Package 'InterCellar'

September 16, 2021

Title InterCellar: an R-Shiny app for interactive analysis and exploration of cell-cell communication in single-cell transcriptomics

Version 1.0.0

Description InterCellar is implemented as an R/Bioconductor Package containing a Shiny app that allows users to interactively analyze cell-cell communication from scRNA-seq data. Starting from precomputed ligand-receptor interactions, InterCellar provides filtering options, annotations and multiple visualizations to explore clusters, genes and functions. Finally, the user can define interaction-pairs modules and link them to significant functional terms from Pathways or Gene Ontology.

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Imports config, golem, shiny, DT, shinydashboard, shinyFiles, shinycssloaders, data.table, fs, dplyr, tidyr, circlize, colourpicker, dendextend, factoextra, ggplot2, plotly, plyr, shinyFeedback, shinyalert, tibble, umap, visNetwork, wordcloud2, readxl, htmlwidgets, colorspace, signal, scales, htmltools, ComplexHeatmap, grDevices, stats, tools, utils, biomaRt, rlang, fmsb

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Config/testthat/edition 3

URL https://github.com/martaint/InterCellar

BugReports https://github.com/martaint/InterCellar/issues

VignetteBuilder knitr

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Depends R (>= 4.1)

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R topics documented:

`annotateGO` *Perform GO annotation of input data*

Description

Perform GO annotation of input data

Usage

```
annotateGO(
  input_select_ensembl,
  input_go_evidence_exclude,
  input_go_sources_checkbox,
  input.data
)
```

Arguments

`input_select_ensembl`	ensembl version selected by user
`input_go_evidence_exclude`	evidence codes to exclude by user
`input_go_sources_checkbox`	GO sources to use by user
`input.data`	preprocessed input data

Value

GO_annotation

`annotatePathways` *Annotate pathways for input data*

Description

Annotate pathways for input data

Usage

```
annotatePathways(selected.db, input.data)
```

Arguments

`selected.db`	pathways sources to use
`input.data`	filtered input data

Value

pathways_annotation

`buildPairsbyFunctionMatrix` *Build binary matrix with int-pairs in rows, functions in cols*

Description

Build binary matrix with int-pairs in rows, functions in cols

Usage

```
buildPairsbyFunctionMatrix(functions_df)
```

Arguments

`functions_df`	annotated df (GO/path/combined)

Value

binary matrix

checkLL_RR *Manually change the annotation of L-L and R-R pairs*

Description

Manually change the annotation of L-L and R-R pairs

Usage

```
checkLL_RR(input.data)
```

Arguments

input.data	preprocessed table

Value

input.data

Examples

```
data(input.data)
checked.input.data <- checkLL_RR(input.data)
```

circlePlot *Plot circle plot*

Description

Plot circle plot

Usage

```
circlePlot(data, cluster_colors, ipm_color, int_flow, link.color)
```

Arguments

data	subset of input data by flow / intpair module
cluster_colors	global
ipm_color	single color for chosen int-pair module
int_flow	string specifying the flow
link.color	string specifying variable by which to color links

Value

circle plot

combineAnnotations *Combine GO annotation and pathways in a unique object*

Description

Combine GO annotation and pathways in a unique object

Usage

```
combineAnnotations(GO_annotation, pathways_annotation)
```

Arguments

GO_annotation	data
pathways_annotation	data

Value

combined annotation dataframe

createBarPlot1_ggplot *Create ggplot barplot to be saved in tiff*

Description

Create ggplot barplot to be saved in tiff

Usage

```
createBarPlot1_ggplot(barplotDF, input_cluster_selected_checkbox)
```

Arguments

barplotDF	dataframe with N interactions per cluster (auto/para)
input_cluster_selected_checkbox	checkbox input

Value

ggplot barplot

createBarPlot2_CV *Create barplot of number of interaction for selected cluster*

Description

Create barplot of number of interaction for selected cluster

Usage

```
createBarPlot2_CV(
  barplotDF2,
  input_cluster_selected_checkbox,
  input_clust_barplot2
)
```

Arguments

barplotDF2	dataframe with barplot data
input_cluster_selected_checkbox	selected clusters to keep
input_clust_barplot2	selected cluster to plot

Value

plotly fig

createBarPlot2_ggplot *Create ggplot barplot of Nint per cluster selected*

Description

Create ggplot barplot of Nint per cluster selected

Usage

```
createBarPlot2_ggplot(
  barplotDF2,
  input_cluster_selected_checkbox,
  input_clust_barplot2
)
```

Arguments

`barplotDF2`	dataframe with barplot data
`input_cluster_selected_checkbox`	selected clusters to keep
`input_clust_barplot2`	selected cluster to plot

Value

ggplot barplot

`createBarPlot_CV` *Create Barplot cluster-verse*

Description

Create Barplot cluster-verse

Usage

```
createBarPlot_CV(barplotDF, input_cluster_selected_checkbox)
```

Arguments

`barplotDF`	dataframe with N interactions per cluster (auto/para)
`input_cluster_selected_checkbox`	checkbox input

Value

plotly barplot

`createNetwork` *Create Network of clusters*

Description

Create Network of clusters

Usage

```
createNetwork(data.filt.cluster)
```

Arguments

`data.filt.cluster`
: filtered input data (by clusters)

Value

list containing nodes and edges for network

---

dendroIntPairModules *Get dendrogram of int pair modules*

Description

Get dendrogram of int pair modules

Usage

```
dendroIntPairModules(pairs_func_matrix)
```

Arguments

`pairs_func_matrix`
: binary matrix pairs x functions

Value

list with dendrogram, hclust and umap

---

elbowPoint *Determine the elbow point on a curve (from package akmedoids)*

Description

Given a list of x, y coordinates on a curve, function determines the elbow point of the curve.

Usage

```
elbowPoint(x, y)
```

Arguments

`x`	vector of x coordinates of points on the curve
`y`	vector of y coordinates of points on the curve

Details

highlight the maximum curvature to identify the elbow point (credit: 'github.com/agentlans')

Value

an x, y coordinates of the elbow point.

---

ensemblLink *Get html link to ensembl*

Description

Get html link to ensembl

Usage

```
ensemblLink(ensembl)
```

Arguments

ensembl	symbol

Value

html link to website

---

getBack2BackBarplot *Get back-to-back barplot for 2 conditions comparison*

Description

Get back-to-back barplot for 2 conditions comparison

Usage

```
getBack2BackBarplot(tab_c1, tab_c2, lab_c1, lab_c2)
```

Arguments

tab_c1	table from csv file (barplot#1) containing data for condition 1
tab_c2	table from csv file (barplot#1)containing data for condition 2
lab_c1	label for condition 1
lab_c2	label for condition 2

Value

ggplot object

getBarplotDF *Get dataframe for plotting barplot (all clusters)*

Description

Get dataframe for plotting barplot (all clusters)

Usage

```
getBarplotDF(data.filt.bar, input_cluster_selected_checkbox)
```

Arguments

`data.filt.bar`	filtered object (checkbox auto/para)
`input_cluster_selected_checkbox`	checkbox input

Value

dataframe with number of interactions per cluster auto/para

getBarplotDF2 *Get dataframe for barplot (by cluster)*

Description

Get dataframe for barplot (by cluster)

Usage

```
getBarplotDF2(filt.data, input_cluster_selected_checkbox, input_clust_barplot2)
```

Arguments

`filt.data`	input data filtered in cluster-verse
`input_cluster_selected_checkbox`	selected clusters to keep
`input_clust_barplot2`	selected cluster to plot

Value

dataframe with num int per cluster

getClusterNames *Get clusters names from initial input data*

Description

Get clusters names from initial input data

Usage

```
getClusterNames(input.data)
```

Arguments

input.data	preprocessed input data

Value

named list of clusters

Examples

```
data(input.data)
cluster_list <- getClusterNames(input.data)
```

getClusterNetwork *Creating edges dataframe for network of clusters*

Description

Creating edges dataframe for network of clusters

Usage

```
getClusterNetwork(input.data)
```

Arguments

input.data	preprocessed input data

Value

edges dataframe

getClusterSize *Get Clusters size*

Description

Get Clusters size

Usage

```
getClusterSize(cl, edges.df)
```

Arguments

cl	cluster name
edges.df	dataframe with edges for network

Value

sum of interactions for that cluster

getDotPlot_selInt *Functions to plot DotPlots*

Description

Functions to plot DotPlots

Usage

```
getDotPlot_selInt(
  selected_tab,
  clust.order,
  low_color = "aquamarine",
  high_color = "#131780"
)
```

Arguments

selected_tab	table of selected rows from gene tableeeeeee
clust.order	how to order clusters
low_color	of dotplot
high_color	of dotplot

Value

list with modified selected data and ggplot2 dotplot

getGeneTable *Get table for gene-verse*

Description

Get table for gene-verse

Usage

```
getGeneTable(input.data)
```

Arguments

input.data	preprocessed input data

Value

gene table with unique intpairs (no connection to clusters)

Examples

```
data(input.data)
gene_table <- getGeneTable(input.data)
```

getGObiomaRt *Connection to Ensembl via biomaRt to get GO terms*

Description

Connection to Ensembl via biomaRt to get GO terms

Usage

```
getGObiomaRt(input_select_ensembl, input.data)
```

Arguments

input_select_ensembl	chosen version of Ensembl
input.data	filtered input data

Value

dataframe with GO annotation

getHitsf *Subfunction to calculate significant functions by permutation test*

Description

Subfunction to calculate significant functions by permutation test

Usage

```
getHitsf(mat, gpModules_assign)
```

Arguments

mat	binary matrix of functional terms by int-pairs
gpModules_assign	assignment of intpairs to modules

Value

matrix with hits

getIntFlow *Get subset of interactions corresponding to a certain viewpoint and flow*

Description

Get subset of interactions corresponding to a certain viewpoint and flow

Usage

```
getIntFlow(vp, input.data, flow)
```

Arguments

vp	viewpoint cluster
input.data	preprocessed/filtered input data
flow	one among directed_out, directed_in or undirected

Value

subset of data

Examples

```
data(input.data)
caf_out <- getIntFlow(vp = "CAF", input.data, flow = "directed_out")
```

getNtermsBYdb *Calculate number of terms of a database*

Description

Calculate number of terms of a database

Usage

```
getNtermsBYdb(annotation)
```

Arguments

annotation	data from either pathways, GO or combined

Value

number of terms by dataset

getNumLR *Get number of unique ligands and receptors*

Description

Get number of unique ligands and receptors

Usage

```
getNumLR(gene.table, type)
```

Arguments

gene.table	gene table of unique int-pairs
type	either L or R

Value

number of L or R genes

getRadarPlot — *Get radar plot of relative numbers of interactions for a certain cell type*

Description

Get radar plot of relative numbers of interactions for a certain cell type

Usage

```
getRadarPlot(tab_c1, tab_c2, lab_c1, lab_c2, cell_name)
```

Arguments

tab_c1	table from csv file (barplot#2) containing data for condition 1
tab_c2	table from csv file (barplot#2) containing data for condition 2
lab_c1	label for condition 1
lab_c2	label for condition 2
cell_name	label of cell type of interest

Value

plot

getRankedTerms — *Get table with ranked functional terms*

Description

Get table with ranked functional terms

Usage

```
getRankedTerms(data.fun.annot, gene.table)
```

Arguments

data.fun.annot	annotated df (GO/path/combined)
gene.table	of unique intpairs

Value

table with ranking

getSignificantFunctions *Calculate significant function per intpair module*

Description

Calculate significant function per intpair module

Usage

```
getSignificantFunctions(
  subGenePairs_func_mat,
  gpModules_assign,
  rank.terms,
  input_maxPval
)
```

Arguments

subGenePairs_func_mat	subset of binary mat
gpModules_assign	assignment of intpairs to modules
rank.terms	table of ranked functions
input_maxPval	threshold of significance

Value

table with significant functions

getSunburst *Get Sunburst plot of selected functional terms*

Description

Get Sunburst plot of selected functional terms

Usage

```
getSunburst(sel.data, func_selected, int_p_fun, cluster.colors)
```

Arguments

sel.data	dataframe of selected functions
func_selected	the selected functional term
int_p_fun	dataframe with int pairs annotated to this function
cluster.colors	for plotting

Value

plotly figure

---

getUMAPipModules *Get UMAP for IP modules*

Description

Get UMAP for IP modules

Usage

```
getUMAPipModules(
  intPairs.dendro,
  gpModules_assign,
  gene.table,
  ipm_colors,
  input_ipM_UMAPcolors
)
```

Arguments

intPairs.dendro	list output of dendrogram
gpModules_assign	named vector of module assignment
gene.table	unique intpairs table
ipm_colors	for intpair modules
input_ipM_UMAPcolors	user choice for coloring umap

Value

plotly umap

getUniqueDotplot *Plot dotplot containing only unique int-pair/cluster pairs with many conditions*

Description

Plot dotplot containing only unique int-pair/cluster pairs with many conditions

Usage

```
getUniqueDotplot(data_dotplot)
```

Arguments

data_dotplot	table with selected int_pairs for multiple conditions

Value

ggplot object

goLink *Get GO link*

Description

Get GO link

Usage

```
goLink(go_id)
```

Arguments

go_id	string

Value

html link to website

input.data *Input Data example*

Description

A dataset obtained from Tirosh et al melanoma dataset, running CellPhoneDBv2. This data is generated by InterCellar running read.CPDBv2()

Usage

```
input.data
```

Format

A data frame with 5638 rows and 11 variables:

int_pair interaction pair name, geneA & geneB

geneA name, hgnc_symbol

geneB name, hgnc_symbol

typeA molecular type of geneA, either L (ligand) or R (receptor)

typeB molecular type of geneB, either L (ligand) or R (receptor)

clustA name of first cluster, either character or number

clustB name of second cluster, either character or number

score int-pair score as avg expression of geneA and geneB over clustA and clustB, decimal

p_value int-pair pvalue, decimal

annotation_strategy database from which the int-pair was retrieved

int.type either autocrine or paracrine

read.CPDBv2 *Read output from CellPhoneDB v2.*

Description

Output is a folder containing 4 .txt files - deconvoluted.txt: containing list of single genes and their mean expression in each cluster (not considered); - means.txt: containing list of interacting pairs with info regarding L/R, annotation strategy and mean value of all pairs over cluster couples. - pvalues.txt: same as means, but containing pvalue of each pair, for each cluster couple. - significant_means.txt: only means of those pairs that have pvalue < 0.05. Has one more column:rank. If the statistical analysis is not run, the folder would contain only deconvoluted and means

Usage

```
read.CPDBv2(folder)
```

Arguments

folder	folder containing output

Value

input.data which is the pre-processed object with annotated L-R pairs

---

read.customInput *Read custom input file and re-structure it with InterCellar format*

Description

Read custom input file and re-structure it with InterCellar format

Usage

```
read.customInput(tab, separator)
```

Arguments

tab	custom input table
separator	character that separates two elements of an interaction pair

Value

preprocessed table

---

read.SCsignalR *Read output from SingleCellSignalR*

Description

SCSR description: the output folder is a collection of txt files, one for each clusters pair considered. The "paracrine" option looks for ligands expressed in cluster A and their associated receptors according to LRdb that are expressed in any other cluster but A. These interactions are labelled "paracrine". The interactions that involve a ligand and a receptor, both differentially expressed in their respective cell clusters according to the **edgeR** analysis performed by the **cluster_analysis()** function, are labelled "specific". The "autocrine" option searches for ligands expressed in cell cluster A and their associated receptors also expressed in A. These interactions are labelled "autocrine". Additionally, it searches for those associated receptors in the other cell clusters (not A) to cover the part of the signaling that is "autocrine" and "paracrine" simultaneously. These interactions are labelled "autocrine/paracrine". This file is a 4-column table: ligands, receptors, interaction types ("paracrine", "autocrine", "autocrine/paracrine" and "specific"), and the associated LRscore. InterCellar: rename autocrine|paracrine to paracrine

Usage

```
read.SCsignalR(folder)
```

Arguments

folder	containing output from SingleCellSignalR, named cell-signaling

Value

input.data: preprocessed object with annotated L-R pairs

`run_app` *Run the Shiny Application*

Description

Run the Shiny Application

Usage

```
run_app(reproducible = TRUE)
```

Arguments

reproducible	boolean for setting a seed, making plots reproducible

Value

a running instance of InterCellar

Examples

```
## Not run:
run_app()

## End(Not run)
```

subsetFuncMatBYFlow *Subset pairs-function matrix by selected flow*

Description

Subset pairs-function matrix by selected flow

Usage

```
subsetFuncMatBYFlow(pairs_func_matrix, flow_df)
```

Arguments

pairs_func_matrix	binary
flow_df	subset of input data by flow

Value

subset of binary mat

swap.RLint *Swaps interaction pairs that are R-L to L-R*

Description

Swaps interaction pairs that are R-L to L-R

Usage

```
swap.RLint(RLint)
```

Arguments

RLint	subset of R-L interactions

Value

input data with ordered L-R pairs and L-L/R-R

uniprotLink *Get html link to uniprot*

Description

Get html link to uniprot

Usage

```
uniprotLink(uniprot)
```

Arguments

uniprot	symbol

Value

html link to website

updateInputLR *Function that orders all interaction pairs as L-R. Leaves unchanged the R-R and L-L*

Description

Function that orders all interaction pairs as L-R. Leaves unchanged the R-R and L-L

Usage

```
updateInputLR(input.data)
```

Arguments

input.data	uploaded data

Value

ordered input data

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