

# Package ‘cTRAP’

April 12, 2022

**Title** Identification of candidate causal perturbations from differential gene expression data

**Version** 1.12.0

**Description** Compare differential gene expression results with those from known cellular perturbations (such as gene knock-down, overexpression or small molecules) derived from the Connectivity Map. Such analyses allow not only to infer the molecular causes of the observed difference in gene expression but also to identify small molecules that could drive or revert specific transcriptomic alterations.

**Depends** R (>= 4.0)

**License** MIT + file LICENSE

**Encoding** UTF-8

**LazyData** true

**biocViews** DifferentialExpression, GeneExpression, RNASeq, Transcriptomics, Pathways, ImmunoOncology, GeneSetEnrichment

**URL** <https://nuno-agostinho.github.io/cTRAP>,  
<https://github.com/nuno-agostinho/cTRAP>

**BugReports** <https://github.com/nuno-agostinho/cTRAP/issues>

**Suggests** testthat, knitr, covr, rmarkdown, spelling, biomaRt, remotes

**RoxygenNote** 7.1.2

**Imports** AnnotationDbi, AnnotationHub, binr, cowplot, data.table, dplyr, DT, fastmatch, fgsea, ggplot2, ggrepel, graphics, highcharter, htmltools, httr, limma, methods, parallel, pbapply, purrr, qs, R.utils, readxl, reshape2, rhdf5, rlang, scales, shiny (>= 1.7.0), shinycssloaders, stats, tibble, tools, utils

**VignetteBuilder** knitr

**Language** en-GB

**Collate** 'utils.R' 'CMap.R' 'ENCODE.R' 'cTRAP-package.r'  
'cmapR\_subset.R' 'compare.R' 'drugSensitivity.R'  
'drugSetEnrichment.R' 'floweRy.R' 'plots.R' 'shinyInterface.R'  
'shinyInterface\_session.R'

**git\_url** <https://git.bioconductor.org/packages/cTRAP>

**git\_branch** RELEASE\_3\_14

**git\_last\_commit** 8282ad2

**git\_last\_commit\_date** 2021-10-26

**Date/Publication** 2022-04-12

**Author** Bernardo P. de Almeida [aut],  
Nuno Saraiva-Agostinho [aut, cre],  
Nuno L. Barbosa-Morais [aut, led]

**Maintainer** Nuno Saraiva-Agostinho <nunodanielagostinho@gmail.com>

## R topics documented:

analyseDrugSetEnrichment . . . . .	3
as.table.referenceComparison . . . . .	4
convertENSEMBLtoGeneSymbols . . . . .	5
convertGeneIdentifiers . . . . .	6
cTRAP . . . . .	7
dimnames.expressionDrugSensitivityAssociation . . . . .	8
downloadENCODeknockdownMetadata . . . . .	9
filterCMapMetadata . . . . .	10
getCMapConditions . . . . .	11
getCMapPerturbationTypes . . . . .	12
launchCMapDataLoader . . . . .	13
launchDiffExprLoader . . . . .	14
launchDrugSetEnrichmentAnalyser . . . . .	14
launchMetadata Viewer . . . . .	15
launchResultPlotter . . . . .	16
listExpressionDrugSensitivityAssociation . . . . .	16
loadCMapData . . . . .	17
loadCMapZscores . . . . .	18
loadDrugDescriptors . . . . .	19
loadENCODEsamples . . . . .	20
loadExpressionDrugSensitivityAssociation . . . . .	20
parseCMapID . . . . .	21
performDifferentialExpression . . . . .	22
plot.perturbationChanges . . . . .	23
plot.referenceComparison . . . . .	25
plotDrugSetEnrichment . . . . .	27
plotTargetingDrugsVSSimilarPerturbations . . . . .	29
predictTargetingDrugs . . . . .	30
prepareCMapPerturbations . . . . .	32
prepareDrugSets . . . . .	33
prepareENCODegeneExpression . . . . .	34
print.similarPerturbations . . . . .	35
rankSimilarPerturbations . . . . .	36

---

analyseDrugSetEnrichment  
*Analyse drug set enrichment*

---

## Description

Analyse drug set enrichment

## Usage

```
analyseDrugSetEnrichment(
  sets,
  stats,
  col = NULL,
  nperm = 10000,
  maxSize = 500,
  ...,
  keyColSets = NULL,
  keyColStats = NULL
)
```

## Arguments

sets	Named list of characters: named sets containing compound identifiers (obtain drug sets by running <code>prepareDrugSets()</code> )
stats	Named numeric vector or either a <code>similarPerturbations</code> or a <code>targetingDrugs</code> object (obtained after running <code>rankSimilarPerturbations</code> or <code>predictTargetingDrugs</code> , respectively)
col	Character: name of the column to use for statistics (only required if class of stats is either <code>similarPerturbations</code> or <code>targetingDrugs</code> )
nperm	Number of permutations to do. Minimal possible nominal p-value is about $1/nperm$
maxSize	Maximal size of a gene set to test. All pathways above the threshold are excluded.
...	Arguments passed on to <code>fgsea::fgseaSimple</code>
minSize	Minimal size of a gene set to test. All pathways below the threshold are excluded.
scoreType	This parameter defines the GSEA score type. Possible options are ("std", "pos", "neg")
nproc	If not equal to zero sets BPPARAM to use nproc workers (default = 0).
gseaParam	GSEA parameter value, all gene-level statis are raised to the power of 'gseaParam' before calculation of GSEA enrichment scores.

	BPPARAM Parallelization parameter used in bplapply. Can be used to specify cluster to run. If not initialized explicitly or by setting 'nproc' default value 'bpparam()' is used.
keyColSets	Character: column from sets to compare with column keyColStats from stats; automatically selected if NULL
keyColStats	Character: column from stats to compare with column keyColSets from sets; automatically selected if NULL

**Value**

Enrichment analysis based on GSEA

**See Also**

Other functions for drug set enrichment analysis: [loadDrugDescriptors\(\)](#), [plotDrugSetEnrichment\(\)](#), [prepareDrugSets\(\)](#)

**Examples**

```
descriptors <- loadDrugDescriptors()
drugSets <- prepareDrugSets(descriptors)

# Analyse drug set enrichment in ranked targeting drugs for a differential
# expression profile
data("diffExprStat")
gdsc <- loadExpressionDrugSensitivityAssociation("GDSC")
predicted <- predictTargetingDrugs(diffExprStat, gdsc)

analyseDrugSetEnrichment(drugSets, predicted)
```

---

as.table.referenceComparison  
*Cross Tabulation and Table Creation*

---

**Description**

Cross Tabulation and Table Creation

**Usage**

```
## S3 method for class 'referenceComparison'
as.table(x, ..., clean = TRUE)
```

**Arguments**

x	referenceComparison object
...	Extra parameters not currently used
clean	Boolean: only show certain columns (to avoid redundancy)?

**Value**

Complete table with metadata based on a targetingDrugs object

**See Also**

Other functions related with the ranking of CMap perturbations: [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSsimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

Other functions related with the prediction of targeting drugs: [listExpressionDrugSensitivityAssociation\(\)](#), [loadExpressionDrugSensitivityAssociation\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSsimilarPer](#), [predictTargetingDrugs\(\)](#)

---

convertENSEMBLtoGeneSymbols

*Convert ENSEMBL gene identifiers to gene symbols*

---

**Description**

Convert ENSEMBL gene identifiers to gene symbols

**Usage**

```
convertENSEMBLtoGeneSymbols(  
  genes,  
  dataset = "hsapiens_gene_ensembl",  
  mart = "ensembl"  
)
```

**Arguments**

genes	Character: ENSEMBL gene identifiers
dataset	Character: biomaRt dataset name
mart	Character: biomaRt database name

**Value**

Named character vector where names are the input ENSEMBL gene identifiers and the values are the matching gene symbols

---

 convertGeneIdentifiers

*Convert gene identifiers*


---

## Description

Convert gene identifiers

## Usage

```
convertGeneIdentifiers(
  genes,
  annotation = "Homo sapiens",
  key = "ENSEMBL",
  target = "SYMBOL",
  ignoreDuplicatedTargets = TRUE
)
```

## Arguments

genes	Character: genes to be converted
annotation	OrgDb with genome wide annotation for an organism or character with species name to query OrgDb, e.g. "Homo sapiens"
key	Character: type of identifier used, e.g. ENSEMBL; read ?AnnotationDbi::columns
target	Character: type of identifier to convert to; read ?AnnotationDbi::columns
ignoreDuplicatedTargets	Boolean: if TRUE, identifiers that share targets with other identifiers will not be converted

## Value

Character vector of the respective targets of gene identifiers. The previous identifiers remain other identifiers have the same target (in case ignoreDuplicatedTargets = TRUE) or if no target was found.

## Examples

```
genes <- c("ENSG0000012048", "ENSG00000083093", "ENSG00000141510",
           "ENSG00000051180")
convertGeneIdentifiers(genes)
convertGeneIdentifiers(genes, key="ENSEMBL", target="UNIPROT")

# Explicit species name to automatically look for its OrgDb database
sp <- "Homo sapiens"
genes <- c("ENSG0000012048", "ENSG00000083093", "ENSG00000141510",
           "ENSG00000051180")
convertGeneIdentifiers(genes, sp)
```

```
# Alternatively, set the annotation database directly
ah <- AnnotationHub::AnnotationHub()
sp <- AnnotationHub::query(ah, c("OrgDb", "Homo sapiens"))[[1]]
columns(sp) # these attributes can be used to change the attributes

convertGeneIdentifiers(genes, sp)
```

---

cTRAP

*cTRAP package*


---

## Description

Compare differential gene expression results with those from big datasets (e.g. CMap), allowing to infer which types of perturbations may explain the observed difference in gene expression.

Optimised to run in ShinyProxy with Celery/Flower backend with argument `shinyproxy = TRUE`.

## Usage

```
cTRAP(
  ...,
  commonPath = "data",
  expire = 14,
  fileSizeLimitMiB = 50,
  flowerURL = NULL,
  port = getOption("shiny.port"),
  host = getOption("shiny.host", "127.0.0.1")
)
```

## Arguments

...	Objects
commonPath	Character: path where to store data common to all sessions
expire	Character: days until a session expires (message purposes only)
fileSizeLimitMiB	Numeric: file size limit in MiB
flowerURL	Character: Flower REST API's URL (NULL to avoid using Celery/Flower backend)
port	The TCP port that the application should listen on. If the <code>port</code> is not specified, and the <code>shiny.port</code> option is set (with <code>options(shiny.port = XX)</code> ), then that port will be used. Otherwise, use a random port between 3000:8000, excluding ports that are blocked by Google Chrome for being considered unsafe: 3659, 4045, 5060, 5061, 6000, 6566, 6665:6669 and 6697. Up to twenty random ports will be tried.
host	The IPv4 address that the application should listen on. Defaults to the <code>shiny.host</code> option, if set, or "127.0.0.1" if not. See Details.

## Details

**Input:** To use this package, a named vector of differentially expressed gene metric is needed, where its values represent the significance and magnitude of the differentially expressed genes (e.g. t-statistic) and its names are gene symbols.

**Workflow:** The differentially expressed genes will be compared against selected perturbation conditions by:

- Spearman or Pearson correlation with z-scores of differentially expressed genes after perturbations from CMap. Use function `rankSimilarPerturbations` with `method = "spearman"` or `method = "pearson"`
- Gene set enrichment analysis (GSEA) using the (around) 12 000 genes from CMap. Use function `rankSimilarPerturbations` with `method = gsea`.

Available perturbation conditions for CMap include:

- Cell line(s).
- Perturbation type (gene knockdown, gene upregulation or drug intake).
- Drug concentration.
- Time points.

Values for each perturbation type can be listed with `getCMapPerturbationTypes()`

**Output:** The output includes a data frame of ranked perturbations based on the associated statistical values and respective p-values.

## Value

Launches result viewer and plotter (returns NULL)

## See Also

Other visual interface functions: `launchCMapDataLoader()`, `launchDiffExprLoader()`, `launchDrugSetEnrichmentAnalysis()`, `launchMetadataViewer()`, `launchResultPlotter()`

---

dimnames.expressionDrugSensitivityAssociation

*Operations on expressionDrugSensitivityAssociation objects*

---

## Description

Operations on expressionDrugSensitivityAssociation objects



**Usage**

```
## S3 method for class 'expressionDrugSensitivityAssociation'
dimnames(x)

## S3 method for class 'expressionDrugSensitivityAssociation'
dim(x)

## S3 method for class 'expressionDrugSensitivityAssociation'
x[i, j, drop = FALSE, ...]
```

**Arguments**

x	An expressionDrugSensitivityAssociation object
i, j	Character or numeric indexes specifying elements to extract
drop	Boolean: coerce result to the lowest possible dimension?
...	Extra arguments given to other methods

**Value**

Subset, dimension or dimension names

---

downloadENCODeknockdownMetadata

*Download metadata for ENCODE knockdown experiments*

---

**Description**

Download metadata for ENCODE knockdown experiments

**Usage**

```
downloadENCODeknockdownMetadata(
  cellLine = NULL,
  gene = NULL,
  file = "ENCODEmetadata.rds"
)
```

**Arguments**

cellLine	Character: cell line
gene	Character: target gene
file	Character: RDS filepath with metadata (if file doesn't exist, it will be created)

**Value**

Data frame containing ENCODE knockdown experiment metadata

**See Also**

Other functions related with using ENCODE expression data: [loadENCODEsamples\(\)](#), [performDifferentialExpression\(\)](#), [prepareENCODEgeneExpression\(\)](#)

**Examples**

```
downloadENCODEknockdownMetadata("HepG2", "EIF4G1")
```

---

filterCMapMetadata      *Filter CMap metadata*

---

**Description**

Filter CMap metadata

**Usage**

```
filterCMapMetadata(
  metadata,
  cellline = NULL,
  timepoint = NULL,
  dosage = NULL,
  perturbationType = NULL
)
```

**Arguments**

metadata	Data frame (CMap metadata) or character (respective filepath)
cellline	Character: cell line (if NULL, all values are loaded)
timepoint	Character: timepoint (if NULL, all values are loaded)
dosage	Character: dosage (if NULL, all values are loaded)
perturbationType	Character: type of perturbation (if NULL, all perturbation types are loaded)

**Value**

Filtered CMap metadata

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

**Examples**

```
cmapMetadata <- loadCMapData("cmapMetadata.txt", "metadata")
filterCMapMetadata(cmapMetadata, cellLine="HEPG2", timepoint="2 h",
                  dosage="25 ng/mL")
```

---

getCMapConditions      *List available conditions in CMap datasets*

---

**Description**

Downloads metadata if not available

**Usage**

```
getCMapConditions(
  metadata,
  cellLine = NULL,
  timepoint = NULL,
  dosage = NULL,
  perturbationType = NULL,
  control = FALSE
)
```

**Arguments**

metadata	Data frame (CMap metadata) or character (respective filepath)
cellLine	Character: cell line (if NULL, all values are loaded)
timepoint	Character: timepoint (if NULL, all values are loaded)
dosage	Character: dosage (if NULL, all values are loaded)
perturbationType	Character: type of perturbation (if NULL, all perturbation types are loaded)
control	Boolean: show controls for perturbation types?

**Value**

List of conditions in CMap datasets

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

## Examples

```
## Not run:  
cmapMetadata <- loadCMapData("cmapMetadata.txt", "metadata")  
  
## End(Not run)  
getCMapConditions(cmapMetadata)
```

---

```
getCMapPerturbationTypes  
Get CMap perturbation types
```

---

## Description

Get CMap perturbation types

## Usage

```
getCMapPerturbationTypes(control = FALSE)
```

## Arguments

control            Boolean: return perturbation types used as control?

## Value

Perturbation types and respective codes as used by CMap datasets

## See Also

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSsimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

## Examples

```
getCMapPerturbationTypes()
```

---

launchCMapDataLoader *Load CMap data via a visual interface*

---

## Description

Load CMap data via a visual interface

## Usage

```
launchCMapDataLoader(  
  metadata = "cmapMetadata.txt",  
  zscores = "cmapZscores.gctx",  
  geneInfo = "cmapGeneInfo.txt",  
  compoundInfo = "cmapCompoundInfo.txt",  
  cellLine = NULL,  
  timepoint = NULL,  
  dosage = NULL,  
  perturbationType = NULL  
)
```

## Arguments

metadata	Data frame (CMap metadata) or character (respective filepath)
zscores	Data frame (GCTX z-scores) or character (respective filepath to load data from file)
geneInfo	Data frame (CMap gene info) or character (respective filepath to load data from file)
compoundInfo	Data frame (CMap compound info) or character (respective filepath to load data from file)
cellLine	Character: cell line (if NULL, all values are loaded)
timepoint	Character: timepoint (if NULL, all values are loaded)
dosage	Character: dosage (if NULL, all values are loaded)
perturbationType	Character: type of perturbation (if NULL, all perturbation types are loaded)

## Value

CMap data

## See Also

Other visual interface functions: [cTRAP\(\)](#), [launchDiffExprLoader\(\)](#), [launchDrugSetEnrichmentAnalyser\(\)](#), [launchMetadataViewer\(\)](#), [launchResultPlotter\(\)](#)

---

launchDiffExprLoader *Load differential expression data via a visual interface*

---

### Description

Currently only supports loading data from ENCODE knockdown experiments

### Usage

```
launchDiffExprLoader(  
  cellLine = NULL,  
  gene = NULL,  
  file = "ENCODEmetadata.rds",  
  path = "."  
)
```

### Arguments

cellLine	Character: cell line
gene	Character: target gene
file	Character: RDS filepath with metadata (if file doesn't exist, it will be created)
path	Character: path where to download files

### Value

Differential expression data

### See Also

Other visual interface functions: [cTRAP\(\)](#), [launchCMapDataLoader\(\)](#), [launchDrugSetEnrichmentAnalyser\(\)](#), [launchMetadataViewer\(\)](#), [launchResultPlotter\(\)](#)

---

launchDrugSetEnrichmentAnalyser  
*View and plot results via a visual interface*

---

### Description

View and plot results via a visual interface

### Usage

```
launchDrugSetEnrichmentAnalyser(sets, ...)
```

**Arguments**

sets	Named list of characters: named sets containing compound identifiers (obtain drug sets by running prepareDrugSets())
...	Objects

**Value**

Launches result viewer and plotter (returns NULL)

**See Also**

Other visual interface functions: [cTRAP\(\)](#), [launchCMapDataLoader\(\)](#), [launchDiffExprLoader\(\)](#), [launchMetadataViewer\(\)](#), [launchResultPlotter\(\)](#)

---

launchMetadataViewer *View metadata via a visual interface*

---

**Description**

View metadata via a visual interface

**Usage**

```
launchMetadataViewer(...)
```

**Arguments**

...	Objects
-----	---------

**Value**

Metadata viewer (returns NULL)

**See Also**

Other visual interface functions: [cTRAP\(\)](#), [launchCMapDataLoader\(\)](#), [launchDiffExprLoader\(\)](#), [launchDrugSetEnrichmentAnalyser\(\)](#), [launchResultPlotter\(\)](#)

launchResultPlotter    *View and plot results via a visual interface*

---

**Description**

View and plot results via a visual interface

**Usage**

```
launchResultPlotter(...)
```

**Arguments**

...                    Objects

**Value**

Launches result viewer and plotter (returns NULL)

**See Also**

Other visual interface functions: [cTRAP\(\)](#), [launchCMapDataLoader\(\)](#), [launchDiffExprLoader\(\)](#), [launchDrugSetEnrichmentAnalyser\(\)](#), [launchMetadataViewer\(\)](#)

---

listExpressionDrugSensitivityAssociation

*List available gene expression and drug sensitivity correlation matrices*

---

**Description**

List available gene expression and drug sensitivity correlation matrices

**Usage**

```
listExpressionDrugSensitivityAssociation(url = FALSE)
```

**Arguments**

url                    Boolean: return download link?

**Value**

Character vector of available gene expression and drug sensitivity correlation matrices



### See Also

Other functions related with the prediction of targeting drugs: [as.table.referenceComparison\(\)](#), [loadExpressionDrugSensitivityAssociation\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPer](#), [predictTargetingDrugs\(\)](#)

### Examples

```
listExpressionDrugSensitivityAssociation()
```

---

loadCMapData	<i>Load CMap data</i>
--------------	-----------------------

---

### Description

Load CMap data (if not found, file will be automatically downloaded)

### Usage

```
loadCMapData(  
  file,  
  type = c("metadata", "geneInfo", "zscores", "compoundInfo"),  
  zscoresID = NULL  
)
```

### Arguments

file	Character: path to file
type	Character: type of data to load (metadata, geneInfo, zscores or compoundInfo)
zscoresID	Character: identifiers to partially load z-scores file (for performance reasons; if NULL, all identifiers will be loaded)

### Value

Metadata as a data table

### Note

If type = "compoundInfo", two files from **The Drug Repurposing Hub** will be downloaded containing information about drugs and perturbations. The files will be named file with `_drugs` and `_samples` before their extension, respectively.

### See Also

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapZScores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPertu](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

**Examples**

```
# Load CMap metadata (data is automatically downloaded if not available)
cmapMetadata <- loadCMapData("cmapMetadata.txt", "metadata")

# Load CMap gene info
loadCMapData("cmapGeneInfo.txt", "geneInfo")
## Not run:
# Load CMap zscores based on filtered metadata
cmapMetadataKnockdown <- filterCMapMetadata(
  cmapMetadata, cellLine="HepG2",
  perturbationType="Consensus signature from shRNAs targeting the same gene")
loadCMapData("cmapZscores.gctx.gz", "zscores", cmapMetadataKnockdown$sig_id)

## End(Not run)
```

---

loadCMapZscores	<i>Load matrix of CMap perturbation's differential expression z-scores (optional)</i>
-----------------	---

---

**Description**

Load matrix of CMap perturbation's differential expression z-scores (optional)

**Usage**

```
loadCMapZscores(data, inheritAttrs = FALSE, verbose = TRUE)
```

**Arguments**

data	perturbationChanges object
inheritAttrs	Boolean: convert to perturbationChanges object and inherit attributes from data?
verbose	Boolean: print additional details?

**Value**

Matrix containing CMap perturbation z-scores (genes as rows, perturbations as columns)

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

## Examples

```
metadata <- loadCMapData("cmapMetadata.txt", "metadata")
metadata <- filterCMapMetadata(metadata, cellLine="HepG2")
## Not run:
perts <- prepareCMapPerturbations(metadata, "cmapZscores.gctx",
                                   "cmapGeneInfo.txt")
zscores <- loadCMapZscores(perts[, 1:10])

## End(Not run)
```

---

loadDrugDescriptors    *Load table with drug descriptors*

---

## Description

Load table with drug descriptors

## Usage

```
loadDrugDescriptors(
  source = c("NCI60", "CMap"),
  type = c("2D", "3D"),
  file = NULL,
  path = NULL
)
```

## Arguments

source	Character: source of compounds used to calculate molecular descriptors (NCI60 or CMap)
type	Character: load 2D or 3D molecular descriptors
file	Character: filepath to drug descriptors (automatically downloaded if file does not exist)
path	Character: folder where to find files (optional; file may contain the full filepath if preferred)

## Value

Data table with drug descriptors

## See Also

Other functions for drug set enrichment analysis: [analyseDrugSetEnrichment\(\)](#), [plotDrugSetEnrichment\(\)](#), [prepareDrugSets\(\)](#)

## Examples

```
loadDrugDescriptors()
```

loadENCODEsamples      *Load ENCODE samples*

---

**Description**

Samples are automatically downloaded if they are not found in the current working directory.

**Usage**

```
loadENCODEsamples(metadata, path = ".")
```

**Arguments**

metadata	Character: ENCODE metadata
path	Character: path where to download files

**Value**

List of loaded ENCODE samples

**See Also**

Other functions related with using ENCODE expression data: [downloadENCODEknockdownMetadata\(\)](#), [performDifferentialExpression\(\)](#), [prepareENCODEgeneExpression\(\)](#)

**Examples**

```
if (interactive()) {  
  # Load ENCODE metadata for a specific cell line and gene  
  cellLine <- "HepG2"  
  gene <- c("EIF4G1", "U2AF2")  
  ENCODEmetadata <- downloadENCODEknockdownMetadata(cellLine, gene)  
  
  # Load samples based on filtered ENCODE metadata  
  loadENCODEsamples(ENCODEmetadata)  
}
```

---

loadExpressionDrugSensitivityAssociation  
*Load gene expression and drug sensitivity correlation matrix*

---

**Description**

Load gene expression and drug sensitivity correlation matrix

**Usage**

```
loadExpressionDrugSensitivityAssociation(  
  source,  
  file = NULL,  
  path = NULL,  
  rows = NULL,  
  cols = NULL,  
  loadValues = FALSE  
)
```

**Arguments**

source	Character: source of matrix to load; see <a href="#">listExpressionDrugSensitivityAssociation</a>
file	Character: filepath to gene expression and drug sensitivity association dataset (automatically downloaded if file does not exist)
path	Character: folder where to find files (optional; file may contain the full filepath if preferred)
rows	Character or integer: rows
cols	Character or integer: columns
loadValues	Boolean: load data values (if available)? If FALSE, downstream functions will load and process directly from the file chunk by chunk, resulting in a lower memory footprint

**Value**

Correlation matrix between gene expression (rows) and drug sensitivity (columns)

**See Also**

Other functions related with the prediction of targeting drugs: [as.table.referenceComparison\(\)](#), [listExpressionDrugSensitivityAssociation\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPe](#), [predictTargetingDrugs\(\)](#)

**Examples**

```
gdsc <- listExpressionDrugSensitivityAssociation()[[1]]  
loadExpressionDrugSensitivityAssociation(gdsc)
```

---

parseCMapID

*Parse CMap identifier*

---

**Description**

Parse CMap identifier

**Usage**

```
parseCMapID(id, cellLine = FALSE)
```

**Arguments**

id	Character: CMap identifier
cellLine	Boolean: if TRUE, return cell line information from CMap identifier; else, return the CMap identifier without the cell line

**Value**

Character vector with information from CMap identifiers

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plot.TargetingDrugsVSsimilarP](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

**Examples**

```
id <- c("CVD001_HEPG2_24H:BRD-K94818765-001-01-0:4.8",
        "CVD001_HEPG2_24H:BRD-K96188950-001-04-5:4.3967",
        "CVD001_HUH7_24H:BRD-A14014306-001-01-1:4.1")
parseCMapID(id, cellLine=TRUE)
parseCMapID(id, cellLine=FALSE)
```

---

```
performDifferentialExpression
```

*Perform differential gene expression based on ENCODE data*

---

**Description**

Perform differential gene expression based on ENCODE data

**Usage**

```
performDifferentialExpression(counts)
```

**Arguments**

counts	Data frame: gene expression
--------	-----------------------------

**Value**

Data frame with differential gene expression results between knockdown and control

**See Also**

Other functions related with using ENCODE expression data: [downloadENCODEknockdownMetadata\(\)](#), [loadENCODEsamples\(\)](#), [prepareENCODEgeneExpression\(\)](#)

**Examples**

```
if (interactive()) {
  # Download ENCODE metadata for a specific cell line and gene
  cellLine <- "HepG2"
  gene <- "EIF4G1"
  ENCODEmetadata <- downloadENCODEknockdownMetadata(cellLine, gene)

  # Download samples based on filtered ENCODE metadata
  ENCODEsamples <- loadENCODEsamples(ENCODEmetadata)[[1]]

  counts <- prepareENCODEgeneExpression(ENCODEsamples)

  # Remove low coverage (at least 10 counts shared across two samples)
  minReads <- 10
  minSamples <- 2
  filter <- rowSums(counts[ , -c(1, 2)] >= minReads) >= minSamples
  counts <- counts[filter, ]

  # Convert ENSEMBL identifier to gene symbol
  counts$gene_id <- convertGeneIdentifiers(counts$gene_id)

  # Perform differential gene expression analysis
  diffExpr <- performDifferentialExpression(counts)
}
```

---

plot.perturbationChanges

*Operations on a perturbationChanges object*

---

**Description**

Operations on a perturbationChanges object

**Usage**

```
## S3 method for class 'perturbationChanges'
plot(
  x,
  perturbation,
  input,
  method = c("spearman", "pearson", "gsea"),
  geneSize = 150,
  genes = c("both", "top", "bottom"),
```

```

    ...,
    title = NULL
)

## S3 method for class 'perturbationChanges'
x[i, j, drop = FALSE, ...]

## S3 method for class 'perturbationChanges'
dim(x)

## S3 method for class 'perturbationChanges'
dimnames(x)

```

### Arguments

x	perturbationChanges object
perturbation	Character (perturbation identifier) or a similarPerturbations table (from which the respective perturbation identifiers are retrieved)
input	Named numeric vector of differentially expressed genes whose names are gene identifiers and respective values are a statistic that represents significance and magnitude of differentially expressed genes (e.g. t-statistics); or character of gene symbols composing a gene set that is tested for enrichment in reference data (only used if method includes gsea)
method	Character: comparison method (spearman, pearson or gsea; multiple methods may be selected at once)
geneSize	Numeric: number of top up-/down-regulated genes to use as gene sets to test for enrichment in reference data; if a 2-length numeric vector, the first index is the number of top up-regulated genes and the second index is the number of down-regulated genes used to create gene sets; only used if method includes gsea and if input is not a gene set
genes	Character: when plotting gene set enrichment analysis (GSEA), plot most up-regulated genes (genes = "top"), most down-regulated genes (genes = "bottom") or both (genes = "both"); only used if method = "gsea" and geneset = NULL
...	Extra arguments
title	Character: plot title (if NULL, the default title depends on the context; ignored when plotting multiple perturbations)
i, j	Character or numeric indexes specifying elements to extract
drop	Boolean: coerce result to the lowest possible dimension?

### Value

Subset, plot or return dimensions or names of a perturbationChanges object

### See Also

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#),



```
loadCMapZscores(), parseCMapID(), plot.referenceComparison(), plotTargetingDrugsVSSimilarPerturbations(),
prepareCMapPerturbations(), print.similarPerturbations(), rankSimilarPerturbations()
```

## Examples

```
data("diffExprStat")
data("cmapPerturbationsKD")

compareKD <- rankSimilarPerturbations(diffExprStat, cmapPerturbationsKD)
EIF4G1knockdown <- grep("EIF4G1", compareKD[[1]], value=TRUE)
plot(cmapPerturbationsKD, EIF4G1knockdown, diffExprStat, method="spearman")
plot(cmapPerturbationsKD, EIF4G1knockdown, diffExprStat, method="pearson")
plot(cmapPerturbationsKD, EIF4G1knockdown, diffExprStat, method="gsea")

data("cmapPerturbationsCompounds")
pert <- "CVD001_HEPG2_24H:BRD-A14014306-001-01-1:4.1"
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="spearman")
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="pearson")
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="gsea")

# Multiple cell line perturbations
pert <- "CVD001_24H:BRD-A14014306-001-01-1:4.1"
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="spearman")
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="pearson")
plot(cmapPerturbationsCompounds, pert, diffExprStat, method="gsea")
```

---

```
plot.referenceComparison
```

*Plot data comparison*

---

## Description

If element = NULL, comparison is plotted based on all elements. Otherwise, show scatter or GSEA plots for a single element compared with previously given differential expression results.

## Usage

```
## S3 method for class 'referenceComparison'
plot(
  x,
  element = NULL,
  method = c("spearman", "pearson", "gsea", "rankProduct"),
  n = c(3, 3),
  showMetadata = TRUE,
  plotNonRankedPerturbations = FALSE,
  alpha = 0.3,
  genes = c("both", "top", "bottom"),
  ...,
  zscores = NULL,
```

```

    title = NULL
  )

```

### Arguments

x	referenceComparison object: obtained after running <a href="#">rankSimilarPerturbations()</a> or <a href="#">predictTargetingDrugs()</a>
element	Character: identifier in the first column of x
method	Character: method to plot results; choose between spearman, pearson, gsea or rankProduct (the last one is only available if element = NULL)
n	Numeric: number of top and bottom genes to label (if a vector of two numbers is given, the first and second numbers will be used as the number of top and bottom genes to label, respectively); only used if element = NULL
showMetadata	Boolean: show available metadata information instead of identifiers (if available)? Only used if element = NULL
plotNonRankedPerturbations	Boolean: plot non-ranked data in grey? Only used if element = NULL
alpha	Numeric: transparency; only used if element = NULL
genes	Character: when plotting gene set enrichment analysis (GSEA), plot most up-regulated genes (genes = "top"), most down-regulated genes (genes = "bottom") or both (genes = "both"); only used if method = "gsea" and geneset = NULL
...	Extra arguments currently not used
zscores	Data frame (GCTX z-scores) or character (respective filepath to load data from file)
title	Character: plot title (if NULL, the default title depends on the context; ignored when plotting multiple perturbations)

### Value

Plot illustrating the reference comparison

### See Also

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

Other functions related with the prediction of targeting drugs: [as.table.referenceComparison\(\)](#), [listExpressionDrugSensitivityAssociation\(\)](#), [loadExpressionDrugSensitivityAssociation\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#), [predictTargetingDrugs\(\)](#)

### Examples

```

# Example of a differential expression profile
data("diffExprStat")

```

```
## Not run:
# Download and load CMap perturbations to compare with
cellLine <- "HepG2"
cmapMetadataKD <- filterCMapMetadata(
  "cmapMetadata.txt", cellLine=cellLine,
  perturbationType="Consensus signature from shRNAs targeting the same gene")

cmapPerturbationsKD <- prepareCMapPerturbations(
  cmapMetadataKD, "cmapZscores.gctx", "cmapGeneInfo.txt", loadZscores=TRUE)

## End(Not run)

# Rank similar CMap perturbations
compareKD <- rankSimilarPerturbations(diffExprStat, cmapPerturbationsKD)

# Plot ranked list of CMap perturbations
plot(compareKD, method="spearman")
plot(compareKD, method="spearman", n=c(7, 3))
plot(compareKD, method="pearson")
plot(compareKD, method="gsea")

# Plot results for a single perturbation
pert <- compareKD[[1, 1]]
plot(compareKD, pert, method="spearman", zscores=cmapPerturbationsKD)
plot(compareKD, pert, method="pearson", zscores=cmapPerturbationsKD)
plot(compareKD, pert, method="gsea", zscores=cmapPerturbationsKD)

# Predict targeting drugs based on a given differential expression profile
gdsc <- loadExpressionDrugSensitivityAssociation("GDSC 7")
predicted <- predictTargetingDrugs(diffExprStat, gdsc)

# Plot ranked list of targeting drugs
plot(predicted, method="spearman")
plot(predicted, method="spearman", n=c(7, 3))
plot(predicted, method="pearson")
plot(predicted, method="gsea")

# Plot results for a single targeting drug
drug <- predicted$compound[[4]]
plot(predicted, drug, method="spearman")
plot(predicted, drug, method="pearson")
plot(predicted, drug, method="gsea")
```

---

plotDrugSetEnrichment *Plot drug set enrichment*

---

## Description

Plot drug set enrichment

**Usage**

```
plotDrugSetEnrichment(  
  sets,  
  stats,  
  col = "rankProduct_rank",  
  selectedSets = NULL,  
  keyColSets = NULL,  
  keyColStats = NULL  
)
```

**Arguments**

sets	Named list of characters: named sets containing compound identifiers (obtain drug sets by running <code>prepareDrugSets()</code> )
stats	Named numeric vector or either a <code>similarPerturbations</code> or a <code>targetingDrugs</code> object (obtained after running <code>rankSimilarPerturbations</code> or <code>predictTargetingDrugs</code> , respectively)
col	Character: name of the column to use for statistics (only required if class of stats is either <code>similarPerturbations</code> or <code>targetingDrugs</code> )
selectedSets	Character: drug sets to plot (if NULL, plot all)
keyColSets	Character: column from sets to compare with column <code>keyColStats</code> from stats; automatically selected if NULL
keyColStats	Character: column from stats to compare with column <code>keyColSets</code> from sets; automatically selected if NULL

**Value**

List of GSEA plots per drug set

**See Also**

Other functions for drug set enrichment analysis: `analyseDrugSetEnrichment()`, `loadDrugDescriptors()`, `prepareDrugSets()`

**Examples**

```
descriptors <- loadDrugDescriptors()  
drugSets <- prepareDrugSets(descriptors)  
  
# Analyse drug set enrichment in ranked targeting drugs for a differential  
# expression profile  
data("diffExprStat")  
gdsc <- loadExpressionDrugSensitivityAssociation("GDSC")  
predicted <- predictTargetingDrugs(diffExprStat, gdsc)  
  
plotDrugSetEnrichment(drugSets, predicted)
```

---

`plotTargetingDrugsVSSimilarPerturbations`*Plot similar perturbations against predicted targeting drugs*

---

## Description

Plot similar perturbations against predicted targeting drugs

## Usage

```
plotTargetingDrugsVSSimilarPerturbations(  
  targetingDrugs,  
  similarPerturbations,  
  column,  
  labelBy = "pert_iname",  
  quantileThreshold = 0.25,  
  showAllScores = FALSE,  
  keyColTargetingDrugs = NULL,  
  keyColSimilarPerturbations = NULL  
)
```

## Arguments

<code>targetingDrugs</code>	targetingDrugs object
<code>similarPerturbations</code>	similarPerturbations object
<code>column</code>	Character: column to plot (must be available in both databases)
<code>labelBy</code>	Character: column in <code>as.table(similarPerturbations)</code> or <code>as.table(targetingDrugs)</code> to be used for labelling
<code>quantileThreshold</code>	Numeric: quantile (between 0 and 1) to highlight values of interest
<code>showAllScores</code>	Boolean: show all scores? If FALSE, only the best score per compound will be plotted
<code>keyColTargetingDrugs</code>	Character: column from <code>targetingDrugs</code> to compare with column <code>keyColSimilarPerturbations</code> from <code>similarPerturbations</code> ; automatically selected if NULL
<code>keyColSimilarPerturbations</code>	Character: column from <code>similarPerturbations</code> to compare with column <code>keyColTargetingDrugs</code> from <code>targetingDrugs</code> ; automatically selected if NULL

## Value

ggplot2 plot

### See Also

Other functions related with the ranking of CMap perturbations: `as.table.referenceComparison()`, `filterCMapMetadata()`, `getCMapConditions()`, `getCMapPerturbationTypes()`, `loadCMapData()`, `loadCMapZscores()`, `parseCMapID()`, `plot.perturbationChanges()`, `plot.referenceComparison()`, `prepareCMapPerturbations()`, `print.similarPerturbations()`, `rankSimilarPerturbations()`

Other functions related with the prediction of targeting drugs: `as.table.referenceComparison()`, `listExpressionDrugSensitivityAssociation()`, `loadExpressionDrugSensitivityAssociation()`, `plot.referenceComparison()`, `predictTargetingDrugs()`

### Examples

```
# Rank similarity against CMap compound perturbations
similarPerts <- rankSimilarPerturbations(diffExprStat,
                                       cmapPerturbationsCompounds)

# Predict targeting drugs
gdsc <- loadExpressionDrugSensitivityAssociation("GDSC 7")
predicted <- predictTargetingDrugs(diffExprStat, gdsc)

plotTargetingDrugsVSimilarPerturbations(predicted, similarPerts,
                                       "spearman_rank")
```

---

predictTargetingDrugs *Predict targeting drugs*

---

### Description

Identify compounds that may target the phenotype associated with a user-provided differential expression profile by comparing such against a correlation matrix of gene expression and drug sensitivity.

### Usage

```
predictTargetingDrugs(
  input,
  expressionDrugSensitivityCor,
  method = c("spearman", "pearson", "gsea"),
  geneSize = 150,
  isDrugActivityDirectlyProportionalToSensitivity = NULL,
  threads = 1,
  chunkGiB = 1,
  verbose = FALSE
)
```

**Arguments**

input	Named numeric vector of differentially expressed genes whose names are gene identifiers and respective values are a statistic that represents significance and magnitude of differentially expressed genes (e.g. t-statistics); or character of gene symbols composing a gene set that is tested for enrichment in reference data (only used if method includes gsea)
expressionDrugSensitivityCor	Matrix or character: correlation matrix of gene expression (rows) and drug sensitivity (columns) across cell lines or path to file containing such data; see <a href="#">loadExpressionDrugSensitivityAssociation()</a> .
method	Character: comparison method (spearman, pearson or gsea; multiple methods may be selected at once)
geneSize	Numeric: number of top up-/down-regulated genes to use as gene sets to test for enrichment in reference data; if a 2-length numeric vector, the first index is the number of top up-regulated genes and the second index is the number of down-regulated genes used to create gene sets; only used if method includes gsea and if input is not a gene set
isDrugActivityDirectlyProportionalToSensitivity	Boolean: are the values used for drug activity directly proportional to drug sensitivity? If NULL, the argument expressionDrugSensitivityCor must have a non-NULL value for attribute isDrugActivityDirectlyProportionalToSensitivity.
threads	Integer: number of parallel threads
chunkGiB	Numeric: if second argument is a path to an HDF5 file (.h5 extension), that file is loaded and processed in chunks of a given size in gibibytes (GiB); lower values decrease peak RAM usage (see details below)
verbose	Boolean: print additional details?

**Value**

Data table with correlation and/or GSEA score results

**Process data by chunks**

If a file path to a valid HDF5 (.h5) file is provided instead of a data matrix, that file can be loaded and processed in chunks of size chunkGiB, resulting in decreased peak memory usage.

The default value of 1 GiB (1 GiB = 1024<sup>3</sup> bytes) allows loading chunks of ~10000 columns and 14000 rows (10000 \* 14000 \* 8 bytes / 1024<sup>3</sup> = 1.04 GiB).

**GSEA score**

When method = "gsea", weighted connectivity scores (WTCS) are calculated ([https://clue.io/connectopedia/cmap\\_algorithms](https://clue.io/connectopedia/cmap_algorithms)).

**See Also**

Other functions related with the prediction of targeting drugs: [as.table.referenceComparison\(\)](#), [listExpressionDrugSensitivityAssociation\(\)](#), [loadExpressionDrugSensitivityAssociation\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSSimilarPerturbations\(\)](#)

**Examples**

```
# Example of a differential expression profile
data("diffExprStat")

# Load expression and drug sensitivity association derived from GDSC data
gdsc <- loadExpressionDrugSensitivityAssociation("GDSC 7")

# Predict targeting drugs on a differential expression profile
predictTargetingDrugs(diffExprStat, gdsc)
```

---

```
prepareCMapPerturbations
```

*Prepare CMap perturbation data*

---

**Description**

Prepare CMap perturbation data

**Usage**

```
prepareCMapPerturbations(
  metadata,
  zscores,
  geneInfo,
  compoundInfo = NULL,
  ...,
  loadZscores = FALSE
)
```

**Arguments**

metadata	Data frame (CMap metadata) or character (respective filepath to load data from file)
zscores	Data frame (GCTX z-scores) or character (respective filepath to load data from file)
geneInfo	Data frame (CMap gene info) or character (respective filepath to load data from file)
compoundInfo	Data frame (CMap compound info) or character (respective filepath to load data from file)
...	Arguments passed on to <a href="#">filterCMapMetadata</a>
cellLine	Character: cell line (if NULL, all values are loaded)
timepoint	Character: timepoint (if NULL, all values are loaded)
dosage	Character: dosage (if NULL, all values are loaded)
perturbationType	Character: type of perturbation (if NULL, all perturbation types are loaded)



`loadZscores` Boolean: load matrix of perturbation z-scores? Not recommended in systems with less than 30GB of RAM; if FALSE, downstream functions will load and process the file directly chunk by chunk, resulting in a lower memory footprint

### Value

CMap perturbation data attributes and filename

### See Also

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSsimilarPerturbations\(\)](#), [print.similarPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

### Examples

```
metadata <- loadCMapData("cmapMetadata.txt", "metadata")
metadata <- filterCMapMetadata(metadata, cellLine="HepG2")
## Not run:
prepareCMapPerturbations(metadata, "cmapZscores.gctx", "cmapGeneInfo.txt")

## End(Not run)
```

---

`prepareDrugSets`

*Prepare drug sets from a table with compound descriptors*

---

### Description

Create a list of drug sets for each character and numeric column. For each character column, drugs are split across that column's unique values (see argument `maxUniqueElems`). For each numeric column, drugs are split across evenly-distributed bins.

### Usage

```
prepareDrugSets(
  table,
  id = 1,
  maxUniqueElems = 15,
  maxBins = 15,
  k = 5,
  minPoints = NULL
)
```

**Arguments**

table	Data frame: drug descriptors
id	Integer or character: index or name of the identifier column
maxUniqueElems	Numeric: ignore character columns with more unique elements than maxUniqueElems
maxBins	Numeric: maximum number of bins for numeric columns
k	Numeric: constant; the higher the constant, the smaller the bin size (check minpts)
minPoints	Numeric: minimum number of points in a bin (if NULL, the minimum number of points is the number of non-missing values divided by maxBins divided by k)

**Value**

Named list of characters: named drug sets with respective compound identifiers as list elements

**See Also**

Other functions for drug set enrichment analysis: [analyseDrugSetEnrichment\(\)](#), [loadDrugDescriptors\(\)](#), [plotDrugSetEnrichment\(\)](#)

**Examples**

```
descriptors <- loadDrugDescriptors("NCI60")
prepareDrugSets(descriptors)
```

---

```
prepareENCODEgeneExpression
```

*Load ENCODE gene expression data*

---

**Description**

Load ENCODE gene expression data

**Usage**

```
prepareENCODEgeneExpression(samples)
```

**Arguments**

samples	List of loaded ENCODE samples
---------	-------------------------------

**Value**

Data frame containing gene read counts

**See Also**

[convertGeneIdentifiers\(\)](#)

Other functions related with using ENCODE expression data: [downloadENCODEknockdownMetadata\(\)](#), [loadENCODEsamples\(\)](#), [performDifferentialExpression\(\)](#)

**Examples**

```
if (interactive()) {
  # Load ENCODE metadata for a specific cell line and gene
  cellLine <- "HepG2"
  gene <- "EIF4G1"
  ENCODEmetadata <- downloadENCODEknockdownMetadata(cellLine, gene)

  # Load samples based on filtered ENCODE metadata
  ENCODEsamples <- loadENCODEsamples(ENCODEmetadata)[[1]]

  prepareENCODEgeneExpression(ENCODEsamples)
}
```

---

```
print.similarPerturbations
```

*Print a similarPerturbations object*

---

**Description**

Print a similarPerturbations object

**Usage**

```
## S3 method for class 'similarPerturbations'
print(x, perturbation = NULL, ...)
```

**Arguments**

x	similarPerturbations object
perturbation	Character (perturbation identifier) or numeric (perturbation index)
...	Extra parameters passed to print

**Value**

Information on perturbationChanges object or on specific perturbations

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plotTargetingDrugsVSsimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [rankSimilarPerturbations\(\)](#)

---

rankSimilarPerturbations

*Rank differential expression profile against CMap perturbations by similarity*

---

## Description

Compare differential expression results against CMap perturbations.

## Usage

```
rankSimilarPerturbations(
  input,
  perturbations,
  method = c("spearman", "pearson", "gsea"),
  geneSize = 150,
  cellLineMean = "auto",
  rankPerCellLine = FALSE,
  threads = 1,
  chunkGiB = 1,
  verbose = FALSE
)
```

## Arguments

input	Named numeric vector of differentially expressed genes whose names are gene identifiers and respective values are a statistic that represents significance and magnitude of differentially expressed genes (e.g. t-statistics); or character of gene symbols composing a gene set that is tested for enrichment in reference data (only used if method includes gsea)
perturbations	perturbationChanges object: CMap perturbations (check <a href="#">prepareCMapPerturbations()</a> )
method	Character: comparison method (spearman, pearson or gsea; multiple methods may be selected at once)
geneSize	Numeric: number of top up-/down-regulated genes to use as gene sets to test for enrichment in reference data; if a 2-length numeric vector, the first index is the number of top up-regulated genes and the second index is the number of down-regulated genes used to create gene sets; only used if method includes gsea and if input is not a gene set
cellLineMean	Boolean: add rows with the mean of method across cell lines? If cellLineMean = "auto" (default), rows will be added when data for more than one cell line is available.
rankPerCellLine	Boolean: rank results based on both individual cell lines and mean scores across cell lines (TRUE) or based on mean scores alone (FALSE)? If cellLineMean = FALSE, individual cell line conditions are always ranked.

threads	Integer: number of parallel threads
chunkGiB	Numeric: if second argument is a path to an HDF5 file (.h5 extension), that file is loaded and processed in chunks of a given size in gibibytes (GiB); lower values decrease peak RAM usage (see details below)
verbose	Boolean: print additional details?

**Value**

Data table with correlation and/or GSEA score results

**Process data by chunks**

If a file path to a valid HDF5 (.h5) file is provided instead of a data matrix, that file can be loaded and processed in chunks of size chunkGiB, resulting in decreased peak memory usage.

The default value of 1 GiB (1 GiB =  $1024^3$  bytes) allows loading chunks of ~10000 columns and 14000 rows ( $10000 * 14000 * 8 \text{ bytes} / 1024^3 = 1.04 \text{ GiB}$ ).

**GSEA score**

When method = "gsea", weighted connectivity scores (WTCS) are calculated ([https://clue.io/connectopedia/cmap\\_algorithms](https://clue.io/connectopedia/cmap_algorithms)).

**See Also**

Other functions related with the ranking of CMap perturbations: [as.table.referenceComparison\(\)](#), [filterCMapMetadata\(\)](#), [getCMapConditions\(\)](#), [getCMapPerturbationTypes\(\)](#), [loadCMapData\(\)](#), [loadCMapZscores\(\)](#), [parseCMapID\(\)](#), [plot.perturbationChanges\(\)](#), [plot.referenceComparison\(\)](#), [plot.TargetingDrugsVSsimilarPerturbations\(\)](#), [prepareCMapPerturbations\(\)](#), [print.similarPerturbations\(\)](#)

**Examples**

```
# Example of a differential expression profile
data("diffExprStat")

## Not run:
# Download and load CMap perturbations to compare with
cellLine <- c("HepG2", "HUH7")
cmapMetadataCompounds <- filterCMapMetadata(
  "cmapMetadata.txt", cellLine=cellLine, timepoint="24 h",
  dosage="5 \u00B5M", perturbationType="Compound")

cmapPerturbationsCompounds <- prepareCMapPerturbations(
  cmapMetadataCompounds, "cmapZscores.gctx", "cmapGeneInfo.txt",
  "cmapCompoundInfo_drugs.txt", loadZscores=TRUE)

## End(Not run)
perturbations <- cmapPerturbationsCompounds

# Rank similar CMap perturbations (by default, Spearman's and Pearson's
# correlation are used, as well as GSEA with the top and bottom 150 genes of
```

```
# the differential expression profile used as reference)
rankSimilarPerturbations(diffExprStat, perturbations)

# Rank similar CMap perturbations using only Spearman's correlation
rankSimilarPerturbations(diffExprStat, perturbations, method="spearman")
```

# Index

- \* **functions for drug set enrichment analysis**
  - analyseDrugSetEnrichment, 3
  - loadDrugDescriptors, 19
  - plotDrugSetEnrichment, 27
  - prepareDrugSets, 33
- \* **functions for gene expression**
  - pre-processing**
    - convertGeneIdentifiers, 6
  - \* **functions related with the prediction of targeting drugs**
    - as.table.referenceComparison, 4
    - listExpressionDrugSensitivityAssociation, 16
    - loadExpressionDrugSensitivityAssociation, 20
    - plot.referenceComparison, 25
    - plotTargetingDrugsVSSimilarPerturbations, 29
    - predictTargetingDrugs, 30
  - \* **functions related with the ranking of CMap perturbations**
    - as.table.referenceComparison, 4
    - filterCMapMetadata, 10
    - getCMapConditions, 11
    - getCMapPerturbationTypes, 12
    - loadCMapData, 17
    - loadCMapZscores, 18
    - parseCMapID, 21
    - plot.perturbationChanges, 23
    - plot.referenceComparison, 25
    - plotTargetingDrugsVSSimilarPerturbations, 29
    - prepareCMapPerturbations, 32
    - print.similarPerturbations, 35
    - rankSimilarPerturbations, 36
  - \* **functions related with using ENCODE expression data**
    - downloadENCODEknockdownMetadata, 9
    - loadENCODEsamples, 20
    - performDifferentialExpression, 22
    - prepareENCODEgeneExpression, 34
- \* **visual interface functions**
  - cTRAP, 7
  - launchCMapDataLoader, 13
  - launchDiffExprLoader, 14
  - launchDrugSetEnrichmentAnalyser, 14
  - launchMetadataViewer, 15
  - launchResultPlotter, 16
  - [.expressionDrugSensitivityAssociation (dimnames.expressionDrugSensitivityAssociation), 8
  - [.perturbationChanges (plot.perturbationChanges), 23
  - analyseDrugSetEnrichment, 3, 19, 28, 34
  - as.table.referenceComparison, 4, 10–12, 17, 18, 21, 22, 24, 26, 30, 31, 33, 35, 37
  - compareAgainstCMap (rankSimilarPerturbations), 36
  - convertENSEMBLtoGeneSymbols, 5
  - convertGeneIdentifiers, 6, 35
  - cTRAP, 7, 13–16
  - dim.expressionDrugSensitivityAssociation (dimnames.expressionDrugSensitivityAssociation), 8
  - dim.perturbationChanges (plot.perturbationChanges), 23
  - dimnames.expressionDrugSensitivityAssociation, 8
  - dimnames.perturbationChanges (plot.perturbationChanges), 23
  - downloadENCODEknockdownMetadata, 9, 20, 23, 35
  - fgsea::fgseaSimple, 3

`filterCMapMetadata`, 5, 10, 11, 12, 17, 18, 22, 24, 26, 30, 32, 33, 35, 37

`getCMapConditions`, 5, 10, 11, 12, 17, 18, 22, 24, 26, 30, 33, 35, 37

`getCMapPerturbationTypes`, 5, 10, 11, 12, 17, 18, 22, 24, 26, 30, 33, 35, 37

`launchCMapDataLoader`, 8, 13, 14–16

`launchDiffExprLoader`, 8, 13, 14, 15, 16

`launchDrugSetEnrichmentAnalyser`, 8, 13, 14, 14, 15, 16

`launchMetadataViewer`, 8, 13–15, 15, 16

`launchResultPlotter`, 8, 13–15, 16

`listExpressionDrugSensitivityAssociation`, 5, 16, 21, 26, 30, 31

`loadCMapData`, 5, 10–12, 17, 18, 22, 24, 26, 30, 33, 35, 37

`loadCMapZscores`, 5, 10–12, 17, 18, 22, 25, 26, 30, 33, 35, 37

`loadDrugDescriptors`, 4, 19, 28, 34

`loadENCODEsamples`, 10, 20, 23, 35

`loadExpressionDrugSensitivityAssociation`, 5, 17, 20, 26, 30, 31

`parseCMapID`, 5, 10–12, 17, 18, 21, 25, 26, 30, 33, 35, 37

`performDifferentialExpression`, 10, 20, 22, 35

`plot.perturbationChanges`, 5, 10–12, 17, 18, 22, 23, 26, 30, 33, 35, 37

`plot.referenceComparison`, 5, 10–12, 17, 18, 21, 22, 25, 25, 30, 31, 33, 35, 37

`plotDrugSetEnrichment`, 4, 19, 27, 34

`plotTargetingDrugsVSSimilarPerturbations`, 5, 10–12, 17, 18, 21, 22, 25, 26, 29, 31, 33, 35, 37

`predictTargetingDrugs`, 3, 5, 17, 21, 26, 28, 30, 30

`prepareCMapPerturbations`, 5, 10–12, 17, 18, 22, 25, 26, 30, 32, 35–37

`prepareDrugSets`, 4, 19, 28, 33

`prepareENCODEgeneExpression`, 10, 20, 23, 34

`print.similarPerturbations`, 5, 10–12, 17, 18, 22, 25, 26, 30, 33, 35, 37

`rankSimilarPerturbations`, 3, 5, 8, 10–12, 17, 18, 22, 25, 26, 28, 30, 33, 35, 36