Package 'scaper'

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Title Single Cell Transcriptomics-Level Cytokine Activity Prediction and Estimation

Version 0.2.0

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Description Generates cell-level cytokine activity estimates using relevant information from gene sets constructed with the 'CytoSig' and the 'Reactome' databases and scored using the modified 'Variance-adjusted Mahalanobis (VAM)' framework for single-cell RNA-sequencing (scRNA-seq) data. 'CytoSig' database is described in: Jiang at al., (2021) <doi:10.1038/s41592-021-01274-5>. 'Reactome' database is described in: Gillespie et al., (2021) <doi:10.1093/nar/gkab1028>. The 'VAM' method is outlined in: Frost (2020) <doi:10.1093/nar/gkaa582>.

Suggests knitr, pheatmap, rmarkdown, usethis

Imports magrittr, xml2, stringr, dplyr, Seurat, SeuratObject, VAM, utils

License GPL (>= 2)

Encoding UTF-8

RoxygenNote 7.2.3

VignetteBuilder knitr

Depends R (>= 3.5.0)

NeedsCompilation no

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Contents

`genesetCytoSig` *CytoSig gene set construction.*

Description

Returns the gene set associated with input cytokine(s) from the CytoSig database given manually specified cytokine-specific output csv file(s) under the extdata directory with file name beginning with the specified cytokine (i.e., 'IL6_output.csv') as currently provided for the IL6 cytokine.

Usage

```
genesetCytoSig(cytokine.eval, file.name)
```

Arguments

`cytokine.eval`	Cytokine(s) associated with the query.
`file.name`	List of XML file(s) associated with the cytokine(s) beginning with the specific cytokine name.

Value

Dataframe consisting of genes and the associated log2 fold change values associated with the specific cytokine(s).

Examples

```
file.name.cytosig1 <- system.file("extdata", "IL6_output.csv", package = "scaper")
genesetCytoSig(cytokine.eval = "IL6", file.name = file.name.cytosig1) %>% head(10)
```

`genesetReactome` *Reactome gene set construction.*

Description

Returns the gene set consisting of genes on the Reactome pathway hierarchy given input cytokine(s) and specified list of pathway hierarchy xml file(s) with file name beginning with the specified cytokine (i.e., 'IL6_Interleukin6_signaling.xml') as currently provided for the IL6 cytokine.

Usage

```
genesetReactome(cytokine.eval, file.name)
```

Arguments

`cytokine.eval`	Cytokine(s) associated with the query.
`file.name`	List of XML file(s) associated with the cytokine(s) beginning with the specific cytokine name.

Value

Dataframe consisting of list of genes on the molecular pathway associated with the specified cytokine(s).

Examples

```
file.name.reactome1 <- system.file("extdata", "IL6_Interleukin6_signaling.xml",
package = "scaper")
genesetReactome(cytokine.eval = "IL6", file.name = file.name.reactome1) %>% head(10)
```

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scape *Cytokine activity scores for a normalized matrix.*

Description

Computes cell-level estimates of cytokine activity for a normalized scRNA-seq count matrix using the SCAPE method. SCAPE activity estimates are computed by scoring weighted genes sets from the CytoSig or Reactome databases using the `VAM::vamForCollection()` function. Individual gene sets for subsequent scoring can be reconstructed using the `genesetCytoSig` and the `genesetReactome` functions for the CytoSig and the Reactome database, respectively.

Usage

```
scape(counts.matrix, database = "cytosig", cytokine = "all")
```

Arguments

`counts.matrix`	A mxn normalized counts matrix with m samples and n genes.
`database`	Database used for gene set construction and set scoring. • "cytosig" performs scoring for up to 41 cytokines using the CytoSig database. • "reactome" performs scoring for up to 30 cytokines using the Reactome database.
`cytokine`	Vector of cytokine names to score for activity. The default value of "all" will score all 41 cytokines supported by CytoSig or 31 supported by Reactome. Please see function `supportedCytokines` to view all the CytoSig or the Reactome specific scored cytokines.

Value

A mxp matrix consisting of the cell-level cytokine activity scores for p cytokines.

See Also

genesetCytoSig, genesetReactome

Examples

```
library(Seurat)
library(SeuratObject)
pbmc_small <- NormalizeData(pbmc_small)
counts.matrix <- as.data.frame(t(as.matrix(pbmc_small@assays$RNA@data)))
CytoSig.score.output <- scape(counts.matrix = counts.matrix,
database = "cytosig")
head(CytoSig.score.output)[,1:3]
CytoSig.score.output.specific <- scape(counts.matrix = counts.matrix,
database = "cytosig", cytokine = c("IL4", "IL13"))
head(CytoSig.score.output.specific)
```

---

scapeForSeurat *Cytokine activity scores for a Seurat matrix.*

Description

Computes cell-level estimates of cytokine activity for a scRNA-seq Seurat count matrix using the scapeForSeurat method. SCAPE activity estimates are computed by scoring weighted gene sets from the CytoSig or Reactome databases using the Variance-adjusted Mahalanobis (VAM) method as implemented in the VAM::vamForSeurat() function. Individual gene sets for subsequent scoring can be reconstructed using the genesetCytoSig and the genesetReactome functions for the CytoSig and the Reactome database, respectively.

Usage

```
scapeForSeurat(
  seurat.object,
  database = "cytosig",
  cytokine = "all",
  normalize = TRUE
)
```

Arguments

seurat.object	Seurat counts matrix.
database	Database used for gene set construction and set scoring. • "cytosig" (default) performs scoring for up to 41 cytokines using the CytoSig database. • "reactome" performs scoring for up to 30 cytokines using the Reactome database.

cytokine	Vector of cytokine names to score for activity. The default value of "all" will score all 41 cytokines supported by CytoSig or 31 supported by Reactome. Please see function supportedCytokines to view all the CytoSig or the Reactome specific scored cytokines.
normalize	Boolean indicator for whether normalization should be performed before performing gene set scoring.

Value

Seurat object consisting of cell-level cytokine activity scores returned as a separate assay (scape for scoring via the CytoSig database and VAMcdf for scoring via the Reactome database).

See Also

genesetCytoSig, genesetReactome, scape

Examples

```
library(SeuratObject)
CytoSig.score.output.all <- scapeForSeurat(seurat.object = pbmc_small,
database = "cytosig", cytokine = "all", normalize=TRUE)
(as.data.frame(CytoSig.score.output.all@assays$scape@data))[1:6,1:3]
CytoSig.score.output.specific <- scapeForSeurat(seurat.object = pbmc_small,
database = "cytosig", cytokine = c("IL4", "IL13"), normalize=TRUE)
(as.data.frame(CytoSig.score.output.specific@assays$scape@data))[,1:3]
```

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supportedCytokines *Gene set to score for the CytoSig or the Reactome databases.*

Description

Returns the names of the cytokines supported by either the CytoSig or the Reactome databases.

Usage

```
supportedCytokines(database = "cytosig")
```

Arguments

database	Database used for gene set construction and set scoring. • "cytosig" returns the 41 cytokines scored using the CytoSig database. • "reactome" returns the 30 cytokines scored using the Reactome database.

Value

List of cytokines associated with the CytoSig or the Reactome databases.

Examples

```
supportedCytokines(database = "cytosig")
supportedCytokines(database = "reactome")
```

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