

Package ‘MoonlightR’

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Type Package

Title Identify oncogenes and tumor suppressor genes from omics data

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Depends R (>= 3.5), doParallel, foreach

Imports parmigene, randomForest, SummarizedExperiment, gplots, circlize, RColorBrewer, HiveR, clusterProfiler, DOSE, Biobase, limma, grDevices, graphics, TCGAbiolinks, GEOquery, stats, RISmed, grid, utils

Description Motivation: The understanding of cancer mechanism requires the identification of genes playing a role in the development of the pathology and the characterization of their role (notably oncogenes and tumor suppressors). Results: We present an R/bioconductor package called MoonlightR which returns a list of candidate driver genes for specific cancer types on the basis of TCGA expression data. The method first infers gene regulatory networks and then carries out a functional enrichment analysis (FEA) (implementing an upstream regulator analysis, URA) to score the importance of well-known biological processes with respect to the studied cancer type. Eventually, by means of random forests, MoonlightR predicts two specific roles for the candidate driver genes: i) tumor suppressor genes (TSGs) and ii) oncogenes (OCGs). As a consequence, this methodology does not only identify genes playing a dual role (e.g. TSG in one cancer type and OCG in another) but also helps in elucidating the biological processes underlying their specific roles. In particular, MoonlightR can be used to discover OCGs and TSGs in the same cancer type. This may help in answering the question whether some genes change role between early stages (I, II) and late stages (III, IV) in breast cancer. In the future, this analysis could be useful to determine the causes of different resistances to chemotherapeutic treatments.

License GPL (>= 3)

biocViews DNAMethylation, DifferentialMethylation, GeneRegulation, GeneExpression, MethylationArray, DifferentialExpression, Pathways, Network, Survival, GeneSetEnrichment, NetworkEnrichment

Suggests BiocStyle, knitr, rmarkdown, testthat, devtools, roxygen2, png

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BugReports <https://github.com/ELELAB/MoonlightR/issues>

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| | |
|-----------------------|---|
| <code>dataFilt</code> | <i>Gene Expression (Rnaseqv2) data from TCGA LUAD</i> |
|-----------------------|---|

Description

A data set containing the following data:

Usage

`data(dataFilt)`

Format

A 13742x20 matrix

Details

- `dataFilt` matrix with 13742 rows (genes) and 20 columns samples with TCGA's barcodes (10TP, 10NT)

Value

a 13742x20 matrix

| | |
|---------|---|
| dataGRN | <i>GRN gene regulatory network output</i> |
|---------|---|

Description

output from GRN function

Usage

```
data(dataGRN)
```

Format

A large list of 2 elements

Details

- dataGRN list of 2 elements miTFGenes, maxmi from GRN function

Value

a large list of 2 elements

| | |
|---------|--|
| dataURA | <i>Output example from function Upstram Regulator Analysis</i> |
|---------|--|

Description

A data set containing the following data:

Usage

```
data(dataURA)
```

Format

A data frame with 100 rows and 2 variables

Details

- dataURA matrix with 100 rows (genes) and 2 columns "apoptosis" "proliferation of cells"

Value

a 100x2 matrix

DEGsmatrix

DEG Differentially expressed genes

Description

A data set containing the following data:

Usage

```
data(DEGsmatrix)
```

Format

A 3502x5 matrix

Details

- DEGsmatrix matrix with 3502 rows (genes) and five columns "logFC" "logCPM" "LR" "PValue" "FDR"

Value

the 3502x5 matrix

DiseaseList

Information on 101 biological processes

Description

A data set containing the following data:

Usage

```
data(DiseaseList)
```

Format

A list of 101 matrices

Details

- DiseaseList list for 101 biological processes, each containing a matrix with five columns: ID, Genes.in.dataset, Prediction based on expression direction, Log ratio, Findings

Value

list of 101 matrices

DPA

DPA

Description

This function carries out the differential phenotypes analysis

Usage

```
DPA(  
  dataType,  
  dataFilt,  
  dataConsortium = "TCGA",  
  fdr.cut = 0.01,  
  logFC.cut = 1,  
  diffmean.cut = 0.25,  
  samplesType,  
  colDescription,  
  gset,  
  gsetFile = "gsetFile.RData"  
)
```

Arguments

| | |
|-----------------------------|---|
| <code>dataType</code> | selected |
| <code>dataFilt</code> | obtained from <code>getDataTCGA</code> |
| <code>dataConsortium</code> | is TCGA or GEO, default TCGA |
| <code>fdr.cut</code> | is a threshold to filter DEGs according their p-value corrected |
| <code>logFC.cut</code> | is a threshold to filter DEGs according their logFC |
| <code>diffmean.cut</code> | <code>diffmean.cut</code> for DMR |
| <code>samplesType</code> | <code>samplesType</code> |
| <code>colDescription</code> | <code>colDescription</code> |
| <code>gset</code> | <code>gset</code> |
| <code>gsetFile</code> | <code>gsetFile</code> |

Value

result matrix from differential phenotype analysis

Examples

```
dataDEGs <- DPA(dataFilt = dataFilt, dataType = "Gene expression")
```

EAGenes

Information about genes

Description

A data set containing the following data:

Usage

```
data(EAGenes)
```

Format

A 20038x5 matrix

Details

- EAGenes matrix with 20038 rows (genes) and five columns "ID" "Gene" "Description" "Location" "Family"

Value

a 20038x5 matrix

FEA

FEA

Description

This function carries out the functional enrichment analysis (FEA)

Usage

```
FEA(BPname = NULL, DEGsmatrix)
```

Arguments

| | |
|------------|---|
| BPname | BPname biological process such as "proliferation of cells", "ALL" (default) if FEA should be carried out for all 101 biological processes |
| DEGsmatrix | DEGsmatrix output from DEA such as dataDEGs" |

Value

matrix from FEA

Examples

```
dataDEGs <- DPA(dataFilt = dataFilt,  
dataType = "Gene expression")  
dataFEA <- FEA(DEGsmatrix = dataDEGs)
```

GDCprojects*Information on GDC projects*

Description

A character vector of GDC projects:

Usage

```
data(GDCprojects)
```

Format

A character vector of 39 elements

Details

- character vector for GDC projects.

Value

character vector of 39 elements

geneInfo*Information about genes for normalization*

Description

A data set containing the following data:

Usage

```
data(geneInfo)
```

Format

A data frame with 20531 rows and 3 variables

Details

- geneInfo matrix with 20531 rows (genes) and 3 columns "geneLength" "gcContent" "chr"

Value

a 20531x3 matrix

| | |
|-------------|--|
| GEO_TCGAtab | <i>Information on GEO data (and overlap with TCGA)#' A data set containing the following data:</i> |
|-------------|--|

Description

- GEO_TCGAtab a 18x12 matrix that provides the GEO data set we matched to one of the 18 given TCGA cancer types

Usage

```
data(GEO_TCGAtab)
```

Format

A 101x3 matrix

Value

a 101x3 matrix

| | |
|------------|-------------------|
| getDataGEO | <i>getDataGEO</i> |
|------------|-------------------|

Description

This function retrieves and prepares GEO data

Usage

```
getDataGEO(GEOobject = "GSE39004", platform = "GPL6244", TCGAtumor = NULL)
```

Arguments

| | |
|-----------|------------|
| GEOobject | GEOobject |
| platform | platform |
| TCGAtumor | tumor name |

Value

return GEO gset

Examples

```
## Not run:
dataGEO <- getDataGEO(GEOobject = "GSE20347",platform = "GPL571")

## End(Not run)
```

 getDataTCGA

getDataTCGA

Description

This function retrieves and prepares TCGA data

Usage

```
getDataTCGA(
  cancerType,
  dataType,
  directory,
  cor.cut = 0.6,
  qnt.cut = 0.25,
  nSample,
  stage = "ALL",
  subtype = 0,
  samples = NULL
)
```

Arguments

| | |
|------------|--|
| cancerType | select cancer type for which analysis should be run. panCancer for all available cancer types in TCGA. Defaults to panCancer |
| dataType | is dataType such as gene expression, cnv, methylation etc. |
| directory | Directory/Folder where the data was downloaded. Default: GDCdata |
| cor.cut | cor.cut |
| qnt.cut | qnt.cut |
| nSample | nSample |
| stage | stage |
| subtype | subtype |
| samples | samples |

Value

returns filtered TCGA data

Examples

```
## Not run:
dataFilt <- getDataTCGA(cancerType = "LUAD",
  dataType = "Gene expression", directory = "data", nSample = 4)

## End(Not run)
```

GRN

*Generate network***Description**

This function carries out the gene regulatory network inference using parmigene

Usage

```
GRN(
  TFs,
  DEGsmatrix,
  DiffGenes = FALSE,
  normCounts,
  kNearest = 3,
  nGenesPerm = 10,
  nBoot = 10
)
```

Arguments

| | |
|------------|---|
| TFs | a vector of genes. |
| DEGsmatrix | DEGsmatrix output from DEA such as dataDEGs |
| DiffGenes | if TRUE consider only diff.expr genes in GRN |
| normCounts | is a matrix of gene expression with genes in rows and samples in columns. |
| kNearest | the number of nearest neighbors to consider to estimate the mutual information. Must be less than the number of columns of normCounts. |
| nGenesPerm | nGenesPerm |
| nBoot | nBoot |

Value

an adjacent matrix

Examples

```
dataDEGs <- DEGsmatrix
dataGRN <- GRN(TFs = rownames(dataDEGs)[1:100],
  DEGsmatrix = dataDEGs,
  DiffGenes = TRUE,
  normCounts = dataFilt)
```

GSEA

GSEA

Description

This function carries out the GSEA enrichment analysis.

Usage

```
GSEA(DEGsmatrix, top, plot = FALSE)
```

Arguments

| | |
|------------|---|
| DEGsmatrix | DEGsmatrix output from DEA such as dataDEGs |
| top | is the number of top BP to plot |
| plot | if TRUE return a GSEA's plot |

Value

return GSEA result

Examples

```
dataDEGs <- DEGsmatrix  
# dataFEA <- GSEA(DEGsmatrix = dataDEGs)
```

knownDriverGenes*Information on known cancer driver gene from COSMIC*

Description

A data set containing the following data:

Usage

```
data(knownDriverGenes)
```

Format

A 101x3 matrix

Details

- TSG known tumor suppressor genes
- OCG known oncogenes

Value

a 101x3 matrix

| | |
|---------------|-----------------------------------|
| listMoonlight | <i>Output list from Moonlight</i> |
|---------------|-----------------------------------|

Description

A list containing the following data:

Usage

```
data(listMoonlight)
```

Format

A Large list with 5 elements

Details

- listMoonlight output from moonlight's pipeline containing dataDEGs, dataURA, listCandidates

Value

output from moonlight pipeline

| | |
|-----|------------|
| LPA | <i>LPA</i> |
|-----|------------|

Description

This function carries out the literature phenotype analysis (LPA)

Usage

```
LPA(dataDEGs, BP, BPlist)
```

Arguments

| | |
|----------|----------------------------------|
| dataDEGs | is output from DEA |
| BP | is biological process |
| BPlist | is list of genes annotated in BP |

Value

table with number of pubmed that affects, increase or decrease genes annotated in BP

Examples

```
data(DEGsmatrix)
BPselected <- c("apoptosis")
BPannotations <- DiseaseList[[match(BPselected, names(DiseaseList))]]$ID
```

moonlight

moonlight pipeline

Description

moonlight is a tool for identification of cancer driver genes. This function wraps the different steps of the complete analysis workflow. Providing different solutions:

1. MoonlighR::FEA
2. MoonlighR::URA
3. MoonlighR::PIA

Usage

```
moonlight(  
  cancerType = "panCancer",  
  dataType = "Gene expression",  
  directory = "GDCdata",  
  BPname = NULL,  
  cor.cut = 0.6,  
  qnt.cut = 0.25,  
  Genelist = NULL,  
  fdr.cut = 0.01,  
  logFC.cut = 1,  
  corThreshold = 0.6,  
  kNearest = 3,  
  nGenesPerm = 10,  
  DiffGenes = FALSE,  
  nBoot = 100,  
  nTF = NULL,  
  nSample = NULL,  
  thres.role = 0,  
  stage = NULL,  
  subtype = 0,  
  samples = NULL  
)
```

Arguments

| | |
|--------------|---|
| cancerType | select cancer type for which analysis should be run. panCancer for all available cancer types in TCGA. Defaults to panCancer |
| dataType | dataType |
| directory | directory |
| BPname | biological processes to use, if NULL: all processes will be used in analysis, RF for candidate; if not NULL the candidates for these processes will be determined (no learning) |
| cor.cut | cor.cut Threshold |
| qnt.cut | qnt.cut Threshold |
| Genelist | Genelist |
| fdr.cut | fdr.cut Threshold |
| logFC.cut | logFC.cut Threshold |
| corThreshold | corThreshold |
| kNearest | kNearest |
| nGenesPerm | nGenesPerm |
| DiffGenes | DiffGenes |
| nBoot | nBoot |
| nTF | nTF |
| nSample | nSample |
| thres.role | thres.role |
| stage | stage |
| subtype | subtype |
| samples | samples |

Value

table with cancer driver genes TSG and OCG.

Examples

```
dataDEGs <- DPA(dataFilt = dataFilt, dataType = "Gene expression")
# to change with moonlight
```

MoonlightR

MoonlightR

Description

MoonlightR is a package designed for the identification of cancer driver genes. Please see the documentation on our Bioconductor page for more details: <https://www.bioconductor.org/packages/release/bioc/html/MoonlightR>
If you experience issues with the package, please open an Issue on our GitHub repository: <https://github.com/ELELAB/MoonlightR>
If you use this package in your research, please cite this paper: <https://doi.org/10.1038/s41467-019-13803-0>

`plotCircos`*plotCircos*

Description

This function visualize the plotCircos

Usage

```
plotCircos(  
  listMoonlight,  
  listMutation = NULL,  
  additionalFilename = NULL,  
  intensityColOCG = 0.5,  
  intensityColTSG = 0.5,  
  intensityColDual = 0.5,  
  fontSize = 1  
)
```

Arguments

| | |
|---------------------------------|---------------------------------|
| <code>listMoonlight</code> | output Moonlight function |
| <code>listMutation</code> | <code>listMutation</code> |
| <code>additionalFilename</code> | <code>additionalFilename</code> |
| <code>intensityColOCG</code> | <code>intensityColOCG</code> |
| <code>intensityColTSG</code> | <code>intensityColTSG</code> |
| <code>intensityColDual</code> | <code>intensityColDual</code> |
| <code>fontSize</code> | <code>fontSize</code> |

Value

no return value, plot is saved

Examples

```
plotCircos(listMoonlight = listMoonlight, additionalFilename = "_ncancer5")
```

plotFEA

plotFEA

Description

This function visualize the functional enrichment analysis (FEA)'s barplot

Usage

```
plotFEA(  
  dataFEA,  
  topBP = 10,  
  additionalFilename = NULL,  
  height,  
  width,  
  offsetValue = 5,  
  angle = 90,  
  xleg = 35,  
  yleg = 5,  
  titleMain,  
  minY = -5,  
  maxY = 10,  
  mycols = c("#8DD3C7", "#FFFB3", "#BEBADA")  
)
```

Arguments

| | |
|--------------------|----------------------------|
| dataFEA | dataFEA |
| topBP | topBP |
| additionalFilename | additionalFilename |
| height | Figure height |
| width | Figure width |
| offsetValue | offsetValue |
| angle | angle |
| xleg | xleg |
| yleg | yleg |
| titleMain | title of the plot |
| minY | minY |
| maxY | maxY |
| mycols | colors to use for the plot |

Value

no return value, FEA result is plotted

Examples

```
dataFEA <- FEA(DEGsmatrix = DEGsmatrix)
plotFEA(dataFEA = dataFEA, additionalFilename = "_example",height = 20,width = 10)
```

| | |
|-----------------|---|
| plotNetworkHive | <i>plotNetworkHive: Hive network plot</i> |
|-----------------|---|

Description

This function visualizes the GRN as a hive plot

Usage

```
plotNetworkHive(dataGRN, namesGenes, thres, additionalFilename = NULL)
```

Arguments

| | |
|--------------------|-----------------------------------|
| dataGRN | output GRN function |
| namesGenes | list TSG and OCG to define axes |
| thres | threshold of edges to be included |
| additionalFilename | additionalFilename |

Value

no results Hive plot is executed

Examples

```
data(knownDriverGenes)
data(dataGRN)
plotNetworkHive(dataGRN = dataGRN, namesGenes = knownDriverGenes, thres = 0.55)
```

| | |
|---------|---|
| plotURA | <i>plotURA: Upstream regulatory analysis heatmap plot</i> |
|---------|---|

Description

This function visualizes the URA in a heatmap

Usage

```
plotURA(dataURA, additionalFilename = "URApot")
```

Arguments

| | |
|--------------------|---------------------|
| dataURA | output URA function |
| additionalFilename | figure name |

Value

heatmap

Examples

```
data(dataURA)
dataDual <- PRA(dataURA = dataURA,
BPname = c("apoptosis", "proliferation of cells"),
thres.role = 0)
TSGs_genes <- names(dataDual$TSG)
OCGs_genes <- names(dataDual$OCG)
plotURA(dataURA = dataURA[c(TSGs_genes, OCGs_genes),], additionalFilename = "_example")
```

| | |
|-----|---|
| PRA | <i>Pattern Recognition Analysis (PRA)</i> |
|-----|---|

Description

This function carries out the pattern recognition analysis

Usage

```
PRA(dataURA, BPname, thres.role = 0)
```

Arguments

| | |
|------------|---------------------|
| dataURA | output URA function |
| BPname | BPname |
| thres.role | thres.role |

Value

returns list of TSGs and OCGs when biological processes are provided, otherwise a randomForest based classifier that can be used on new data

Examples

```
data(dataURA)
dataDual <- PRA(dataURA = dataURA,
BPname = c("apoptosis", "proliferation of cells"),
thres.role = 0)
```

| | |
|--------------|---|
| tabGrowBlock | <i>Information growing/blocking characteristics for 101 selected biological processes</i> |
|--------------|---|

Description

A data set containing the following data:

Usage

```
data(tabGrowBlock)
```

Format

A 101x3 matrix

Details

- tabGrowBlock matrix that defines if a process is growing or blocking cancer development, for each 101 biological processing

Value

a 101x3 matrix

Description

This function carries out the upstream regulator analysis

Usage

```
URA(dataGRN, DEGsmatrix, BPname, nCores = 1)
```

Arguments

| | |
|------------|------------------------|
| dataGRN | output GNR function |
| DEGsmatrix | output DPA function |
| BPname | biological processes |
| nCores | number of cores to use |

Value

an adjacent matrix

Examples

```
dataDEGs <- DEGsmatrix
dataGRN <- GRN(TFs = rownames(dataDEGs)[1:100],
  DEGsmatrix = dataDEGs,
  DiffGenes = TRUE,
  normCounts = dataFilt)
dataURA <- URA(dataGRN = dataGRN,
  DEGsmatrix = dataDEGs,
  BPname = c("apoptosis",
    "proliferation of cells"))
```

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