Package 'methyl.O'

March 30, 2021

```
Title Annotate, Score and Visualize Differentially Methylated Regions
Version 1.0.0
Depends R (>= 3.5.0)
biocViews
Imports EnsDb.Hsapiens.v75,
     EnsDb.Hsapiens.v86,
     TxDb.Hsapiens.UCSC.hg19.knownGene (>= 3.2.2),
     GenomicRanges (>= 1.38.0),
     biomaRt (>= 2.42.1),
     S4Vectors (>= 0.24.4),
     Gviz (>= 1.30.0),
     ensembldb (>= 2.10.2),
     DT (>= 0.17),
     shiny (>= 1.6.0),
     shinycssloaders (>= 1.0.0),
      shinythemes (>= 1.2.0),
     shinyWidgets (>= 0.5.7),
     shinyLP (>= 1.1.2),
     shinyBS (>= 0.61),
     shinyalert (>= 2.0.0),
     colourpicker (>= 1.1.0),
      ggplot2 (>= 3.3.3),
      we sanders on (>= 0.3.6),
      enrichR
Manteiner Gianluca Mattei < gianluca.mattei@unifi.it>
Author Gianluca Mattei
Description Methods annotateDMRs() to retrieve annotations for DMRs and scoreAnnotated-
     DMRs() to assign a score to the annotated DMRs. Method annotateEhancers() is used to asso-
     ciate enhancers to genes. Method plotDMRs() used to visualize the annotated regions.
License LGPL (>= 2.1)
URL https://github.com/GianlucaMattei/methyl.0
BugReports https://github.com/GianlucaMattei/methyl.O/issues
Repository CRAN
Encoding UTF-8
LazyData true
```

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```
Roxygen list(markdown = TRUE)
RoxygenNote 7.1.1
Suggests knitr, rmarkdown, BiocStyle
VignetteBuilder knitr
```

R topics documented:

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annotatedDMRs2Enrichr Query different databases to find enriched proceses.

Description

Query gene symbols from resulting annotations list in order to find enriched proceses.

Usage

```
annotatedDMRs2Enrichr(
  annotatedDMRs,
  active.features = c("promoters", "heads"),
  stat.filter = "P.value",
  stat.thr = 0.01,
  db = NULL
)
```

Arguments

```
\label{eq:ddmrs} annotated DMRs \ list resulting from annotate DMRs() or score Annotated DMRs() \\ active.features \\ annotation level from the gene symbols are taken. \ Default = c('promoters', 'heads')
```

annotatedDMRs2Exprs

```
character indicating which type of statistics use for filtering results. Accepted values: 'P.value', 'Adjusted.P.value' or 'Overlap'. Default 'P.value'.

stat.thr

numeric value indicating the threshold to use for selcted statistical test. Default 0.01.

db

vector of characters indicating DBs to query. Default c("ClinVar_2019", "OMIM_Disease", "Elsevier_Pathway_Collection", "MSigDB_Hallmark_2020", "MSigDB_Oncogenic_Signatures", "GO_Biological_Process_2018", "Human_Phenotype_Ontology", "KEGG_2016", "NCI-Nature_2016", "Panther_2016", "Reactome_2016", "WikiPathways_2019_Human")
```

Value

data.frame with enriched processes

annotatedDMRs2Exprs

Compute correlation between expression and methylation levels.

Description

Compute correlation between expression and methylation levels.

```
annotatedDMRs2Exprs(
  annotatedDMRs,
  expressionProfile,
  active.features = c("promoters", "heads"),
  col.genes = 0,
  col.stat = 6,
  stat.thr = 0.05,
  col.logFC = 2,
  logfc.thr = 0,
  convert.genes = FALSE,
  convert.from,
  beta.thr = 0.3,
  overlap.param.thr = 100,
  param.type = "overlap.length",
  line.col = "lightgrey",
  lmfit.col1 = "red",
  lmfit.col2 = "green",
  pal = "RdGy",
  plot.type = "splitted",
  show.text = FALSE,
  cor.type = "pearson";
  filter.by.genes = NULL,
  return.table = FALSE
)
```

Arguments

 $annotated DMRs \ \ anotated \ DMRs \ list \ resulting from \ annotate DMRs() \ or \ score Annotated DMRs() \ expression Profile$

data.frame, expression profile.

active.features

character vectors, containing features to correlate. Must be from names of resulting list from annotateDMRs. Additional feature names can be first exons (exons1) or first intron (intron1). To use more than one feature use c(). Default = c("promoters", "heads")

col.genes numeric, the column of expressionProfile data.frame with gene Ids. If NULL geneIDs will be taken from rownames() of expressionProfile. Default = 0.

col.stat numeric, the column of expressionProfile data.frame with the statistics to use.

Default = 6.

stat.thr numeric, threshold for statistical significance. Default = 0.05

col.logFC numeric, the column of expressionProfile data.frame with log. fold change. De-

fault = 2

logfc.thr numeric, threshold value for log. fold change. Default = 0.

convert.genes boolean, used to indicate if gene ids have to be translated in official gene sym-

bols. Default = FALSE

convert.from character, used annotation for gene in expressionProfile to be converted to sym-

bols gene IDs. Accepted: c("ENTREZID" ,"EXONID" ,"GENEBIOTYPE" ,"GENEID" ,"GENENAME" ,"PROTDOMID" ,"PROTEINDOMAINID" ,"PROTEINDOMAINSOURCE" ,"PROTEINID" ,""SEQSTRAND" ,"SYMBOL" ,"TXBIO-

TYPE", "TXID", "TXNAME", "UNIPROTID")

beta. thr numeric, beta difference threshold value. Default = 0.3.

overlap.param.thr

nuemric, threshold value for selected parameter to filter methylations overlap-

ping the selected features. Default = 100

param.type character, threshold parameter to filter methylations overlapping the selected

features. Accetped c("dmr.length", "overlap.length", "overlap.percentage"). De-

fault = "overlap.length".

line.col character, color of lines at x=0, y=0. Default = "lightgray"

lmfit.col1 character, color of linear model line 1 or for simple plot. Default = "red"

lmfit.col2 character, color of linear model line 2. Default = "green"

pal character, color palette. hcl.pals() to show available. Default = "RdGy"

plot.type character, compute or not different linear models for upregulated and downreg-

ulated genes. Accepted: "simple" or "splitted". Default = "splitted".

show. text logical, indicating if print gene names in the final plot. Accepted values: TRUE

or FALSE. Default = FALSE.

cor.type character, correlation method. Available "pearson", "kendall" or "spearman"

correlation, Default = "pearson"

filter.by.genes

character vectors, gene symbols used for filtering output

return.table logical, TRUE return a data.frame instead a plot. Default = FALSE

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Value

plot of correlation or (if return.table = TRUE) a data.frame of genes expression associated to beta methylation values.

annotatedEnh2Exprs

Compute expression methylation correlation

Description

Compute and plot correlation between expression and methylation

Usage

```
annotatedEnh2Exprs(
  annotatedEnhancers,
  expressionProfile,
  hg = "hg19",
  enhancer.db = "FANTOM5",
  col.genes = 0,
  col.stat = 6,
  stat.thr = 0.05,
  col.logFC = 2,
  logfc.thr = 0.5,
  convert.genes = FALSE,
  convert.from,
  beta.thr = 0.3,
  overlap.param.thr = 40,
  param.type = "overlap.percentage",
  line.col = "lightgrey",
  lmfit.col1 = "red",
  lmfit.col2 = "green";
  pal = "RdGy"
  plot.type = "splitted",
  show.text = FALSE,
  cor.type = "pearson";
  return.table = FALSE
)
```

Arguments

```
annotatedEnhancers
data.frame. It corresponds to resulting list from annotateEnhancers()
expressionProfile
expression profile data.frame
hg character, "hg19", "hg38". Version of the enhancer database. Default = "hg19"
enhancer.db character, which database to use between 'FANTOM5' or '4DGenome'. Default = "FANTOM5"

col.genes numeric, the column of expressionProfile data.frame with gene Ids. If NULL geneIDs will be taken from rownames() of expressionProfile. Default = 0.
```

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col.stat	numeric, the column of expression Profile data.frame with the statistics to use. Default $= 6$.
stat.thr	threshold for statistical significance. Default = 0.05
col.logFC	numeric, the column of expression Profile data.frame with log. fold change. Default = 2
logfc.thr	numeric, threshold value for log. fold change. Default = 0 .
convert.genes	logical, used to indicate if gene ids have to be translated in official gene symbols. Default = FALSE
convert.from	character, used annotation for gene in expressionProfile to be converted to symbols gene IDs. Accepted: c("ENTREZID" ,"EXONID" ,"GENEBIOTYPE" ,"GENEID" ,"GENENAME" ,"PROTDOMID" ,"PROTEINDOMAINID" ,"PROTEINDOMAINSOURCE" ,"PROTEINID" ,""SEQSTRAND" ,"SYMBOL" ,"TXBIOTYPE" ,"TXID" ,"TXNAME" ,"UNIPROTID")
beta.thr	numeric, beta difference threshold value. Default = 0.3.
overlap.param.	thr
	numeric, threshold value for selected parameter to filter methylations overlapping the selected features. Default = 100
param.type	character, threshold parameter to filter methylations overlapping the selected features. Accetped c("dmr.length", "overlap.length", "overlap.percentage"). Default = "overlap.length".
line.col	character, color of lines at $x=0$, $y=0$. Defalt = "lightgray"
lmfit.col1	character, color of linear model line 1 or for simple plot. Defalt = "red"
lmfit.col2	character, color of linear model line 2. Defalt = "green"
pal	character, color palette. hcl.pals() to show available. Default = "RdGy"
plot.type	character, compute or not different linear models for upregulated and downreg- ulated genes. Accepted: "simple" or "splitted". Default = "splitted".
show.text	logical, indicating if print gene names in the final plot. Accepted values: TRUE or FALSE. Default = FALSE.
cor.type	character, correlation method. Available "pearson", "kendall" or "spearman" correlation, Default = "pearson"
return.table	logical, TRUE return a data.frame instead a plot. Default = FALSE

Value

plot of correlation or (if return.table = TRUE) a data.frame of genes expression associated to beta methylation values of enhancers.

annotateDMRs	Annotates the the differentially methylated regions.	

Description

Maps DMRs on genes returning a list for each features.

annotateDMRs 7

Usage

```
annotateDMRs(
  DMRsRanges,
  prom.length = 1500,
  head.length = 1500,
  longest.trx = TRUE,
  annotation = "ensembl",
  hg = "hg19",
  annotation.fast = TRUE,
  thr.beta = 0.3,
  thr.cgis = 0.4,
  col.betadiff = 4,
  col.beta1 = NULL,
  col.beta2 = NULL
)
```

Arguments

DMRsRanges	data.frame, the DMRs ranges, it must have the following columns: chr, start, end, beta diff. Other columns will be stored in the resulting output under the column other.
prom.length	numeric, length of promoters. Default = 1500
head.length	numeric, length of the first part of the gene, named head, starting from the TSS. If longer than the gene, the entire txs will be considered as head. Default = 1500
longest.trx	logical, option to use the longest transcript to represent the gene
annotation	character, database to use for transcripts mapping. Available "ensembl" or "ucsc". Default ="ensembl"
hg	character, Available "hg19", "hg38". Genome assembly version. Default = "hg19" $$
annotation.fast	
	logical, compute 1:1 mapping or 1:many - many:1 - many:many mapping. Default = TRUE
thr.beta	numeric, beta difference threshold to consider methylations. Default = 0.3
thr.cgis	numeric, length, in percentage, of methylated CGIs in order to be considered altered. Default = 0.4
col.betadiff	nuemric, column position for beta diff. in input table. Default = 4
col.beta1	numeric, column position for first sample beta values in input table
col.beta2	numeric, column position for second sample beta values in input table

Value

list, features overlapped by annotated DMRs

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annotateEnhancers

Query database to find enhancer.

Description

Query database of annotations results list to enhancer database in order to associate differentially methylated segments to genes.

Usage

```
annotateEnhancers(
  DMRsRanges,
  hg = "hg19",
  thr.beta = 0.3,
  overlap.param.thr = 40,
  param.type = "overlap.percentage",
  score.modifier = 0.5,
  col.betadiff = 4
)
```

Arguments

DMRsRanges the DMRs ranges, it must have the following columns: chr, start, end, beta diff.

Other columns will be stored in the resulting output under the column other.

hg character, Available "hg19", "hg38". Genome assembly version. Default =

"hg19"

thr. beta numeric, beta difference threshold to consider methylations. Default = 0.3

overlap.param.thr

numeric, threshold value for selected parameter to filter methylations overlap-

ping the selected features. Default = 100

param.type character, threshold parameter to filter methylations overlapping the selected

features. Accetped c("dmr.length", "overlap.length", "overlap.percentage"). De-

fault = "overlap.length".

score.modifier numeric, value between 0-1. It specifies how the final score is computed by

assigning different weights to the methylation charactersistics of enhancers or to genes already involved in pathologies. By increasing this value to 1, resulting scores will be focused on discovering segments affecting gene expression. A value equal to 0 will focus the results on enaheners involving genes associated

to pathologies, not considering the effect of methylation. Default = 0.5

col.betadiff numeric, column position for beta diff. in input table. Default = 4

Value

a vector of presence or a data.frame

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associateTFs2Exprs

Associate target genes to TFs and retrieve their expression

Description

For each TF find and associate the target genes, within the annotation results, and retrieve expression

Usage

```
associateTFs2Exprs(
  annotatedDMRs,
  expressionProfile,
  active.features = c("promoters", "heads"),
  col.genes = 0,
  col.stat = 6,
  stat.thr = 0.05,
  col.logFC = 2,
  logfc.thr = 0,
  convert.genes = FALSE,
  convert.from,
  beta.thr = 0.3,
 overlap.param.thr = 30,
  param.type = "overlap.percentage"
)
```

Arguments

annotatedDMRs anotated DMRs list resultingfrom annotateDMRs() or scoreAnnotatedDMRs() expressionProfile expression data.frame

active.features

character vectors containing features to correlate. Must be from names of resulting list from annotateDMRs. Additional feature names can be first exons (exons1) or first intron (intron1). To use more than one feature use c(). Default = c("promoters", "heads")

col.genes numeric, the column of expressionProfile data.frame with gene Ids. If NULL

geneIDs will be taken from rownames() of expressionProfile. Default = 0.

col.stat numeric, the column of expressionProfile data.frame with the statistics to use.

Default = 6.

stat.thr numeric, threshold for statistical significance. Default = 0.05

col.logFC numeric, the column of expressionProfile data.frame with log. fold change. De-

logfc.thr numeric, threshold value for \log fold change. Default = 0.

convert.genes logical, used to indicate if gene ids have to be translated in official gene symbols.

Default = FALSE

convert.from character, used annotation for gene in expressionProfile to be converted to sym-

> bols gene IDs. Accepted: c("ENTREZID", "EXONID", "GENEBIOTYPE" ,"GENEID", "GENENAME", "PROTDOMID", "PROTEINDOMAINID", "PRO-TEINDOMAINSOURCE", "PROTEINID", ""SEQSTRAND", "SYMBOL", "TXBIO-

TYPE", "TXID", "TXNAME", "UNIPROTID")

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```
beta.thr numeric, beta difference threshold value. Default = 0.3.

overlap.param.thr

numeric, threshold value for selected parameter to filter methylations overlapping the selected features. Default = 100

param.type character, threshold parameter to filter methylations overlapping the selected features. Accetped c("dmr.length", "overlap.length", "overlap.percentage"). Default = "overlap.length".
```

Value

data.frame with TF methylation levels, target.genes expression

formatDMRsInput Convert input table to proper format.

Description

Convert input table to proper format. The firts three column of the input table must have chr, start, end coordinates.

Usage

```
formatDMRsInput(
  tableIn,
  thr.beta,
  col.betadiff = 4,
  col.beta1 = NULL,
  col.beta2 = NULL
)
```

Arguments

thr.beta	numeric, beta difference threshold to consider methylations. Default = 0.3
col.betadiff	numeric, column position for beta diff. in input table. Default = 4
col.beta1	numeric, column position for first sample beta values in input table
col.beta2	numeric, column position for second sample beta values in input table
DMRsRanges	the DMRs ranges, it must have the following columns: chr, start, end, beta diff. Other columns will be stored in the resulting output under the column other.

Value

data.frame of DMR ranges

genesToNCG 11

annoc.	エヘいへん
genes	LONCG

Find genes annotated in NCG.

Description

Assess the presence of genes in results from annotateDMRs() in NCG database.

Usage

```
genesToNCG(annotatedDMRs, ncg, return.table = FALSE)
```

Arguments

Value

data.frame or vector of presences

plotDMRs

Converts annotated DMRs in a plot

Description

This function allows to track in a plot the beta value of a methylated segment mapped on a transcript of the human genome

```
plotDMRs(
  annotatedDMRs,
  symbol,
  annotation = "ensembl",
  hg = "hg19",
  beta1.name = NULL,
  beta2.name = NULL,
  beta.colors = c("red", "navy"),
  blackandwhite = FALSE,
  show.all.transcripts = FALSE,
  prom.width = 1500,
  path = NULL,
  coord.zoom = NULL,
  smartzoom = TRUE,
  height.pdf = 9,
  width.pdf = 16
)
```

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Arguments

anotated DMRs list resultingfrom annotateDMRs() or scoreAnnotatedDMRs() $annotated {\tt DMRs}$ symbol character, gene symbol to plot. annotation character, "ensembl" or "ucsc". Annotation used to track the plot. Default = "esembl". character, "hg19" or "hg38". Genome Assembly version. Default = "hg19". hg beta1.name character, if unsued beta difference is plotted. character string identifying beta value of first sample in "other" column in results from annotateDMRs() or indentifying colname in input table used in annotateDMRs() character, it identifies beta value of second sample in "other" column in results beta2.name from annotateDMRs() or it identifies colname in input table used in annotateDMRs() beta.colors character vectors, colors of tracks for the first and the second byalue, respectivetely. Default is c("red", "navy"). If beta diff is plotted, only the first element of vector is considered. blackandwhite logical, it allows to get all the plot in greyscale. Default = FALSE. show.all.transcripts logical, if TRUE all transcripts of genes are tracked, if FALSE only the longest transcript is tracked. Default = FALSE. prom.width integer, promoter lenght. Default = 1500. logical, path where the plot is saved in a pdf file. If NULL the plot is not saved. path Default = NULL. coord.zoom numeric vectors, coordinates of zoom region. If NULL the plot is not zoomed. Default = NULL. logical, automatic zoom on the methylated region. Default = TRUE. smartzoom height.pdf integer, hight pdf file. Default = 9. width.pdf integer, width pdf file. Default = 16.

Value

Plot of the beta value(s) mapped on transcript(s).

plotDMRs2Enrichr	Plot EnrichR Results
PIOCENING ZEIN TCIN	1 tot Entrem Resuits

Description

Visualize enrichment results and the contributes of hyper-metyhlated and hypo-methylated genes.

```
plotDMRs2Enrichr(
  enrichr.results,
  annotatedDMRs,
  stat = "P.value",
  n = 25,
```

```
plot.type = "barplot",
pal.col = "Dynamic",
col.hyper = "#ff0000",
col.hypo = "#00b3ff",
thrs = c(0.01, 0.05),
thrs.cols = c("green", "yellow")
```

Arguments

enrichr.results

data.frame resulting list from annotatedDMTs2Enrichr().

annotatedDMRs anotated DMRs list resultingfrom annotateDMRs() or scoreAnnotatedDMRs() character, statistics to visualize. Accepted "P.value", "Adjusted.P.value" or "Overstat lap". Default = 'P.value'. numeric, value indicating the number of enrichment to plot, starting from the n most enriched, to visualize. Default = 25. plot.type character, compute or not different linear models for upregulated and downregulated genes. Accepted: "simple" or "splitted". Default = "splitted". pal.col character, the palette color for plot.type = 'lollipop'. Must be one from hcl.pals(). Default = 'Dynamic'. col.hyper character, the color representing hyper-methylated genes. Default = 'Grey70'. col.hypo character, the color representing hyper-methylated genes. Default = 'Grey30'. thrs

numeric vectors, statistical thresholds to plot. Default = c(0.01, 0.05) characters vector, the colors to use for thresholds. Default = c('green', "yel-

low").

Value

plot of enrichR results

thrs.cols

plotMethylationOverview

Plot a simple distribution of methylations.

Description

Plot distribution of beta values on chromosomes, this function has mainly an internal utility and is design for shinyApp version of package

Usage

```
plotMethylationOverview(annotatedDMRs, plot.type, palette)
```

Arguments

${\tt annotatedDMRs}$	$anotated\ DMRs\ list\ resulting from\ annotate DMRs()\ or\ score Annotated DMRs()$
plot.type	character, compute or not different linear models for upregulated and downregulated genes. Accepted: "simple" or "splitted". Default = "splitted".
palette	character, color palette of plot. It must be one resulting from hcl.pals()

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Value

plot of enrichR results

plotTFs2Exprs

Plot the beta value of TF and related target genes expression

Description

Barplot of the beta value of TF and the expression of the target genes

Usage

```
plotTFs2Exprs(
  associatedTFs2Expr,
  symbol,
  col.meth = "#8e0000",
  pals.bars = "Cold"
)
```

Arguments

associated TFs 2 Expr

data.frame, results from associateTFs2Exprs().

symbol character, feature to correlate. Must be from na

character, feature to correlate. Must be from names of resulting list from anno-

tateDMRs. Additional feature names can be first exons (exons1) or first intron

(intron1). To use more than one feature use c().

col.meth character, color for beta value. Defaut = "#8e0000" (red)

pals.bars character, palette for gene expresion. hcl.pals() to show available. Default =

"Cold"

Value

plot showing methylation levels of TF and expresion of target genes

queryDatabase

Query database to find pathologic genes.

Description

Query elements of resulting annotations list to specified database in order to find pathogenic genes.

```
queryDatabase(
   DMRsRanges,
   db,
   return.table = TRUE,
   hold.columns,
   is.genomic.ranges = FALSE,
   thr = 0
)
```

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Arguments

DMRsRanges DMRs ranges

db character, database to query

return.table logical, optition to return a table instead a vector of presence. Default = TRUE

hold.columns numeric vectors, column positions to hold when return.table=TRUE

is.genomic.ranges

logical, specifies if database is a GenomicRange objet or a data.frame. Default

= FALSE

thr numeric, threshold for beta difference values. Default = 0

Value

a vector of presence or a data.frame

runOnDesktop

Start Graphical User Interface

Description

Start Graphical User Interface

Usage

```
runOnDesktop()
```

Value

GUI

 ${\tt scoreAnnotatedDMRs}$

Score the annotated methylation segments.

Description

Assigns a score to annotated methylated segments resulting from annotateDMRs() function

```
scoreAnnotatedDMRs(
  annotatedDMRs,
  active.features = c("promoters", "heads"),
  score.modifier = 0.5
)
```

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Arguments

anotated DMRs list resultingfrom annotateDMRs() annotatedDMRs active.features

> character vectors, containing features to correlate. Must be from names of resulting list from annotateDMRs. Additional feature names can be first exons (exons1) or first intron (intron1). To use more than one feature use c(). Default = c("promoters", "heads")

score.modifier numeric, value between 0-1. It specifies how the final score is computed by assigning different weights to the methylation charactersistics of enhacners or to genes already involved in pathologies. By increasing this value to 1, resulting scores will be focused on discovering segments affecting gene expression. A value equal to 0 will focus the results on enahcners involving genes associated to pathologies, not considering the effect of methylation. Default = 0.5

Value

data.frame of annotated DMRs with assigned scores

tfs2Enrichr

Query different databases to find enriched proceses.

Description

Query TF's targeted genes in order to find enriched proceses.

Usage

```
tfs2Enrichr(
 associatedTFs2Expr,
 logfc.thr = 1,
 stat.filter = "P.value",
 stat.thr = 0.01,
 db = NULL
```

Arguments

associatedTFs2Expr

data.frame. Corresponding to resulting data.frame from associateTFs2Exprs().

logfc.thr numeric value indicating logFC threshold. Default = 1.

stat.filter character indicating which type of statistics use for filtering results. Accepted

values: 'P.value' or 'Adjusted.P.value'. Default 'P.value'.

stat.thr numeric value indicating the threshold to use for selcted statistical test. Default

0.01.

db vector of characters indicating DBs to query. Default c("ClinVar 2019", "OMIM Disease",

"Elsevier_Pathway_Collection", "MSigDB_Hallmark_2020", "MSigDB_Oncogenic_Signatures",

"NCI-Nature_2016", "Panther_2016", "Reactome_2016", "WikiPathways_2019_Human")

"GO_Biological_Process_2018", "Human_Phenotype_Ontology", "KEGG_2016",

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Value

data.frame with enriched processes

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