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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Description
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(0,4,10,Inf))
```

Description
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)
```
download_KEGGfile

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)<-1000:5999
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

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')

download_latest_pathway

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

- `keggpathway2gene`: a list with the genes for each pathway
- `pathway2name`: a list with the names for each pathway

Examples

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

```r
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 stastic`: 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

```r
data(pho_sites_count)
#the 300 genes with most phospholation sites quantified
genes<-names(rev(sort(pho_sites_count[,1])))[1:300])
pho_KEGGresult<-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
convertIdTable<-paste("New",c(1,2,2,1,3,4,4,5,5))
names(convertIdTable)<-paste("Old",1:length(convertIdTable))
temp<-matrix(rnorm(20),ncol=2)
row.names(temp)<-names(convertIdTable)
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 information 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_XML_file(pathway_id = "04110", species = "hsa", database_dir = system.file("extdata", package = "KEGGprofile"))
```

<table>
<thead>
<tr>
<th>pho_sites_count</th>
<th>number of phosphorylation sites quantified for each gene</th>
</tr>
</thead>
</table>

**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**


<table>
<thead>
<tr>
<th>plot_pathway</th>
<th>plot_pathway</th>
</tr>
</thead>
</table>

**Description**

A wrapper for function `download_KEGGfile`, `parse(XML_file)` 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

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)

#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",max_dist=2)
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")
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**

```r
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**

```r
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)
```

The function `plot_profile` plots gene expression profiles on KEGG pathway maps.
Usage

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' chose 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
The line width when type='lines'

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

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.

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

XML2database <- parse.XMLfile(pathway_id="04110",species="hsa",database.dir=system.file("extdata",package="KEGGprofile"))
data(pro_pho_expr)
temp <- plot_profile(pro_pho_expr,pathway_name="hsa04110",KEGG_database=XML2database,line_col=c("brown1","sea"))

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.

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