

# Package ‘dominoSignal’

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**Title** Cell Communication Analysis for Single Cell RNA Sequencing

**Version** 1.0.0

**Description** dominoSignal is a package developed to analyze cell signaling through ligand - receptor - transcription factor networks in scRNAseq data. It takes as input information transcriptional data, requiring counts, z-scored counts, and cluster labels, as well as information on transcription factor activation (such as from SCENIC) and a database of ligand and receptor pairings (such as from CellPhoneDB). This package creates an object storing ligand - receptor - transcription factor linkages by cluster and provides several methods for exploring, summarizing, and visualizing the analysis.

**BugReports** <https://github.com/FertigLab/dominoSignal/issues>

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**Author** Christopher Cherry [aut] (<<https://orcid.org/0000-0002-5481-0055>>),  
 Jacob T Mitchell [aut, cre] (<<https://orcid.org/0000-0002-5370-9692>>),  
 Sushma Nagaraj [aut] (<<https://orcid.org/0000-0001-5166-1309>>),  
 Kavita Krishnan [aut] (<<https://orcid.org/0000-0003-1345-0249>>),  
 Dmitrijs Lvovs [aut],  
 Elana Fertig [ctb] (<<https://orcid.org/0000-0003-3204-342X>>),  
 Jennifer Elisseeff [ctb] (<<https://orcid.org/0000-0002-5066-1996>>)  
**Maintainer** Jacob T Mitchell <jtmitch81@jhmi.edu>

## Contents

add_rl_column . . . . .	3
build_domino . . . . .	4
CellPhoneDB . . . . .	5
check_arg . . . . .	5
circos_ligand_receptor . . . . .	6
convert_genes . . . . .	7
conv_py_bools . . . . .	8
cor_heatmap . . . . .	8
cor_scatter . . . . .	9
count_linkage . . . . .	10
create_domino . . . . .	11
create_regulon_list_scenic . . . . .	13
create_rl_map_cellphonedb . . . . .	13
domino-class . . . . .	14
dom_clusters . . . . .	15
dom_correlations . . . . .	16
dom_counts . . . . .	16
dom_database . . . . .	17
dom_de . . . . .	17
dom_info . . . . .	18
dom_linkages . . . . .	18
dom_network_items . . . . .	19
dom_signaling . . . . .	20
dom_tf_activation . . . . .	20
dom_zscores . . . . .	21
do_norm . . . . .	21
feat_heatmap . . . . .	22
gene_network . . . . .	23
ggplot_col_gen . . . . .	24
incoming_signaling_heatmap . . . . .	24
lc . . . . .	26
linkage_summary-class . . . . .	26
mean_ligand_expression . . . . .	27
mock_linkage_summary . . . . .	27
PBMC . . . . .	28
plot_differential_linkages . . . . .	28
print,domino-method . . . . .	29
read_if_char . . . . .	30
rename_clusters . . . . .	30
SCENIC . . . . .	31

<i>add_rl_column</i>	3
show,domino-method . . . . .	31
signaling_heatmap . . . . .	32
signaling_network . . . . .	33
summarize_linkages . . . . .	34
table_convert_genes . . . . .	35
test_differential_linkages . . . . .	36
<b>Index</b>	<b>38</b>

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<code>add_rl_column</code>	<i>Adds a column to the RL signaling data frame.</i>
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---

### Description

This function adds a column to the internal rl 'map' used to map all receptor and receptor complexes to all ligand and ligand complexes.

### Usage

```
add_rl_column(map, map_ref, conv, new_name)
```

### Arguments

<code>map</code>	RL signaling data frame.
<code>map_ref</code>	Name of column to match new data to
<code>conv</code>	Data frame matching current data in map to new data.
<code>new_name</code>	Name of new column to be created in RL map

### Value

An updated RL signaling data frame

### Examples

```
example(create_rl_map_cellphonedb, echo = FALSE)
lr_name <- data.frame("abbrev" = c("L", "R"), "full" = c("Ligand", "Receptor"))
rl_map_expanded <- add_rl_column(map = rl_map_tiny, map_ref = "type_A",
conv = lr_name, new_name = "type_A_full")
```

---

 build\_domino

 Calculate a signaling network for a domino object
 

---

### Description

This function calculates a signaling network. It requires a domino object preprocessed from `create_domino` and returns a domino object prepared for plotting with the various plotting functions in this package.

### Usage

```
build_domino(
  dom,
  max_tf_per_clust = 5,
  min_tf_pval = 0.01,
  max_rec_per_tf = 5,
  rec_tf_cor_threshold = 0.15,
  min_rec_percentage = 0.1
)
```

### Arguments

<code>dom</code>	Domino object from <code>create_domino()</code> .
<code>max_tf_per_clust</code>	Maximum number of transcription factors called active in a cluster.
<code>min_tf_pval</code>	Minimum p-value from differential feature score test to call a transcription factor active in a cluster.
<code>max_rec_per_tf</code>	Maximum number of receptors to link to each transcription factor.
<code>rec_tf_cor_threshold</code>	Minimum Spearman correlation used to consider a receptor linked with a transcription factor. Increasing this will decrease the number of receptors linked to each transcription factor.
<code>min_rec_percentage</code>	Minimum percentage of cells in cluster expressing a receptor for the receptor to be linked to transcription factors in that cluster.

### Value

A domino object with a signaling network built

### Examples

```
example(create_domino, echo = FALSE)

#a relaxed example
pbmc_dom_built_tiny <- build_domino(
  dom = pbmc_dom_tiny, min_tf_pval = .05, max_tf_per_clust = Inf,
  max_rec_per_tf = Inf, rec_tf_cor_threshold = .1, min_rec_percentage = 0.01
)
```

---

CellPhoneDB	<i>CellPhoneDB subset</i>
-------------	---------------------------

---

**Description**

A list of four subsets of CellPhoneDB data.

**Usage**

```
data("CellPhoneDB")
```

**Format**

A list of:

**genes\_tiny** A subset of CellPhoneDB gene\_input.csv

**proteins\_tiny** A subset of CellPhoneDB protein\_input.csv

**complexes\_tiny** A subset of CellPhoneDB complex\_input.csv

**interactions\_tiny** A subset of CellPhoneDB interaction\_input.csv

**Source**

<https://github.com/ventolab/cellphonedb-data/archive/refs/tags/v4.0.0.tar.gz>

---

check_arg	<i>Check input arguments</i>
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---

**Description**

Accepts an object and rules to check against; stops if requirements are not met

**Usage**

```
check_arg(  
  arg,  
  allow_class = NULL,  
  allow_len = NULL,  
  allow_range = NULL,  
  allow_values = NULL,  
  need_vars = c(NULL),  
  need_colnames = FALSE,  
  need_rownames = FALSE,  
  need_names = FALSE  
)
```

**Arguments**

arg	the argument to check
allow_class	vector of allowed classes
allow_len	vector of allowed lengths
allow_range	range of minimum and maximum values i.e. c(1, 5)
allow_values	vector of allowed values
need_vars	vector of required variables
need_colnames	logical for whether colnames are required
need_rownames	logical for whether rownames are required
need_names	logical for whether names are required

**Value**

Logical indicating whether the argument meets the requirements

---

circos\_ligand\_receptor

*Plot expression of a receptor's ligands by other cell types as a chord plot*

---

**Description**

Creates a chord plot of expression of ligands that can activate a specified receptor where chord widths correspond to mean ligand expression by the cluster.

**Usage**

```
circos_ligand_receptor(
  dom,
  receptor,
  ligand_expression_threshold = 0.01,
  cell_idents = NULL,
  cell_colors = NULL
)
```

**Arguments**

dom	Domino object that has undergone network building with <code>build_domino()</code>
receptor	Name of a receptor active in at least one cell type in the domino object
ligand_expression_threshold	Minimum mean expression value of a ligand by a cell type for a chord to be rendered between the cell type and the receptor
cell_idents	Vector of cell types from cluster assignments in the domino object to be included in the plot.
cell_colors	Named vector of color names or hex codes where names correspond to the plotted cell types and the color values

**Value**

Renders a circos plot to the active graphics device

**Examples**

```
example(build_domino, echo = FALSE)
#basic usage
circos_ligand_receptor(pbmc_dom_built_tiny, receptor = "CXCR3")
#specify colors
cols = c("red", "orange", "green")
names(cols) = dom_clusters(pbmc_dom_built_tiny)
circos_ligand_receptor(pbmc_dom_built_tiny, receptor = "CXCR3", cell_colors = cols)
```

---

convert_genes	<i>Use biomaRt to convert genes</i>
---------------	-------------------------------------

---

**Description**

This function reads in a vector of genes and converts the genes to specified symbol type

**Usage**

```
convert_genes(
  genes,
  from = c("ENSMUSG", "ENSG", "MGI", "HGNC"),
  to = c("MGI", "HGNC"),
  host = "https://www.ensembl.org"
)
```

**Arguments**

genes	Vector of genes to convert.
from	Format of gene input (ENSMUSG, ENSG, MGI, or HGNC)
to	Format of gene output (MGI or HGNC)
host	Host to connect to. Defaults to <a href="https://www.ensembl.org">https://www.ensembl.org</a> following the useMart default, but can be changed to archived hosts if useMart fails to connect.

**Value**

A data frame with input genes as column 1 and converted genes as column 2

---

conv_py_bools	<i>Change cases of True/False syntax from Python to TRUE/FALSE R syntax</i>
---------------	---

---

**Description**

Change cases of True/False syntax from Python to TRUE/FALSE R syntax

**Usage**

```
conv_py_bools(obj)
```

**Arguments**

obj	object that will be converted
-----	-------------------------------

**Value**

The converted object

---

cor_heatmap	<i>Create a heatmap of correlation between receptors and transcription factors</i>
-------------	--

---

**Description**

Creates a heatmap of correlation values between receptors and transcription factors either with boolean threshold or with continuous values displayed

**Usage**

```
cor_heatmap(
  dom,
  bool = FALSE,
  bool_thresh = 0.15,
  title = TRUE,
  feats = NULL,
  recs = NULL,
  mark_connections = FALSE,
  ...
)
```

**Arguments**

dom	Domino object with network built ( <a href="#">build_domino()</a> )
bool	Boolean indicating whether the heatmap should be continuous or boolean. If boolean then bool_thresh will be used to determine how to define activity as positive or negative.



bool_thresh	Numeric indicating the threshold separating 'on' or 'off' for feature activity if making a boolean heatmap.
title	Either a string to use as the title or a boolean describing whether to include a title. In order to pass the 'main' parameter to <a href="#">ComplexHeatmap::Heatmap()</a> you must set title to FALSE.
feats	Either a vector of features to include in the heatmap or 'all' for all features. If left NULL then the features selected for the signaling network will be shown.
recs	Either a vector of receptors to include in the heatmap or 'all' for all receptors. If left NULL then the receptors selected in the signaling network connected to the features plotted will be shown.
mark_connections	Boolean indicating whether to add an 'x' in cells where there is a connected receptor or TF. Default FALSE.
...	Other parameters to pass to <a href="#">ComplexHeatmap::Heatmap()</a> . Note that to use the 'main' parameter of <a href="#">ComplexHeatmap::Heatmap()</a> you must set title = FALSE and to use 'annCol' or 'annColors' ann_cols must be FALSE.

**Value**

A heatmap rendered to the active graphics device

**Examples**

```
example(build_domino, echo = FALSE)
#basic usage
cor_heatmap(pbmc_dom_built_tiny, title = "PBMC R-TF Correlations")
#show correlations above a specific value
cor_heatmap(pbmc_dom_built_tiny, bool = TRUE, bool_thresh = 0.1)
#identify combinations that are connected
cor_heatmap(pbmc_dom_built_tiny, bool = FALSE, mark_connections = TRUE)
```

---

cor\_scatter

*Create a correlation plot between TF and receptor*


---

**Description**

Create a correlation plot between transcription factor activation score and receptor expression

**Usage**

```
cor_scatter(dom, tf, rec, remove_rec_dropout = TRUE, ...)
```

**Arguments**

dom	Domino object with network built ( <a href="#">build_domino()</a> )
tf	Target TF for plotting AUC score
rec	Target receptor for plotting expression
remove_rec_dropout	Whether to remove cells with zero expression for plot. This should match the same setting as in <a href="#">build_domino()</a> .
...	Other parameters to pass to <a href="#">ggpubr::ggscatter()</a> .

**Value**

A ggplot scatter plot rendered in the active graphics device

**Examples**

```
example(build_domino, echo = FALSE)
cor_scatter(pbmc_dom_built_tiny, "FLI1", "CXCR3")
```

---

count_linkage	<i>Count occurrences of linkages across multiple domino results from a linkage summary</i>
---------------	--

---

**Description**

Count occurrences of linkages across multiple domino results from a linkage summary

**Usage**

```
count_linkage(
  linkage_summary,
  cluster,
  group.by = NULL,
  linkage = "rec_lig",
  subject_names = NULL
)
```

**Arguments**

linkage_summary	a <code>linkage_summary()</code> object
cluster	the name of the cell cluster being compared across multiple domino results
group.by	the name of the column in <code>linkage_summary@subject_meta</code> by which to group subjects for counting. If <code>NULL</code> , only total counts of linkages for linkages in the cluster across all subjects is given.
linkage	a stored linkage from the domino object. Can compare any of <code>'tfs'</code> , <code>'rec'</code> , <code>'incoming_lig'</code> , <code>'tfs_rec'</code> , or <code>'rec_lig'</code>
subject_names	a vector of <code>subject_names</code> from the <code>linkage_summary</code> to be compared. If <code>NULL</code> , all <code>subject_names</code> in the linkage summary are included in counting.

**Value**

A data frame with columns for the unique linkage features and the counts of how many times the linkage occurred across the compared domino results. If `group.by` is used, counts of the linkages are also provided as columns named by the unique values of the `group.by` variable.

**Examples**

```
count_linkage(
  linkage_summary = mock_linkage_summary(), cluster = "C1",
  group.by = "group", linkage = "rec")
```

---

create_domino	<i>Create a domino object and prepare it for network construction</i>
---------------	---

---

## Description

This function reads in a receptor ligand signaling database, cell level features of some kind (ie. output from pySCENIC), z-scored single cell data, and cluster id for single cell data, calculates a correlation matrix between receptors and other features (this is transcription factor module scores if using pySCENIC), and finds features enriched by cluster. It will return a domino object prepared for `build_domino()`, which will calculate a signaling network.

## Usage

```
create_domino(
  rl_map,
  features,
  counts = NULL,
  z_scores = NULL,
  clusters = NULL,
  use_clusters = TRUE,
  tf_targets = NULL,
  verbose = TRUE,
  use_complexes = TRUE,
  rec_min_thresh = 0.025,
  remove_rec_dropout = TRUE,
  tf_selection_method = "clusters",
  tf_variance_quantile = 0.5
)
```

## Arguments

<code>rl_map</code>	Data frame where each row describes a receptor-ligand interaction with required columns <code>gene_A</code> & <code>gene_B</code> including the gene names for the receptor and ligand and <code>type_A</code> & <code>type_B</code> annotating if genes A and B are a ligand (L) or receptor (R)
<code>features</code>	Either a path to a csv containing cell level features of interest (ie. the auc matrix from pySCENIC) or named matrix with cells as columns and features as rows.
<code>counts</code>	Counts matrix for the data. This is only used to threshold receptors on dropout.
<code>z_scores</code>	Matrix containing z-scored expression data for all cells with cells as columns and features as rows.
<code>clusters</code>	Named factor containing cell cluster with names as cells.
<code>use_clusters</code>	Boolean indicating whether to use clusters.
<code>tf_targets</code>	Optional. A list where names are transcription factors and the stored values are character vectors of genes in the transcription factor's regulon.
<code>verbose</code>	Boolean indicating whether or not to print progress during computation.
<code>use_complexes</code>	Boolean indicating whether you wish to use receptor/ligand complexes in the receptor ligand signaling database. If FALSE, receptor/ligand pairs where either functions as a protein complex will not be considered when constructing the signaling network.

`rec_min_thresh` Minimum expression level of receptors by cell. Default is 0.025 or 2.5 percent of all cells in the data set. This is important when calculating correlation to connect receptors to transcription activation. If this threshold is too low then correlation calculations will proceed with very few cells with non-zero expression.

`remove_rec_dropout`

Whether to remove receptors with 0 expression counts when calculating correlations. This can reduce false positive correlation calculations when receptors have high dropout rates.

`tf_selection_method`

Selection of which method to target transcription factors. If 'clusters' then differential expression for clusters will be calculated. If 'variable' then the most variable transcription factors will be selected. If 'all' then all transcription factors in the feature matrix will be used. Default is 'clusters'. Note that if you wish to use clusters for intercellular signaling downstream to MUST choose clusters.

`tf_variance_quantile`

What proportion of variable features to take if using variance to threshold features. Default is 0.5. Higher numbers will keep more features. Ignored if `tf_selection_method` is not 'variable'

## Value

A domino object

## Examples

```
example(create_rl_map_cellphonedb, echo = FALSE)
example(create_regulon_list_scenic, echo = FALSE)
data(SCENIC)
data(PBMC)
```

```
pbmc_dom_tiny <- create_domino(
  rl_map = rl_map_tiny, features = SCENIC$auc_tiny,
  counts = PBMC$RNA_count_tiny, z_scores = PBMC$RNA_zscore_tiny,
  clusters = PBMC$clusters_tiny, tf_targets = regulon_list_tiny,
  use_clusters = TRUE, use_complexes = TRUE, remove_rec_dropout = FALSE,
  verbose = FALSE
)
```

```
pbmc_dom_tiny_no_clusters <- create_domino(
  rl_map = rl_map_tiny, features = SCENIC$auc_tiny,
  counts = PBMC$RNA_count_tiny, z_scores = PBMC$RNA_zscore_tiny,
  clusters = PBMC$clusters_tiny, tf_targets = regulon_list_tiny,
  use_clusters = FALSE, use_complexes = FALSE,
  rec_min_thresh = 0.1, remove_rec_dropout = TRUE,
  tf_selection_method = "all",
  verbose = FALSE
)
```

---

```
create_regulon_list_scenic
```

*Create a list of genes in regulons inferred by SCENIC*

---

**Description**

Generates a list of transcription factors and the genes targeted by the transcription factor as part of their regulon inferred by pySCENIC

**Usage**

```
create_regulon_list_scenic(regulons)
```

**Arguments**

regulons            Data frame or file path to the table of the output of the ctx function from pySCENIC

**Value**

A list where names are transcription factors and the stored values are character vectors of genes in the inferred regulons

**Examples**

```
data(SCENIC)
regulon_list_tiny <- create_regulon_list_scenic(regulons = SCENIC$regulons_tiny)
```

---

```
create_rl_map_cellphonedb
```

*Create a receptor - ligand map from a CellPhoneDB signaling database*

---

**Description**

Generates a data frame of ligand-receptor interactions from a CellPhoneDB database annotating the genes encoding the interacting ligands and receptors to be queried in transcriptomic data.

**Usage**

```
create_rl_map_cellphonedb(
  genes,
  proteins,
  interactions,
  complexes = NULL,
  database_name = "CellPhoneDB",
  gene_conv = NULL,
  gene_conv_host = "https://www.ensembl.org",
  alternate_convert = FALSE,
  alternate_convert_table = NULL
)
```

**Arguments**

genes	data frame or file path to table of gene names in uniprot, hgnc_symbol, or ensembl format in CellPhoneDB database format
proteins	data frame or file path to table of protein features in CellPhoneDB format
interactions	data frame or file path to table of protein-protein interactions in CellPhoneDB format
complexes	optional: data frame or file path to table of protein complexes in CellPhoneDB format
database_name	name of the database being used, stored in output
gene_conv	a tuple of (from, to) or (source, target) if gene conversion to orthologs is desired; options are ENSMUSG, ENSG, MGI, or HGNC
gene_conv_host	host for conversion; default ensembl, could also use mirrors if desired
alternate_convert	boolean if you would like to use a non-ensembl method of conversion (must supply table; not recommended, use only if ensembl is down)
alternate_convert_table	supplied table for non-ensembl method of conversion

**Value**

Data frame where each row describes a possible receptor-ligand interaction

**Examples**

```
data(CellPhoneDB)
rl_map_tiny <- create_rl_map_cellphonedb(genes = CellPhoneDB$genes_tiny,
  proteins = CellPhoneDB$proteins_tiny,
  interactions = CellPhoneDB$interactions_tiny,
  complexes = CellPhoneDB$complexes_tiny)
```

---

domino-class

*The domino class*

---

**Description**

The domino class contains all information necessary to calculate receptor-ligand signaling. It contains z-scored expression, cell cluster labels, feature values, and a referenced receptor-ligand database formatted as a receptor-ligand map. Calculated intermediate values are also stored.

**Value**

An instance of class domino

**Slots**

db\_info List of data sets from ligand - receptor database  
 counts Raw count gene expression data  
 z\_scores Matrix of z-scored expression data with cells as columns  
 clusters Named factor with cluster identity of each cell  
 features Matrix of features (TFs) to correlate receptor - ligand expression with. Cells are columns and features are rows.  
 cor Correlation matrix of receptor expression to features.  
 linkages List of lists containing info linking cluster->tf->rec->lig  
 clust\_de Data frame containing differential expression results for features by cluster.  
 misc List of miscellaneous info pertaining to run parameters etc.  
 cl\_signaling\_matrices Incoming signaling matrix for each cluster  
 signaling Signaling matrix between all clusters.

---

dom_clusters	<i>Access clusters</i>
--------------	------------------------

---

**Description**

A function to pull cluster information from a domino object

**Usage**

```
dom_clusters(dom, labels = FALSE)
```

**Arguments**

dom	a domino object that has been created with <a href="#">create_domino()</a>
labels	a boolean for whether to return the cluster labels for each cell or the clusters used for inferring communication

**Value**

A vector containing either the names of the clusters used OR factors of the cluster label for each individual cell

**Examples**

```

example(build_domino, echo = FALSE)
cluster_names <- dom_clusters(pbmc_dom_built_tiny)
cell_cluster_label <- dom_clusters(pbmc_dom_built_tiny, labels = TRUE)

```

---

dom\_correlations      *Access correlations*

---

### Description

A function to pull receptor-transcription factor correlations from a domino object

### Usage

```
dom_correlations(dom, type = "rl")
```

### Arguments

dom	a domino object that has been created with <a href="#">create_domino()</a>
type	either "rl" or "complex", to select between the receptor-ligand or complex correlation matrix

### Value

A matrix containing the correlation values for each receptor (row) by transcription factor (column)

### Examples

```
example(build_domino, echo = FALSE)
cor_matrix <- dom_correlations(pbmc_dom_built_tiny, "rl")
```

---

dom\_counts      *Access counts*

---

### Description

A function to pull gene expression from a domino object

### Usage

```
dom_counts(dom)
```

### Arguments

dom	a domino object that has been created with <a href="#">create_domino()</a>
-----	--

### Value

A matrix containing the gene expression values for each gene (row) by cell (column)

### Examples

```
example(build_domino, echo = FALSE)
counts <- dom_counts(pbmc_dom_built_tiny)
```



---

dom_database	<i>Access database</i>
--------------	------------------------

---

**Description**

A function to pull database information from a domino object

**Usage**

```
dom_database(dom, name_only = TRUE)
```

**Arguments**

dom	a domino object that has been created
name_only	a boolean for whether to return only the name of the database used or the entire database that is stored. Default TRUE.

**Value**

A vector of unique databases used in building the domino object OR a data frame that includes the database information used in the domino object creation

**Examples**

```
example(build_domino, echo = FALSE)
database_name <- dom_database(pbmc_dom_built_tiny)
full_database <- dom_database(pbmc_dom_built_tiny, name_only = FALSE)
```

---

dom_de	<i>Access differential expression</i>
--------	---------------------------------------

---

**Description**

A function to pull differential expression p-values from a domino object

**Usage**

```
dom_de(dom)
```

**Arguments**

dom	a domino object that has been created with <a href="#">create_domino()</a>
-----	--

**Value**

A matrix containing the p-values for differential expression of transcription factors (rows) in each cluster (columns)

### Examples

```
example(build_domino, echo = FALSE)
de_mat <- dom_de(pbmc_dom_built_tiny)
```

---

dom\_info                      *Access build information*

---

### Description

A function to pull the parameters used when running `build_domino()` from a domino object

### Usage

```
dom_info(dom)
```

### Arguments

dom                      a domino object that has been created with `create_domino()`

### Value

A list containing booleans for whether the object has been created and built and a list of the build parameters that were used in `build_domino()` to infer the signaling network

### Examples

```
example(build_domino, echo = FALSE)
build_details <- dom_info(pbmc_dom_built_tiny)
```

---

dom\_linkages                      *Access linkages*

---

### Description

A function to pull linkages from a domino object

### Usage

```
dom_linkages(
  dom,
  link_type = c("complexes", "receptor-ligand", "tf-target", "tf-receptor", "receptor",
    "incoming-ligand"),
  by_cluster = FALSE
)
```

**Arguments**

dom	a domino object that has been created with <code>create_domino()</code>
link_type	one value (out of "complexes", "receptor-ligand", "tf-target", "tf-receptor", "receptor", "incoming-ligand") used to select the desired type of linkage
by_cluster	a boolean to indicate whether the linkages should be returned overall or by cluster

**Value**

A list containing linkages between some combination of receptors, ligands, transcription factors, and clusters

**Examples**

```
example(build_domino, echo = FALSE)
complexes <- dom_linkages(pbmc_dom_built_tiny, "complexes")
tf_rec_by_cluster <- dom_linkages(pbmc_dom_built_tiny, "tf-receptor", TRUE)
```

---

dom_network_items	<i>Access all features, receptors, or ligands present in a signaling network.</i>
-------------------	---

---

**Description**

This function collates all of the features, receptors, or ligands found in a signaling network anywhere in a list of clusters. This can be useful for comparing signaling networks across two separate conditions. In order to run this `build_domino()` must be run on the object previously.

**Usage**

```
dom_network_items(dom, clusters = NULL, return = NULL)
```

**Arguments**

dom	a domino object containing a signaling network (i.e. <code>build_domino()</code> was run)
clusters	vector indicating clusters to collate network items from. If left as NULL then all clusters will be included.
return	string indicating whether to collate "features", "receptors", or "ligands". If "all" then a list of all three will be returned.

**Value**

A vector containing all features, receptors, or ligands in the data set or a list containing all three.

**Examples**

```
example(build_domino, echo = FALSE)
monocyte_receptors <- dom_network_items(pbmc_dom_built_tiny, "CD14_monocyte", "receptors")
all_tfs <- dom_network_items(pbmc_dom_built_tiny, return = "features")
```

---

dom\_signaling      *Access signaling*

---

**Description**

A function to pull signaling matrices from a domino object

**Usage**

```
dom_signaling(dom, cluster = NULL)
```

**Arguments**

dom                    a domino object that has been created with `create_domino()`  
cluster                either NULL to indicate global signaling or a specific cluster for which a signaling matrix is desired

**Value**

A data frame containing the signaling score through each ligand (row) by each cluster (column) OR a data frame containing the global summed signaling scores between receptors (rows) and ligands (columns) of each cluster

**Examples**

```
example(build_domino, echo = FALSE)  
monocyte_signaling <- dom_signaling(pbmc_dom_built_tiny, cluster = "CD14_monocyte")
```

---

dom\_tf\_activation      *Access transcription factor activation*

---

**Description**

A function to pull transcription factor activation scores from a domino object

**Usage**

```
dom_tf_activation(dom)
```

**Arguments**

dom                    a domino object that has been created with `create_domino()`

**Value**

A matrix containing the transcription factor activation scores for each TF (row) by cell (column)

**Examples**

```
example(build_domino, echo = FALSE)  
tf_activation <- dom_tf_activation(pbmc_dom_built_tiny)
```

---

dom_zscores	<i>Access z-scores</i>
-------------	------------------------

---

**Description**

A function to pull z-scored expression from a domino object

**Usage**

```
dom_zscores(dom)
```

**Arguments**

dom                    a domino object that has been created with `create_domino()`

**Value**

A matrix containing the z-scored gene expression values for each gene (row) by cell (column)

**Examples**

```
example(build_domino, echo = FALSE)
zscores <- dom_zscores(pbmc_dom_built_tiny)
```

---

do_norm	<i>Normalize a matrix to its max value by row or column</i>
---------	---

---

**Description**

Normalizes a matrix to its max value by row or column

**Usage**

```
do_norm(mat, dir)
```

**Arguments**

mat                    Matrix to be normalized  
dir                    Direction to normalize the matrix (either "row" for row or "col" for column)

**Value**

A normalized matrix in the direction specified.

---

feat_heatmap	<i>Create a heatmap of features organized by cluster</i>
--------------	--

---

### Description

Creates a heatmap of transcription factor activation scores by cells grouped by cluster.

### Usage

```
feat_heatmap(
  dom,
  feats = NULL,
  bool = FALSE,
  bool_thresh = 0.2,
  title = TRUE,
  norm = FALSE,
  cols = NULL,
  ann_cols = TRUE,
  min_thresh = NULL,
  max_thresh = NULL,
  ...
)
```

### Arguments

dom	Domino object with network built ( <a href="#">build_domino()</a> )
feats	Either a vector of features to include in the heatmap or 'all' for all features. If left NULL then the features selected for the signaling network will be shown.
bool	Boolean indicating whether the heatmap should be continuous or boolean. If boolean then bool_thresh will be used to determine how to define activity as positive or negative.
bool_thresh	Numeric indicating the threshold separating 'on' or 'off' for feature activity if making a boolean heatmap.
title	Either a string to use as the title or a boolean describing whether to include a title. In order to pass the 'main' parameter to <a href="#">ComplexHeatmap::Heatmap()</a> you must set title to FALSE.
norm	Boolean indicating whether or not to normalize the transcription factors to their max value.
cols	Named vector of colors to annotate cells by cluster color. Values are taken as colors and names as cluster. If left as NULL then default ggplot colors will be generated.
ann_cols	Boolean indicating whether to include cell cluster as a column annotation. Colors can be defined with cols. If FALSE then custom annotations can be passed to <a href="#">ComplexHeatmap::Heatmap()</a> .
min_thresh	Minimum threshold for color scaling if not a boolean heatmap
max_thresh	Maximum threshold for color scaling if not a boolean heatmap
...	Other parameters to pass to <a href="#">ComplexHeatmap::Heatmap()</a> . Note that to use the 'main' parameter of <a href="#">ComplexHeatmap::Heatmap()</a> you must set title = FALSE and to use 'annCol' or 'annColors' ann_cols must be FALSE.

**Value**

A heatmap rendered to the active graphics device

**Examples**

```
#basic usage
example(build_domino, echo = FALSE)
feat_heatmap(pbmc_dom_built_tiny)
#using thresholds
feat_heatmap(
  pbmc_dom_built_tiny, min_thresh = 0.1,
  max_thresh = 0.6, norm = TRUE, bool = FALSE)
```

---

gene_network	<i>Create a gene association network</i>
--------------	--

---

**Description**

Create a gene association network for genes from a given cluster. The selected cluster acts as the receptor for the gene association network, so only ligands, receptors, and features associated with the receptor cluster will be included in the plot.

**Usage**

```
gene_network(
  dom,
  clust = NULL,
  OutgoingSignalingClust = NULL,
  class_cols = c(lig = "#FF685F", rec = "#47a7ff", feat = "#39C740"),
  cols = NULL,
  lig_scale = 1,
  layout = "grid",
  ...
)
```

**Arguments**

dom	Domino object with network built ( <a href="#">build_domino()</a> )
clust	Receptor cluster to create the gene association network for. A vector of clusters may be provided.
OutgoingSignalingClust	Vector of clusters to plot the outgoing signaling from
class_cols	Named vector of colors used to color classes of vertices. Values must be colors and names must be classes ('rec', 'lig', and 'feat' for receptors, ligands, and features.).
cols	Named vector of colors for individual genes. Genes not included in this vector will be colored according to class_cols.
lig_scale	FALSE or a numeric value to scale the size of ligand vertices based on z-scored expression in the data set.

layout           Type of layout to use. Options are 'grid', 'random', 'sphere', 'circle', 'fr' for Fruchterman-Reingold force directed layout, and 'kk' for Kamada Kawai for directed layout.

...               Other parameters to pass to plot() with an **igraph** object. See **igraph** manual for options.

**Value**

An igraph plot rendered to the active graphics device

**Examples**

```
#basic usage
example(build_domino, echo = FALSE)
gene_network(
  pbmc_dom_built_tiny, clust = "CD8_T_cell",
  OutgoingSignalingClust = "CD14_monocyte")
```

---

ggplot\_col\_gen           *Generate ggplot colors*

---

**Description**

Accepts a number of colors to generate and generates a ggplot color spectrum.

**Usage**

```
ggplot_col_gen(n)
```

**Arguments**

n                Number of colors to generate

**Value**

A vector of colors according to ggplot color generation.

---

incoming\_signaling\_heatmap  
*Create a cluster incoming signaling heatmap*

---

**Description**

Creates a heatmap of a cluster incoming signaling matrix. Each cluster has a list of ligands capable of activating its enriched transcription factors. The function creates a heatmap of cluster average expression for all of those ligands. A list of all cluster incoming signaling matrices can be found in the cl\_signaling\_matrices slot of a domino option as an alternative to this plotting function.



**Usage**

```
incoming_signaling_heatmap(
  dom,
  rec_clust,
  clusts = NULL,
  min_thresh = -Inf,
  max_thresh = Inf,
  scale = "none",
  normalize = "none",
  title = TRUE,
  ...
)
```

**Arguments**

dom	Domino object with network built ( <a href="#">build_domino()</a> )
rec_clust	Which cluster to select as the receptor. Must match naming of clusters in the domino object.
clusts	Vector of clusters to be included. If NULL then all clusters are used.
min_thresh	Minimum signaling threshold for plotting. Defaults to -Inf for no threshold.
max_thresh	Maximum signaling threshold for plotting. Defaults to Inf for no threshold.
scale	How to scale the values (after thresholding). Options are 'none', 'sqrt' for square root, or 'log' for log10.
normalize	Options to normalize the matrix. Accepted inputs are 'none' for no normalization, 'rec_norm' to normalize to the maximum value with each receptor cluster, or 'lig_norm' to normalize to the maximum value within each ligand cluster
title	Either a string to use as the title or a boolean describing whether to include a title. In order to pass the 'main' parameter to <a href="#">ComplexHeatmap::Heatmap()</a> you must set title to FALSE.
...	Other parameters to pass to <a href="#">ComplexHeatmap::Heatmap()</a> . Note that to use the 'column_title' parameter of <a href="#">ComplexHeatmap::Heatmap()</a> you must set title = FALSE

**Value**

a Heatmap rendered to the active graphics device

**Examples**

```
example(build_domino, echo = FALSE)
#incoming signaling of the CD8 T cells
incoming_signaling_heatmap(pbmc_dom_built_tiny, "CD8_T_cell")
```

---

lc	<i>Pulls all items from a list pooled into a single vector</i>
----	--

---

**Description**

Helper function to convert from a nested series of lists to a single vector.

**Usage**

```
lc(list, list_names)
```

**Arguments**

list	List to pull items from
list_names	Names of items in list to pool

**Value**

A vector containing all items in the list by list\_names

---

linkage\_summary-class *The domino linkage summary class*

---

**Description**

The linkage summary class contains linkages established in multiple domino objects through gene regulatory network inference and reference to receptor- ligand data bases. A data frame summarizing meta features that describe the domino objects compared in the linkage summary facilitates comparisons of established linkages and differential signaling interactions across categorical sample covariates.

**Value**

an instance of class linkage\_summary

**Slots**

subject_names	unique names for each domino result included in the summary
subject_meta	data.frame with each row describing one subject and columns describing features of the subjects by which to draw comparisons of signaling networks
subject_linkages	nested list of linkages inferred for each subject. Lists are stored in a heirarchical structure of subject-cluster-linkage where linkages include transcription factors (tfs), linkages between transcription factors and receptors (tfs_rec), active receptors (rec), possible receptor-ligand interactions (rec_lig), and incoming ligands (incoming_lig)

---

`mean_ligand_expression`*Calculate mean ligand expression as a data frame for plotting in circos plot*

---

**Description**

Creates a data frame of mean ligand expression for use in plotting a circos plot of ligand expression and saving tables of mean expression. us

**Usage**

```
mean_ligand_expression(x, ligands, cell_ident, cell_barcodes, destination)
```

**Arguments**

<code>x</code>	Gene by cell expression matrix
<code>ligands</code>	Character vector of ligand genes to be quantified
<code>cell_ident</code>	Vector of cell type (identity) names for which to calculate mean ligand gene expression
<code>cell_barcodes</code>	Vector of cell barcodes (colnames of <code>x</code> ) belonging to <code>cell_ident</code> to calculate mean expression across
<code>destination</code>	Name of the receptor with which each ligand interacts

**Value**

A data frame of ligand expression targeting the specified receptor

**Examples**

```
example(build_domino, echo = FALSE)
counts <- dom_counts(pbmc_dom_built_tiny)
mean_exp <- mean_ligand_expression(counts,
  ligands = c("PTPRC", "FASLG"), cell_ident = "CD14_monocyte",
  cell_barcodes = colnames(counts), destination = "FAS")
```

---

`mock_linkage_summary` *Create a mock linkage summary object*

---

**Description**

Create a mock linkage summary object

**Usage**

```
mock_linkage_summary()
```

**Value**

obj a linkage summary object

---

PBMC

*PBMC RNAseq data subset*

---

### Description

A subset of the results of PBMC RNA-seq data.

### Usage

```
data("PBMC")
```

### Format

A list of::

**RNA\_count\_tiny** A subset of PBMC RNA-seq data: counts assay

**RNA\_zscore\_tiny** A subset of PBMC RNA-seq data: zscore assay

**clusters\_tiny** A subset of PBMC RNA-seq data: clusters as defined by cell\_type

### Source

[https://zenodo.org/records/10951634/files/pbmc3k\\_sce.rds](https://zenodo.org/records/10951634/files/pbmc3k_sce.rds)

---

plot\_differential\_linkages

*Plot differential linkages among domino results ranked by a comparative statistic*

---

### Description

Plot differential linkages among domino results ranked by a comparative statistic

### Usage

```
plot_differential_linkages(  
  differential_linkages,  
  test_statistic,  
  stat_range = c(0, 1),  
  stat_ranking = c("ascending", "descending"),  
  group_palette = NULL  
)
```

**Arguments**

differential_linkages	a data frame output from the <code>test_differential_linkages()</code> function
test_statistic	column name of differential_linkages where the test statistic used for ranking linkages is stored (ex. 'p.value')
stat_range	a two value vector of the minimum and maximum values of test_statistic for plotting linkage features
stat_ranking	'ascending' (lowest value of test statistic is colored red and plotted at the top) or 'descending' (highest value of test statistic is colored red and plotted at the top).
group_palette	a named vector of colors to use for each group being compared

**Value**

A heatmap-class object of features ranked by test\_statistic annotated with the proportion of subjects that showed active linkage of the features.

**Examples**

```
example(build_domino, echo = FALSE)
example(test_differential_linkages, echo = FALSE)
plot_differential_linkages(
  differential_linkages = tiny_differential_linkage_c1,
  test_statistic = "p.value",
  stat_ranking = "ascending"
)
```

---

```
print,domino-method  Print domino object
```

---

**Description**

Prints a summary of a domino object

**Usage**

```
## S4 method for signature 'domino'
print(x, ...)
```

**Arguments**

x	A domino object
...	Additional arguments to be passed to other methods

**Value**

A printed description of the number of cells and clusters in the domino object

**Examples**

```
example(build_domino, echo = FALSE)
print(pbm_dom_built_tiny)
```

---

read_if_char	<i>Read in data if an object looks like path to it</i>
--------------	--

---

**Description**

Read in data if an object looks like path to it

**Usage**

```
read_if_char(obj)
```

**Arguments**

obj	object to read if not already object
-----	--------------------------------------

**Value**

Object itself or data read in from path

---

rename_clusters	<i>Renames clusters in a domino object</i>
-----------------	--

---

**Description**

This function renames the clusters used to build a domino object

**Usage**

```
rename_clusters(dom, clust_conv, warning = FALSE)
```

**Arguments**

dom	a domino object to rename clusters in
clust_conv	named vector of conversions from old to new clusters. Values are taken as new clusters IDs and names as old cluster IDs.
warning	logical. If TRUE, will warn if a cluster is not found in the conversion table. Default is FALSE.

**Value**

A domino object with clusters renamed in all applicable slots.

**Examples**

```
example(build_domino, echo = FALSE)
new_clust <- c("CD8_T_cell" = "CD8+ T Cells",
  "CD14_monocyte" = "CD14+ Monocytes", "B_cell" = "B Cells")
pbmc_dom_built_tiny <- rename_clusters(pbmc_dom_built_tiny, new_clust)
```

---

SCENIC	<i>SCENIC AUC subset</i>
--------	--------------------------

---

**Description**

A subset of SCENIC AUCs as applied to PBMC data.

**Usage**

```
data("SCENIC")
```

**Format**

A list of:

**auc\_tiny** A subset of SCENIC AUCs

**regulons\_tiny** A subset of SCENIC regulons

**Source**

<https://zenodo.org/records/10951634/files>

---

show,domino-method	<i>Show domino object information</i>
--------------------	---------------------------------------

---

**Description**

Shows content overview of domino object

**Usage**

```
## S4 method for signature 'domino'
show(object)
```

**Arguments**

object            A domino object

**Value**

A printed description of cell numbers and clusters in the object

**Examples**

```
example(build_domino, echo = FALSE)
show(pbmc_dom_built_tiny)
```

---

signaling\_heatmap      *Create a network heatmap*

---

### Description

Creates a heatmap of the signaling network. Alternatively, the network matrix can be accessed directly in the signaling slot of a domino object using the `dom_signaling()` function.

### Usage

```
signaling_heatmap(
  dom,
  clusts = NULL,
  min_thresh = -Inf,
  max_thresh = Inf,
  scale = "none",
  normalize = "none",
  ...
)
```

### Arguments

dom	domino object with network built ( <code>build_domino()</code> )
clusts	vector of clusters to be included. If NULL then all clusters are used.
min_thresh	minimum signaling threshold for plotting. Defaults to -Inf for no threshold.
max_thresh	maximum signaling threshold for plotting. Defaults to Inf for no threshold.
scale	how to scale the values (after thresholding). Options are 'none', 'sqrt' for square root, or 'log' for log10.
normalize	options to normalize the matrix. Normalization is done after thresholding and scaling. Accepted inputs are 'none' for no normalization, 'rec_norm' to normalize to the maximum value with each receptor cluster, or 'lig_norm' to normalize to the maximum value within each ligand cluster
...	other parameters to pass to <code>ComplexHeatmap::Heatmap()</code>

### Value

A heatmap rendered to the active graphics device

### Examples

```
example(build_domino, echo = FALSE)
#basic usage
signaling_heatmap(pbmc_dom_built_tiny)
#scale
signaling_heatmap(pbmc_dom_built_tiny, scale = "sqrt")
#normalize
signaling_heatmap(pbmc_dom_built_tiny, normalize = "rec_norm")
```



---

signaling_network	<i>Create a cluster to cluster signaling network diagram</i>
-------------------	--

---

### Description

Creates a network diagram of signaling between clusters. Nodes are clusters and directed edges indicate signaling from one cluster to another. Edges are colored based on the color scheme of the ligand expressing cluster

### Usage

```
signaling_network(
  dom,
  cols = NULL,
  edge_weight = 0.3,
  clusts = NULL,
  showOutgoingSignalingClusts = NULL,
  showIncomingSignalingClusts = NULL,
  min_thresh = -Inf,
  max_thresh = Inf,
  normalize = "none",
  scale = "sq",
  layout = "circle",
  scale_by = "rec_sig",
  vert_scale = 3,
  plot_title = NULL,
  ...
)
```

### Arguments

dom	a domino object with network built ( <a href="#">build_domino()</a> )
cols	named vector indicating the colors for clusters. Values are colors and names must match clusters in the domino object. If left as NULL then ggplot colors are generated for the clusters
edge_weight	weight for determining thickness of edges on plot. Signaling values are multiplied by this value
clusts	vector of clusters to be included in the network plot
showOutgoingSignalingClusts	vector of clusters to plot the outgoing signaling from
showIncomingSignalingClusts	vector of clusters to plot the incoming signaling on
min_thresh	minimum signaling threshold. Values lower than the threshold will be set to the threshold. Defaults to -Inf for no threshold
max_thresh	maximum signaling threshold for plotting. Values higher than the threshold will be set to the threshold. Defaults to Inf for no threshold
normalize	options to normalize the signaling matrix. Accepted inputs are 'none' for no normalization, 'rec_norm' to normalize to the maximum value with each receptor cluster, or 'lig_norm' to normalize to the maximum value within each ligand cluster

scale	how to scale the values (after thresholding). Options are 'none', 'sqrt' for square root, 'log' for log10, or 'sq' for square
layout	type of layout to use. Options are 'random', 'sphere', 'circle', 'fr' for Fruchterman-Reingold force directed layout, and 'kk' for Kamada Kawai for directed layout
scale_by	how to size vertices. Options are 'lig_sig' for summed outgoing signaling, 'rec_sig' for summed incoming signaling, and 'none'. In the former two cases the values are scaled with asinh after summing all incoming or outgoing signaling
vert_scale	integer used to scale size of vertices with or without variable scaling from size_verts_by.
plot_title	text for the plot's title.
...	other parameters to be passed to plot when used with an igraph object.

**Value**

An igraph plot rendered to the active graphics device

**Examples**

```
example(build_domino, echo = FALSE)
#basic usage
signaling_network(pbmc_dom_built_tiny, edge_weight = 2)
# scaling, thresholds, layouts, selecting clusters
signaling_network(
  pbmc_dom_built_tiny, showOutgoingSignalingClusts = "CD14_monocyte",
  scale = "none", norm = "none", layout = "fr", scale_by = "none",
  vert_scale = 5, edge_weight = 2)
```

---

summarize\_linkages      *Summarize linkages from multiple domino objects*

---

**Description**

Creates a `linkage_summary()` object storing the linkages learned in different domino objects as nested lists to facilitate comparisons of networks learned by domino across subject covariates.

**Usage**

```
summarize_linkages(domino_results, subject_meta, subject_names = NULL)
```

**Arguments**

domino_results	list of domino result with one domino object per subject. Names from the list must match subject_names
subject_meta	data frame that includes the subject features by which the objects could be grouped. The first column should must be subject names
subject_names	vector of subject names in domino_results. If NULL, defaults to first column of subject_meta.

**Value**

A linkage summary class object consisting of nested lists of the active transcription factors, active receptors, and incoming ligands for each cluster across multiple domino results

**Examples**

```
example(build_domino, echo = FALSE)

#create alternative clustering by shuffling cluster assignments
clusters_tiny_alt <- setNames(
  PBMC$clusters_tiny[c(121:240, 1:120, 241:360)],
  names(PBMC$clusters_tiny)
)
clusters_tiny_alt <- as.factor(clusters_tiny_alt)

#build an alternative domino object
pbmc_dom_tiny_alt <- create_domino(
  rl_map = rl_map_tiny,
  features = SCENIC$auc_tiny,
  counts = PBMC$RNA_count_tiny,
  z_scores = PBMC$RNA_zscore_tiny,
  clusters = clusters_tiny_alt,
  tf_targets = regulon_list_tiny,
  use_clusters = TRUE,
  use_complexes = TRUE,
  remove_rec_dropout = FALSE
)

pbmc_dom_built_tiny_alt <- build_domino(
  dom = pbmc_dom_tiny_alt,
  min_tf_pval = .05,
  max_tf_per_clust = Inf,
  max_rec_per_tf = Inf,
  rec_tf_cor_threshold = .1,
  min_rec_percentage = 0.01
)

#create a list of domino objects
dom_ls <- list(
  dom1 = pbmc_dom_built_tiny,
  dom2 = pbmc_dom_built_tiny_alt
)

#compare the linkages across the two domino objects
meta_df <- data.frame("ID" = c("dom1", "dom2"), "group" = c("A", "B"))
summarize_linkages(
  domino_results = dom_ls, subject_meta = meta_df,
  subject_names = meta_df$ID
)
```

**Description**

Takes a vector of gene inputs and a conversion table and returns a converted gene table

**Usage**

```
table_convert_genes(genes, from, to, conversion_table)
```

**Arguments**

genes	the genes to convert
from	gene symbol type of the input (ENSG, ENSMUSG, HGNC, MGI)
to	desired gene symbol type for the output (HGNC, MGI)
conversion_table	a data frame with column names corresponding to gene symbol types (mm.ens, hs.ens, mgi, hgnc) and rows corresponding to the gene symbols themselves

**Value**

A data frame of genes with original and corresponding converted symbols

---

```
test_differential_linkages
```

*Statistical test for differential linkages across multiple domino results*

---

**Description**

Statistical test for differential linkages across multiple domino results

**Usage**

```
test_differential_linkages(
  linkage_summary,
  cluster,
  group.by,
  linkage = "rec_lig",
  subject_names = NULL,
  test_name = "fishers.exact"
)
```

**Arguments**

linkage_summary	a <code>linkage_summary()</code> object
cluster	the name of the cell cluster being compared across multiple domino results
group.by	the name of the column in <code>linkage_summary@subject_meta</code> by which to group subjects for counting.
linkage	a stored linkage from the domino object. Can compare any of 'tfs', 'rec', 'incoming_lig', 'tfs_rec', or 'rec_lig'

- `subject_names` a vector of `subject_names` from the `linkage_summary` to be compared. If `NULL`, all `subject_names` in the linkage summary are included in counting.
- `test_name` the statistical test used for comparison.
- `'fishers.exact'` : Fisher's exact test for the dependence of the proportion of subjects with an active linkage in the cluster on which group the subject belongs to in the `group.by` variable. Provides an odds ratio, p-value, and a Benjamini-Hochberg FDR-adjusted p-value (`p.adj`) for each linkage tested.

### Value

A data frame of results from the test of the differential linkages. Rows correspond to each linkage tested. Columns correspond to:

- `'cluster'` : the name of the cell cluster being compared
- `'linkage'` : the type of linkage being compared
- `'group.by'` : the grouping variable
- `'test_name'` : the test used for comparison
- `'feature'` : individual linkages compared
- `'test statistics'` : test statistics provided are based on test method. `'fishers.exact'` provides a odds ratio, p-value, and fdr-adjusted p-value.
- `'total_count'` : total number of subjects where the linkage is active
- `'X_count'` : number of subjects in each category of `group.by` (`X`) where the linkage is active
- `'total_n'` : number of total subjects compared
- `'X_n'` : total number of subjects in each category of `group.by` (`X`)

### Examples

```
tiny_differential_linkage_c1 <- test_differential_linkages(  
  linkage_summary = mock_linkage_summary(), cluster = "C1", group.by = "group",  
  linkage = "rec", test_name = "fishers.exact"  
)
```

# Index

- \* **datasets**
  - CellPhoneDB, 5
  - PBMC, 28
  - SCENIC, 31
- \* **internal**
  - check\_arg, 5
  - conv\_py\_bools, 8
  - convert\_genes, 7
  - do\_norm, 21
  - ggplot\_col\_gen, 24
  - lc, 26
  - read\_if\_char, 30
  - table\_convert\_genes, 35
- add\_rl\_column, 3
- build\_domino, 4
- build\_domino(), 6, 8, 9, 11, 18, 19, 22, 23, 25, 32, 33
- CellPhoneDB, 5
- check\_arg, 5
- circos\_ligand\_receptor, 6
- ComplexHeatmap::Heatmap(), 9, 22, 25, 32
- conv\_py\_bools, 8
- convert\_genes, 7
- cor\_heatmap, 8
- cor\_scatter, 9
- count\_linkage, 10
- create\_domino, 11
- create\_domino(), 4, 15–21
- create\_regulon\_list\_scenic, 13
- create\_rl\_map\_cellphonedb, 13
- do\_norm, 21
- dom\_clusters, 15
- dom\_correlations, 16
- dom\_counts, 16
- dom\_database, 17
- dom\_de, 17
- dom\_info, 18
- dom\_linkages, 18
- dom\_network\_items, 19
- dom\_signaling, 20
- dom\_signaling(), 32
- dom\_tf\_activation, 20
- dom\_zscores, 21
- domino (domino-class), 14
- domino-class, 14
- feat\_heatmap, 22
- gene\_network, 23
- ggplot\_col\_gen, 24
- ggpubr::ggscatter(), 9
- incoming\_signaling\_heatmap, 24
- lc, 26
- linkage\_summary
  - (linkage\_summary-class), 26
- linkage\_summary(), 10, 34, 36
- linkage\_summary-class, 26
- mean\_ligand\_expression, 27
- mock\_linkage\_summary, 27
- PBMC, 28
- plot\_differential\_linkages, 28
- print, domino-method, 29
- read\_if\_char, 30
- rename\_clusters, 30
- SCENIC, 31
- show, domino-method, 31
- signaling\_heatmap, 32
- signaling\_network, 33
- summarize\_linkages, 34
- table\_convert\_genes, 35
- test\_differential\_linkages, 36
- test\_differential\_linkages(), 29