Package 'scTHI'

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Title Indentification of significantly activated ligand-receptor interactions across clusters of cells from single-cell RNA sequencing data

Version 1.21.0

Description scTHI is an R package to identify active pairs of ligand-receptors from single cells in order to study,among others, tumor-host interactions. scTHI contains a set of signatures to classify cells from the tumor microenvironment.

Depends R (>= 4.0)

License GPL-2

Encoding UTF-8

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VignetteBuilder knitr

biocViews Software,SingleCell

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`scTHI` *single cell Tumor Hist Interaction (scTHI)*

Description

Indentification of significantly activated ligand-receptor interactions across clusters of cells from single-cell RNA sequencing data. Single-cell RNA sequencing is the reference technique to characterize the heterogeneity of tumor microenvironment. The composition of the various cell types making up the microenvironment can significantly affect the way in which the immune system activates cancer rejection mechanisms. Understanding the cross-talk signals between immune cells and cancer cells is a fundamental for the identification immuno-oncology therapeutic targets. scTHI is a novel method, single cell Tumor-Host Interaction tool (scTHI), to identify significantly activated ligand-receptor interactions across clusters of cells from single-cell RNA sequencing data. cTHI is based on the hypothesis that when patterns of interaction are active, they are also simultaneously and highly expressed in homogeneous cell populations. We also model the autocrine and paracrine signalling effects of L-R partners

Details

Please have a look at the vignette for a in-depth introduction to the package.

`scTHI_plotCluster` *scTHI_plotCluster*

Description

Graphs the output of scTHI_runTsne, labeling cells by clusters.

Usage

```
scTHI_plotCluster(scTHIresult, cexPoint = 0.8, legendPos = c("topleft",
  "topright", "bottomright", "bottomleft"))
```

Arguments

`scTHIresult`	scTHI object.
`cexPoint`	Set the point size.
`legendPos`	Character string to custom the legend position.

Value

None

Examples

```
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
                       cellCusterA = colnames(scExample)[1:30],
                       cellCusterB = colnames(scExample)[31:100],
                       cellCusterAName = "ClusterA",
                       cellCusterBName = "ClusterB", filterCutoff = 0,
                       pvalueCutoff = 1, nPermu = 100, ncore = 8)
result <- scTHI_runTsne(result)
scTHI_plotCluster(result)
```

`scTHI_plotPairs` *scTHI_plotPairs*

Description

Generates a plot on the t-SNE coordinates to show the expression levels of an interaction pair of interest. Each cell is colored according to the corresponding gene expression value.

Usage

```
scTHI_plotPairs(scTHIresult, cexPoint = 0.8, interactionToplot)
```

Arguments

`scTHIresult`	scTHI object.
`cexPoint`	Set the point size.
`interactionToplot`	Interaction pair to plot.

Value

None

Examples

```
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
                cellCusterA = colnames(scExample)[1:30],
                cellCusterB = colnames(scExample)[31:100],
                cellCusterAName = "ClusterA",
                cellCusterBName = "ClusterB", filterCutoff = 0,
                pvalueCutoff = 1, nPermu = 100, ncore = 8)
result <- scTHI_runTsne(result)
scTHI_plotPairs(result,interactionToplot = "CXCL12_CD4")
```

scTHI_plotResult *scTHI_plotResult*

Description

Creates barplots of scTHI_score results.

Usage

```
scTHI_plotResult(scTHIresult, cexNames = 0.8, plotType = c("score",
  "pair"), nRes = NULL)
```

Arguments

scTHIresult	scTHI object.
cexNames	Size of names in barplot.
plotType	Type of plot to be generated. Default is "score", can be also "pair". The "score" option will generate a barplot for each resulted interaction pair, representing the calculated interaction score and the related p-Value.The "pair" option will generate two barplot for each resulted interaction pair, representing the percentage of cells of each cluster expressing partnerA and partnerB gene, respectively.
nRes	Number of pairs to plot (all if NULL).

Value

None

Examples

```
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
                       cellCusterA = colnames(scExample)[1:30],
                       cellCusterB = colnames(scExample)[31:100],
                       cellCusterAName = "ClusterA",
                       cellCusterBName = "ClusterB", filterCutoff = 0,
                       pvalueCutoff = 1, nPermu = 100, ncore = 8)

scTHI_plotResult(result, plotType = "score")
scTHI_plotResult(result, plotType = "pair")
```

scTHI_runTsne *scTHI_runTsne*

Description

Runs t-SNE dimensionality reduction on selected features based on Rtsne package.

Usage

```
scTHI_runTsne(scTHIresult)
```

Arguments

scTHIresult	scTHI object.

Value

The same object as scTHI_score with a fifth item tsneData (data.frame)

Examples

```
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
                       cellCusterA = colnames(scExample)[1:30],
                       cellCusterB = colnames(scExample)[31:100],
                       cellCusterAName = "ClusterA",
                       cellCusterBName = "ClusterB", filterCutoff = 0,
                       pvalueCutoff = 1, nPermu = 100, ncore = 8)
result <- scTHI_runTsne(result)
```

---

scTHI_score *scTHI_score*

Description

This function allows the user to compute a score for a set of ligand-receptor pairs, from a single cell gene expression matrix, and detect specific Tumor-Host interactions. You must specify at least two clusters of cells (for example tumor cells and immune cells).

Usage

```
scTHI_score(expMat, cellCusterA, cellCusterB, cellCusterAName,
  cellCusterBName, topRank = 10, autocrineEffect = TRUE,
  fileNameBase = "scTHI", filterCutoff = 0.5, PValue = TRUE,
  pvalueCutoff = 0.05, nPermu = 1000, ncore = 8)
```

Arguments

expMat	ScRNA-seq gene expression matrix where rows are genes presented with Hugo Symbols and columns are cells. Gene expression values should be counts or normalized counts.
cellCusterA	Vector of columns of expMat that belong to the first cluster.
cellCusterB	Vector of columns of expMat that belong to the second cluster.
cellCusterAName	A character string labeling the clusterA.
cellCusterBName	A character string labeling the clusterB.
topRank	Filter threshold. Set to 10 (default) means that each gene of the interaction pair will be considered as expressed in a cell if it's in the top rank 10 percent.
autocrineEffect	if TRUE remove the paracrine filter

fileNameBase	Project name.
filterCutoff	Score threshold (default is 0.50). For each interaction pair, if the score calculated (for the partnerA or partnerB) will be less than filterCutoff the interaction pair will be discarded.
PValue	Logical, set to TRUE (default) compute statistical iterations. If p.value < 0.05, the value will be returned.
pvalueCutoff	cutoff of the p-value
nPermu	Number of iterations to perform (default is 1000).
ncore	Number of processors to use.

Value

A list of results, with four items: result (data.frame), expMat (matrix), clusterA (character), clusterA (character)

Examples

```
######################## example of scTHI_score
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
      cellCusterA = colnames(scExample)[1:30],
      cellCusterB = colnames(scExample)[31:100],
      cellCusterAName = "ClusterA",
      cellCusterBName = "ClusterB", filterCutoff = 0,
     pvalueCutoff = 1, nPermu = 100, ncore = 8)
```

TME_classification *TME_classification*

Description

The function allows the user to classify non-tumor cells in tumor microenvironment. It implements the Mann-Whitney-Wilcoxon Gene Set Test (MWW-GST) algorithm and tests for each cell the enrichment of a collection of signatures of different cell types.

Usage

```
TME_classification(expMat, minLenGeneSet = 10,
  alternative = "two.sided", pvalFilter = FALSE, fdrFilter = TRUE,
  pvalCutoff = 0.01, nesCutoff = 0.58, nNES = 1)
```

Arguments

expMat	Gene expression matrix where rows are genes presented with Hugo Symbols and columns are cells. Gene expression values should be normalized counts.
minLenGeneSet	Minimum gene set length
alternative	a character string specifying the alternative hypothesis of wilcoxon test, must be one of "two.sided" (default), "greater" or "less".

pvalFilter	Logical, if TRUE results will be filtered for p-Value. Defoult is FALSE.
fdrFilter	Logical, if TRUE results will be filtered for FDR.
pvalCutoff	Numeric p-Value (or FDR) threshold. Gene set with p-Value (or FDR) greater than pvalCutoff will be discarded (default is 0.01).
nesCutoff	Numeric threshold. Gene set with NES greater than nesCutoff will be discarded (default is 0.58)
nNES	Default is 0.58, so each cell is classified with a specific phenotype based on the first significant enriched gene set.

Value

A list with two items: Class (character) and ClassLegend (character)

Examples

```
library(scTHI.data)
data(scExample)
Class <- TME_classification(scExample)
```

TME_plot *TME_plot*

Description

Generates a plot on the t-SNE coordinates, labeling cells by TME classification.

Usage

```
TME_plot(tsneData, Class, cexPoint = 0.8)
```

Arguments

tsneData	X and y coordinates of points in the plot.
Class	Object returned by TME_classification function.
cexPoint	Set the point size.

Value

None

Examples

```
library(scTHI.data)
data(scExample)
result <-  scTHI_score(scExample,
           cellCusterA = colnames(scExample)[1:30],
           cellCusterB = colnames(scExample)[31:100],
           cellCusterAName = "ClusterA",
           cellCusterBName = "ClusterB", filterCutoff = 0,
           pvalueCutoff = 1, nPermu = 100, ncore = 8)
result <- scTHI_runTsne(result)
Class <- TME_classification(scExample)
TME_plot(tsneData = result$tsneData, Class)
```

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