Package 'miRsponge'

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Type Package

Title Identification and analysis of miRNA sponge interaction networks and modules

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Description This package provides several functions to study miRNA sponge (also called ceRNA or miRNA decoy), including popular methods for identifying miRNA sponge interactions, and the integrative method to integrate miRNA sponge interactions from different methods, as well as the functions to validate miRNA sponge interactions, and infer miRNA sponge modules, conduct enrichment analysis of modules, and conduct survival analysis of modules.

Depends R (>= 3.4.1)

License GPL-3

URL <https://github.com/zhangjunpeng411/miRsponge>

Encoding UTF-8

LazyData true

biocViews GeneExpression, BiomedicalInformatics, NetworkEnrichment, Survival, Microarray, Software

RoxygenNote 6.0.1

Imports corpcor, parallel, igraph, ProNet, clusterProfiler, ReactomePA, DOSE, survival, grDevices, graphics, stats, varhandle, utils

Suggests BiocStyle, knitr, rmarkdown, testthat, org.Hs.eg.db

VignetteBuilder knitr

NeedsCompilation no

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`integrateMethod` *Integrate method for identifying miRNA sponge interactions by integrating different methods*

Description

Integrate method for identifying miRNA sponge interactions by integrating different methods.

Usage

```
integrateMethod(Interlist, Intersect_num)
```

Arguments

`Interlist`	List object, a list of miRNA sponge interactions from different methods.
`Intersect_num`	The least number of different methods intersected for integration. The value of 1 means the union of miRNA sponge interactions from different methods.

Value

A list of integrated miRNA sponge interactions.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

Examples

```
ExpDatacsv <- system.file("extdata","ExpData.csv",package="miRsponge")
ExpData <- read.csv(ExpDatacsv, header=FALSE, sep=",")
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
miRHomologyceRInt <- spongeMethod(miRTarget, method = "miRHomology")
pcceRInt <- spongeMethod(miRTarget, ExpData, method = "pc")
sppcceRInt <- spongeMethod(miRTarget, ExpData, method = "sppc")
Interlist <- list(miRHomologyceRInt[, 1:2], pcceRInt[, 1:2], sppcceRInt[, 1:2])
IntegrateceRInt <- integrateMethod(Interlist, 2)
```

moduleDEA *Disease enrichment analysis of modules*

Description

Disease enrichment analysis of modules. The disease ontology databases have three types including DO: Disease Ontology database (http://disease-ontology.org/), DGN: DisGeNET database (http://www.disgenet.org/), and NCG: Network of Cancer Genes database (http://ncg.kcl.ac.uk/).

Usage

```
moduleDEA(Modulelist, OrgDb = "org.Hs.eg.db", ont = "DO",
padjustvaluecutoff = 0.05, padjustedmethod = "BH",plot = FALSE)
```

Arguments

Modulelist	A list of miRNA sponge modules.
OrgDb	OrgDb
ont	One of "DO", and "DOLite" subontologies.
padjustvaluecutoff	A cutoff value of adjusted p-values.
padjustedmethod	Adjusted method of p-values, can select one of "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none".
plot	A logical value, plot or not.

Value

A list of disease enrichment analysis results.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

References

Yu G, Wang L, Yan G, et al. DOSE: an R/Bioconductor package for Disease Ontology Semantic and Enrichment analysis. Bioinformatics, 2015, 31(4):608-609.

Examples

```
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
miRHomologyceRInt <- spongeMethod(miRTarget, method = "miRHomology")
spongenetwork_Cluster <- netModule(miRHomologyceRInt[, 1:2])
sponge_Module_DEA <- moduleDEA(spongenetwork_Cluster)
```

moduleFEA *Functional GO, KEGG and Reactome enrichment analysis of modules*

Description

Functional GO, KEGG and Reactome enrichment analysis of modules. GO: Gene Ontology database (http://www.geneontology.org/), KEGG: Kyoto Encyclopedia of Genes and Genomes Pathway Database (http://www.genome.jp/kegg/) and Reactome: Reactome Pathway Database (http://reactome.org/).

Usage

```
moduleFEA(Modulelist, ont = "BP", KEGGorganism = "hsa",
Reactomeorganism = "human", OrgDb = "org.Hs.eg.db",
padjustvaluecutoff = 0.05, padjustedmethod = "BH", plot = FALSE)
```

Arguments

Modulelist	A list of miRNA sponge modules.
ont	One of "MF", "BP", and "CC" subontologies.
KEGGorganism	Organism, supported organism listed in http://www.genome.jp/kegg/catalog/org_list.html
Reactomeorganism	Organism, one of "human", "rat", "mouse", "celegans", "yeast", "zebrafish", "fly".
OrgDb	OrgDb
padjustvaluecutoff	A cutoff value of adjusted p-values.
padjustedmethod	Adjusted method of p-values, can select one of "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none".
plot	A logical value, plot or not.

Value

A list of functional GO, KEGG and Reactome enrichment analysis results.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

References

1. Yu G, Wang L, Han Y, et al. clusterProfiler: an R package for comparing biological themes among gene clusters. OMICS: A Journal of Integrative Biology, 2012, 16(5):284-287.

2. Yu G and He Q. ReactomePA: an R/Bioconductor package for reactome pathway analysis and visualization. Molecular BioSystems, 2016, 12(12), pp. 477-479.

Examples

```
## Not run:
ExpDatacsv <- system.file("extdata","ExpData.csv",package="miRsponge")
ExpData <- read.csv(ExpDatacsv, header=FALSE, sep=",")
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
pcceRInt <- spongeMethod(miRTarget, ExpData, method = "pc")
spongenetwork_Cluster <- netModule(pcceRInt[, 1:2])
sponge_Module_FEA <- moduleFEA(spongenetwork_Cluster)

## End(Not run)
```

`moduleSurvival` *Survival analysis of modules*

Description

Survival analysis of modules.

Usage

```
moduleSurvival(Modulelist, ExpData, SurvData,
devidePercentage=.5, plot = FALSE)
```

Arguments

`Modulelist`	A list of miRNA sponge modules.
`ExpData`	An input expression data, the columns are genes and the rows are samples.
`SurvData`	An input survival data, three columns contain the information of sample, time (Months) and status, respectively.
`devidePercentage`	A percentage value, the percentage of high risk group.
`plot`	A logical value, plot or not.

Value

Survival analysis result of modules.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

References

Terry M. Therneau and Patricia M. Grambsch. Modeling Survival Data: Extending the Cox Model. Springer, New York. ISBN 0-387-98784-3, 2000.

Examples

```
ExpDatacsv <- system.file("extdata","ExpData.csv",package="miRsponge")
ExpData <- read.csv(ExpDatacsv, header=FALSE, sep=",")
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
SurvDatacsv <- system.file("extdata", "SurvData.csv", package="miRsponge")
SurvData <- read.csv(SurvDatacsv, header=TRUE, sep=",")
pcceRInt <- spongeMethod(miRTarget, ExpData, method = "pc")
spongenetwork_Cluster <- netModule(pcceRInt[, 1:2])
sponge_Module_Survival <- moduleSurvival(spongenetwork_Cluster,
ExpData, SurvData)
```

`netModule` *Identifying miRNA sponge modules from network*

Description

Identifying miRNA sponge modules from network. Possible methods include FN, MCL, LINKCOMM and MCODE.

Usage

```
netModule(spongenetwork, method = "MCL", directed = FALSE, save = FALSE)
```

Arguments

`spongenetwork`	Input miRNA sponge interaction network.
`method`	Cluster method, can select one of FN, MCL, LINKCOMM and MCODE.
`directed`	A logical value, the network is directed or not.
`save`	A logical value, save the identified modules or not.

Value

A list of miRNA sponge modules.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

References

1. Clauset A, Newman ME, Moore C. Finding community structure in very large networks. Phys Rev E Stat Nonlin Soft Matter Phys., 2004, 70(6 Pt 2):066111.

2. Enright AJ, Van Dongen S, Ouzounis CA. An efficient algorithm for large-scale detection of protein families. Nucleic Acids Res., 2002, 30(7):1575-84.

3. Kalinka AT, Tomancak P. linkcomm: an R package for the generation, visualization, and analysis of link communities in networks of arbitrary size and type. Bioinformatics, 2011, 27(14):2011-2.

4. Bader GD, Hogue CW. An automated method for finding molecular complexes in large protein interaction networks. BMC Bioinformatics, 2003, 4:2.

Examples

```
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
miRHomologyceRInt <- spongeMethod(miRTarget, method = "miRHomology")
spongenetwork_Cluster <- netModule(miRHomologyceRInt[, 1:2])
```

---

querymiRTargetbinding *Query miRNA-target interactions by combining expression data and putative miRNA-target interactions*

Description

Query miRNA-target interactions by combining expression data and putative miRNA-target interactions.

Usage

```
querymiRTargetbinding(ExpData, miRTarget)
```

Arguments

ExpData	An input gene expression data frame, the rows are samples and the columns are genes.
miRTarget	An input miRNA-target interaction data frame, the first column is miRNA with name "mir" and the second column is target with name "gene".

Value

A list of queried miRNA-target interactions

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

Examples

```
ExpDatacsv <- system.file("extdata", "ExpData.csv", package="miRsponge")
ExpData <- read.csv(ExpDatacsv, header=FALSE, sep=",")
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
miR2Target_queried <- querymiRTargetbinding(ExpData, miRTarget)
```

spongeMethod *Identifying miRNA sponge interactions using spongeMethod*

Description

Identifying miRNA sponge interactions using spongeMethod. We implement seven popular methods (miRHomology, pc, sppc, ppc, hermes, muTaME, and cernia) to identify miRNA sponge interactions.

Usage

```
spongeMethod(miRTarget, ExpData = NULL, mres = NULL, minSharedmiR = 3,
poscorcutoff = 0, num_perm = 100, padjustvaluecutoff = 0.01,
padjustmethod = "BH", senscorcutoff = 0.3, scorecutoff = 0.5,
method = c("miRHomology", "pc", "sppc", "ppc", "hermes", "muTaME", "cernia"))
```

Arguments

`miRTarget`	Putative miRNA-target interactions.
`ExpData`	An input expression data frame, the columns are genes and the rows are samples.
`mres`	Putative MiRNA Response Elements (mres) data frame, each row contains five elements: Mirna, Target, energy, gap_l, gap_r.
`minSharedmiR`	The minimum number of shared miRNAs between targets.
`poscorcutoff`	A cutoff value of positive correlation.
`num_perm`	The number of permutations.
`padjustvaluecutoff`	A cutoff value of adjusted p-values.
`padjustmethod`	Adjusted method of p-values, can select one of "holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none".
`senscorcutoff`	A cutoff value of sensitivity partial pearson correlation.
`scorecutoff`	A cutoff value of normalized score (range from 0 to 1).
`method`	Select a method for identifying miRNA sponge interactions, can select one of "miRHomology", "pc", "sppc", "ppc", "hermes", "muTaME", "cernia".

Value

A list of identified miRNA sponge interactions.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

References

1. Le TD, Zhang J, Liu L, et al. Computational methods for identifying miRNA sponge interactions. Brief Bioinform., 2017, 18(4):577-590.

2. Li JH, Liu S, Zhou H, et al. starBase v2.0: decoding miRNA-ceRNA, miRNA-ncRNA and protein-RNA interaction networks from large-scale CLIP-Seq data. Nucleic Acids Res., 2014, 42(Database issue):D92-7.

3. Sarver AL, Subramanian S. Competing endogenous RNA database. Bioinformation, 2012, 8(15):731-3.

4. Zhou X, Liu J, Wang W, Construction and investigation of breast-cancer-specific ceRNA network based on the mRNA and miRNA expression data. IET Syst Biol., 2014, 8(3):96-103.

5. Xu J, Li Y, Lu J, et al. The mRNA related ceRNA-ceRNA landscape and significance across 20 major cancer types. Nucleic Acids Res., 2015, 43(17):8169-82.

6. Paci P, Colombo T, Farina L, Computational analysis identifies a sponge interaction network between long non-coding RNAs and messenger RNAs in human breast cancer. BMC Syst Biol., 2014, 8:83.

7. Sumazin P, Yang X, Chiu HS, et al. An extensive microRNA-mediated network of RNA-RNA interactions regulates established oncogenic pathways in glioblastoma. Cell, 2011, 147(2):370-81.

8. Tay Y, Kats L, Salmena L, et al. Coding-independent regulation of the tumor suppressor PTEN by competing endogenous mRNAs. Cell, 2011, 147(2):344-57.

9. Sardina DS, Alaimo S, Ferro A, et al. A novel computational method for inferring competing endogenous interactions. Brief Bioinform., 2016, DOI: 10.1093/bib/bbw084.

Examples

```
ExpDatacsv <- system.file("extdata","ExpData.csv",package="miRsponge")
ExpData <- read.csv(ExpDatacsv, header=FALSE, sep=",")
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")

# miRHomology method
miRHomologyceRInt <- spongeMethod(miRTarget, method = "miRHomology")

# pc method
pcceRInt <- spongeMethod(miRTarget, ExpData, method = "pc")

# sppc method
sppcceRInt <- spongeMethod(miRTarget, ExpData, senscorcutoff = 0.1, method = "sppc")
```

---

spongeValidate *Validation of computationally predicted miRNA sponge interactions*

Description

Validation of computationally predicted miRNA sponge interactions. The groundtruth of miRNA sponge interactions are from miRSponge v2.0 (http://www.bio-bigdata.net/miRSponge/).

Usage

```
spongeValidate(spongenetwork, Groundtruth)
```

Arguments

spongenetwork	Input miRNA sponge interaction network.
Groundtruth	The groundtruth of miRNA sponge interactions.

Value

A list of experimentally validated miRNA sponge interactions.

Author(s)

Junpeng Zhang (https://www.researchgate.net/profile/Junpeng_Zhang3)

Examples

```
miR2Target <- system.file("extdata", "miR2Target.csv", package="miRsponge")
miRTarget <- read.csv(miR2Target, header=TRUE, sep=",")
miRHomologyceRInt <- spongeMethod(miRTarget, method = "miRHomology")
Groundtruthcsv <- system.file("extdata", "Groundtruth.csv", package="miRsponge")
Groundtruth <- read.csv(Groundtruthcsv, header=TRUE, sep=",")
spongenetwork_validated <- spongeValidate(miRHomologyceRInt[, 1:2], Groundtruth)
```

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