DRviaSPCNDData". "DRviaSPCNDData" has been uploaded to the
#github repository. Users can download and install through "install_github"
#function and set parameter url="hanjunwei-lab/DRviaSPCNDData".
#After installing and loading package "DRviaSPCNDData",
#users can use the following command to get the data.
#DrugPscoreMatrix<-Getlist('DrugPscoreMatrix')
DE2SubPathresult<-GetExample("DE2SubPathresult")
GEP<-GetExample("GEP")
label<-GetExample("label")

SubPathscore<-getSubpathscore(DE2SubPathresult=DE2SubPathresult, inexpData=GEP, Label=label)
#Run the function
Opdrugresult<-optimaldrugs(SubPathscore=SubPathscore, Drug_Pscore_matrix=DrugPscoreMatrix,
                           nperm=1000, cut='p', topcut=20, pcut=0.01, weight=FALSE)
```

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PackageLoaded

*PackageLoaded*

---

### Description

Determine if the package is loaded, if no package is loaded.

### Usage

```
PackageLoaded(name)
```

### Arguments

name                      A character which is the name of package.

### Value

A boolean value.

plotSPW

*Plot subpathway network graph***Description**

The function plotSPW can visualize subpathway network graph.

**Usage**

```
plotSPW(
  subpathwayID,
  layout = NULL,
  margin = 0,
  vertex.label.cex = 0.8,
  vertex.label.font = 0.8,
  vertex.label.dist = 1,
  vertex.size = 12,
  edge.arrow.width = 3,
  edge.label.cex = 0.6,
  vertex.label.color = "black",
  vertex.color = "#F08080",
  vertex.frame.color = "dimgray",
  edge.color = "grey70",
  edge.label.color = "dimgray",
  sub = NULL,
  main = NULL
)
```

**Arguments**

subpathwayID	Subpathway id .A character vector.
layout	A matrix of x-y coordinates with two dims. Determine the placement of the nodes for drawing a graph.
margin	A numeric. The value is usually between -0.5 and 0.5, which is able to zoom in or out a subpathway graph. The default is 0.
vertex.label.cex	A numeric vector of node label size.
vertex.label.font	A numeric vector of label font.
vertex.label.dist	A numeric vector of label dist.
vertex.size	A numeric vector of Node size. See plot.igraph.
edge.arrow.width	Edge arrow width. The default is 3.
edge.label.cex	Edge label size.
vertex.label.color	A vector of node label colors. The default is black.
vertex.color	A vector of node colors. The default is the KEGG node color.

<code>vertex.frame.color</code>	A vector of node frame color. The default is <code>dimgray</code> .
<code>edge.color</code>	A vector of edge color. The default is <code>dimgray</code> .
<code>edge.label.color</code>	A vector of edge label color. The default is <code>dimgray</code> .
<code>sub</code>	A character string of subtitle.
<code>main</code>	A character string of main title.

**Value**

a subpathway map

**Examples**

```
# load depend package
library(igraph)
# plot network graph of the subpathway "00020_4"
plotSPW("00020_4")
```

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