Package 'mirIntegrator'

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Type Package

Title Integrating microRNA expression into signaling pathways for pathway analysis

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Imports graph,ROntoTools, ggplot2, org.Hs.eg.db, AnnotationDbi, Rgraphviz

Suggests RUnit, BiocGenerics

Description Tools for augmenting signaling pathways to perform pathway analysis of microRNA and mRNA expression levels.

License GPL (>=3)

URL http://datad.github.io/mirIntegrator/

biocViews Network, Microarray, GraphAndNetwork, Pathways, KEGG

NeedsCompilation no

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`augmented_pathways` *Signaling pathways augmented with miRNA.*

Description

Human signaling KEGG pathways augmented with validated miRNA-target interactions from mirTarBase using the mirIntegrator package. These interactions represent the biological miRNA repression over its target genes and are included in the model as negative links.

Usage

```
data("augmented_pathways")
```

Value

A list of graphNEL objects where each graph is a pathway that were augmented with miRNA-target interactions. The name of each pathway is its KEGG pathway identifier.

Source

Generated using the mirIntegrator package. A script that constructs the augmented_pathways object may be found in 'inst/scripts/get_augmented_pathways.R', see the example.

References

M. Kanehisa and S. Goto, *KEGG: Kyoto Encyclopedia of Genes and Genomes*, Nucleic Acids Research, vol. 28, pp. 27-30, January 2000.

S.-D. Hsu, Y.-T. Tseng, S. Shrestha, Y.-L. Lin, A. Khaleel, C.-H. Chou, C.-F. Chu, H.-Y. Huang, C.-M. Lin, S.-Y. Ho, T.-Y. Jian, F.-M. Lin, T.-H. Chang, S.-L. Weng, K.-W. Liao, I.-E. Liao, C.-C. Liu, and H.-D. Huang, *miRTarBase update 2014: an information resource for experimentally validated miRNA-target interactions*, Nucleic Acids Research, vol. 42, pp. D78 - D85, Jan. 2014.

See Also

`mirTarBase` and `kegg_pathways`

Examples

```
data(augmented_pathways)
head(augmented_pathways)

script <- system.file("scripts", "get_augmented_pathways.R",
                      package = "mirIntegrator")
script
readLines(script)
```

GSE43592_miRNA *Top table of preprocessed miRNA of GSE43592 dataset.*

Description

A data.frame with the Log fold change and p-value of preprocessed miRNA expression of GSE43592 dataset.

Usage

```
data(GSE43592_miRNA)
```

Value

A data frame with 881 miRNAs with the following 8 variables: entre, ID, logFC, AveExpr, t, P.Value, adj.P.Val, B.

Source

Raw data obtained from http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE43592 and preprocessed with the limma package version 3.24.0.

References

M. Jernas, C. Malmestrom, M. Axelsson, I. Nookaew, H. Wadenvik, J. Lycke, and B. Olsson,*MicroRNA regulate immune pathways in t-cells in multiple sclerosis (MS),* BMC immunology, vol. 14, p. 32, 2013.

Ritchie ME, Phipson B, Wu D, Hu Y, Law CW, Shi W and Smyth GK (2015). *limma powers differential expression analyses for RNA-sequencing and microarray studies.* Nucleic Acids Research, 43(7), pp. e47.

Examples

```
data(GSE43592_miRNA)
head(GSE43592_miRNA)
```

GSE43592_mRNA *Top table of preprocessed mRNA of GSE43592 dataset.*

Description

A data.frame with the Log fold change and p-value of preprocessed mRNA expression of GSE43592 dataset.

Usage

```
data(GSE43592_mRNA)
```

Value

A data frame with 19611 mRNAs with the following 8 variables: entre, ID, logFC, AveExpr, t, P.Value, adj.P.Val, B.

Source

Raw data obtained from http://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE43592 and preprocessed with the limma package version 3.24.0.

References

M. Jernas, C. Malmestrom, M. Axelsson, I. Nookaew, H. Wadenvik, J. Lycke, and B. Olsson,*MicroRNA regulate immune pathways in t-cells in multiple sclerosis (MS),* BMC immunology, vol. 14, p. 32, 2013.

Ritchie ME, Phipson B, Wu D, Hu Y, Law CW, Shi W and Smyth GK (2015). *limma powers differential expression analyses for RNA-sequencing and microarray studies.* Nucleic Acids Research, 43(7), pp. e47.

Examples

```
data(GSE43592_mRNA)
head(GSE43592_mRNA)
```

integrate_mir *Produce augmented pathways*

Description

This function takes each pathway of the input list of signaling pathways and adds the miRNAs that are related to it.

Usage

```
integrate_mir(original_pathways, targets_db)
```

Arguments

original_pathways	A list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Gene IDs used to identify the nodes must be the same gene IDs used to identify the genes on the miRNA-target interactions data.frame, targets_db. i.e. If the genes are identified by Entrez ID on the original_pathways graph::graphNEL list, then the targets_db data.frame must identify the genes by Entrez ID as well. Nodes of each graph::graphNEL represent the genes involved in the pathway and edges represent the biological interactions (activation or repression) among those genes (activation or repression).
targets_db	A data.frame with columns: 'miRNA' which names the miRNAs and 'Target.ID' which gives the gene ID of the target gene. The Gene IDs used to identify the "Target.ID" column must be the same gene IDs used on the nodes of the original_pathways. i.e. If the genes are identified by Entrez ID on the original_pathways graph::graphNEL list, then the targets_db data.frame must identify the genes by Entrez ID as well.

Value

Gene signaling pathways augmented with miRNA interactions. This is a list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent genes and miRNAs involved in the pathway and edges represent the biological interactions (activation or repression) among them.

Author(s)

Diana Diaz <dmd at wayne dot edu>

Examples

```
data(kegg_pathways)
data(mirTarBase)
kegg_pathways <- kegg_pathways[1:5] #delete this for augmenting all pathways.
augmented_pathways <- integrate_mir(kegg_pathways, mirTarBase)
```

---

kegg_pathways *List of KEGG signaling pathways of human.*

Description

This dataset contains 149 KEGG signaling pathways of human. The original pathways were parsed to a list of graphNEL objects using the ROntoTools package. The original KEGG pathways were published by Kanehisa Laboratories, release 73.0+/01-03, Jan 2015.

Usage

```
data("kegg_pathways")
```

Value

A list of graphNEL objects where each graph represents one KEGG signaling pathway. The name of each pathway is its KEGG pathway identifier.

Source

Obtained using the ROntoTools package Version 1.2.0 with KEGG database release 73.0+/01-03, Jan 2015. A script that constructs the kegg_pathways object may be found in 'inst/scripts/get_kegg_pathways.R', see the example.

References

M. Kanehisa and S. Goto, *KEGG: Kyoto Encyclopedia of Genes and Genomes*, Nucleic Acids Research, vol. 28, pp. 27-30, January 2000.

C. Voichita, M. Donato, and S. Draghici, *Incorporating gene significance in the impact analysis of signaling pathways*, in 2012 11th International Conference on Machine Learning and Applications (ICMLA), vol. 1, pp. 126-131, Dec. 2012.

Examples

```
data(kegg_pathways)
head(kegg_pathways)

script <- system.file("scripts", "get_kegg_pathways.R",
                      package = "mirIntegrator")
script
readLines(script)
```

---

mirTarBase *MicroRNA-target interactions in human.*

Description

Dataset of miRNA-target interactions in human obtained from mirTarBase release 4.5: Nov. 1, 2013.

Usage

```
data(mirTarBase)
```

Format

A data.frame with 39083 interactions and 9 variables. The columns needed for this package are:

- `miRNA`: which contains the miRNA ID,
- `Target.ID`: contains the entrez ID of the gene targeted by the `miRNA`

Details

This dataset is licensed by its authors (Hsu et al.), see http://mirtarbase.mbc.nctu.edu.tw/cache/download/LICENSE.

Value

A data.frame with human miRNA-targets interactions

Source

Downloaded from http://mirtarbase.mbc.nctu.edu.tw/ on 4/1/2015. A script which downloads the file and constructs the mirTarBase object may be found in 'inst/scripts/get_mirTarBase.R', see the example.

References

S.-D. Hsu, Y.-T. Tseng, S. Shrestha, Y.-L. Lin, A. Khaleel, C.-H. Chou, C.-F. Chu, H.-Y. Huang, C.-M. Lin, S.-Y. Ho, T.-Y. Jian, F.-M. Lin, T.-H. Chang, S.-L. Weng, K.-W. Liao, I.-E. Liao, C.-C. Liu, and H.-D. Huang, *miRTarBase update 2014: an information resource for experimentally validated miRNA-target interactions*, Nucleic Acids Research, vol. 42, pp. D78 - D85, Jan. 2014.

Examples

```
data(mirTarBase)
head(mirTarBase)

script <- system.file("scripts", "get_mirTarBase.R",
                      package = "mirIntegrator")
script
readLines(script)
```

---

names_pathways *List of KEGG signaling pathways' names.*

Description

Names of the KEGG signaling pathways in human obtained with the ROntoTools package. The original KEGG pathways were published by Kanehisa Laboratories, release 73.0+/01-03, Jan 2015.

Usage

```
data("names_pathways")
```

Value

A list of KEGG signaling pathways' names.

Source

Obtained using the ROntoTools package Version 1.2.0 with KEGG database release 73.0+/01-03, Jan 2015. A script that constructs the names_pathways object may be found in 'inst/scripts/get_names_pathways.R', see the example.

References

M. Kanehisa and S. Goto, *KEGG: Kyoto Encyclopedia of Genes and Genomes*, Nucleic Acids Research, vol. 28, pp. 27-30, January 2000.

C. Voichita, M. Donato, and S. Draghici, *Incorporating gene significance in the impact analysis of signaling pathways*, in 2012 11th International Conference on Machine Learning and Applications (ICMLA), vol. 1, pp. 126-131, Dec. 2012.

Examples

```
data(names_pathways)
head(names_pathways)

script <- system.file("scripts", "get_names_pathways.R",
                      package = "mirIntegrator")
script
readLines(script)
```

`pathways2pdf` *Export augmented pathways to pdf*

Description

This function creates a pdf file with plottings of a list of augmented pathways.

Usage

```
pathways2pdf(original_pathways, augmented_pathways, pathway_names, file)
```

Arguments

`original_pathways`
: A list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent the genes involved in the pathway and edges represent the biological interactions (activation or repression) among those genes (activation or repression).

augmented_pathways
: A list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent genes and miRNAs involved in the pathway and edges represent the biological interactions (activation or repression) among them.

pathway_names
: A list of names of the pathways named by '<pathway_ID>'.

file
: The name of the file where the plots will be saved.

Value

A pdf file with the plottings of the augmented pathways.

Author(s)

Diana Diaz <dmd at wayne dot edu>

Examples

```
data(augmented_pathways)
data(kegg_pathways)
data(names_pathways)
#The following instruction writes a pfd with three pathways
pathways2pdf(kegg_pathways[18:20],augmented_pathways[18:20],
             names_pathways[18:20], "three_pathways.pdf")
#The following instruction writes a pfd with all the pathways:
#NOTE: It may take time.
# pathways2pdf(kegg_pathways,augmented_pathways,
#              names_pathways, "all_pathways.pdf")
```

---

plot_augmented_pathway

Plotting of augmented pathway

Description

Functions for plotting a particular augmented pathway. In the plot, miRNAs that were added to the original pathway are differentiated from proteins that were originally in the pathway. Blue boxes represent the proteins that were part of the original pathway, and black boxes represent the miRNAs that were added during augmentation.

Usage

```
plot_augmented_pathway(original_pathway, augmented_pathway,
  pathway_name = " ", ...)
```

Arguments

original_pathway	A graph::graphNEL object where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent the genes involved in the pathway and edges represent the biological interactions (activation or repression) among those genes.
augmented_pathway	A graph::graphNEL object where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent genes and miRNAs involved in the pathway and edges represent the biological interactions (activation or repression) among them.
pathway_name	The name of the pathway.
...	Other arguments for the '<plotPathway2Colors>' function.

Value

A plot of one augmented pathway with the new nodes highlighted in black.

Author(s)

Diana Diaz <dmd at wayne dot edu>

Examples

```
data(augmented_pathways)
data(kegg_pathways)
data(names_pathways)

plot_augmented_pathway(kegg_pathways[[18]], augmented_pathways[[18]],
                       pathway_name = names_pathways[[18]])
```

---

plot_change *Plotting the change in pathways order*

Description

Function for plotting a lines plot of the difference in pathways' order. The resultant plot shows the comparison between the order of the original pathways and the order of the augmented pathways. It also contains a line with the order difference (order of the augmented pathways minus order of the original pathways). The order of a biological pathway is the number of genes that are involved in it.

Usage

```
plot_change(original_pathways, augmented_pathways, pathway_names, ...)
```

Arguments

original_pathways	A list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent the genes involved in the pathway and edges represent the biological interactions (activation or repression) among those genes (activation or repression).
augmented_pathways	A list of graph::graphNEL objects where each of the nodes is named with '<gene_ID>'. Nodes of each graph::graphNEL represent genes and miRNAs involved in the pathway and edges represent the biological interactions (activation or repression) among them.
pathway_names	A list of names of the pathways named by '<pathway_ID>'.
...	Other arguments for the '<plotLines>' function.

Value

A lines plot of the comparison of pathways order.

Author(s)

Diana Diaz <dmd at wayne dot edu>

Examples

```
data(augmented_pathways)
data(kegg_pathways)
data(names_pathways)
plot_change(kegg_pathways,augmented_pathways, names_pathways)
```

---

smallest_pathway *Get the smallest pathway*

Description

Find the pathway with the fewer number of nodes among a list of pathways. This simple function is an example of how to navigate the genes on a list of pathways.

Usage

```
smallest_pathway(pathways)
```

Arguments

pathways	A list of graph::graphNEL objects.

Value

The index of the pathway with fewer number of nodes.

Author(s)

Diana Diaz <dmd at wayne dot edu>

Examples

```
data(augmented_pathways)
smallest_pathway(augmented_pathways)
smallest_pathway
```

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