Package ‘KEGGprofile’

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Type  Package

Title  An annotation and visualization package for multi-types and multi-groups expression data in KEGG pathway

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Description  KEGGprofile is an annotation and visualization tool which integrated the expression profiles and the function annotation in KEGG pathway maps. The multi-types and multi-groups expression data can be visualized in one pathway map. KEGGprofile facilitated more detailed analysis about the specific function changes inner pathway or temporal correlations in different genes and samples.

License  GPL (>= 2)

LazyLoad  yes

Imports  AnnotationDbi, png, TeachingDemos, XML, KEGG.db, KEGGREST, biomaRt

biocViews  Pathways, KEGG

NeedsCompilation  no

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The function will transfer a numeric matrix into a matrix of colors, in which the colors represent the values of numeric matrix.

**Usage**

```r
col_by_value(x, col, range = NA, breaks = NA, showColorBar = T)
```

**Arguments**

- **x**: a numeric matrix
- **col**: colors used to represent the values. (See also ‘Details’)
- **range**: values out of the range will be modified to in the range.
- **breaks**: a numeric vector of three or more cut points giving the number of intervals into which x is to be cut. See also ‘Details’
- **showColorBar**: Logical. Indicates display the colorbar or not. The default value is TRUE.

**Details**

A colorbar would also be plotted. The returned colors of the function can be used in function `plot_profile`. If breaks not equal to NA, col must have the same length with breaks-1.

**Value**

A matrix equal to x, but the values were instead by colors.

**Examples**

```r
data(pho_sites_count)
col<-col_by_value(pho_sites_count,col=colorRampPalette(c('white','khaki2'))(4),breaks=c(0,1,4,10,Inf))
```

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**convertId**

A function to convert ID based on the biomaRt package.

**Usage**

```r
convertId(x, dataset = "hsapiens_gene_ensembl", filters = "uniprot_swissprot_accession", attributes = c(filters, "entrezgene"), genesKept = c("foldchange", "first", "random", "var", "abs"), keepNoId = T, keepMultipleId = F, verbose = F)
```
Arguments

x       the expression data matrix.
dataset Dataset you want to use. To see the different datasets available within a biomaRt you can e.g. do: mart = useMart('ensembl'), followed by listDatasets(mart).
filters Filters (one or more) that should be used in the query. A possible list of filters can be retrieved using the function listFilters.
attributes Attributes you want to retrieve. A possible list of attributes can be retrieved using the function listAttributes.
genesKept The method to select target gene in more than one targets. "var"/"foldchange"/"abs" means selecting the gene with largest variation/fold change/absolute value. "first" means selecting the first target and "random" means randomly selection.
keepNoId Logical. Indicate keep the source IDs without target IDs or not.
keepMultipleId Logical. Indicate keep the multiple target IDs related to one source ID or not.
verbose Logical. Indicate report extra information on progress or not.

Details

A function to convert ID based on the biomaRt package.

Examples

temp<-cbind(rnorm(10),rnorm(10))
row.names(temp)<-c("Q04837","P0C0L4","P0C0L5","Q75379","Q13068","A2MYD1","P60709","P30462","P30475","P30479")
colnames(temp)<-c("Exp1","Exp2")
convertId(temp,filters="uniprot_swissprot",keepMultipleId=TRUE)

## Not run:
temp<-cbind(rnorm(5000),rnorm(5000),rnorm(5000),rnorm(5000),rnorm(5000),rnorm(5000))
row.names(temp)<-1:5999
colnames(temp)<-c("Control1","Control2","Control3","Treatment1","Treatment2","Treatment3")
convertId(temp,filters="entrezgene",attributes =c("entrezgene","uniprot_swissprot"),keepNoId=FALSE)

## End(Not run)

download_KEGGfile

Description

The function download XML files and png files from KEGG website to local disk

Usage

download_KEGGfile(pathway_id = "00010", species = "hsa", target_dir = getwd())

Arguments

pathway_id the KEGG pathway id, such as '00010'
species the species id in KEGG database, 'hsa' means human, 'mmu' means mouse, 'rno' means rat, etc
target_dir the local directory where the downloaded files are saved
Details

If pathway_id is set as ‘all’, all KEGG pathway ids in KEGG.db package will be used and downloaded from KEGG website.

Examples

download_KEGGfile(pathway_id="00010",species='hsa')

Description

The function will download the latest pathway gene link from KEGG website.

Usage

download_latest_pathway(species)

Arguments

species the species id in KEGG database, ‘hsa’ means human, ‘mmu’ means mouse, ‘rno’ means rat, etc

Details

The function will download the latest pathway gene link from KEGG website.

Value

a list with two parts

name keggpathway2gene
   description a list with the genes for each pathway

name pathway2name
   description a list with the names for each pathway

Examples

## Not run: download_latest_pathway(species="hsa")
Description

The function will map the genes in KEGG pathway database, and then hypergeometric tests would be used to estimate the significance of enrichment for each pathway.

Usage

```
find_enriched_pathway(gene, species = "hsa", returned_pvalue = 0.01, returned_adjpvalue = 0.05, returned_genenumber = 5, download_latest = FALSE)
```

Arguments

- **gene**: a numeric matrix
- **species**: the species id in KEGG database, 'hsa' means human, 'mmu' means mouse, 'rno' means rat, etc
- **returned_pvalue**: the minimum p value for enriched pathways
- **returned_adjpvalue**: the minimum adjusted p value for enriched pathways
- **returned_genenumber**: the minimum number of annotated genes for enriched pathways
- **download_latest**: logical. Indicate if the function will download the latest pathway/gene link from KEGG website. As the KEGG.db package was not updated for a long time due to the KEGG policy change, we provided this parameter so that the users could get the latest KEGG database.

Details

Only the pathways with p value <= returned_pvalue in hypergeometric tests and number of annotated genes >= returned_genenumber would be taken as enriched and returned.

Value

- a list with two parts
  - **name stactic**: description a matrix containing the pathway IDs of enriched pathways, and their names, p values, number of annotated genes
  - **name detail**: description a list with the genes annotated for each pathway

Examples

```
data(pho_sites_count)
# the 300 genes with most phospholation sites quantified
genes<-names(rev(sort(pho_sites_count[,1])))[1:300])
pho KEKGresult<-find_enriched_pathway(genes,species='hsa')
```
newIdMatrix

Description
A function to convert ID.

Usage
newIdMatrix(x, convertIdTable, genesKept = c("var", "foldchange", "abs", "first", "random"))

Arguments
- **x**: the expression data matrix.
- **convertIdTable**: A vector. The names should be the source IDs, and the values should be the target IDs.
- **genesKept**: The method to select target gene in more than one targets. "var"/"foldchange"/"abs" means selecting the gene with largest variation/fold change/absolute value. "first" means selecting the first target and "random" means randomly selection.

Details
A function to convert ID.

Examples
```r
correctIdTable<-paste("New",c(1,2,2,1,3,4,4,5,5))
names(correctIdTable)<-paste("Old",1:length(correctIdTable))
temp<-matrix(rnorm(20),ncol=2)
row.names(temp)<-names(correctIdTable)
colnames(temp)<-c("Exp1","Exp2")
newIdMatrix(temp,genesKept="foldchange",convertIdTable)
```

parse_XMLfile

Description
The function parses KEGG XML (KGML) files

Usage
parse_XMLfile(pathway_id, species, database_dir = getwd())

Arguments
- **pathway_id**: the KEGG pathway id, such as ‘00010’
- **species**: the species id in KEGG database, ‘hsa’ means human, ‘mmu’ means mouse, ‘rno’ means rat, etc
- **database_dir**: the directory where the XML files and png files are located
**Details**

This function will parse the KEGG XML (KGML) file. Then a matrix with genes in this pathway and related informations will be returned. This matrix can be used for plot the expression profiles on the pathway figure.

**Value**

a matrix containing genes in this pathway, and their names, locations etc, which could be used in the function plot_profile as param KEGG_database

**Examples**

```r
XML2database<-parse_XMLfile(pathway_id="04110",species="hsa",database_dir=system.file("extdata",package="KEGGprofile"))
```

---

**pho_sites_count**

| pho_sites_count | number of phosphorylation sites quantified for each gene |

**Description**

This data set is a data.frame with number of phosphorylation sites quantified for each gene in the analysis.

**Usage**

```r
pho_sites_count
```

**Source**


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**plot_pathway**

**plot_pathway**

**Description**

A wrapper for function download_KEGGfile, parse_XMLfile and plot_profile

**Usage**

```r
plot_pathway(gene_expr, line_col, groups, pathway_id = "00010", species = "hsa", pathway_min = 5, database_dir = getwd(), speciesRefMap = TRUE, ...)
```
Arguments

- **gene_expr**
  - the matrix for gene expression, row.names should be NCBI gene ID, such as 67040, 93683
- **line_col**
  - line color for expression in different samples in the pathway map, valid when `type='lines'
- **groups**
  - a character used to indicate expression values from different types of samples
- **pathway_id**
  - the KEGG pathway id, such as '00010'
- **species**
  - the species id in KEGG database, 'hsa' means human, 'mmu' means mouse, 'rno' means rat, etc
- **pathway_min**
  - The pathways with number of annotated genes less than `pathway_min` would be ignored
- **database_dir**
  - the directory where the XML files and png files are located
- **speciesRefMap**
  - Logical, use the species specific figure as reference map. If set as FALSE, the reference pathway figure without species information will be used
- ... any other Arguments for function `plot_profile`

Details

This wrapper function is developed to make the visualization process more easier. Firstly the existence of XML file and png file would be checked, if not, the `download_KEGGfile` function would be used to download the files. Then the `parse_XMLfile` function would be used to parse the XML file. At last the `plot_profile` function would be used to generate the pathway map.

See Also

- `download_KEGGfile`, `parse_XMLfile`, `plot_profile`

Examples

```r
data(pro_pho_expr)
data(pho_sites_count)
#type='lines'
col<-col_by_value(pho_sites_count,col=colorRampPalette(c('white','khaki2'))(4),breaks=c(0,1,4,10,Inf))
temp<-plot_pathway(pro_pho_expr,bg_col=col,line_col=c("brown1","seagreen3"),groups=c(rep("Proteome",6),rep("Phosphoproteome",6)),magnify=1.2,species="hsa",database_dir=system.file("extdata",package="KEGGprofile"),pathway_id="04110",max_dist=5)

#type='bg'
pho_expr<-pro_pho_expr[,7:12]
temp<apply(pho_expr,1,function(x) length(which(is.na(x))))
pho_expr<pho_expr[which(temp==0),]
col<-col_by_value(pho_expr,col=colorRampPalette(c('green','black','red'))(1024),range=c(-6,6))
temp<-plot_pathway(pho_expr,type="bg",bg_col=col,text_col="white",magnify=1.2,species="hsa",database_dir=system.file("extdata",package="KEGGprofile"),pathway_id="04110")

#Compound and gene data
set.seed(124)
testData1<-rbind(rnorm(6),rnorm(6),rnorm(6),rnorm(6),rnorm(6),rnorm(6),rnorm(6),rnorm(6))
row.names(testData1)<-c("4967","55753","1743","8802","47","50","cpd:C15972","cpd:C16255")
colnames(testData1)<-c("Control0","Control2","Control5","Sample0","Sample2","Sample5")
temp<-plot_pathway(testData1,type="lines",line_col=c("brown1","seagreen3"),groups=c(rep("Control",3),rep("Sample",3)),magnify=1.2,species="hsa",database_dir=system.file("extdata",package="KEGGprofile"),pathway_id="00020")

testData2<-testData1[4:6]-testData1[1:3]
col<-col_by_value(testData2,col=colorRampPalette(c('green','black','red'))(1024),range=c(-2,2))
temp<-plot_pathway(testData2,type="bg",bg_col=col,text_col="white",magnify=1.2,species="hsa",database_dir=system.file("extdata",package="KEGGprofile"),pathway_id="00020")
```
plot_pathway_cor

Description

The function will plot the correlation distributions for each enriched pathway (result from find_enriched_pathway function), and then Wilcoxon tests would be used to estimate the significance of correlations distribution between genes in each pathway and all genes.

Usage

plot_pathway_cor(gene_expr, kegg_enriched_pathway, groups = NULL, side = c("both", "pos", "neg"), alternative = NULL)

Arguments

gene_expr  
the matrix for gene expression, row.names should be NCBI gene ID, such as 67040, 93683

kegg_enriched_pathway  
The returned value from find_enriched_pathway function, the enriched pathways.

groups  
a character used to indicate expression values from different types of samples

side  
a character string specifying the correlation directions interested, must be one of "both" (default), "pos" or "neg".

alternative  
a character string specifying the alternative hypothesis, must be one of "two.sided" (default), "greater" or "less". You can specify just the initial letter.

Value

p values for Wilcoxon tests in each pathway

Examples

data(pro_pho_expr)
data(pho_sites_count)
genes<-row.names(pho_sites_count)[which(pho_sites_count>=10)]
pho_KEGGresult<-find_enriched_pathway(genes,species='hsa')
result<-plot_pathway_cor(gene_expr=pro_pho_expr,kegg_enriched_pathway=pho_KEGGresult)

plot_profile

Description

The function plot gene expression profiles on KEGG pathway maps
### Usage

```r
plot_profile(gene_expr, pathway_name, result_name = paste(pathway_name, 
"_profile_", type, ".png", sep = ""), KEGG_database, groups, 
bg_col = "white", text_col = "black", line_col, border_col = "grey", 
text_cex = 0.25, magnify = 1, type = c("lines", "bg"), 
pathway_min = 5, genes_kept = c("foldchange", "first", "random", "var", 
"abs"), species = "hsa", database_dir = getwd(), max_dist, lwd = 1.2, 
speciesRefMap = TRUE)
```

### Arguments

- **gene_expr**: the matrix for gene expression, row.names should be NCBI gene ID, such as 67040, 93683
- **pathway_name**: the species id and KEGG pathway id, such as 'hsa00010'
- **result_name**: the name of figure file generated by KEGGprofile. The default name is pathway_name+'_profile_'+type+'.png', such as 'hsa04110_profile_lines.png'
- **KEGG_database**: the matrix returned by function parse_XMLfile, which contains genes in this pathway, and their names, locations etc
- **groups**: a character used to indicate expression values from different types of samples
- **bg_col**: background color for gene rectangles in the pathway map
- **text_col**: the colors for text in the pathway map. A color matrix generated by function `col_by_value` can be used here
- **line_col**: line color for expression in different samples in the pathway map, valid when type='lines'
- **border_col**: border color for gene rectangles in the pathway map. A color matrix generated by function `col_by_value` can be used here
- **text_cex**: cex for text in the pathway map. A color matrix generated by function `col_by_value` can be used here
- **magnify**: the coefficient used to magnify the gene rectangles
- **type**: the type of pathway map visualization, could be 'bg' or 'lines'. Default is 'bg'. See also 'Details'
- **pathway_min**: The pathways with number of annotated genes less than pathway_min would be ignored
- **genes_kept**: methods used for choosing genes when several genes corresponding to one location in pathway map. Default is 'foldchange', which kept the gene with largest fold changes. 'first' kept the first gene. 'random' chosed gene random. 'var' kept the gene with largest variation. 'abs' kept the gene with largest absolute value
- **species**: the species id in KEGG database, 'hsa' means human, 'mmu' means mouse, 'rno' means rat, etc
- **database_dir**: the directory where the XML files and png files are located
- **max_dist**: The expression changes that represented by the distance from the bottom to the top of gene rectangle, valid when type='lines'. This param is used to ensure the dynamic changes of lines in different gene polygon represent equal variation. It would be calculated from the maximum changes of genes in this pathway by default. If max_dist=NA, then the lines would be plotted from top to bottom in each gene rectangle
**pro_pho_expr**

1wd

The line width when `type='lines'`

speciesRefMap

Logical, use the species specific figure as reference map. If set as FALSE, the reference pathway figure without species information will be used.

**Details**

There are two visualization methods to represent gene expression profiles: 'background' and 'lines'. The first one is applicable for analysis with only one sample or one type of data, which divides the gene polygon into several sub-polygons to represent different time points. And each sub-polygon has a specific background color to represent expression changes in that time point. The second method plots lines with different colors in the gene polygon to represent different samples or different types of data. The dynamic changes of lines mean the profiles of genes in different time points.

**Value**

A matrix containing genes mapped in this pathway, and their names, expressions.

**Examples**

```r
XML2database<-'parse.XMLfile(pathway_id="04110",species="hsa",database_dir=system.file("extdata",package="KEGGprofile"),package="KEGGprofile")
temp<-plot_profile(pro_pho_expr,pathway_name="hsa04110",KEGG_database=XML2database,line_col=c("brown1","seagreen3"),groups=rep("Phosphorylation ",6),rep("Phosphoproteome ",6)),magnify=1.2,database_dir=system.file("extdata",package="KEGGprofile"),max_dist=5)
```

**Description**

This data set is from a previously published data of proteome and phosphoproteome analysis in different cell phase. The column 1-6 are proteome data and column 7-12 are phosphoproteome data in this data.frame. The 6 time points are G1, G1/S, Early S, Late S, G2, Mitosis.

**Usage**

`pro_pho_expr`

**Source**

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