Package 'cageminer'

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Title Candidate Gene Miner

Version 1.12.0

Description This package aims to integrate GWAS-derived SNPs and coexpression networks to mine candidate genes associated with a particular phenotype. For that, users must define a set of guide genes, which are known genes involved in the studied phenotype. Additionally, the mined candidates can be given a score that favor candidates that are hubs and/or transcription factors. The scores can then be used to rank and select the top n most promising genes for downstream experiments.

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URL https://github.com/almeidasilvaf/cageminer

BugReports https://support.bioconductor.org/t/cageminer

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Contents

`chr_length` *Pepper chromosome lengths*

Description

Lengths of pepper chromosomes 1-12 in a GRanges object. The genome for which lengths were calculated (v1.55) was downloaded from http://peppergenome.snu.ac.kr/download.php

Usage

```
data(chr_length)
```

Format

A GRanges object

Examples

```
data(chr_length)
```

gcn — *Simulation of the output list from BioNERO::exp2gcn() with pepper data*

Description

This object is a list as returned by BioNERO::exp2gcn(), but only the element genes_and_modules is included. For running time issues, only genes in the cyan module were kept in the element genes_and_modules. All other list elements have been assigned NULL. The network was inferred using the code from the vignette.

Usage

```
data(gcn)
```

Format

A list with the elements returned by BioNERO::exp2gcn().

Examples

```
data(gcn)
```

gene_ranges — *Genomic coordinates of pepper genes*

Description

GRanges object with genomic coordinates of pepper genes downloaded from http://peppergenome.snu.ac.kr/download.ph

Usage

```
data(gene_ranges)
```

Format

A GRanges object

Examples

```
data(gene_ranges)
```

guides *Guide genes associated with defense and resistance to oomycetes*

Description

The GO annotation was retrieved from PLAZA 4.0 Dicots.

Usage

```
data(guides)
```

Format

A data frame with genes in the first column and GO description in the second column.

References

Van Bel, M., Diels, T., Vancaester, E., Kreft, L., Botzki, A., Van de Peer, Y., ... & Vandepoele, K. (2018). PLAZA 4.0: an integrative resource for functional, evolutionary and comparative plant genomics. Nucleic acids research, 46(D1), D1190-D1196.

Examples

```
data(guides)
```

hubs *Example hub genes for the network stored in the gcn object*

Description

The data frame was created using the code from the vignette.

Usage

```
data(hubs)
```

Format

Data frame with gene IDs, module and intramodular degree.

Examples

```
data(hubs)
```

mine2 *Example output from mine_step2()*

Description

The list was created using the example code from mine_step().

Usage

```
data(mine2)
```

Format

List with elements 'candidates' (character vector) and 'enrichment' (data frame).

Examples

```
data(mine2)
```

mined_candidates *Example output from mined_candidates()*

Description

The data frame was created using the code from the vignette.

Usage

```
data(mined_candidates)
```

Format

Data frame with an example of the output from mined_candidates

Examples

```
data(mined_candidates)
```

`mine_candidates` *Mine high-confidence candidate genes in a single step*

Description

Mine high-confidence candidate genes in a single step

Usage

```
mine_candidates(
  gene_ranges = NULL,
  marker_ranges = NULL,
  window = 2,
  expand_intervals = TRUE,
  gene_col = "ID",
  exp = NULL,
  gcn = NULL,
  guides = NULL,
  metadata,
  metadata_cols = 1,
  sample_group,
  min_cor = 0.2,
  alpha = 0.05,
  ...
)
```

Arguments

`gene_ranges`	A GRanges object with genomic coordinates of all genes in the genome.
`marker_ranges`	Genomic positions of SNPs. For a single trait, a GRanges object. For multiple traits, a GRangesList or CompressedGRangesList object, with each element of the list representing SNP positions for a particular trait.
`window`	Sliding window (in Mb) upstream and downstream relative to each SNP. Default: 2.
`expand_intervals`	Logical indicating whether or not to expand markers that are represented by intervals. This is particularly useful if users want to use a custom interval defined by linkage disequilibrium, for example. Default: TRUE.
`gene_col`	Column of the GRanges object containing gene ID. Default: "ID", the default for gff/gff3 files imported with rtracklayer::import.
`exp`	Expression data frame with genes in row names and samples in column names or a SummarizedExperiment object.
`gcn`	Gene coexpression network returned by `BioNERO::exp2gcn()`.
`guides`	Guide genes as a character vector or as a data frame with genes in the first column and gene annotation class in the second column.
`metadata`	Sample metadata with samples in row names and sample information in the first column. Ignored if `exp` is a SummarizedExperiment object, as the colData will be extracted from the object.

metadata_cols	A vector (either numeric or character) indicating which columns should be extracted from column metadata if **exp** is a SummarizedExperiment object. The vector can contain column indices (numeric) or column names (character). By default, all columns are used.
sample_group	Level of sample metadata to be used for filtering in gene-trait correlation.
min_cor	Minimum correlation value for BioNERO::gene_significance(). Default: 0.2
alpha	Numeric indicating significance level. Default: 0.05
...	Additional arguments to BioNERO::gene_significance.

Value

A data frame with mined candidate genes and their correlation to the condition of interest.

Examples

```
data(pepper_se)
data(snp_pos)
data(gene_ranges)
data(guides)
data(gcn)
set.seed(1)
candidates <- mine_candidates(gene_ranges, snp_pos, exp = pepper_se,
                              gcn = gcn, guides = guides$Gene,
                              sample_group = "PRR_stress")
```

---

mine_step1 *Step 1: Get all putative candidate genes for a given sliding window*

Description

For a user-defined sliding window relative to each SNP, this function will subset all genes whose genomic positions overlap with the sliding window.

Usage

```
mine_step1(gene_ranges, marker_ranges, window = 2, expand_intervals = TRUE)
```

Arguments

gene_ranges	A GRanges object with genomic coordinates of all genes in the genome.
marker_ranges	Genomic positions of SNPs. For a single trait, a GRanges object. For multiple traits, a GRangesList or CompressedGRangesList object, with each element of the list representing SNP positions for a particular trait.
window	Sliding window (in Mb) upstream and downstream relative to each SNP. Default: 2.
expand_intervals	Logical indicating whether or not to expand markers that are represented by intervals. This is particularly useful if users want to use a custom interval defined by linkage disequilibrium, for example. Default: TRUE.

Value

A GRanges or GRangesList object with the genomic positions of all putative candidate genes.

See Also

findOverlaps-methods

Examples

```
data(snp_pos)
data(gene_ranges)
genes <- mine_step1(gene_ranges, snp_pos, window = 2)
```

---

mine_step2 *Step 2: Get candidates in modules enriched in guide genes*

Description

Step 2: Get candidates in modules enriched in guide genes

Usage

```
mine_step2(exp, gcn, guides, candidates, ...)
```

Arguments

exp	Expression data frame with genes in row names and samples in column names or a SummarizedExperiment object.
gcn	Gene coexpression network returned by BioNERO::exp2gcn().
guides	Guide genes as a character vector or as a data frame with genes in the first column and gene annotation class in the second column.
candidates	Character vector of all candidates genes to be inspected.
...	Additional arguments to BioNERO::module_enrichment

Value

A list of 2 elements:

candidates Character vector of candidates after step 2

enrichment Data frame of results for enrichment analysis

Examples

```
data(pepper_se)
data(guides)
data(gcn)
set.seed(1)
mine2 <- mine_step2(
    exp = pepper_se,
    gcn = gcn,
    guides = guides$Gene,
    candidates = rownames(pepper_se)
)
```

mine_step3 *Step 3: Select candidates based on gene significance*

Description

Step 3: Select candidates based on gene significance

Usage

```
mine_step3(
  exp,
  metadata,
  metadata_cols = 1,
  candidates,
  sample_group,
  min_cor = 0.2,
  alpha = 0.05,
  ...
)
```

Arguments

exp	Expression data frame with genes in row names and samples in column names or a SummarizedExperiment object.
metadata	Sample metadata with samples in row names and sample information in the first column. Ignored if exp is a SummarizedExperiment object, as the colData will be extracted from the object.
metadata_cols	A vector (either numeric or character) indicating which columns should be extracted from column metadata if **exp** is a SummarizedExperiment object. The vector can contain column indices (numeric) or column names (character). By default, all columns are used.
candidates	Character vector of candidate genes to be inspected.
sample_group	Level of sample metadata to be used for filtering in gene-trait correlation.
min_cor	Minimum correlation value for BioNERO::gene_significance(). Default: 0.2
alpha	Numeric indicating significance level. Default: 0.05
...	Additional arguments to BioNERO::gene_significance.

Value

A data frame with mined candidate genes and their correlation to the condition of interest.

Examples

```
data(pepper_se)
data(snp_pos)
data(gene_ranges)
data(guides)
data(gcn)
data(mine2)
set.seed(1)
```

```
mine3 <- mine_step3(
    exp = pepper_se,
    candidates = mine2$candidates,
    sample_group = "PRR_stress"
)
```

`pepper_se` *Gene expression data from Kim et al., 2018.*

Description

The data were filtered to keep only the top 4000 genes with highest RPKM values in PRR stress-related samples.

Usage

```
data(pepper_se)
```

Format

A SummarizedExperiment object.

References

Kim, MS., Kim, S., Jeon, J. et al. Global gene expression profiling for fruit organs and pathogen infections in the pepper, Capsicum annuum L.. Sci Data 5, 180103 (2018). https://doi.org/10.1038/sdata.2018.103

Examples

```
data(pepper_se)
```

`plot_snp_circos` *Circos plot of SNP distribution across chromosomes*

Description

Circos plot of SNP distribution across chromosomes

Usage

```
plot_snp_circos(genome_ranges, gene_ranges, marker_ranges)
```

Arguments

`genome_ranges`	A GRanges object with chromosome lengths.
`gene_ranges`	A GRanges object with genomic coordinates of all genes in the genome.
`marker_ranges`	Genomic positions of SNPs. For a single trait, a GRanges object. For multiple traits, a GRangesList or CompressedGRangesList object, with each element of the list representing SNP positions for a particular trait.

Value

A ggplot object with a circos plot of molecular marker distribution across chromosomes.

Examples

```
data(snp_pos)
data(gene_ranges)
data(chr_length)
p <- plot_snp_circos(chr_length, gene_ranges, snp_pos)
```

---

plot_snp_distribution *Plot a barplot of SNP distribution across chromosomes*

Description

Plot a barplot of SNP distribution across chromosomes

Usage

```
plot_snp_distribution(marker_ranges)
```

Arguments

marker_ranges	Genomic positions of SNPs. For a single trait, a GRanges object. For multiple traits, a GRangesList or CompressedGRangesList object, with each element of the list representing SNP positions for a particular trait. List elements must have names for proper labelling.

Value

A ggplot object.

Examples

```
data(snp_pos)
p <- plot_snp_distribution(snp_pos)
```

---

score_genes *Score candidate genes and select the top n genes*

Description

Score candidate genes and select the top n genes

Usage

```
score_genes(
  mined_candidates,
  hubs = NULL,
  tfs = NULL,
  pick_top = 10,
  weight_tf = 2,
  weight_hub = 2,
  weight_both = 3
)
```

Arguments

mined_candidates	Data frame resulting from `mine_candidates()` or `mine_step()`.
hubs	Character vector of hub genes.
tfs	Character vector of transcription factors.
pick_top	Number of top genes to select. Default: 10.
weight_tf	Numeric scalar with the weight to which correlation coefficients will be multiplied if the gene is a TF. Default: 2.
weight_hub	Numeric scalar with the weight to which correlation coefficients will be multiplied if the gene is a hub. Default: 2.
weight_both	Numeric scalar with the weight to which correlation coefficients will be multiplied if the gene is both a TF and a hub. Default: 3.

Value

Data frame with top n candidates and their scores.

Examples

```
data(tfs)
data(hubs)
data(mined_candidates)
set.seed(1)
scored <- score_genes(mined_candidates, hubs$Gene, tfs$Gene_ID)
```

---

simulate_windows *Simulate number of genes for each sliding window*

Description

This function counts genes that are contained in sliding windows related to each SNP.

Usage

```
simulate_windows(
  gene_ranges,
  marker_ranges,
  windows = seq(0.1, 2, by = 0.1),
  expand_intervals = TRUE
)
```

Arguments

gene_ranges	A GRanges object with genomic coordinates of all genes in the genome.
marker_ranges	Genomic positions of SNPs. For a single trait, a GRanges object. For multiple traits, a GRangesList or CompressedGRangesList object, with each element of the list representing SNP positions for a particular trait.
windows	Sliding windows (in Mb) upstream and downstream relative to each SNP. Default: seq(0.1, 2, by = 0.1).
expand_intervals	Logical indicating whether or not to expand markers that are represented by intervals. This is particularly useful if users want to use a custom interval defined by linkage disequilibrium, for example. Default: TRUE.

Details

By default, the function creates 20 sliding windows by expanding upstream and downstream boundaries for each SNP from 0.1 Mb (100 kb) to 2 Mb.

Value

A ggplot object summarizing the results of the simulations.

See Also

findOverlaps-methods

Examples

```
data(snp_pos)
data(gene_ranges)
simulate_windows(gene_ranges, snp_pos)
```

---

snp_pos *Capsicum annuum SNPs associated with resistance to Phytophthora root rot.*

Description

The SNPs in this data set were retrieved from Siddique et al., 2019, and they are associated to resistance to Phytophthora root rot.

Usage

```
data(snp_pos)
```

Format

A GRanges object.

References

Siddique, M.I., Lee, HY., Ro, NY. et al. Identifying candidate genes for Phytophthora capsici resistance in pepper (Capsicum annuum) via genotyping-by-sequencing-based QTL mapping and genome-wide association study. Sci Rep 9, 9962 (2019). https://doi.org/10.1038/s41598-019-46342-1

Examples

```
data(snp_pos)
```

`tfs` *Pepper transcription factors*

Description

Pepper transcription factors and their families retrieved from PlantTFDB 4.0.

Usage

```
data(tfs)
```

Format

A data frame with gene IDs in the first column and TF families in the second column.

References

Jin, J., Tian, F., Yang, D. C., Meng, Y. Q., Kong, L., Luo, J., & Gao, G. (2016). PlantTFDB 4.0: toward a central hub for transcription factors and regulatory interactions in plants. Nucleic acids research, gkw982.

Examples

```
data(tfs)
```

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