Package 'scMINER'

April 27, 2023

```
Type Package
Title scMINER
Version 1.0.0
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Description
      Mutual information-based single-cell clustering and network-enabled hidden driver analysis
License Apache License
Encoding UTF-8
LazyData TRUE
Roxygen list(markdown = TRUE)
RoxygenNote 7.2.3
Depends R (>= 4.0.3),
      Biobase (>= 2.50.0),
      ggplot2 (>= 3.3.3),
      RColorBrewer (\geq 1.1.2),
      reshape 2 (>= 1.4.4),
      rmarkdown (>= 2.8),
      kableExtra (>= 1.3.4),
      dplyr (>= 1.0.6),
      grDevices (>= 4.0.3),
      scales (>= 1.1.1),
      limma (>= 3.46.0),
      anndata (>= 0.7.5.3)
Imports plyr (>= 1.8.6),
      Matrix (>= 1.5.3),
      stats (>= 4.0.3),
      methods (>= 4.0.3),
      ComplexHeatmap (>= 2.6.2),
      igraph (>= 1.2.6),
      rhdf5 (>= 2.34.0)
Suggests NetBID2 (>= 2.0.3),
      openxlsx (>= 4.2.3),
      knitr (>= 1.33),
      testthat (>= 3.0.0)
```

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VignetteBuilder knitr

$\textbf{Config/testthat/edition} \ \ 3$

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Description

 ${\tt combinePvalVector}\ is\ a\ function\ to\ combine\ multiple\ comparison's\ P\ values\ using\ Fisher's\ method\ or\ Stouffer's\ method.$

```
combinePvalVector(pvals, method = "Stouffer", signed = TRUE, twosided = TRUE)
```

ConvertNet2List 3

Arguments

pvals	a vector of numerics, the P values from multiple comparison need to be combined.
method	character, users can choose between "Stouffer" and "Fisher". Default is "Stouffer".
signed	logical, if TRUE, will give a sign to the P value to indicate the direction of testing. Default is TRUE.
twosided	logical, if TRUE, P value is calculated in a one-tailed test. If FALSE, P value is calculated in a two-tailed test, and it falls within the range 0 to 0.5. Default is TRUE.

Value

Return a vector contains the "Z-statistics" and "P.Value".

Examples

```
combinePvalVector(c(0.1,1e-3,1e-5))
combinePvalVector(c(0.1,1e-3,-1e-5))
```

ConvertNet2List	Convert Pairwise Network Data Frame to Driver-to-
	Target List ConvertNet2List is a helper function in the
	get.SJAracne.network. But if users have their own pairwise
	gene network files, they can convert it to driver-to-target list object.

Description

Convert Pairwise Network Data Frame to Driver-to-Target List ConvertNet2List is a helper function in the get.SJAracne.network. But if users have their own pairwise gene network files, they can convert it to driver-to-target list object.

Usage

```
ConvertNet2List(net_dat = NULL)
```

Arguments

net_dat data.fr

data.frame, must contain two columns with column names "source" (driver) and "target" (target genes). "MI" (mutual information) and "spearman" (spearman correlation coefficient) columns are optional, but strongly suggested to use. If "MI" and "spearman" columns are missing, errors may occur in some following steps (e.g. es.method='weightedmean' in cal.Activity).

Value

Return a list. The names of the list elements are drivers. Each element is a data frame, contains three columns. "target", target gene names; "MI", mutual information; "spearman", spearman correlation coefficient.

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Examples

CreateSparseEset

CreateSparseEset

Description

Create a S4 class which utilize 'ExpressionSet' template yet compatible with sparseMatrix type of assaydata

Usage

```
CreateSparseEset(
  data = NULL,
  meta.data = NULL,
  feature.data = NULL,
  add.meta = T
)
```

Arguments

data Sparse expression data, could be from either of these class:c('matrix','dgTMatrix','dgCMatrix').Requ

meta.data phenotype data which rownames should be the same as data colnames; Optional;

Default as NULL

feature.data feature data which rownames should be the same as data rownames; Optional;

Default as NULL

add.meta logical; Whether or not calculate extra pheonotype info including total number

of UMI, number of non-zero gene for each cell, mitochondrial percentage and

spike-in gene expression percentage and store them in Biobase::pData

Value

A customized S4 class using ExpressionSet class as prototype

DAG_ttest

DAG_ttest

Description

DAG_ttest

```
DAG_ttest(d, group)
```

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draw.bubblePlot2

Inner function for simple bubbleplots

Description

Inner function for simple bubbleplots

Usage

```
draw.bubblePlot2(
  df = NULL,
  xlab,
  ylab,
  clab,
  slab,
  low.col = "#004C99",
  high.col = "#CC0000",
  plot.title = NULL
)
```

Arguments

```
df
                  re-structured data.frame for bubble plots
xlab
                  string
ylab
                  string
clab
                  string
slab
                  string
                  string,default as "#004C99"
low.col
high.col
                  string, default as "CC0000
plot.title
                  string
```

Value

a ggplot object

draw.group.barplot

Draw barplot for composition study

Description

Draw barplot for composition study

```
draw.group.barplot(input_eset, group_by, color_by, colors = NULL)
```

6 draw.marker.bbp

Arguments

input_eset ExpressionSet that include group information in phenotype data
group_by Group criteria for bars, should be a variable stored in Biobase::pData(input_eset)

color_by Coloring criteria of bar fractions, should be a variable stored in Biobase::pData(input_eset)

colors color values to feed in scale_fill_manual, default as NULL; If NULL, then default color for ggplot will be used

Value

a ggplot object

Examples

draw.marker.bbp

Generate visualization for marker scores via bubble plot

Description

Marker visualizatoin from known markers/signatures, requires knowledge-based marker list as input

Usage

```
draw.marker.bbp(
  ref = NULL,
  input_eset,
  feature = "geneSymbol",
  group_name = "ClusterRes",
  save_plot = FALSE,
  width = 8,
  height = 5,
  plot_name = "AnnotationBubbleplot.png"
)
```

Arguments

reference dataframe, includes positive or negative markers for different cell types; Specify first column as different cell types, second columns as markers, third columns as weight (postive or negative marker)

input_eset expressionSet/SparseExpressionSet object with clustering membership stored in Biobase::pData

feature feature type from second column of your reference, should be in colnames(Biobase::fData(eset))

group_name a character, the variable containing clustering label in Biobase::pData(eset); or any other group information stored in Biobase::pData(eset)

draw.scRNAseq.QC 7

save_plot logical, whether or not save your plot; if TRUE, plot will be saved as plot_name width default as 8, inch as unit default as 5, inch as unit plot_name plot name, please include plot type

Details

Visualize marker score of different cell types on bubbleplot

Value

A ggplot object

Examples

draw.scRNAseq.QC

draw.scRNAseq.QC

Description

generated a scRNA-seq quality control report in html with Rmarkdown

```
draw.scRNAseq.QC(
   SparseEset,
   project.name,
   plot.dir = "./QC/",
   output.cutoff = TRUE,
   group = "group"
)
```

8 feature_heatmap

Arguments

SparseEset an SparseEset generated by CreateSparseEset project.name a character, project name to print on report plot.dir a character, output directory for QC reports

output.cutoff logical, whether or not return a list of suggested thresholds for filtering

group a character, a variable name indicate groupping information (stored in Biobase::pData)

to help generate violin plots

Details

```
draw.scRNAseq.QC
```

Value

an R markdown QC report and a list of suggested threshold (if specify)

Examples

feature_heatmap

Visualize gene expression level on scRNA-seq data via heatmap

Description

This plot will visualiz feature info in scatter plot by outputing a ggplot object

```
feature_heatmap(
  input_eset,
  target,
  feature = "geneSymbol",
  group_name = "label",
  name = "log2Exp",
  save_plot = TRUE,
  width = 4,
  height = 8,
  cluster_rows = FALSE,
  colors = rev(colorRampPalette(brewer.pal(10, "RdYlBu"))(256)),
  plot_name = "GeneHeatmap.png",
  ...
)
```

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Arguments

input_eset Input expression set target a character or a character vector indicating feature names feature a character, which feature to visualize group_name a character, label to visualize on the top of heatmap character, name of value visualized in color scale name save_plot logical, whether to save plots or not width numerical height numerical $cluster_rows$ logical, if or not cluster rows colors color palette plot_name character, name of heamap

Value

. . .

a ggplot object

Examples

parameter to be passed to ComplexHeatmap::Heatmap

feature_highlighting feature_highlighting

Description

This plot will visualize feature info on scatter plot by outputing a ggplot object

10 feature_highlighting

Usage

```
feature_highlighting(
  input_eset,
  target = NULL,
  feature = "geneSymbol",
  x = "X",
  y = "Y",
  wrap_by = NULL,
  ylabel = "Expression",
  pct.size = 0.8,
  title.size = 15,
  ncol = 4,
  alpha = 0.8,
  colors = colorRampPalette(c("#E3E3E3", "#BCA2FC", "#4900FE"), interpolate =
    "linear")(8)
)
```

Arguments

input_eset	Input expression set
target	a character vector, the list of feature to visualize
feature	character, which feature to visualize
X	cordinates for x axis
у	cordinates for y axis
wrap_by	character, variable to wrap plot with
ylabel	a characterm, title of y axis
pct.size	numrical, point size
title.size	numerical, default as 5
ncol	cordinates for y axis
alpha	numerical, default as 0.8
colors	color palette for feature highlighting

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feature_vlnplot	feature_vlnplot
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Description

This plot will visualize feature info in violin plot by outputing a ggplot object

Usage

```
feature_vlnplot(
   input_eset,
   target = NULL,
   feature = "geneSymbol",
   group_by = "celltype",
   ylabel = "Expression",
   color_by = NULL,
   colors = NULL,
   ncol = 3,
   stat = "median",
   boxplot = FALSE,
   title.size = 5
)
```

Arguments

input_eset	Input expression set
target	a character vector, the list of feature to visualize
feature	character, which feature to visualize
group_by	character, which group info to visualize as x axis
ylabel	a character, title of y axis
color_by	character, which group info to define color, if NULL, then violin plots will be colored by 'group_by'
colors	character vector, default as NULL, will use ggplot default color palette
ncol	cordinates for y axis
stat	a character, whether to plot median or mean as a black dot on violinplot
boxplot	logical, whether to plot boxplot on violinplot
title.size	numerical, default as 5

```
target = genes_of_interest,
feature = "geneSymbol",
group_by = "ClusterRes",
ylabel = "log2Exp", ncol = 4)
```

generateMICAinput

Generate MICA input accepted txt or h5ad file

Description

A utility function that helps generate MICA input from a data matrix with rownames and colnames

Usage

```
generateMICAinput(d, filename="project_name_MICAinput.h5")
```

Arguments

scminer.par list for the parameter settings in scMINER pipeline, optional.

d matrix with colnames as cell/sample info, rownames as gene/feature info filename of your MICA input file, supported format: txt or h5

Value

A txt file or a h5 file that could be read in MICA

Examples

generateSJARACNeInput Generate SJARACNE input with designed folder structure

Description

This function helps to generate appropriate input files for SJARACNe pipeline. It can take transcription factor/signaling gene reference from internal(stored in package) or external (manual define)

```
generateSJARACNeInput(
  input_eset,
  ref = NULL,
  funcType = NULL,
  wd.src,
  group_name
)
```

get.DA

Arguments

```
input_eset An expressionSet

ref c("hg", "mm"), could be a manually defined geneSymbol vector

funcType c("TF","SIG", NULL), if NULL then both TF and SIG will be considered

wd.src output path

group_name name of group for sample identification
```

Details

generate SJARACNe Input

Value

SJARACNe input files for each subgroups

Examples

get.DA

Find differential activity genes from activity matrix

Description

get.DA is a wraper of (DAG_test, and getDE.limma), which helps to conduct two_sided t.test on all genes in specific group VS Others to find differential activity genes, a table with essential statistics will be outputted.

```
get.DA(
  input_eset = NULL,
  group_name = "celltype",
  group_case = NULL,
  group_ctrl = NULL,
  method = "t.test"
)
```

Arguments

input_eset	ExpressionSet that stores group information in Biobase::pData
group_name	a character string, column name in Biobase::pData(input_eset) that indicates group info
group_case	NULL(If do get.DA for all group vs others) or a character string (one specific group vs others) of column name in Biobase::pData(input_eset) that indicates group info
group_ctrl	NULL(If one vs Others); a character indicate case group if do pairwise analysis
method	a character from c("t.test", "limma"), which method will be used to identify differential activity gene

Value

output would be a data.frame containing: t.statistics, p.value, log2FC, z.score, and mean Activity value

Examples

```
demo_file <- system.file('PBMC14KDS_DemoDataSet/SJAR/DATA/celltype_Activity.RData',</pre>
                                              package = "scMINER")
load(demo_file)
DAG_result_tf <- get.DA(input_eset = AC_eset$AC.TF,
                        group_name = "celltype")
```

get.network.scMINER

Read SJARACNe Network Result and Return it as List Object(adapted from NetBID2)

Description

get.network.scMINER reads SJARACNe network construction result and returns a list object with network data frame, driver-to-target list and igraph object wrapped inside.

Usage

```
get.network.scMINER(network_file = NULL)
```

Arguments

network_file

character, the path for storing network file. For the output of SJAracne, the name of the network file will be "consensus_network_ncol_.txt" under the output directory.

Details

In the demo, "consensus_network_ncol_.txt" file will be read and convert into a list object. This list contains three elements, network_data, target_list and igraph_obj. network_dat is a data.frame, contains all the information of the network SJARACNe constructed. target_list is a driver-to-target list object. Please check details in get_net2target_list. igraph_obj is an igraph object used to save this directed and weighted network. Each edge of the network has two attributes, weight and sign. weight is the "MI (mutual information)" value and sign is the sign of the spearman correlation coefficient (1, positive regulation; -1, negative regulation).

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Value

Return a list containing three elements, network_dat, target_list and igraph_obj.

Examples

get.Topdrivers

get.Topdrivers

Description

Help quick pick top master regulators from previous differential activity analysis results

Usage

```
get.Topdrivers(
  DAG_result = DAG_result,
  n = 5,
  degree_filter = c(50, 500),
  celltype = NULL
)
```

Arguments

DAG_result Output table from function FindDAG

n threshold to pick top master regulators(top n)

degree_filter filter out drivers with target number less than certain value celltype character, output top hits are from which celltype

Value

A list of top master regulators among different groups

```
GetActivityFromSJARACNe
```

GetActivityFromSJARACNe

Description

Allocate network information from SJARACNe and calculate activity score for each hub genes.

Usage

```
GetActivityFromSJARACNe(
   SJARACNe_output_path = NA,
   SJARACNe_input_eset = NA,
   functype = "tf",
   group_name = NA,
   activity.method = "unweighted",
   activity.norm = TRUE,
   save_network_file = FALSE,
   save_path = NULL
)
```

Arguments

```
SJARACNe_output_path
                  Path to SJARACNe output folder(s)
SJARACNe_input_eset
                  Expressionset that you generate input from
                  character c("tf", "sig"); If NULL, both activity from TF and SIG network will be
functype
                  calculated; default as NULL
group_name
                  a string, group name stored in Biobase::pData that defines expression matrix
                  separation
activity.method
                  c("weighted,unweighted), default to "unweighted"
                 logical, default to TRUE.
activity.norm
save_network_file
                  logical, default to FALSE
                  Path to save network file
save_path
```

Value

An expressionset with activity values

Author(s)

```
Chenxi Qian, <chenxi.qian@stjude.org>
```

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Examples

getDE.limma

Differential Expression Analysis and Differential Activity Analysis Between 2 Sample Groups Using Limma

Description

getDE.1imma is a function performs differential gene expression analysis and differential driver activity analysis between control group (parameter G0) and experimental group (parameter G1), using limma related functions.

Usage

```
getDE.limma(
  eset = NULL,
  G1 = NULL,
  G0 = NULL,
  G1_name = NULL,
  G0_name = NULL,
  verbose = TRUE,
  random_effect = NULL)
```

Arguments

eset	ExpressionSet class object, contains gene expression data or driver activity data.
G1	a vector of characters, the sample names of experimental group.
G0	a vecotr of characters, the sample names of control group.
G1_name	character, the name of experimental group (e.g. "Male"). Default is "G1".
G0_name	character, the name of control group (e.g. "Female"). Default is "G0".
verbose	logical, if TRUE, sample names of both groups will be printed. Default is TRUE.
random_effect	a vector of characters, vector or factor specifying a blocking variable. Default is NULL, no random effect will be considered.

18 get_activity

Value

Return a data frame. Rows are genes/drivers, columns are "ID", "logFC", "AveExpr", "t", "P.Value", "adj.P.Val", "B", "Z-statistics", "Ave.G1" and "Ave.G0". Names of the columns may vary from different group names. Sorted by P-values.

Examples

```
## Not run:
analysis.par <- list()</pre>
analysis.par$out.dir.DATA <- system.file('demo1','driver/DATA/',package = "NetBID2")</pre>
NetBID.loadRData(analysis.par=analysis.par,step='ms-tab')
phe_info <- Biobase::pData(analysis.par$cal.eset)</pre>
each_subtype <- 'G4'
GO <- rownames(phe_info)[which(phe_info$`subgroup`!=each_subtype)] # get sample list for GO
G1 <- rownames(phe_info)[which(phe_info$`subgroup`==each_subtype)] # get sample list for G1
DE_gene_limma <- getDE.limma(eset=analysis.par$cal.eset,</pre>
                                 G1=G1, G0=G0,
                                  G1_name=each_subtype,
                                  G0_name='other')
DA_driver_limma <- getDE.limma(eset=analysis.par$merge.ac.eset,
                                  G1=G1, G0=G0,
                                 G1_name=each_subtype,
                                 G0_name='other')
## End(Not run)
```

get_activity

Calculate activity from network file or gene list

Description

Calculate activity from network file or gene list

Usage

```
get_activity(
  Net = NULL,
  eset,
  tag = NULL,
  genelist = NULL,
  use.symbol = FALSE,
  feature = "geneSymbol",
  es.method = "mean",
  activity.method = "weighted",
  normalize = TRUE,
  sep.symbol = "."
)
```

Arguments

Net Network data frame

eset ExpressionSet/SparseExpressionSet with expression data

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tag If network is TF network or SIG network

genelist A list of signature gene list

use.symbol logical, in network file, use geneSymbol or use geneID

feature character, use which feature as ID in Biobase::fData(eset)

es.method character, which method to use to calculate activity value ("mean","maxmean")

activity.method character, which method to use to estimate activity ("weighted","unweighted")

normalize logical, if normalize or not

Details

sep.symbol

If network object was loaded by get.network.scMINER function, then network dataframe is could be retrieved under network_dat slot.

which symbol to sparate name and tag

Examples

MICAplot

plot MICA clustering results or other meta variables

Description

This function helps to generate a ggplot object for phenotypic visualization

```
MICAplot(
  input_eset,
  color_by = "ClusterRes",
  colors = NULL,
  X = NULL,
  Y = NULL,
  show_label = FALSE,
  label.size = 10,
  title.size = 20,
  title.name = "",
  pct = 0.5,
  alpha = 1
)
```

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Arguments

input_eset	ExpressionSet that include visualization coordinates in phenotype data
color_by	Coloring criteria of data points, should be a variable stored in Biobase::pData(input_eset)
colors	character, color values, if NULL then use ggplot default color
X	character, column name of x axis
Υ	character, column name of y axis
show_label	logical, whether or not to show label on tSNE plot
label.size	numerical, size of label ploted on figure
title.size	numerical, size of plot title, default as 10
title.name	character, title of plot, default as NULL
pct	numerical, size of point, default as 0.5
aplha	numerical, indicate point transparency

Examples

preMICA.filtering

preMICA.filtering

Description

scRNA-seq filtering function

```
preMICA.filtering(
   SparseEset,
   cutoffs,
   gene_filter = T,
   nGene_filter = T,
   nUMI_filter = T,
   ERCC_filter = T,
   Mito_filter = T
```

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Arguments

SparseEset	the sparseEset object outputted from draw.scRNAseq.QC
cutoffs	a list outputted by draw.scRNAseq.QC, if NULL, manual input will be required
gene_filter	logical; or a numerical number, indicating lower threshold for gene filtering based on how many non-zero cells each gene expressed in
nGene_filter	logical; a numerical number, indicating lower threshold put on number of gene expression in each cell for cell filtering
nUMI_filter	logical;a vector of two numerical number, indicating lower threshold and upper threshold put on number of total UMI for cell filtering
ERCC_filter	logical; a numerical number, indicating upper threshold put on ERCC percentage for cell filtering
Mito_filter	logical;a numerical number, indicating upper threshold put on Mitochondrial gene expression fraction for cell filtering

Details

preMICA.filtering

Value

A Sparse expression set

Examples

readMICAoutput readMICAoutput

Description

Read MICA input and output to create an expressionSet for downstream analysis

Usage

```
readMICAoutput(eset = NULL, input_file, output_file, load_ClusterRes = TRUE)
```

Arguments

eset a SparseMatrix Eset

input_file input expression txt file of MICA pipeline
output_file output ClusterMem.txt file from MICA pipeline

load_ClusterRes

logical, if TRUE, clustering results will be store at Biobase::pData(eset)\$label

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Value

A sparse expressionSet object

Examples

readscRNAseqData

readscRNAseqData

Description

read scRNA-seq data, a wrapper of conventional data reading (read.delim) and 10x genomics data standarad output reading

Usage

```
readscRNAseqData(
  file,
  is.10x = TRUE,
  CreateSparseEset = TRUE,
  add.meta = F,
  sep = ","
)
```

Arguments

file data path to 10x genomics output folder, which normally contains 3 files (ma-

trix.mtx, gene or feature.tsv and barcode.csv), or data path to data txt/csv/tsv

file

is.10x logical, whether or not inputs are from CellRanger standard output

 ${\tt CreateSparseEset}$

logical, whether or not create sparse matrix incorporated expression set

add.meta logical, whether or not calculate metadata info from expression matrixm, this is

not suggested before merging/downsampling your data

 \dots parameters pass to read.delim if is.10x = FALSE

Value

A list or sparse matrix expression set

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scMINER.dir.create

Manipulation of Working Directories for scMINER pipeline

Description

scMINER.dir.create is used to help users create an organized working directory for the network construction step in scMINER analysis. However, it is not essential for the analysis. It creates a hierarchical working directory and returns a list contains this directory information.

Usage

```
scMINER.dir.create(project_main_dir = NULL, project_name = NULL)
```

Arguments

Details

This function needs users to define the main working directory and the project's name. It creates a main working directory with a subdirectory of the project. It also automatically creates five subfolders (DATA, SJAR, MICA, QC, PLOT) within the project folder. DATA/, storing data files; SJAR/, storing files needed for running SJAracne; MICA/, storing files needed for running MICA; QC/, storing Quality Control related plots; PLOT/, storing plot files; This function also returns a list object (example, scminer.par in the demo) with directory information wrapped inside.

Value

scMINER.dir.create returns a list object, containing main.dir (path of the main working directory), project.name (project name), out.dir (path of the project folder).

ARACNe_filter	
---------------	--

Description

This is the inner function to help generate SJARACNe input for scRNA-seq data, all non-informative (zero genes) will be filtered in by this function

Usage

```
SJARACNe_filter(eset.sel, tf.ref, sig.ref, wd.src, grp.tag)
```

Arguments

eset.sel	ExpressionSet to generate SJaracne input
tf.ref	A vector of reference transcription factors
sig.ref	A vector of reference signaling genes
wd.src	path to store SjAracne input
grp.tag	name of group for identification

Details

Non-expressed genes in subgroups are filtered. tf.ref should be coordinate with featureNames(eset.sel).

Value

A folder with picked master regulator and filtered gene expression matrix

```
SparseExpressionSet-class
SparseExpressionSet
```

Description

SparseExpressionSet

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