

# Package ‘anamiR’

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**Type** Package

**Title** An integrated analysis package of miRNA and mRNA expression data

**Version** 1.6.1

**Description** This package is intended to identify potential interactions of miRNA-target gene interactions from miRNA and mRNA expression data. It contains functions for statistical test, databases of miRNA-target gene interaction and functional analysis.

**biocViews** Software, AssayDomain, GeneExpression, BiologicalQuestion, GeneSetEnrichment, GeneTarget, Normalization, Pathways, DifferentialExpression, GeneRegulation, ResearchField, Genetics, Technology, Microarray, Sequencing, miRNA, WorkflowStep

**License** GPL-2

**URL** <https://github.com/AllenTiTaiWang/anamiR>

**BugReports** <https://github.com/AllenTiTaiWang/anamiR/issues>

**LazyData** TRUE

**Imports** stats, DBI, limma, lumi, agricolae, RMySQL, DESeq2, SummarizedExperiment, gplots, gage, S4Vectors

**Depends** R (>= 3.3.3), SummarizedExperiment(>= 1.1.6)

**RoxygenNote** 6.0.1

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**Suggests** knitr, rmarkdown, data.table

**VignetteBuilder** knitr

**NeedsCompilation** no

## R topics documented:

anamiR	2
database_support	3
differExp_continuous	4
differExp_discrete	5
egSymb	7

enrichment . . . . .	7
GSEA_ana . . . . .	9
GSEA_res . . . . .	10
heat_vis . . . . .	11
mirna . . . . .	13
miR_converter . . . . .	14
mrna . . . . .	15
msigdb.gs . . . . .	16
multi_Differ . . . . .	17
negative_cor . . . . .	18
normalization . . . . .	19
pheno.mirna . . . . .	20
pheno.mrna . . . . .	21
table_pre . . . . .	21

<b>Index</b>	<b>22</b>
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anamiR	<i>anamiR: An integrated analysis package of miRNA and mRNA expression data.</i>
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## Description

The anamiR package is used to identify miRNA-target genes interactions. The anamiR package provides a whole workflow, which contains important functions: ‘normalization’, ‘differExp\_discrete’, ‘negative\_cor’, ‘miR\_converter’, ‘database\_support’, ‘enrichment’.

### normalization

The normalization function is used to normalize the expression data with one of three methods, including normal, quantile, rank.invariant.

### differExp\_discrete

The differExp\_discrete function is used to find the differential genes or miRNAs from given expression data with one of three statistical methods, including t.test, wilcox.test, limma and DESeq. The miRNA would remain if its p-value lower than the cutoff value.

### miR\_converter

The miR\_annotation function is used to convert the older miRNA annotation to the miRBase 21 version.

### negative\_cor

The negative\_cor function is used to identify the possible miRNA-target gene interactions from given miRNA and mRNA expression data by calculating the correlation coefficient between each miRNA and gene. interaction would remain if its correlation coefficient is negative and lower than cutoff value.

**database\_support**

The database\_support function would search information about miRNA-target gene interactions from an integrated database, which contains 8 algorithm predicted databases and 2 experiment validated databases. Eventually return a big table, which is in data.frame format and contains extra 10 columns for those 10 databases to count if interactions were predicted or validated by these databases.

**enrichment**

The enrichment function is used to do the functional analysis from the output of 'database\_support'. Not only p-value from hypergeometric test but empirical p-value from 10000 times of permutation would be provided by this function.

---

database_support	<i>Intersect with databases for potential miRNA-target gene interactions</i>
------------------	--

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**Description**

This function will intersect potential miRNA-target gene interactions from the input matrix, which is generated by [negative\\_cor](#) or [miR\\_converter](#), with 8 predict databases and 2 validate databases about miRNA-target gene interactions. If the input contains hundreds of interactions, it would take a few minutes to intersect all of them.

**Usage**

```
database_support(cor_data, org = "hsa", Sum.cutoff = 2)
```

**Arguments**

cor_data	matrix format generated from <a href="#">negative_cor</a> or <a href="#">miR_converter</a> , including miRNA, gene, correlation coefficient for column names.
org	species of genes and miRNAs, only support "hsa", "mmu"
Sum.cutoff	a Threshold for total hits by predict databases. This one should not be greater than 8. Default is 2.

**Value**

data.frame format. Each row represent one potential interaction. The first four columns are information about interactions: miRNA, gene symbol, Ensembl ID, gene ID, as for column 5 to 12 represent the predict dataases, while column 13 to 14 are validate databases. if databases truly hit this interactions, the number in it would be 1. The column 'Sum' means total hits by 8 databases, and column 'Validate' would be TRUE if at least one validate database hit the interaction. Furthermore, 'Fold-Change' and 'P-adjust' can also be found in this output, and if the 'de novo' column contains 1 means that row is not supported by any databases. The column 'evidence' represents if the experiment for validation is strong or limited, considering <http://mirtarbase.mbc.nctu.edu.tw/>.

**Examples**

```

## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())
data("mrna", package = "anamiR", envir = environment())
data("pheno.mrna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## SummarizedExperiment class
require(SummarizedExperiment)
mrna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mrna),
  colData = pheno.mrna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)

## Finding differential mRNA from mRNA expression data with t.test
mrna_d <- differExp_discrete(
  se = mrna_se,
  class = "ER",
  method = "t.test"
)

## Convert annotation to miRBse 21
mirna_21 <- miR_converter(data = mirna_d, original_version = 17)

## Correlation
cor <- negative_cor(mrna_data = mrna_d, mirna_data = mirna_21)

## Intersect with known databases
sup <- database_support(cor_data = cor)

```

---

differExp\_continuous *Find differential expression genes or miRNAs from given expression data*

---

**Description**

This function will apply linear regression model to find differential expression genes or miRNAs with continuous phenotype data, and then filter the genes or miRNAs (rows) which have bigger p-value than cutoff.

**Usage**

```
differExp_continuous(se, class, log2 = FALSE, p_value.cutoff = 0.05)
```

**Arguments**

`se` [SummarizedExperiment](#) for input format.

`class` string. Choose one features from all rows of phenotype data.

`log2` logical, if this data hasn't been log2 transformed yet, this one should be TRUE. Default is FALSE.

`p_value.cutoff` an numeric value indicating a threshold of p-value for every genes or miRNAs (rows). Default is 0.05.

**Value**

data expression data in matrix format, with sample name in columns and gene symbol or miRNA name in rows.

**See Also**

[lm](#) for fitting linear models.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## Finding differential miRNA from miRNA expression data with lm
differExp_continuous(
  se = mirna_se, class = "Survival"
)
```

---

differExp_discrete	<i>Find differential expression genes or miRNAs from given expression data</i>
--------------------	--

---

**Description**

This function will apply one of three statistical methods, including `t.test`, `wilcox.test` and `limma`, to find differential expression genes or miRNAs with, discrete phenotype data, and then filter the genes or miRNAs (rows) which have bigger p-value than cutoff.

**Usage**

```
differExp_discrete(se, class, method = c("t.test", "limma", "wilcox.test",
  "DESeq"), limma.trend = FALSE, t_test.var = FALSE, log2 = FALSE,
  p_value.cutoff = 0.05, p_adjust.method = "BH", logratio = 0.5)
```

**Arguments**

<code>se</code>	<code>SummarizedExperiment</code> for input format.
<code>class</code>	string. Choose one features from all rows of phenotype data.
<code>method</code>	statistical method for finding differential genes or miRNAs, including "t.test", "wilcox.test", "limma". Default is "t.test".
<code>limma.trend</code>	logical, only matter when limma is chosen to be the method. From function <code>eBayes</code> .
<code>t_test.var</code>	logical, only matter when limma is chosen to be the method. Whether to treat the two variances as being equal. From function <code>t.test</code>
<code>log2</code>	logical, if this data hasn't been log2 transformed yet, this one should be TRUE Default is FALSE.
<code>p_value.cutoff</code>	an numeric value indicating a threshold of p-value for every genes or miRNAs (rows). Default is 0.05.
<code>p_adjust.method</code>	Correction method for multiple testing. (If you are using DESeq for method, this param would not affect the result) From function <code>p.adjust</code> . Default is "BH".
<code>logratio</code>	an numeric value indicating a threshold of logratio for every genes or miRNAs (rows). Default is 0.5.

**Value**

data expression data in matrix format, with sample name in columns and gene symbol or miRNA name in rows.

**See Also**

`t.test` for Student's t-Test; `wilcox.test` for Wilcoxon Rank Sum and Signed Rank Tests.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)
```

---

 egSymb

*A table with information of gene symbol and gene ID*


---

**Description**

This table is originally from [gage](#), including 40784 genes.

**Usage**

```
egSymb
```

**Format**

A large matrix with 40784 rows and 2 columns:

**eg** gene ID, in column

**sym** gene symbol, in column

**Value**

matrix

**Source**

[gage](https://bioconductor.org/packages/release/bioc/html/gage.html) <https://bioconductor.org/packages/release/bioc/html/gage.html>

---

 enrichment

*Enrich pathways with genes from putative miRNA-target gene interactions.*


---

**Description**

This function will do function analysis with genes from potential miRNA-target gene interactions in the input data.frame, which is generated by [database\\_support](#), with total 4 kinds of pathway databases, including mouse and human two species, besides, this function will permute 5000 times (Default) for each pathway to show an empirical p\_value to avoid the bias from hypergeometric p-value, this indicating that it would take a few minutes to do functional analysis.

**Usage**

```
enrichment(data_support, org = c("hsa", "mmu"), per_time = 5000)
```

**Arguments**

**data\_support** matrix format generated from [database\\_support](#).

**org** species of genes and miRNAs, only support "hsa", "mmu"

**per\_time** Times of permutation about each enriched pathways, higher times, more precise empirical p-value user can obtain, meanwhile, this function would cost more time. Default is 5000.

**Value**

matrix format. There are 7 columns in it, including database, term, total genes of the term, targets in the term, targets in total genes of the term ( p-value.

**See Also**

[phyper](#) for details.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())
data("mrna", package = "anamiR", envir = environment())
data("pheno.mrna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## SummarizedExperiment class
require(SummarizedExperiment)
mrna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mrna),
  colData = pheno.mrna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)

## Finding differential mRNA from mRNA expression data with t.test
mrna_d <- differExp_discrete(
  se = mrna_se,
  class = "ER",
  method = "t.test"
)

## Convert annotation to miRBse 21
mirna_21 <- miR_converter(data = mirna_d, original_version = 17)

## Correlation
cor <- negative_cor(mrna_data = mrna_d, mirna_data = mirna_21)

## Intersect with known databases
sup <- database_support(cor_data = cor)

## Functional analysis
pat <- enrichment(data_support = sup, org = "hsa", per_time = 100)
```



---

GSEA\_ana

*This function will do function driven analysis.*

---

## Description

This function will do GSEA analysis through the function [gage](#). After obtaining the ranking of pathways, this function will choose the top five (default) pathways, and then find the related miRNAs based on their gene set.

## Usage

```
GSEA_ana(mrna_se, mirna_se, class, compare = "unpaired", eg2sym = TRUE,
         pathway_num = 5)
```

## Arguments

mrna_se	<a href="#">SummarizedExperiment</a> for input format and it contains mRNA information.
mirna_se	<a href="#">SummarizedExperiment</a> for input format, and it contains miRNA information.
class	string. Choose one features from all rows of phenotype data.
compare	character, if the length of case is the same as control, use "paired".Default is "unpaired".
eg2sym	logical. conversion between Entrez Gene IDs and official gene symbols for human genes.
pathway_num	The number of chosen pathways from the result of GSEA analysis.

## Value

list format containing both selected gene and miRNA expression data for each chosen pathway.

## See Also

[gage](#) for GSEA analysis.

## Examples

```
require(data.table)

## Load example data
aa <- system.file("extdata", "GSE19536_mrna.csv", package = "anamiR")
mrna <- fread(aa, fill = TRUE, header = TRUE)

bb <- system.file("extdata", "GSE19536_mirna.csv", package = "anamiR")
mirna <- fread(bb, fill = TRUE, header = TRUE)

cc <- system.file("extdata", "pheno_data.csv", package = "anamiR")
pheno.data <- fread(cc, fill = TRUE, header = TRUE)

## adjust data format
mirna_name <- mirna[["miRNA"]]
mrna_name <- mrna[["Gene"]]
```

```

mirna <- mirna[, -1]
mrna <- mrna[, -1]
mirna <- data.matrix(mirna)
mrna <- data.matrix(mrna)
row.names(mirna) <- mirna_name
row.names(mrna) <- mrna_name
pheno_name <- pheno.data[["Sample"]]
pheno.data <- pheno.data[, -1]
pheno.data <- as.matrix(pheno.data)
row.names(pheno.data) <- pheno_name

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.data)

mrna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mrna),
  colData = pheno.data)

#table <- GSEA_ana(mrna_se = mrna_se,
#mirna_se = mirna_se, class = "ER",
#pathway_num = 2)

```

---

GSEA\_res

*Pipeline of anamiR is applied to given output from [GSEA\\_ana](#).*


---

## Description

This function will use [differExp\\_discrete](#) and [negative\\_cor](#) to do the deeper analysis of given data which is from [GSEA\\_ana](#).

## Usage

```

GSEA_res(table, pheno.data, class, DE_method = c("t.test", "limma",
  "wilcox.test", "DESeq"), limma.trend = FALSE, t_test.var = FALSE,
  log2 = FALSE, p_adjust.method = "BH", cor_cut = -0.3)

```

## Arguments

table	list format containing both selected gene and miRNA expression data for each chosen pathway. output of <a href="#">GSEA_ana</a>
pheno.data	phenotype data.
class	string. Choose one features from all rows of phenotype data.
DE_method	statistical method for finding differential genes or miRNAs, including "t.test", "wilcox.test", "limma". Default is "t.test".
limma.trend	logical, only matter when limma is chosen to be the method. From function <a href="#">eBayes</a> .
t_test.var	logical, only matter when limma is chosen to be the method. Whether to treat the two variances as being equal. From function <a href="#">t.test</a>

log2	logical, if this data hasn't been log2 transformed yet, this one should be TRUE. Default is FALSE.
p_adjust.method	Correction method for multiple testing. (If you are using DESeq for method, this param would not affect the result) From function <a href="#">p.adjust</a> . Default is "BH".
cor_cut	an numeric value indicating a threshold of correlation coefficient for every potential miRNA-genes interactions. Default is -0.3, however, if no interaction pass the threshold, this function would add 0.2 value in threshold until at least one interaction passed the threshold.

### Value

list format containing matrix for each chosen pathway. The format of matrix is like the output from [negative\\_cor](#).

### See Also

[differExp\\_discrete](#) and [negative\\_cor](#).

### Examples

```
## Load example data

require(data.table)

cc <- system.file("extdata", "pheno_data.csv", package = "anamiR")
pheno.data <- fread(cc, fill = TRUE, header = TRUE)

## adjust data format
pheno_name <- pheno.data[["Sample"]]
pheno.data <- pheno.data[, -1]
pheno.data <- as.matrix(pheno.data)
row.names(pheno.data) <- pheno_name
data(table_pre)

result <- GSEA_res(table = table_pre, pheno.data = pheno.data,
  class = "ER", DE_method = "limma", cor_cut = 0)
```

---

heat\_vis

*Using correlation information to draw a heatmaps*

---

### Description

This function would base on Fold-Change information from the output of [negative\\_cor](#), [differExp\\_discrete](#) and show heatmaps to users. Note that if miRNA-gene interactions (row) from input are larger than 100, the lable in plot would be unclear.

### Usage

```
heat_vis(cor_data, mrna_d, mirna_21)
```

**Arguments**

cor_data	matrix format generated from <a href="#">negative_cor</a> .
mrna_d	differential expressed data in data.frame format, with sample name in columns and gene symbol in rows, which is generated by <a href="#">differExp_discrete</a> or <a href="#">differExp_continuous</a> .
mirna_21	differential expressed data in data.frame format, with sample name in columns and miRNA in rows, which is generated by <a href="#">differExp_discrete</a> or <a href="#">differExp_continuous</a> , miRNA should be miRBase 21 version now.

**Value**

heatmap plots of miRNA and gene.

**See Also**

[heatmap.2](#) for plot.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())
data("mrna", package = "anamiR", envir = environment())
data("pheno.mrna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## SummarizedExperiment class
require(SummarizedExperiment)
mrna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mrna),
  colData = pheno.mrna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)

## Finding differential mRNA from mRNA expression data with t.test
mrna_d <- differExp_discrete(
  se = mrna_se,
  class = "ER",
  method = "t.test"
)

## Convert annotation to miRBse 21
mirna_21 <- miR_converter(data = mirna_d, original_version = 17)

## Correlation
```

```
cor <- negative_cor(mrna_data = mrna_d, mirna_data = mirna_21)

## Draw heatmap
heat_vis(cor, mrna_d, mirna_21)
```

---

mirna

*miRNA expression data about breast cancer*

---

### Description

This miRNA expression dataset is originally from GSE19536. To make dataset smaller, we have selected 30 samples in columns and 489 miRNAs in rows.

### Usage

```
mirna
```

### Format

A data frame with 489 obs (miRNAs) and 30 variables:

**BC.M.014** sample name, in column  
**BC.M.015** sample name, in column  
**BC.M.017** sample name, in column  
**BC.M.019** sample name, in column  
**BC.M.023** sample name, in column  
**BC.M.031** sample name, in column  
**BC.M.053** sample name, in column  
**BC.M.083** sample name, in column  
**BC.M.088** sample name, in column  
**BC.M.112** sample name, in column  
**BC.M.119** sample name, in column  
**BC.M.144** sample name, in column  
**BC.M.148** sample name, in column  
**BC.M.150** sample name, in column  
**BC.M.209** sample name, in column  
**BC.M.220** sample name, in column  
**BC.M.221** sample name, in column  
**BC.M.300** sample name, in column  
**BC.M.308** sample name, in column  
**BC.M.309** sample name, in column  
**BC.M.318** sample name, in column  
**BC.M.357** sample name, in column  
**BC.M.381** sample name, in column

**BC.M.388** sample name, in column  
**BC.M.406** sample name, in column  
**BC.M.451** sample name, in column  
**BC.M.457** sample name, in column  
**BC.M.493** sample name, in column  
**BC.M.512** sample name, in column  
**BC.M.709** sample name, in column

**Value**

data.frame

**Source**

NCBI GEO: <http://www.ncbi.nlm.nih.gov/geo/>

---

miR_converter	<i>Convert miRNA annotation to the miRBase 21 version</i>
---------------	---

---

**Description**

This function will convert the miRNA names from the data frame, which is produced by [differ-Exp\\_discrete](#), to the miRBase 21 version of miRNA annotation. If the input contains hundreds of miRNAs, it would take a few minutes to convert all of them.

**Usage**

```
miR_converter(data, remove_old = TRUE, original_version,
              latest_version = 21)
```

**Arguments**

data	expression data in data.frame format, with sample name in columns and miRNA name in rows.
remove_old	logical value, if the miRNA is deleted in miRBase 21, should it be removed from row? Default is TRUE.
original_version	the original version of miRNA in input matrix. This one is necessary.
latest_version	choose an interger under 21, and this function would convert miRNA annotation to that version. Default is 21.

**Value**

expression data in data.frame format, with sample name in columns and miRNA name for miRBase version 21 in rows.

## Examples

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)

## Convert annotation to miRBse 21
mirna_21 <- miR_converter(data = mirna_d, original_version = 17)
```

---

mrna

*mRNA expression data about breast cancer*

---

## Description

This mRNA expression dataset is originally from GSE19536. To make dataset smaller, we have selected 30 samples in columns and 19210 genes in rows.

## Usage

```
mrna
```

## Format

A data frame with 15000 rows (genes) and 30 variables:

**BC.M.014** sample name, in column  
**BC.M.015** sample name, in column  
**BC.M.017** sample name, in column  
**BC.M.019** sample name, in column  
**BC.M.023** sample name, in column  
**BC.M.031** sample name, in column  
**BC.M.053** sample name, in column  
**BC.M.083** sample name, in column  
**BC.M.088** sample name, in column  
**BC.M.112** sample name, in column  
**BC.M.119** sample name, in column

**BC.M.144** sample name, in column  
**BC.M.148** sample name, in column  
**BC.M.150** sample name, in column  
**BC.M.209** sample name, in column  
**BC.M.220** sample name, in column  
**BC.M.221** sample name, in column  
**BC.M.300** sample name, in column  
**BC.M.308** sample name, in column  
**BC.M.309** sample name, in column  
**BC.M.318** sample name, in column  
**BC.M.357** sample name, in column  
**BC.M.381** sample name, in column  
**BC.M.388** sample name, in column  
**BC.M.406** sample name, in column  
**BC.M.451** sample name, in column  
**BC.M.457** sample name, in column  
**BC.M.493** sample name, in column  
**BC.M.512** sample name, in column  
**BC.M.709** sample name, in column

**Value**

data.frame

**Source**

NCBI GEO: <http://www.ncbi.nlm.nih.gov/geo/>

---

msigdb.gs

*MsigDB C2 pathways with gene set information*

---

**Description**

This table is originally from [gage](#), including 4731 pathways.

**Usage**

msigdb.gs

**Format**

A list with 4731 C2 pathways from MsigDB.

**Value**

list

**Source**

GSEA MsigDB <http://software.broadinstitute.org/gsea/msigdb>



---

multi_Differ	<i>Find differential expression groups of each genes or miRNA from expression data</i>
--------------	--

---

## Description

This function will apply anova ,a statistical methods, for each gene or miRNA (row) to find not only whether expression data of multiple groups differential expressed or not, but also tell specifically two groups from all are differential expression.

## Usage

```
multi_Differ(se, class, anova_p_value = 0.05, post_hoc = c("scheffe.test",
  "duncan.test", "HSD.test"), post_hoc_p_value = 0.05)
```

## Arguments

se	<a href="#">SummarizedExperiment</a> for input format.
class	string. Choose one features from all rows of phenotype data.
anova_p_value	an numeric value indicating a threshold of p-value from anova for every genes or miRNAs (rows). Default is 0.05.
post_hoc	post hoc test for anova, including "scheffe.test", "HSD.test", "duncan.test".
post_hoc_p_value	an numeric value indicating a threshold of p-value from post hoc test for every genes or miRNAs (rows). Default is 0.05.

## Value

data.frame format with extra columns containing information about differential expressed groups among all.

## See Also

[aov](#) for fit an analysis of variance model.

## Examples

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mirna),
  colData = pheno.mirna)

## Finding differential miRNA from miRNA expression data with anova
aov <- multi_Differ(se = mirna_se, class = "Subtype",
  post_hoc = "scheffe.test")
```

negative\_cor

*Find the correlation coefficient between each gene and miRNA.***Description**

This function will calculate the correlation coefficient between each gene and miRNA from differential expressed data, which are produced by [differExp\\_discrete](#) or [differExp\\_continuous](#). After filtering the positive and higher than cutoff value of correlation, this function would return a matrix with seven columns, including miRNA, gene, correlation coefficients and Fold change, P-adjust value for miRNA and gene. Each row represents one potential miRNA-target gene interaction.

**Usage**

```
negative_cor(mrna_data, mirna_data, method = c("pearson", "kendall",
  "spearman"), cut.off = -0.5)
```

**Arguments**

mrna_data	differential expressed data in matrix format, with sample name in columns and gene symbol in rows, which is generated by <a href="#">differExp_discrete</a> or <a href="#">differExp_continuous</a> .
mirna_data	differential expressed data in matrix format, with sample name in columns and miRNA in rows, which is generated by <a href="#">differExp_discrete</a> or <a href="#">differExp_continuous</a> , miRNA should be miRBase 21 version now.
method	methods for calculating correlation coefficient, including "pearson", "spearman", "kendall". Default is "pearson". From function <a href="#">cor</a>
cut.off	an numeric value indicating a threshold of correlation coefficient for every potential miRNA-genes interactions. Default is -0.5, however, if no interaction pass the threshold, this function would add 0.2 value in threshold until at least one interaction passed the threshold.

**Value**

matrix format with each row indicating one potential miRNA-target gene interaction and seven columns are miRNA, gene, correlation coefficient and Fold change, P-adjust value for miRNA and gene.

**See Also**

[cor](#) for calculation of correlation.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())
data("pheno.mirna", package = "anamiR", envir = environment())
data("mrna", package = "anamiR", envir = environment())
data("pheno.mrna", package = "anamiR", envir = environment())

## SummarizedExperiment class
require(SummarizedExperiment)
mirna_se <- SummarizedExperiment(
```

```

assays = SimpleList(counts=mirna),
colData = pheno.mirna)

## SummarizedExperiment class
require(SummarizedExperiment)
mrna_se <- SummarizedExperiment(
  assays = SimpleList(counts=mrna),
  colData = pheno.mrna)

## Finding differential miRNA from miRNA expression data with t.test
mirna_d <- differExp_discrete(
  se = mirna_se,
  class = "ER",
  method = "t.test"
)

## Finding differential mRNA from mRNA expression data with t.test
mrna_d <- differExp_discrete(
  se = mrna_se,
  class = "ER",
  method = "t.test"
)

## Correlation
cor <- negative_cor(mrna_data = mrna_d, mirna_data = mirna_d,
  method = "pearson"
)

```

---

normalization

*Normalize expression data*


---

## Description

This function will normalize the given expression data and return it in the same data format.

## Usage

```
normalization(data, method = c("quantile", "normal", "rank.invariant"))
```

## Arguments

data	expression data in matrix format, with sample name in columns and gene symbol or miRNA name in rows.
method	normalization methods, including "quantile", "normal", "rank.invariant". Default is "quantile". As for method "normal", we trim the extreme value and calculate the mean in the data.

## Value

[SummarizedExperiment](#) for return object.

**See Also**

[normalizeQuantiles](#) for quantile normalization; [rankinvariant](#) for rank invariant normalization.

**Examples**

```
## Use the internal dataset
data("mirna", package = "anamiR", envir = environment())

## Normalize miRNA expression data
normalization(data = mirna, method = "quantile")
```

---

pheno.mirna

*phenotype data of [mirna](#) about breast cancer*

---

**Description**

This phenotype dataset is originally from GSE19536. It contains 3 features in row and 30 samples in column.

**Usage**

```
pheno.mirna
```

**Format**

A data frame with 30 obs and 3 variables:

**ER** estrogen receptor status

**Subtype** breast cancer subtype

**Survival** disease free survival time (months)

**Value**

```
data.frame
```

**Source**

NCBI GEO: <http://www.ncbi.nlm.nih.gov/geo/>

---

pheno.mrna	<i>phenotype data of <a href="#">mrna</a> about breast cancer</i>
------------	---

---

**Description**

This phenotype dataset is originally from GSE19536. It contains 3 features in row and 30 samples in column.

**Usage**

```
pheno.mrna
```

**Format**

A data frame with 30 obs and 3 variables:

**ER** estrogen receptor status

**Subtype** breast cancer subtype

**Survival** disease free survival time (months)

**Value**

```
data.frame
```

**Source**

NCBI GEO: <http://www.ncbi.nlm.nih.gov/geo/>

---

table_pre	<i>A list with information of genes and miRNAs.</i>
-----------	---

---

**Description**

This table is generated from [miR\\_converter](#), including 4 files.

**Usage**

```
table_pre
```

**Format**

A large list with 2 gene expression files and 2 miRNAs files

**Value**

```
list
```

**Source**

NCBI GEO: <http://www.ncbi.nlm.nih.gov/geo/>

# Index

## \*Topic **datasets**

- egSymb, [7](#)
- mirna, [13](#)
- mrna, [15](#)
- msigdb.gs, [16](#)
- pheno.mirna, [20](#)
- pheno.mrna, [21](#)
- table\_pre, [21](#)

- anamiR, [2](#)
- anamiR-package (anamiR), [2](#)
- aov, [17](#)

- cor, [18](#)

- database\_support, [3](#), [7](#)
- differExp\_continuous, [4](#), [12](#), [18](#)
- differExp\_discrete, [5](#), [10–12](#), [14](#), [18](#)

- eBayes, [6](#), [10](#)
- egSymb, [7](#)
- enrichment, [7](#)

- gage, [7](#), [9](#), [16](#)
- GSEA\_ana, [9](#), [10](#)
- GSEA\_res, [10](#)

- heat\_vis, [11](#)
- heatmap.2, [12](#)

- lm, [5](#)

- miR\_converter, [3](#), [14](#), [21](#)
- mirna, [13](#), [20](#)
- mrna, [15](#), [21](#)
- msigdb.gs, [16](#)
- multi\_Differ, [17](#)

- negative\_cor, [3](#), [10–12](#), [18](#)
- normalization, [19](#)
- normalizeQuantiles, [20](#)

- p.adjust, [6](#), [11](#)
- pheno.mirna, [20](#)
- pheno.mrna, [21](#)

- phyper, [8](#)

- rankinvariant, [20](#)

- SummarizedExperiment, [5](#), [6](#), [9](#), [17](#), [19](#)

- t.test, [6](#), [10](#)
- table\_pre, [21](#)

- wilcox.test, [6](#)