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.

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

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

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Contents

`dataFilt` *Gene Expression (Rnaseqv2) data from TCGA LUAD*

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` *GRN gene regulatory network output*

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` *Output example from function Upstram Regulator Analysis*

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

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

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` *Information on GEO data (and overlap with TCGA)#' A data set containing the following data:*

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` *getDataGEO*

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` *Output list from Moonlight*

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` *LPA*

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 decrase 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/Moon

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

listMoonlight	output Moonlight function
listMutation	listMutation
additionalFilename	additionalFilename
intensityColOCG	intensityColOCG
intensityColTSG	intensityColTSG
intensityColDual	intensityColDual
fontSize	fontSize

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", "#FFFFB3", "#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` *plotNetworkHive: Hive network plot*

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 *plotURA: Upstream regulatory analysis heatmap plot*

Description

This function visualizes the URA in a heatmap

Usage

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

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 *Pattern Recognition Analysis (PRA)*

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 *Information growing/blocking characteristics for 101 selected biological processes*

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

URA *URA Upstream Regulator Analysis*

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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