# Package 'DRviaSPCN'

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**Type** Package

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

**Version** 0.1.2

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**Description** A systematic biology tool was developed to repurpose drugs via a subpathway crosstalk network. The operation modes include 1) calculating centrality scores of SPs in the context of gene expression data to reflect the influence of SP crosstalk, 2) evaluating drug-disease reverse association based on disease- and drug-induced SPs weighted by the SP crosstalk, 3) identifying cancer candidate drugs through perturbation analysis. 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,
DT

**VignetteBuilder** knitr

## R topics documented:

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DRviaSPCN-package      *The DRviaSPCN package*

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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) CalCentralityScore 2) Optimaldrugs and four visualization functions: 1) plotSPW 2) getMolecularFM 3) Disease2SPheatmap 4) Drug2SPheatmap.

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

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CalCentralityScore      *Calculating eigenvector centrality of subpathways*

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#### Description

The function "CalCentralityScore" is used to calculate the eigenvector centrality of subpathways.

#### Usage

```
CalCentralityScore(ExpData,Label,nperm=1000)
```

#### Arguments

ExpData     A gene expression profile of interest (rows are genes, columns are samples).

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.

nperm       Number of random permutations (default: 1000).

#### Value

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

## Examples

```
library(igraph)
#Obtain input data
GEP<-GetExample('GEP')
Slabel<-GetExample('Slabel')
#Run the function
#CentralityScoreResult<-CalCentralityScore(ExpData=GEP,Label=Slabel,nperm=1000)
```

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Disease2SPheatmap     *Plot a heat map of the subpathways activity regulated by disease*

---

## Description

The "Disease2SPheatmap" function plots a heat map of the subpathways that are regulated by disease. We map subpathways to the disease gene expression through ssgsea to get a subpathway abundance matrix. Then we visualize the matrix by heatmap.

## Usage

```
Disease2SPheatmap(CentralityScore,ExpData,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

CentralityScore

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

| | |
|---|---|
| ExpData | 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 "CentralityScoreResult" is the result of function "CalCentralityScore")
GEP<-GetExample('GEP')
Slabel<-GetExample('Slabel')
CentralityScoreResult<-GetExample('CentralityScoreResult')
#Run the function
#Disease2SPheatmap(CentralityScore=CentralityScoreResult,ExpData=GEP,Label=Slabel,
#                  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)
```

---

Drug2SPheatmap    *Plot a heat map of the subpathways activity regulated by drugs*

---

## Description

The function "Drug2SPheatmap" plots heatmaps of the subpathways that are regulated by drugs. We map subpathways to the disease gene expression through ssgsea to get a subpathway abundance matrix. Then we visualize the matrix by heatmap.

## Usage

```
Drug2SPheatmap(drugname="",DrugSPPvalue,ExpData,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 with specific concentration, cell line and duration. |
|---|---|
| DrugSPPvalue | A matrix which colunms represent drugs and rows respresent subpathways. Values in this matrix is the pvalue of subpathways centrality score regulated by drugs. |

| | |
|---|---|
| ExpData | 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
#Statistic significance of centrality score of subpathways
#induced by each drug were stored in package "DRviaSPCNData".
#"DRviaSPCNData" has been uploaded to the github repository.
#Users can download and install through "install_github" function and
#set parameter url="hanjunwei-lab/DRviaSPCNData".
#After installing and loading package "DRviaSPCNData",
#users can use the following command to get the data:
#DrugSPPvalueMatrix<-GetData('DrugSPPvalueMatrix')
GEP<-GetExample('GEP')
Slabel<-GetExample('Slabel')

#Run the function
#Drug2SPheatmap(drugname = "methotrexate_HL60_6_8.8e-06",
#               DrugSPPvalue=DrugSPPvalueMatrix,
#               ExpData=GEP,Label=Slabel,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)
```

---

envData | *An environment variable which includes some example data*

---

## Description

An environment variable which includes some example data. CentralityScoreResult: The result of function "CalCentralityScore". 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 pair of subpathways with Biological Process. Jaccardscore: Jaccard score shared by a pair of subpathways with Biological Process. Slabel: 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 | *Calculating Log2 Fold Change of genes*

---

## 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.

---

GetExample                    *Get example data*

---

### Description

This function is used to achieve exxample data.

### Usage

```
GetExample(exampleData)
```

### Arguments

exampleData     A character, should be one of"GEP","Slabel", "CentralityScoreResult" and "Op-
                drugresult".

### Value

example data

---

getMolecularFm              *Plot chemical molecular formula of drugs*

---

### 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)
```

---

`Optimaldrugs`                              *Identifying the optimal drugs*

---

**Description**

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

**Usage**

```
Optimaldrugs(ExpData,Label,DrugSPESC,CentralityScore,nperm=1000,
                topcut=10,pcut=0.01,weight=FALSE)
```

**Arguments**

| | |
|---|---|
| ExpData | A gene expression profile of interest (rows are genes, columns are samples). |
| 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. |
| DrugSPESC | 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 induced by each drug. The users could obtain this matrix from our example data. |
| CentralityScore | |
| | The result of function "CalCentralityScore". |
| nperm | Number of random permutations (default: 1000). |
| topcut | The parameter "topcut" represents the number of selected SPs from the top or bottom of the ranked SP list. The topcut defaults to 10. |
| pcut | The parameter "pcut" represents the threshold of statistical significance for screen SPs. The pcut defaults to 0.01. |
| 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),"DES"(drug enrichment score),"p-value"(statistical significance),"FDR"(adjusted statistical significance).

**Examples**

```
##Obtain input data
#Weighted enrichmentscore of subpathways induced by each drug were stored
#in package "DRviaSPCNData". "DRviaSPCNData" has been uploaded to the
#github repository.Users can download and install through "install_github"
#function and set parameter url="hanjunwei-lab/DRviaSPCNData".
#After installing and loading package "DRviaSPCNData",
#users can use the following command to get the data.
#DrugSPESCMatrix<-GetData('DrugSPESCMatrix')
CentralityScoreResult<-GetExample("CentralityScoreResult")
```

```
GEP<-GetExample("GEP")
Slabel<-GetExample("Slabel")
#Run the function
#Opdrugresult<-Optimaldrugs(ExpData=GEP,Label=Slabel,DrugSPESC=DrugSPESCMatrix,
#CentralityScore=CentralityScoreResult,nperm=1000,topcut=10,pcut=0.01,weight=FALSE)
```

---

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. |
| `vertex.frame.color` | |
| | A vector of node frame color. The default is dimgray. |
| `edge.color` | A vector of edge color. The default is dimgray |
| `edge.label.color` | |
| | A vector of edge label color. The default is dimgray. |
| `sub` | A character string of subtitle. |
| `main` | 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")
```

# Index