

Package ‘orthogene’

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Description

orthogene is an R package for easy mapping of orthologous genes across hundreds of species. It pulls up-to-date interspecies gene ortholog mappings across 700+ organisms. It also provides various utility functions to map common objects (e.g. data.frames, gene expression matrices, lists) onto 1:1 gene orthologs from any other species.

URL <https://github.com/neurogenomics/orthogene>

BugReports <https://github.com/neurogenomics/orthogene/issues>

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orthogene-package **orthogene:** *Interspecies gene mapping*

Description

orthogene is an R package for easy mapping of orthologous genes across hundreds of species.

Details

It pulls up-to-date interspecies gene ortholog mappings across 700+ organisms.

It also provides various utility functions to map common objects (e.g. data.frames, gene expression matrices, lists) onto 1:1 gene orthologs from any other species.

Author(s)

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Source

- [GitHub](#) : Source code and Issues submission.
- [Author Site](#) : orthogene was created by Brian M. Schilder.

See Also

Useful links:

- <https://github.com/neurogenomics/orthogene>
- Report bugs at <https://github.com/neurogenomics/orthogene/issues>

aggregate_mapped_genes

Aggregate a gene matrix by gene symbols

Description

Map matrix rownames to standardised gene symbols, and then aggregate many-to-one rows into a new matrix.

Usage

```
aggregate_mapped_genes(
  gene_df,
  species = "human",
  FUN = "sum",
  method = c("monocle3", "stats", "delayedarray"),
  transpose = FALSE,
  gene_map = NULL,
  gene_map_col = "name",
  non121_strategy = "drop_output_species",
  as_sparse = TRUE,
  as_DelayedArray = FALSE,
  dropNA = TRUE,
  sort_rows = FALSE,
  verbose = TRUE
)
```

Arguments

gene_df	Input matrix where row names are genes.
species	Species to map against.
FUN	Aggregation function (<i>DEFAULT</i> : "sum").
method	Aggregation method.
transpose	Transpose gene_df before mapping genes.
gene_map	A user-supplied gene_map. If NULL (<i>DEFAULT</i>), map_genes will be used to create a gene_map.
gene_map_col	Column in gene_map to aggregate gene_df by.

non121_strategy

How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include:

- "drop_both_species" or "dbs" or 1 :
Drop genes that have duplicate mappings in either the input_species or output_species
(*DEFAULT*).
- "drop_input_species" or "dis" or 2 :
Only drop genes that have duplicate mappings in the input_species.
- "drop_output_species" or "dos" or 3 :
Only drop genes that have duplicate mappings in the output_species.
- "keep_both_species" or "kbs" or 4 :
Keep all genes regardless of whether they have duplicate mappings in either species.
- "keep_popular" or "kp" or 5 :
Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max" :
When gene_df is a matrix and gene_output="rownames", these options will aggregate many-to-one gene mappings (input_species-to-output_species) after dropping any duplicate genes in the output_species.

as_sparse Convert aggregated matrix to sparse matrix.

as_DelayedArray

Convert aggregated matrix to [DelayedArray](#).

dropNA Drop genes assigned to NA in groupings.

sort_rows Sort gene_df rows alphanumerically.

verbose Print messages.

Value

Aggregated matrix

Examples

```
data("exp_mouse")
X_agg <- aggregate_mapped_genes(gene_df = exp_mouse, species = "mouse")
```

all_genes

Get all genes

Description

Return all known genes from a given species.

Usage

```
all_genes(  
  species,  
  method = c("gprofiler", "homologene", "babelgene"),  
  ensure_filter_nas = FALSE,  
  verbose = TRUE,  
  ...  
)
```

Arguments

species	Species to get all genes for. Will first be standardised with <code>map_species</code> .
method	R package to use for gene mapping: "gprofiler" (slower but more species and genes) or "homologene" (faster but fewer species and genes).
ensure_filter_nas	Perform an extra check to remove genes that are NAs of any kind.
verbose	Print messages.
...	Additional arguments to be passed to <code>gconvert</code> when <code>method="gprofiler"</code> .

Details

References [homologeneData](#) or [gconvert](#).

Value

Table with all gene symbols from the given species.

Examples

```
genome_mouse <- all_genes(species = "mouse")  
genome_human <- all_genes(species = "human")
```

convert_orthologs	<i>Map genes from one species to another</i>
-------------------	--

Description

Currently supports ortholog mapping between any pair of 700+ species.
Use [map_species](#) to return a full list of available organisms.

Usage

```

convert_orthologs(
  gene_df,
  gene_input = "rownames",
  gene_output = "rownames",
  standardise_genes = FALSE,
  input_species,
  output_species = "human",
  method = c("gprofiler", "homologene", "babelgene"),
  drop_nonorths = TRUE,
  non121_strategy = "drop_both_species",
  mthreshold = Inf,
  as_sparse = FALSE,
  sort_rows = FALSE,
  verbose = TRUE,
  ...
)

```

Arguments

- gene_df** Data object containing the genes (see `gene_input` for options on how the genes can be stored within the object).
Can be one of the following formats:
- `matrix` :
A sparse or dense matrix.
 - `data.frame` :
A `data.frame`, `data.table`. or `tibble`.
 - `codelist` :
A list or character vector.
- Genes, transcripts, proteins, SNPs, or genomic ranges can be provided in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to gene symbols unless specified otherwise with the `...` arguments.
Note: If you set `method="homologene"`, you must either supply genes in gene symbol format (e.g. "Sox2") OR set `standardise_genes=TRUE`.
- gene_input** Which aspect of `gene_df` to get gene names from:
- `"rownames"` :
From row names of `data.frame/matrix`.
 - `"colnames"` :
From column names of `data.frame/matrix`.
 - `<column name>` :
From a column in `gene_df`, e.g. `"gene_names"`.
- gene_output** How to return genes. Options include:

- "rownames" :
As row names of gene_df.
- "colnames" :
As column names of gene_df.
- "columns" :
As new columns "input_gene", "ortholog_gene" (and "input_gene_standard" if standardise_genes=TRUE) in gene_df.
- "dict" :
As a dictionary (named list) where the names are input_gene and the values are ortholog_gene.
- "dict_rev" :
As a reversed dictionary (named list) where the names are ortholog_gene and the values are input_gene.

standardise_genes

If TRUE AND gene_output="columns", a new column "input_gene_standard" will be added to gene_df containing standardised HGNC symbols identified by [gorth](#).

input_species Name of the input species (e.g., "mouse","fly"). Use [map_species](#) to return a full list of available species.

output_species Name of the output species (e.g. "human","chicken"). Use [map_species](#) to return a full list of available species.

method R package to use for gene mapping:

- "gprofiler" : Slower but more species and genes.
- "homologene" : Faster but fewer species and genes.
- "babelgene" : Faster but fewer species and genes. Also gives

(slower but more species and genes) or "homologene" (faster but fewer species and genes).

drop_nonorths Drop genes that don't have an ortholog in the output_species.

non121_strategy

How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include:

- "drop_both_species" or "dbs" or 1 :
Drop genes that have duplicate mappings in either the input_species or output_species
(*DEFAULT*).
- "drop_input_species" or "dis" or 2 :
Only drop genes that have duplicate mappings in the input_species.
- "drop_output_species" or "dos" or 3 :
Only drop genes that have duplicate mappings in the output_species.
- "keep_both_species" or "kbs" or 4 :
Keep all genes regardless of whether they have duplicate mappings in either species.

- "keep_popular" or "kp" or 5 :
Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max" :
When gene_df is a matrix and gene_output="rownames", these options will aggregate many-to-one gene mappings (input_species-to-output_species) after dropping any duplicate genes in the output_species.

mthreshold Maximum number of ortholog names per gene to show. Passed to [gorth](#). Only used when method="gprofiler" (*DEFAULT* : Inf).

as_sparse Convert gene_df to a sparse matrix. Only works if gene_df is one of the following classes:

- matrix
- Matrix
- data.frame
- data.table
- tibble

If gene_df is a sparse matrix to begin with, it will be returned as a sparse matrix (so long as gene_output= "rownames" or "colnames").

sort_rows Sort gene_df rows alphanumerically.

verbose Print messages.

... Additional arguments to be passed to [gorth](#) or [homologene](#).

NOTE: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see [here](#).

Value

gene_df with orthologs converted to the output_species.
Instead returned as a dictionary (named list) if gene_output="dict" or "dict_rev".

Examples

```

data("exp_mouse")
gene_df <- convert_orthologs(
  gene_df = exp_mouse,
  input_species = "mouse"
)

```

create_background *Create gene background*

Description

Create a gene background as the union/intersect of all orthologs between input species (species1 and species2), and the output_species. This can be useful when generating random lists of background genes to test against in analyses with data from multiple species (e.g. enrichment of mouse cell-type markers gene sets in human GWAS-derived gene sets).

Usage

```
create_background(
  species1,
  species2,
  output_species = "human",
  as_output_species = TRUE,
  use_intersect = TRUE,
  bg = NULL,
  gene_map = NULL,
  method = "homologene",
  non121_strategy = "drop_both_species",
  verbose = TRUE
)
```

Arguments

species1	First species.
species2	Second species.
output_species	Species to convert all genes from species1 and species2 to first. Default="human", but can be to either any species supported by orthogene , including species1 or species2.
as_output_species	Return background gene list as output_species orthologs, instead of the gene names of the original input species.
use_intersect	When species1 and species2 are both different from output_species, this argument will determine whether to use the intersect (TRUE) or union (FALSE) of all genes from species1 and species2.
bg	User supplied background list that will be returned to the user after removing duplicate genes.
gene_map	User-supplied gene_map data table from map_orthologs or map_genes .
method	R package to to use for gene mapping: <ul style="list-style-type: none"> • "gprofiler" : Slower but more species and genes. • "homologene" : Faster but fewer species and genes.

- "babelgene" : Faster but fewer species and genes. Also gives (slower but more species and genes) or "homologene" (faster but fewer species and genes).

non121_strategy

How to handle genes that don't have 1:1 mappings between input_species:output_species. Options include:

- "drop_both_species" or "dbs" or 1 :
Drop genes that have duplicate mappings in either the input_species or output_species
(*DEFAULT*).
- "drop_input_species" or "dis" or 2 :
Only drop genes that have duplicate mappings in the input_species.
- "drop_output_species" or "dos" or 3 :
Only drop genes that have duplicate mappings in the output_species.
- "keep_both_species" or "kbs" or 4 :
Keep all genes regardless of whether they have duplicate mappings in either species.
- "keep_popular" or "kp" or 5 :
Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
- "sum", "mean", "median", "min" or "max" :
When gene_df is a matrix and gene_output="rownames", these options will aggregate many-to-one gene mappings (input_species-to-output_species) after dropping any duplicate genes in the output_species.

verbose Print messages.

Value

Background gene list.

Examples

```
bg <- orthogene::create_background(species1 = "mouse",
                                  species2 = "rat",
                                  output_species = "human")
```

exp_mouse

Gene expression data: mouse

Description

Mean pseudobulk single-cell RNA-seq gene expression matrix.

Data originally comes from Zeisel et al., 2018 (Cell).

Usage

```
data("exp_mouse")
```

Format

sparse matrix

Source

Publication `ctd <- ewceData::ctd()` `exp_mouse <- as(ctd[[1]]$mean_exp, "sparseMatrix")`
`usethis::use_data(exp_mouse, overwrite = TRUE)`

exp_mouse_enst	<i>Transcript expression data: mouse</i>
----------------	--

Description

Mean pseudobulk single-cell RNA-seq Transcript expression matrix.

Data originally comes from Zeisel et al., 2018 (Cell).

Usage

```
data("exp_mouse_enst")
```

Format

sparse matrix

Source

Publication `data("exp_mouse")` `mapped_genes <- map_genes(genes = rownames(exp_mouse)[seq(1, 100)],`
`target = "ENST", species = "mouse", drop_na = FALSE)` `exp_mouse_enst <- exp_mouse[mapped_genes$input,]`
`rownames(exp_mouse_enst) <- mapped_genes$target` `all_nas <- orthogene::find_all_nas(rownames(exp_mouse)`
`exp_mouse_enst <- exp_mouse_enst[!all_nas,]` `exp_mouse_enst <- phenomix::add_noise(exp_mouse_enst)`
`usethis::use_data(exp_mouse_enst, overwrite = TRUE)`

gprofiler_orgs	<i>Reference organisms</i>
----------------	----------------------------

Description

Organism for which gene references are available via [gProfiler API](#).

Used as a backup if API is not available.

Usage

```
gprofiler_orgs
```

Format

```
data.frame URL <- 'https://biit.cs.ut.ee/gprofiler/api/util/organisms_list' gprofiler_orgs  
<- jsonlite::fromJSON(URL) gprofiler_orgs <- dplyr::arrange(gprofiler_orgs, scientific_name)  
usethis::use_data(gprofiler_orgs, overwrite = TRUE, internal=TRUE)
```

Source

[gProfiler site](#)

infer_species	<i>Infer species from gene names</i>
---------------	--------------------------------------

Description

Infers which species the genes within gene_df is from. Iteratively test the percentage of gene_df genes that match with the genes from each test_species.

Usage

```
infer_species(  
  gene_df,  
  gene_input = "rownames",  
  test_species = c("human", "monkey", "rat", "mouse", "zebrafish", "fly"),  
  method = c("homologene", "gprofiler", "babelgene"),  
  make_plot = TRUE,  
  show_plot = TRUE,  
  verbose = TRUE  
)
```

Arguments

gene_df	<p>Data object containing the genes (see gene_input for options on how the genes can be stored within the object). Can be one of the following formats:</p> <ul style="list-style-type: none"> • <code>matrix</code> : A sparse or dense matrix. • <code>data.frame</code> : A <code>data.frame</code>, <code>data.table</code>. or <code>tibble</code>. • <code>codelist</code> : A list or character vector. <p>Genes, transcripts, proteins, SNPs, or genomic ranges can be provided in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to gene symbols unless specified otherwise with the <code>...</code> arguments. <i>Note:</i> If you set <code>method="homologene"</code>, you must either supply genes in gene symbol format (e.g. "Sox2") OR set <code>standardise_genes=TRUE</code>.</p>
gene_input	<p>Which aspect of <code>gene_df</code> to get gene names from:</p> <ul style="list-style-type: none"> • <code>"rownames"</code> : From row names of <code>data.frame/matrix</code>. • <code>"colnames"</code> : From column names of <code>data.frame/matrix</code>. • <code><column name></code> : From a column in <code>gene_df</code>, e.g. <code>"gene_names"</code>.
test_species	<p>Which species to test for matches with. If set to <code>NULL</code>, will default to a list of humans and 5 common model organisms. If <code>test_species</code> is set to one of the following options, it will automatically pull all species from that respective package and test against each of them:</p> <ul style="list-style-type: none"> • <code>"homologene"</code> 20+ species (default) • <code>"gprofiler"</code> 700+ species • <code>"babelgene"</code> 19 species
method	<p>R package to use for gene mapping:</p> <ul style="list-style-type: none"> • <code>"gprofiler"</code> : Slower but more species and genes. • <code>"homologene"</code> : Faster but fewer species and genes. • <code>"babelgene"</code> : Faster but fewer species and genes. Also gives (slower but more species and genes) or <code>"homologene"</code> (faster but fewer species and genes).
make_plot	Make a plot of the results.
show_plot	Print the plot of the results.
verbose	Print messages.

Value

An ordered dataframe of `test_species` from best to worst matches.

Examples

```
data("exp_mouse")
matches <- infer_species(gene_df = exp_mouse[1:200,])
```

map_genes	<i>Map genes</i>
-----------	------------------

Description

Input a list of genes, transcripts, proteins, SNPs, or genomic ranges in any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and return a table with standardised gene symbols (the "names" column).

Usage

```
map_genes(
  genes,
  species = "hsapiens",
  target = "ENSG",
  mthreshold = Inf,
  drop_na = FALSE,
  numeric_ns = "",
  verbose = TRUE
)
```

Arguments

genes	Gene list.
species	Species to map against.
target	target namespace.
mthreshold	maximum number of results per initial alias to show. Shows all by default.
drop_na	Drop all genes without mappings. Sets <code>gprofiler2::gconvert(filter_na=)</code> as well an additional round of more comprehensive NA filtering by orthogene .
numeric_ns	namespace to use for fully numeric IDs (list of available namespaces).
verbose	Print messages.

Details

Uses [gconvert](#). The exact contents of the output table will depend on target parameter. See `?gprofiler2::gconvert` for more details.

Value

Table with standardised genes.

Examples

```
genes <- c(
  "Klf4", "Sox2", "TSPAN12", "NM_173007", "Q8BKT6",
  "ENSMUSG00000012396", "ENSMUSG00000074637"
)
mapped_genes <- map_genes(
  genes = genes,
  species = "mouse"
)
```

map_orthologs	<i>Map orthologs</i>
---------------	----------------------

Description

Map orthologs from one species to another.

Usage

```
map_orthologs(
  genes,
  standardise_genes = FALSE,
  input_species,
  output_species = "human",
  method = c("gprofiler", "homologene"),
  mthreshold = Inf,
  verbose = TRUE,
  ...
)
```

Arguments

genes	can be a mixture of any format (HGNC, Ensembl, RefSeq, UniProt, etc.) and will be automatically converted to standardised HGNC symbol format.
standardise_genes	If TRUE AND gene_output="columns", a new column "input_gene_standard" will be added to gene_df containing standardised HGNC symbols identified by gorth .
input_species	Name of the input species (e.g., "mouse", "fly"). Use map_species to return a full list of available species.
output_species	Name of the output species (e.g. "human", "chicken"). Use map_species to return a full list of available species.
method	R package to to use for gene mapping: <ul style="list-style-type: none"> • "gprofiler" : Slower but more species and genes. • "homologene" : Faster but fewer species and genes.

- "babelgene" : Faster but fewer species and genes. Also gives (slower but more species and genes) or "homologene" (faster but fewer species and genes).
- mthreshold** Maximum number of ortholog names per gene to show. Passed to [gorth](#). Only used when method="gprofiler" (*DEFAULT* : Inf).
- verbose** Print messages.
- ...** Additional arguments to be passed to [gorth](#) or [homologene](#).

NOTE: To return only the most "popular" interspecies ortholog mappings, supply `mthreshold=1` here AND set `method="gprofiler"` above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see [here](#).

Details

`map_orthologs()` is a core function within `convert_orthologs()`, but does not have many of the extra checks, such as `non121_strategy`) and `drop_nonorths`.

Value

Ortholog map data.frame with at least the columns "input_gene" and "ortholog_gene".

Examples

```
data("exp_mouse")
gene_map <- map_orthologs(
  genes = rownames(exp_mouse),
  input_species = "mouse"
)
```

map_species	<i>Standardise species names</i>
-------------	----------------------------------

Description

Search gprofiler database for species that match the input text string. Then translate to a standardised species ID.

Usage

```
map_species(
  species = NULL,
  search_cols = c("display_name", "id", "scientific_name", "taxonomy_id"),
  output_format = c("id", "display_name", "scientific_name", "taxonomy_id", "version"),
  method = "gprofiler",
```



```

    use_local = TRUE,
    verbose = TRUE
  )

```

Arguments

species	Species query (e.g. "human", "homo sapiens", "hapiens", or 9606). If given a list, will iterate queries for each item. Set to NULL to return all species.
search_cols	Which columns to search for species substring in metadata API .
output_format	Which column to return.
method	R package to use for gene mapping: <ul style="list-style-type: none"> • "gprofiler" : Slower but more species and genes. • "homologene" : Faster but fewer species and genes. • "babelgene" : Faster but fewer species and genes. Also gives (slower but more species and genes) or "homologene" (faster but fewer species and genes).
use_local	If TRUE <i>default</i> , map_species uses a locally stored version of the species metadata table instead of pulling directly from the gprofiler API. Local version may not be fully up to date, but should suffice for most use cases.
verbose	Print messages.

Value

Species ID of type output_format

Examples

```

ids <- map_species(species = c(
  "human", 9606, "mus musculus",
  "fly", "C elegans"
))

```

report_orthologs	<i>Report orthologs</i>
------------------	-------------------------

Description

Identify the number of orthologous genes between two species.

Usage

```

report_orthologs(
  target_species = "mouse",
  reference_species = "human",
  standardise_genes = FALSE,
  method_all_genes = c("gprofiler", "homologene"),
  method_convert_orthologs = c("gprofiler", "homologene", "babelgene"),
  drop_nonorths = TRUE,
  non121_strategy = "drop_both_species",
  round_digits = 2,
  return_report = TRUE,
  verbose = TRUE,
  ...
)

```

Arguments

`target_species` Target species.

`reference_species`
Reference species.

`standardise_genes`
If TRUE AND `gene_output="columns"`, a new column "input_gene_standard" will be added to `gene_df` containing standardised HGNC symbols identified by [gorth](#).

`method_all_genes`
R package to use in [all_genes](#) step: "gprofiler" (slower but more species and genes) or "homologene" (faster but fewer species and genes).

`method_convert_orthologs`
R package to use in [convert_orthologs](#) step: "gprofiler" (slower but more species and genes) or "homologene" (faster but fewer species and genes).

`drop_nonorths` Drop genes that don't have an ortholog in the `output_species`.

`non121_strategy`
How to handle genes that don't have 1:1 mappings between `input_species:output_species`.
Options include:

- "drop_both_species" or "dbs" or 1 :
Drop genes that have duplicate mappings in either the `input_species` or `output_species` (*DEFAULT*).
- "drop_input_species" or "dis" or 2 :
Only drop genes that have duplicate mappings in the `input_species`.
- "drop_output_species" or "dos" or 3 :
Only drop genes that have duplicate mappings in the `output_species`.
- "keep_both_species" or "kbs" or 4 :
Keep all genes regardless of whether they have duplicate mappings in either species.

- "keep_popular" or "kp" or 5 :
Return only the most "popular" interspecies ortholog mappings. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.
 - "sum", "mean", "median", "min" or "max" :
When gene_df is a matrix and gene_output="rownames", these options will aggregate many-to-one gene mappings (input_species-to-output_species) after dropping any duplicate genes in the output_species.
- round_digits Number of digits to round to when printing percentages.
- return_report Return just the ortholog mapping between two species (FALSE) or return both the ortholog mapping as well a data.frame of the report statistics (TRUE).
- verbose Print messages.
- ... Additional arguments to be passed to [gorth](#) or [homologene](#).

NOTE: To return only the most "popular" interspecies ortholog mappings, supply mthreshold=1 here AND set method="gprofiler" above. This procedure tends to yield a greater number of returned genes but at the cost of many of them not being true biological 1:1 orthologs.

For more details, please see [here](#).

Value

List of ortholog report statistics

Examples

```
orth_fly <- report_orthologs(
  target_species = "fly",
  reference_species = "human"
)
```

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