Package 'SubpathwayLNCE'

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Type Package

Title Identify Signal Subpathways Competitively Regulated by LncRNAs
Based on ceRNA Theory

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Description Identify dysfunctional subpathways competitively regulated by lncRNAs through integrating lncRNA-mRNA expression profile and pathway topologies.

Depends R (>= 2.10), igraph, RBGL, utils, BiasedUrn, graph, graphics,
stats

Suggests XML

Collate ExpProcess.r getBackgroundLnc.r getEdgeLabel.r getEdgeLty.r
getEnvironmentData.r getInteGraphList.r getInteUMGraph.r
getKGeneFromGene.r getLayout.r getLncGenePairs.r
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LazyData Yes

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R topics documented:

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envData   *The variables in the environment variable* envData *of the system*

Description

The variables in the environment variable envData of the system.

Format

An environment variable

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

---

getBackgroundLnc   *Get the background of molecules*

Description

getBackgroundLnc attempts to get the background of user-specified molecules.

Usage

```
getBackgroundLnc(type = "gene_lncRNA")
```

Arguments

type   A character string. Should be one of "gene", "lncRNA" or "gene_lncRNA".

Details

The default background is obtained from the environment variable. For human, the reference gene background is all human genes in KEGG pathways. The reference lncRNA background is collected from GeneCode database.

Value

A character vector.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

[identifyLncGraphW](#)

Examples

```
## Not run:
## get all background of genes
 bgGene <- getBackgroundLnc(type="gene")

## get all background of lncRNAs
 bgLncRNA  <- getBackgroundLnc(type="lncRNA")

## get all background of lncRNAs and genes
 bgGL <- getBackgroundLnc(type="gene_lncRNA")

## End(Not run)
```

GetExampleData   *Get the environment data*

Description

Get variables in current environment.

Usage

```
GetExampleData(exampleData)
```

Arguments

exampleData   A character string. It must be one of them, including "code", "compound", "g2",
                "gene", "gene2path", "gene2symbol", "GeneExp", "keggGene2gene", "lnc2Name",
                "lncBackground", "LncExp", "LncGenePairs", "mart", "nocode", "pp", "resultT"
                and "sub".

Details

The parameter exampleData is "code", which represents to obtain all human coding gene collected from Genecode.

The parameter K2riData is "compound", which represents to obtain all huamn compound.

The parameter K2riData is "g2", which represents to obtain undirect KEGG metabolic pathway graphs with genes as nodes.

The parameter K2riData is "gene", which represents to obtain interseted gene of example.

The parameter K2riData is "gene2symbol", which represents to obtain gene-symbol data.

The parameter K2riData is "gene2path", which represents to obtain gene-pathway data.

The parameter K2riData is "GeneExp", which represents to obtain gene expression profile of example.

The parameter K2riData is "keggGene2gene", which represents to obtain kegggene-gene data.

The parameter K2riData is "lnc2Name", which represents to obtain lncRNA Ensemble-Name data.

The parameter K2riData is "lncBackground", which represents to obtain background of lncRNA, gene or lncRNA-gene.

The parameter K2riData is "LncExp", which represents to obtain lncRNA expression profile of example.

The parameter K2riData is "LncGenePairs", which represents to obtain the cmepetitively regulated lncRNA-mRNA interactions.

The parameter K2riData is "mart", which represents to obtain gene ensemble-name-entrez data.

The parameter K2riData is "nocode", which represents to obtain all huaman lncRNA collected from Genecode.

The parameter K2riData is "resultT", which represents to obtain result of example.

The parameter K2riData is "sub", which represents to obtain subpahtway of example.

The parameter K2riData is "geneLnc", which represents to obtain user-interested genes and lncRNAs of example.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

Examples

```
## Not run:


# obtain lncRNA expression profile #
LncExp <- GetExampleData(exampleData="LncExp")



## End(Not run)
```

---

getInteGraphList *Get the reconstructed signal pathway graphs*

Description

Get the reconstructed KEGG signal pathway graphs embedded by lncRNAs of competitive regulation.

Usage

```
getInteGraphList(graphList,relations)
```

Arguments

graphList	A graphList. There nodes must be represented by genes.
relations	A data frame. It contains two columns, the first is lncRNA names and the second is its target names.

Details

The argument "relations" represents user-interested lncRNA-target interactions, which can be returned from the GetExampleData.

Value

A graph list.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

plotGraphL, getLocSubGraphLnc, GetExampleData

Examples

```
## Not run:
### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  g2<-GetExampleData(exampleData="g2")
  interUMGraph<-getInteGraphList(g2,LncGenePairs)
  #interUMGraph<-getInteUMGraph(LncGenePairs)
### get user-interested lncRNAs and genes sets.
  #geneLnc<-GetExampleData(exampleData="geneLnc")
# get locate subpathways.
  #sub<-getLocSubGraphLnc(geneLnc,interUMGraph,type="gene_lncRNA",n=1,s=8)
  #SubcodeLncResult<-identifyLncGraphW(geneLnc,sub,type="gene_lncRNA",bet=1)
  #resultT<-printGraphW(SubcodeLncResult,detail=TRUE)
```

```
## End(Not run)
```

---

getInteUMGraph   *Get the reconstructed condition-specific lncRNA-regulated signal*
                              pathways

Description

Get the reconstructed condition-specific LncRNA-regulated signal pathways embedded by lncR-NAs of competitive regulation through linking to their regulated-mRNAs.

Usage

```
getInteUMGraph(LncGenePairs)
```

Arguments

LncGenePairs   A data frame. It contains two columns, the first is lncRNA names and the second is mRNA names.

Details

The argument "LncGenePairs" represents competitively regulated lncRNA-mRNA interactions, which can be returned from the getLncGenePairs.

Value

A graph list.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

[getLncGenePairs](#)

Examples

```
## Not run:

### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  inteUMGraph<-getInteUMGraph(LncGenePairs)

## End(Not run)
```

---

getLncGenePairs | *Get the co-express lncRNA-mRNA interactions*

Description

Get the co-express lncRNA-mRNA interactions reached a significant positive threshold. These lncRNAs-mRNAs pairs are competitivly rugulated.

Usage

```
getLncGenePairs(GeneExp,LncExp,a=0.025)
```

Arguments

GeneExp   A gene expression profile. The first row of gene expression profile is names of mRNA, and the gene expression profile and the lncRNA expression profile must be mached.

LncExp   A lncRNA expression profile. The first row of lncRNA expression profile is names of lncRNA, and the gene expression profile and the lncRNA expression profile must be mached.

a   A parameter,namely the significant positive threshold.

Details

Co-express coefficient for any pair of relations in the candidate LncRNA-mRNA network is calculated basing on matched LncRNA and mRNA expression profiles, those relations had reached a significant positive threshold were retained.

Value

A data frame. The data frame has two columns, the fist is lncRNA names, the other is mRNA names.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

Examples

```
## Not run:


 GeneExp<-GetExampleData(exampleData="GeneExp")
 LncExp<-GetExampleData(exampleData="LncExp")
 LncGenePairs<-getLncGenePairs(GeneExp,LncExp,a=0.025)

## End(Not run)
```

---

getLocSubGraphLnc   *Get the located signal subpathways*

Description

Locate signal subpathways competitively regulated by lncRNAs.

Usage

```
getLocSubGraphLnc(moleculeList, graphList, type="gene_lncRNA",
    n=1, s=8, method = "shortestPaths")
```

Arguments

moleculeList   A character vector. Such as competitively regulated lncRNAs and/or differen-
                 tially expressed genes under disease phenotypes. Gene should be geneid.

graphList   A graph list. There nodes must be represented by genes.

type   A character string. Should be one of "gene", "lncRNA" or "gene_lncRNA".

n   An integer. The maximum acceptable quantities of non-signature node at the
                 shortest path between each two interested molecules.

s   An integer. The minimum acceptable quantities of nodes in located subpath-
                 ways.

method   A character string. In which the shorest path algorithms will be used.

Details

We apply lenient distance similarity method to locate signal subpathways competitively regulated by
miRNAs. We first map user competitively regulated lncRNAs and/or interested genes to pathways
as signatures. For a given pathway, we compute the shortest path between any two signatures.
In shortest path, if the number of non-signature nodes between two signatures is no more than
n, then these two signature nodes and other nodes at the shortest path are added into the same
node set. We extract the corresponding subgraph in the pathway graph according to each node
set. We finally define these subgraphs with node number >= s as the subpathway regions of the
pathway. The argument n is maximum number of permitted non-signature nodes at the shortest path
between signature nodes. The default parameter n=1. The argument s is used to filter subpathways
in which the number of nodes are less than the parameter s. The default parameter s=8. The
argument method determines which shortest path algorithms will be used. We set the default value
as "get.shortest.paths".

Value

A list of graphs.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

[getInteGraphList](), [identifyLncGraphW]()

Examples

```
## Not run:

### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  interUMGraph<-getInteUMGraph(LncGenePairs)
### get user-interested lncRNAs and genes sets.
##geneLnc<-c(getBackground(type="gene")[1:3000],unique(LncGenePairs[1,]))
  geneLnc<-GetExampleData(exampleData="geneLnc")
# get locate subpathways.
  sub<-getLocSubGraphLnc(geneLnc,interUMGraph,type="gene_lncRNA",n=1,s=8)


## End(Not run)
```

---

identifyLncGraphW   *Annotate and identify subpathways*

Description

Annotate user-interested molecules to pathways and identify significantly enriched subpathways.

Usage

```
identifyLncGraphW(moleculeList,graphList,type="gene_lncRNA",
          background=getBackgroundLnc(type),
          order="pvalue",decreasing=FALSE,bet=1)
```

Arguments

moleculeList	A character vector. Such as user-interested lncRNAs and/or genes under disease phenotypes.
graphList	A graph list. There nodes must be represented by genes or lncRNAs and genes.
type	A character string. Should be one of "gene", "lncRNA" or "gene_lncRNA".
background	A character vector of molecules.
order	A character string. Should be one of "pvalue", "fdr".
decreasing	A logical. Should the sort be ordered by increasing or decreasing?
bet	A number. A parameter.

Details

The function can support the annotation and identification of metabolic subpathways based on genes, lncRNAs or gene_lncRNAs sets. The argument moleculeList supports three kinds of molecular sets: "genes", "lncRNAs" or "gene_lncRNAs".

The argument type represent the type of input molecules, including one of "genes", "lncRNAs" or "gene_lncRNA".

Detailed background information is provided in the function getBackgroundLnc.

When many correlated subpathways are considered, the parameter order is used to order the pathways on the basis of "pvalue" or "fdr".

The parameter decreasing is set TRUE that represent the order would be performed by decreasing.

Value

A list. It include: 'pathwayId', 'pathwayName', 'annMoleculeList', 'annMoleculeNumber', 'annBg-MoleculeList', 'annBgNumber', 'MoleculeNumber', 'bgNumber','annWeight', 'pvalue', and 'fdr', corresponding to pathway identifier, pathway name, the submitted molecules annotated to a pathway, the number of submitted molecules annotated to a pathway, the background molecules annotated to a pathway, the number of background molecules annotated to a pathway, the number of submitted molecules, the number of background molecules, the weight of lncRNA competitively regulated subpathway p-value of the hypergeometric test, and Benjamini-Hochberg fdr values.

The background molecules annotated to a pathway are equal to all molecules in the pathway. For example, if the submitted molecules are human genes, the background molecules annotated to a pathway are equal to all human genes in the pathway.

The number of background molecules is the number of all molecules. For example, if the submitted molecules are human genes, the number of background molecules is equal to all human genes.

To visualize and save the results, the list can be converted to the data.frame by the function printGraphW.

Note that moleculeList must be a 'character' vector. The genes must be represented by NCBI gene ids, and lncRNAs must be represented by mature lncRNA Ensemble name.

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

printGraphW, getBackgroundLnc, GetExampleData

Examples

```
## Not run:

### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  #LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  #inteUMGraph<-getInteUMGraph(LncGenePairs)
### get user-interested lncRNAs and genes sets.
  geneLnc<-GetExampleData(exampleData="geneLnc")
```

```
# get locate subpathways.
  #sub<-getLocSubGraphLnc(geneLnc,interUMGraph,type="gene_lncRNA",n=1,s=8)
   sub<-GetExampleData(exampleData="sub")
  SubcodeLncResult<-identifyLncGraphW(geneLnc,sub,type="gene_lncRNA",bet=1)

## End(Not run)
```

---

plotAnnGraph   *Visualize annotated pathway graphs*

Description

Visualize annotated pathway graphs.

Usage

```
plotAnnGraph(pathwayId,graphList,ann,gotoKEGG=FALSE,orgSpecific=TRUE,
displayInR=TRUE,match=TRUE,vertex.frame.color="red",...)
```

Arguments

pathwayId	A character vector of pathway identifier, e.g., c("path:00010","path:00020").
graphList	A graph list.
ann	A list, e.g., the return value of the function [identifyLncGraphW]().
gotoKEGG	A logical. If TRUE, go to KEGG web site. The identified nodes are colored red.
orgSpecific	A logical.
match	A logical.
displayInR	A logical. If TRUE, display pathway graphs on the device.
vertex.frame.color	
	A character defining the frame color of the nodes which represent the annotated nodes in the pathway.
...	The arguments passed to or from methods. See [plotGraphL](), [plot.igraph]() and see [plot]().

Details

The function can visualize the annotated pathway (or subpathways) graphs. The red nodes in the result graph represent the nodes which include the submitted molecules.

Author(s)

Xinrui Shi, Chunquan Li, Xia Li

See Also

[plotGraphL](),[identifyLncGraphW](),[printGraphW]()

Examples

```
## Not run:
### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  g2<-GetExampleData(exampleData="g2")
  interUMGraph<-getInteGraphList(g2,LncGenePairs)
  interUMGraph<-getInteUMGraph(LncGenePairs)
### get user-interested lncRNAs and genes sets.
  geneLnc<-GetExampleData(exampleData="geneLnc")
# get locate subpathways.
  sub<-getLocSubGraphLnc(geneLnc,interUMGraph,type="gene_lncRNA",n=1,s=8)
  SubcodeLncResult<-identifyLncGraphW(geneLnc,sub,type="gene_lncRNA",bet=1)
  resultT<-printGraphW(SubcodeLncResult,detail=TRUE)
  plotAnnGraph("path:04020_1",sub,SubcodeLncResult,gotoKEGG=FALSE)


## End(Not run)
```

---

plotGraphL   *Visualize a pathway graph*

Description

Visualize a pathway graph.

Usage

```
plotGraphL(graph,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,vertex.label=V(graph)$graphics_name,
  vertex.shape=V(graph)$graphics_type,layout=getLayout(graph),
  vertex.label.color="black",vertex.color=V(graph)$graphics_bgcolor,
  vertex.frame.color="dimgray",edge.color="dimgray",
  edge.label=getEdgeLabel(graph),edge.label.cex=0.6,
  edge.label.color="dimgray",edge.lty=getEdgeLty(graph),
  axes=FALSE,xlab="",ylab="",sub=NULL,main=NULL,...)
```

Arguments

graph	The igraph object of a pathway graph.
margin	A numeric. The value is usually between -0.5 and 0.5, which is able to zoom in or out a pathway 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.
vertex.label	A vector of node label. The default is graphics_name.
vertex.shape	A vector of node shape. The default is graphics_type.
layout	A matrix of x-y coordinates with two dims. Determine the placement of the nodes for drawing a graph. The default is the KEGG node coordinates that are originally obtained from the KGML file.
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	A vector of edge label.
edge.label.cex	Edge label size.
edge.label.color	
	A vector of edge label color. The default is dimgray.
edge.lty	A vector of line type for the edges.
axes	A logical. whether to plot axes. The default is FALSE.
xlab	A character string. The label of the horizontal axis. The default is the empty string.
ylab	A character string. The label of the vertical axis. The default is the empty string.
sub	A character string of subtitle.
main	A character string of main title.
...	The arguments passed to or from methods. See `plot`.

Details

The function `plotGraphL` is able to display a pathway graph.

The argument `layout` is used to determine the placement of the nodes for drawing a graph. There are mainly two preprocessed methods to determine the placement of the nodes for drawing a pathway graph: the KEGG pathway layout and `layout` provided in the function `plot.igraph` of the igraph package. The default layout is the KEGG layout, for which the coordinates of nodes in KEGG is used to determine the placement of the nodes for drawing a graph. Therefore, the returned figure by the function may be very similar to the KEGG pathway graph when information in the pathway graph is complete relatively. The layouts provided in igraph include `layout.reingold.tilford`, `layout.random`, `layout.circle`, `layout.sphere`,..., .

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

[plot](#), [layout.random](#)

Examples

```
## Not run:
###  get  signal pathway graphs   ###

g<- GetExampleData(exampleData="g2")

# visualize the graph
plotGraphL(g[[9]],layout=layout.random)


## End(Not run)
```

---

printGraphW   *Print the results of graph annotation and identification*

Description

Print the results of graph annotation and identification.

Usage

```
printGraphW(ann,detail=FALSE)
```

Arguments

ann	A list. The value was returned from the function [identifyLncGraphW](#).
detail	A logical. If true, gene lists from the function [identifyLncGraphW](#) are converted into strings, which are used to display and write results with genes.

Value

A data.frame. Columns include pathwayId, pathwayName, annMoleculeRatio, annBgRatio,annWeight, pvalue, 'fdr', annMoleculeList, annBgMoleculeList. Detailed information is provided in [identifyLncGraphW](#).

Author(s)

Xinrui Shi, Chunquan Li and Xia Li

See Also

[identifyLncGraphW](#)

Examples

```
## Not run:
### Integrate lncRNAs of competitive regulation into KEGG pathway graphs ###
  LncGenePairs<-GetExampleData(exampleData="LncGenePairs")
  inteUMGraph<-getInteUMGraph(LncGenePairs)
### get user-interested lncRNAs and genes sets.
  geneLnc<-GetExampleData(exampleData="geneLnc")
# get locate subpathways.
  sub<-getLocSubGraphLnc(geneLnc,inteUMGraph,type="gene_lncRNA",n=1,s=8)
  SubcodeLncResult<-identifyLncGraphW(geneLnc,sub,type="gene_lncRNA",bet=1)
  resultT<-printGraphW(SubcodeLncResult,detail=TRUE)



## End(Not run)
```

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