Package 'SubtypeDrug'

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Type Package

Title Prioritization of Candidate Cancer Subtype Specific Drugs

Version 0.1.9

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Description A systematic biology tool was developed to prioritize cancer subtype-specific drugs by integrating genetic perturbation, drug action, biological pathway, and cancer subtype. The capabilities of this tool include inferring patient-specific subpathway activity profiles in the context of gene expression profiles with subtype labels, calculating differentially expressed subpathways based on cultured human cells treated with drugs in the 'cMap' (connectivity map) database, prioritizing cancer subtype specific drugs according to drug-disease reverse association score based on subpathway, and visualization of results (Castelo (2013) <doi:10.1186/1471-2105-14-7>; Han et al (2019) <doi:10.1093/bioinformatics/btz894>; Lamb and Justin (2006) <doi:10.1126/science.1132939>). Pleasing <doi:10.1093/bioinformatics/btab011>.

License GPL (>= 2)

Depends R (>= 2.10)

Encoding UTF-8

LazyData true

BugReports https://github.com/hanjunwei-lab/SubtypeDrug/issues

RoxygenNote 7.3.0

Imports
BiocGenerics,GSVA,grDevices,graphics,igraph,parallel,pheatmap,rvest,stats,xml2,ChemmineR

Suggests knitr, rmarkdown, testthat (>= 3.0.0)

VignetteBuilder knitr

NeedsCompilation no

Repository CRAN

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R topics documented:

`AccumulateNormal` *SubtypeDrug internal function*

Description

Infering patient-specific subpathway activity profiles.

Usage

```
AccumulateNormal(x_matrix, control_index)
```

Arguments

`x_matrix`	A subpathway activity profile. rows are subpathwyas, columns are samples.
`control_index`	A vector. In the sample of the subpathway activity profile, the position of control samples.

Details

AccumulateNormal

Value

A matrix.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
x<-matrix(c(1:10),ncol = 5)
x1<-AccumulateNormal(x,c(3,5))
```

`CalculateSES` *SubtypeDrug internal function*

Description

Calculate subpathway enrichment score.

Usage

```
CalculateSES(labels.list, correl.vector = NULL)
```

Arguments

`labels.list`	A vector of 0 and 1.
`correl.vector`	A vector. The weight value used to calculate the enrichment score.

Details

CalculateSES

Value

A vector.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
x<-CalculateSES(sample(c(0,1),10,replace = TRUE),c(1:10))
```

Colork *Color*

Description

This variable stores the color data required by the program.

Usage

```
Colork
```

Format

A vector containing 73 values.

Examples

```
data(Colork)
```

Disease_drugs *Simulated result data*

Description

The simulated result data of only two sample types is generated by the functional PrioSubtypeDrug.

Usage

```
Disease_drugs
```

Format

A list containing 8 variables. The variables are as follows:

- Cacner Results table for cacner
- SubpathwayMatrix Subpathway activity natrix
- SampleInformation Cancer sample phenotypic information
- Parameter Parameter of the function PrioSubtypeDrug

Examples

```
# data(Disease_drugs)
```

Drugs_CID — *Correspondence table of drug label and drug ID in PubCham database*

Description

A data frame for the drug and its corresponding PubCham database ID.

Usage

```
Drugs_CID
```

Format

A dataframe with drug label and CID. The variables are as follows:

- Drugs Drug label
- CID Drug ID in PubCham database

Examples

```
data(Drugs_CID)
```

Geneexp — *Simulated gene expression data*

Description

Simulated normalized gene expression profile data.

Usage

```
Geneexp
```

Format

A matrix with 3000 genes and 40 samples.

Examples

```
data(Geneexp)
```

GeneexpT *Gene expression data for testing*

Description

Simulated normalized gene expression profile data.

Usage

```
GeneexpT
```

Format

A matrix with 40 samples.

Examples

```
data(GeneexpT)
```

getDrugMatrix *SubtypeDrug internal function*

Description

Obtaining drug-disease reverse association score matrix.

Usage

```
getDrugMatrix(spw_matrix, drug_target_data, weighted.score)
```

Arguments

spw_matrix	A subpathway activity profile. rows are subpathwyas, columns are samples.
drug_target_data	A list. A list stores a collection of drug up- and down-regulated subpathways.
weighted.score	A binary value of 0 or 1. If the 'weighted.score' = 1, the drug reverse association score will be weighted by the subpathway activity.

Details

getDrugMatrix

Value

A matrix.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(GSVA)
Geneexp<-get("GeneexpT")
UserDS<-get("UserDST")
UserGS<-get("UserGST")
gsvapar <- gsvaParam(Geneexp, UserGS)
spw_matrix<-gsva(gsvapar)
x<-getDrugMatrix(spw_matrix,UserDS,weighted.score=FALSE)
```

---

getDrugSpw *SubtypeDrug internal function*

Description

According to the parameters set by the user, the up-regulatory and down-regulatory subpathway data of drug is obtained.

Usage

```
getDrugSpw(
  drug_target_data,
  spw_matrix_rnames,
  drug.P.value.threshold,
  drug.min.sz,
  drug.max.sz
)
```

Arguments

drug_target_data	A list. A list stores a collection of drug up- and down-regulated subpathways.
spw_matrix_rnames	A vector. A vector consisting of row names of subpathway activity profile.
drug.P.value.threshold	A value. According to the threshold of the significant P value set by parameter 'drug.p.val.threshold', the drug up-regulation and down-regulatory subpathways were screened.
drug.min.sz	A numeric. The drug regulated subpathways intersects with the subpathways in the subpathway activity profile. Then drugs with less than 'drug.spw.min.sz' up- or down-regulated subpathways are removed.
drug.max.sz	A numeric. Similar to parameter 'drug.spw.min.sz', drugs with more than 'drug.spw.max.sz' up- or down-regulated subpathways are removed.

Details

getDrugSpw

Value

a list.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(GSVA)
Geneexp<-get("Geneexp")
UserGS<-get("UserGS")
UserDS<-get("UserDS")
gsvaPar <- GSVA::ssgseaParam(Geneexp,UserGS,minSize=2)
spw_matrix<-gsva(gsvaPar)
x<-getDrugSpw(UserDS,row.names(spw_matrix),0.05,1,100)
```

---

getDrugStructure *Get drug chemical structure diagram data*

Description

'getDrugStructure()' outputs the chemical structure graph data of the drug or compound based on the input drug label by the user. The results can be visualized by the 'plot' function.

Usage

```
getDrugStructure(drug.label = "", main = "", sub = "")
```

Arguments

drug.label	A character string of drug label to determine which drug to use for visualization.
main	An overall title for the chemical structure graph.
sub	A sub title for the chemical structure graph.

Details

getDrugStructure

Value

A sdfset object.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(rvest)
require(ChemmineR)
# Plot the chemical structure of drug pirenperone.
# Chem_str<-getDrugStructure(drug.label="pirenperone.")
# plot(Chem_str)
```

---

isPackageLoaded *SubtypeDrug internal function*

Description

Determine if the package is loaded. If the package is not loaded, the program will prompt the user.

Usage

```
isPackageLoaded(name)
```

Arguments

name	A string. The name of the R package which determines whether it is loaded.

Details

isPackageLoaded

Value

A string, TRUE or FALSE.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
isPackageLoaded("pheatmap")
```

`plotDScoreHeatmap` *Plot a heat map of the normalized drug-disease reverse association scores for cancer samples*

Description

According to the parameter setting, the function 'plotDScoreHeatmap()' displays the heat map of the normalized drug-disease reverse association score for the significant drugs.

Usage

```
plotDScoreHeatmap(
  data,
  subtype.label = "all",
  SDS = "all",
  E_Pvalue.th = 1,
  E_FDR.th = 0.05,
  S_Pvalue.th = 1,
  S_FDR.th = 0.001,
  show.rownames = TRUE,
  show.colnames = FALSE,
  color = colorRampPalette(c("#0A8D0A", "#F8F0EB", "red"))(190),
  subtype_colors = NA,
  drug_colors = NA,
  border_color = "grey60",
  cellwidth = NA,
  cellheight = NA,
  fontsize = 10,
  fontsize.row = 10,
  fontsize.col = 10,
  scale = "row"
)
```

Arguments

`data`	A list of result data generated by function 'PrioSubtypeDrug()'.
`subtype.label`	Character string indicates which sample of the cancer subtype was used to plot the heat map. If subtype.label = "all" (default), all cancer samples will be shown in the heat map.
`SDS`	A string indicates that the range of SDS is used for the heat map. if SDS="all" (default), the SDS will not be filtered. SDS="negative", only drugs with SDS<0 are used. SDS="positive", only drugs with SDS>0 are used.
`E_Pvalue.th`	A numeric.A threshold is used to filter the drug effected P value (default: 1).
`E_FDR.th`	A numeric.A threshold is used to filter the drug effected FDR (default: 0.05).
`S_Pvalue.th`	A numeric.A threshold is used to filter the Subtype specific P value (default: 1).

S_FDR.th	A numeric.A threshold is used to filter the Subtype specific P value (default: 0.001).
show.rownames	Boolean specifying if row names are be shown (default: TRUE).
show.colnames	Boolean specifying if column names are be shown (default: FALSE).
color	Vector of colors used in heatmap.
subtype_colors	Vector of colors is used to annotate the sample subtype. Its length should correspond to the number of sample subtypes.
drug_colors	Vector of colors is used to label subtype-specific drugs.
border_color	Color of cell borders on heatmap, use NA if no border should be drawn.
cellwidth	Individual cell width in points. If left as NA, then the values depend on the size of plotting window.
cellheight	Individual cell height in points. If left as NA, then the values depend on the size of plotting window.
fontsize	Base fontsize for the plot (default: 10).
fontsize.row	Fontsize for rownames (default: 10).
fontsize.col	Fontsize for colnames (default: 10).
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" (default), "column" and "none".

Details

plotDScoreHeatmap

Value

A heat map.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(pheatmap)
## Get the result data of PrioSubtypeDrug().
## The data is based on the simulated breast cancer subtype data.
Subtype_drugs<-get("Subtype_drugs")
## Heat map of all subtype-specific drugs.
#plotDScoreHeatmap(data=Subtype_drugs,E_Pvalue.th=0.05,
#                          S_Pvalue.th=0.05)
## Plot only Basal subtype-specific drugs.
plotDScoreHeatmap(Subtype_drugs,subtype.label="Basal",SDS="all",E_Pvalue.th=0.05,
                  E_FDR.t=1,S_Pvalue.th=0.05,S_FDR.th=1)
```

plotDSpwHeatmap *Plot heat map of the drug regulated subpathway activity score*

Description

The 'plotDSpwHeatmap()' function plots a heat map of the subpathways that are regulated by specified drug and have differential expression between specified cancer subtype and normal.

Usage

```
plotDSpwHeatmap(
  data,
  drug.label = "",
  subtype.label = "",
  show.rownames = TRUE,
  show.colnames = TRUE,
  color = NA,
  phen_colors = NA,
  border_color = "grey60",
  cellwidth = NA,
  cellheight = NA,
  fontsize = 10,
  fontsize.row = 10,
  fontsize.col = 10,
  scale = "row"
)
```

Arguments

data	A list of result data generated by function 'PrioSubtypeDrug()'.
drug.label	A character string of drug labels to determine which drug to use for visualization.
subtype.label	Character string indicates which sample of the cancer subtype was used to plot the heat map.
show.rownames	Boolean specifying if row names are be shown.
show.colnames	Boolean specifying if column names are be shown.
color	Vector of colors used in heatmap.
phen_colors	Vector of colors is used to annotate the sample subtype and control sample.It should be assigned two colors.
border_color	Color of cell borders on heatmap, use NA if no border should be drawn.
cellwidth	Individual cell width in points. If left as NA, then the values depend on the size of plotting window.
cellheight	Individual cell height in points. If left as NA, then the values depend on the size of plotting window.

fontsize	Base fontsize for the plot (default: 10).
fontsize.row	Fontsize for rownames (default: 10).
fontsize.col	Fontsize for colnames (default: 10).
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".

Details

plotDSpwHeatmap

Based on the input cancer subtype, the program draws a heat map of the drug regulated subpathway activity score. If the cancer subtype of input has sutype-specific drug score (SDS)<0, we can observe the drug upregulatory subpathway is lowly expressed in the cancer subtype samples and high in the normal samples; the drug downregulatory subpathway is highly expressed in the cancer subtype samples and low in the normal samples. This indicates that after the drug action, these subpathways activity is converted from the level of the cancer subtype into the level of normal. If the cancer subtype of input has sutype-specific drug score (SDS)>0, it is indicated that the drug action may promote the subpathway expression status of the cancer subtype.

Value

A heat map.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(pheatmap)
## Get the result data of PrioSubtypeDrug().
## The data is based on the simulated breast cancer subtype data.
Subtype_drugs<-get("Subtype_drugs")
plotDSpwHeatmap(data=Subtype_drugs,drug.label="pirenperone(1.02e-05M)",subtype.label="Basal")
##Visualize the results of only two types of samples.
Disease_drugs<-get("Disease_drugs")
plotDSpwHeatmap(data=Disease_drugs,drug.label="W-13(1e-05M)",subtype.label="Cancer")
```

---

plotGlobalGraph *Plot a global graph of the drug*

Description

The 'plotGlobalGraph()' identifies the drug label entered by the user, and plots an integrated diagram including box plot of the normalized drug-disease reverse association scores, null distribution curves of significant P-value, and heat map of cancer subtype sample distribution.

Usage

```
plotGlobalGraph(
  data,
  drug.label = "",
  overall.main = "",
  overall.cex.main = 1.5,
  cex.submap.axis = 1,
  cex.submap.lab = 1,
  cex.submap.main = 1,
  cex.submap.sub = 1,
  cex.legend = 1
)
```

Arguments

`data`	A list of result data generated by function 'PrioSubtypeDrug()'.
`drug.label`	A character string of drug labels to determine which drug to use for visualization.
`overall.main`	An overall title for the whole graph. If the user does not make any input, the title will display a drug label.
`overall.cex.main`	The magnification to be used for overall.main (default: 1.5).
`cex.submap.axis`	The magnification to be used for axis of each submap annotation relative to the current setting of cex.
`cex.submap.lab`	The magnification to be used for x and y labels of each submap relative to the current setting of cex.
`cex.submap.main`	The magnification to be used for main titles of each submap relative to the current setting of cex.
`cex.submap.sub`	The magnification to be used for sub titles of each submap relative to the current setting of cex.
`cex.legend`	fontsize of labels for legend.

Details

plotGlobalGraph

Value

A plot.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
## Get the result data of PrioSubtypeDrug().
## The data is based on the simulated breast cancer subtype data.
Subtype_drugs<-get("Subtype_drugs")
## Plot a global graph of the drug pirenperone(1.02e-05M).
plotGlobalGraph(data=Subtype_drugs,drug.label="pirenperone(1.02e-05M)")
```

`plotSpwNetGraph` *Polt a subpathway network graph*

Description

Visualize a subpathway network graph.

Usage

```
plotSpwNetGraph(
  spwid,
  layout = NULL,
  margin = 0,
  vertex.label.cex = 0.6,
  vertex.label.font = 1,
  vertex.size = 8,
  vertex.size2 = 6,
  edge.arrow.size = 0.2,
  edge.arrow.width = 3,
  edge.label.cex = 0.6,
  vertex.label.color = "black",
  vertex.color = "#BFFFBF",
  vertex.frame.color = "dimgray",
  edge.color = "dimgray",
  edge.label.color = "dimgray",
  sub = NULL,
  main = NULL
)
```

Arguments

`spwid`	The subpathway id which the user wants to plot.
`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.size`
: A numeric vector of Node size. See `plot.igraph`.

`vertex.size2`
: A numeric vector of Node size.

`edge.arrow.size`
: Edge arrow size.The default is 0.2.

`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.

Details

plotSpwNetGraph

The function plotSpwNetGraph is able to display a subpathway graph. The argument layout is used to determine the placement of the nodes for drawing a graph.The layouts provided in igraph include ‘layout_as_star‘, ‘layout_as_tree‘, ‘layout_in_circle‘, ‘layout_nicely‘,‘layout_on_grid‘, ‘layout_on_sphere‘, ‘layout_randomly‘, ‘layout_with_dh‘, ‘layout_with_fr‘, ‘layout_with_gem‘, ‘layout_with_graphopt‘, ‘layout_with_kk‘, ‘layout_with_lgl‘, ‘layout_with_mds‘. The ‘layout_as_tree‘ generates a tree-like layout, so it is mainly for trees. The ‘layout_randomly‘ places the nodes randomly. The ‘layout_in_circle‘ places the nodes on a unit circle. Detailed information on the parameters can be found in `layout_`

Value

a plot

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(igraph)
# plot network graph of the subpathway 00020_4.
plotSpwNetGraph(spwid="00020_4")
```

PrioSubtypeDrug *Prioritization of candidate cancer subtype-specific drugs (PrioSubtypeDrug)*

Description

Integrating drug, gene, and subpathway data to identify drugs specific to cancer subtypes.

Usage

```
PrioSubtypeDrug(
  expr,
  input.cls = "",
  control.label = "",
  subpathway.list,
  spw.min.sz = 10,
  spw.max.sz = Inf,
  spw.score.method = "gsva",
  kcdf = "Gaussian",
  drug.spw.data,
  drug.spw.p.val.th = 0.05,
  drug.spw.min.sz = 10,
  drug.spw.max.sz = Inf,
  weighted.drug.score = TRUE,
  nperm = 1000,
  parallel.sz = 1,
  E_FDR = 0.05,
  S_FDR = 0.001
)
```

Arguments

expr	Matrix of gene expression values (rows are genes, columns are samples).
input.cls	Input sample subtype class vector file in CLS format.
control.label	In the CLS file of 'input.cls', the label of the control sample.
subpathway.list	A list. The subpathway list data is mined from KEGG data is stored in the package 'SubtypeDrugData' and can be downloaded through the connection https://github.com/hanjunwei-lab/SubtypeDrugData. The gene tags included in the subpathway list data should be consistent with those in the gene expression profile. The package 'SubtypeDrugData' provides two choices that include the Entrezid and Symbol tags of the gene. Users can also enter their own pathway or gene set list data.
spw.min.sz	Removes subpathways that contain fewer genes than 'spw.min.sz' (default: 10).
spw.max.sz	Removes subpathways that contain more genes than 'spw.max.sz' (default: Inf).

`spw.score.method`
: Method to employ in the estimation of subpathway enrichment scores per sample. By default this is set to 'gsva' (Hänzelmann et al, 2013) and other options are 'ssgsea' (Barbie et al, 2009).

`kcdf`
: Character string denoting the kernel to use during the non-parametric estimation of the cumulative distribution function of expression levels across samples when 'spw.score.method="gsva"'. By default, 'kcdf="Gaussian"' which is suitable when input expression values are continuous, such as microarray fluorescent units in logarithmic scale, RNA-seq log-CPMs, log-RPKMs or log-TPMs. When input expression values are integer counts, such as those derived from RNA-seq experiments, then this argument should be set to 'kcdf="Poisson"'.

`drug.spw.data`
: A list data of drug regulation. The drug subpathway association data we constructed is stored in package 'SubtypeDrugData' and can be downloaded via connection https://github.com/hanjunwei-lab/SubtypeDrugData. If the input is user-defined drug regulation data, the data should be a list data with each drug as its element. Each drug also contains 'Target_upregulation' and 'Target_downregulation' subpathway or gene set. Subpathway or gene set contained in drug regulation data should exist in input data of parameter 'subpathway.list'.

`drug.spw.p.val.th`
: Parameter used only when 'drug.spw.data="DrugSpwData"'. According to the threshold of the significant P value set by parameter 'drug.spw.p.val.th' (default: 0.05), the drug up-regulation and down-regulatory subpathways were screened.

`drug.spw.min.sz`
: A numeric. The drug regulated subpathways intersects with the subpathways in the subpathway activity profile. Then drugs with less than 'drug.spw.min.sz' (default: 10) up- or down-regulated subpathways are removed.

`drug.spw.max.sz`
: A numeric. Similar to parameter 'drug.spw.min.sz', drugs with more than 'drug.spw.max.sz' (default: Inf) up- or down-regulated subpathways are removed.

`weighted.drug.score`
: A boolean values determines the method for calculating the normalized drug-disease reverse association score of the drug for each sample. 'weighted.drug.score=TRUE' (default): KS random walk statistic with individualized subpathway activity aberrance score as weight was used to calculate the normalized drug-disease reverse association score. 'weighted.drug.score=FALSE': Similar to 'CMap' (Lamb et al., 2006), no weight is needed, and the normalized drug-disease reverse association score is calculated by the rank of the individualized subpathway activity aberrance score.

`nperm`
: Number of random permutations (default: 1000).

`parallel.sz`
: Number of processors to use when doing the calculations in parallel (default value: 1). If parallel.sz=0, then it will use all available core processors unless we set this argument with a smaller number.

`E_FDR`
: Significance threshold for E_FDR for drugs (default: 0.05)

`S_FDR`
: Significance threshold for S_FDR for drugs (default: 0.001)

Details

PrioSubtypeDrug

First, the function PrioSubtypeDrug uses the ‘GSVA‘ or ‘ssgsea‘ method to convert the disease gene expression profile into subpathway activity profile. Parameters ‘subpathway.list‘, ‘spw.min.sz‘ and ‘spw.max.sz‘ are used to process the subpathway list data. ‘spw.score.method‘ and ‘kcdf‘ are used to control the method of constructing the subpathway activity score profile. Individualized subpathway activity aberrance score was estimated using the mean and standard deviation of the Control samples. Subpathways of each cancer sample are ordered in a ranked list according to individualized subpathway activity aberrance score. Next, we calculate the normalized drug-disease reverse association score by enriching drug regulated subpathway tags to the subpathway ranked list. Finlly, all drug-regulated subpathways are enriched into each cancer sample to obtain a normalized drug-disease reverse association score matrix. The ‘drug.spw.p.val.th‘, ‘drug.spw.min.sz‘ and ‘drug.spw.max.sz‘ is used to screen the drug regulated subpathway set. If user-defined drug targeting data is used, drug regulated ‘Target_upregulation‘ and ‘Target_downregulation‘ should already be defined in the data. The ‘weighted.drug.score‘ to control the method of calculating the normalized drug-disease reverse association score. Finally, empirical sample-based permutation test procedure to obtain significative cancer subtype specific drugs. For samples containing only cancer and Control, the subpathways are ranked according to the difference in activity between cancer and Control samples. Subsequently, the subpathway set of drug up- and down-regulated is enriched to the ranking list of subpathway to evaluate the normalized drug-disease reverse association score and subpathway-based permutation test procedure to calculate significance. The subpathway list data and drug subpathway associated data set is stored in package ‘SubtypeDrugData‘ and can be obtained on https://github.com/hanjunwei-lab/SubtypeDrugData.

Value

A list contains the result table of drug scoring and significance, a subpathway activity score matrix, a normalized drug-disease reverse association score matrix, sample information, and user set parameter information.

Author(s)

Xudong Han, Junwei Han, Chonghui Liu

Examples

```
require(GSVA)
require(parallel)
## Get simulated breast cancer gene expression profile data.
Geneexp<-get("Geneexp")
## Obtain sample subtype data and calculate breast cancer subtype-specific drugs.
Subtype<-system.file("extdata", "Subtype_labels.cls", package = "SubtypeDrug")

## Subpathway list data and drug subpathway association data
## were stored in packet `SubtypeDrugData`.
## `SubtypeDrugData` has been uploaded to the github repository.
## If subpathway list data and drug subpathway association data are needed,
## users can download and install through `install_github` function and
## set parameter url=""hanjunwei-lab/SubtypeDrugData".
```

```
## After installing and loading package `SubtypeDrugData`,
## users can use the following command to get the data.
## Get subpathway list data.
## If the gene expression profile contains gene Symbol.
## data(SpwSymbolList)
## If the gene expression profile contains gene Entrezid.
## data(SpwEntrezidList)
## Get drug subpathway association data.
## data(DrugSpwData)

## Identify breast subtype-specific drugs.
## Subtype_drugs<-PrioSubtypeDrug(Geneexp,Subtype,"Control",SpwSymbolList,drug.spw.data=DrugSpwData,
##                                      E_FDR=1,S_FDR=1)

## Identify breast cancer-related drugs in only two types of samples: breast cancer and control.
Cancer<-system.file("extdata", "Cancer_normal_labels.cls", package = "SubtypeDrug")
## Disease_drugs<-PrioSubtypeDrug(Geneexp,Cancer,"Control",SpwSymbolList,drug.spw.data=DrugSpwData,
##                                      E_FDR=1,S_FDR=1)

## The function PrioSubtypeDrug() can also support user-defined data.
Geneexp<-get("GeneexpT")
## User-defined drug regulation data should resemble the structure below
UserDS<-get("UserDST")
str(UserDS)
## Need to load gene set data consistent with drug regulation data.
UserGS<-get("UserGST")
str(UserGS)
Drugs<-PrioSubtypeDrug(Geneexp,Cancer,"Control",UserGS,spw.min.sz=1,
                       drug.spw.data=UserDS,drug.spw.min.sz=1,
                       nperm=10,E_FDR=1,S_FDR=1)
```

`ReadClsFile` *SubtypeDrug internal function*

Description

These are function read sample label file (.cls format).

Usage

```
ReadClsFile(file)
```

Arguments

`file`	Input sample subtype class vector file in CLS format.

Details

ReadClsFile

Value

a list

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Examples

```
Subtype<-system.file("extdata", "Subtype_labels.cls", package = "SubtypeDrug")
x<-ReadClsFile(Subtype)
```

SpwNetworkData *Subpathway network structure data*

Description

A list to store the network data of the genes contained in the subpathway.

Usage

```
SpwNetworkData
```

Format

A list containing 1598 subpathway network.

Examples

```
data(SpwNetworkData)
```

Subtype_drugs *Simulation result data*

Description

The result data of the simulation is generated by the functional OCSSD.

Usage

```
Subtype_drugs
```

Format

A list containing 8 variables. The variables are as follows:

- Basal Results table for basal subtype
- Her2 Results table for Her2 subtype
- LumA Results table for LumA subtype
- LumB Results table for LumB subtype
- DrugMatrix Drug disease reverse association matrix
- SubpathwayMatrix Subpathway activity natrix
- SampleInformation Cancer sample phenotypic information
- Parameter Parameter of the function OCSSD

Examples

```
# data(Subtype_drugs)
```

`UserDS` *Simulated user-defined drug regulator subpathway dataset*

Description

The drug regulator subpathway data set is modeled as a case.

Usage

```
UserDS
```

Format

A list containing 5 drugs.

Examples

```
data(UserDS)
```

UserDST *User-defined drug regulator subpathway dataset for testing*

Description

The drug regulator subpathway data set is modeled as a case.

Usage

```
UserDST
```

Format

A list.

Examples

```
data(UserDST)
```

UserGS *Simulated user-defined gene set data*

Description

Gene set data is simulated for case studies.

Usage

```
UserGS
```

Format

A list containing 50 gene sets.

Examples

```
data(UserDS)
```

UserGST *User-defined gene set data for testing*

Description

Gene set data is simulated for case studies.

Usage

```
UserGST
```

Format

A list.

Examples

```
data(UserGST)
```

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