Package ‘MoonlightR’

March 28, 2024

Type Package

Title Identify oncogenes and tumor suppressor genes from omics data

Version 1.28.0

Date 07-08-2020

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, edgeR

**VignetteBuilder**  knitr

**LazyData**  true

**URL**  https://github.com/ELELAB/MoonlightR

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

**RoxygenNote**  7.2.3

**Encoding**  UTF-8

**git_url**  https://git.bioconductor.org/packages/MoonlightR

**git_branch**  RELEASE_3_18

**git_last_commit**  7dada82

**git_last_commit_date**  2023-10-24

**Repository**  Bioconductor 3.18

**Date/Publication**  2024-03-27

**Author**  Antonio Colaprico [aut], Catharina Olsen [aut], Matthew H. Bailey [aut], Gabriel J. Odom [aut], Thilde Terkelsen [aut], Mona Nourbakhsh [aut], Astrid Saksager [aut], Tiago C. Silva [aut], André V. Olsen [aut], Laura Cantini [aut], Andrei Zinovyev [aut], Emmanuel Barillot [aut], Houtan Noushmehr [aut], Gloria Bertoli [aut], Isabella Castiglioni [aut], Claudia Cava [aut], Gianluca Bontempi [aut], Xi Steven Chen [aut], Elena Papaleo [aut], Matteo Tiberti [cre, aut]

**Maintainer**  Matteo Tiberti <tiberti@cancer.dk>

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**R topics documented:**

- dataFilt
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)
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 Upstream 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

**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

**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

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

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

GDCprojects

<table>
<thead>
<tr>
<th>Information on GDC projects</th>
</tr>
</thead>
</table>

Description

A character vector of GDC projects:

Usage

data(GDCprojects)

Format

A character vector of 39 elements

Details

• character vector for GDC projects.

Value

calendar vector of 39 elements

geneInfo

<table>
<thead>
<tr>
<th>Information about genes for normalization</th>
</tr>
</thead>
</table>

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"
**GEO_TCGAtab**

**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**

```r
data(GEO_TCGAtab)
```

**Format**

A 101x3 matrix

**Value**

a 101x3 matrix

---

**getDataGEO**

**Description**

This function retrieves and prepares GEO data

**Usage**

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

**Arguments**

- GEOobject: GEOobject
- platform: platform
- TCGAtumor: tumor name

**Value**

return GEO gset
getDataTCGA

Examples

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

## End(Not run)

datasetTCGA

datasetTCGA

datasetTCGA

datasetTCGA

datasetTCGA

datasetTCGA

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
**GRN**

Examples

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

## End(Not run)
```

---

**Description**

This function carries out the gene regulatory network inference using parmigene

**Usage**

```r
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**

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

**Description**

This function carries out the GSEA enrichment analysis.

**Usage**

\[
\text{GSEA}(\text{DEGsmatrix}, \text{top}, \text{plot} = \text{FALSE})
\]

**Arguments**

- `DEGsmatrix` \(\text{DEGsmatrix output from DEA such as dataDEGs}\)
- `top` \(\text{is the number of top BP to plot}\)
- `plot` \(\text{if TRUE return a GSEA's plot}\)

**Value**

return GSEA result

**Examples**

\[
\text{dataDEGs <- DEGsmatrix} \\
# \text{dataFEA <- GSEA(DEGsmatrix = dataDEGs)}
\]

### knownDriverGenes

**Information on known cancer driver gene from COSMIC**

**Description**

A data set containing the following data:

**Usage**

\[
\text{data(knownDriverGenes)}
\]

**Format**

A 101x3 matrix

**Details**

- TSG known tumor suppressor genes
- OCG known oncogenes
**listMoonlight**

**Value**

A 101x3 matrix

**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 list 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 decrease genes annotated in BP

Examples

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

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. MoonlightR::FEA
2. MoonlightR::URA
3. MoonlightR::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

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.html
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
### Description

This function visualizes the plotCircos.

### Usage

```r
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

```r
plotCircos(listMoonlight = listMoonlight, additionalFilename = "ncancer5")
```
Description

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

Usage

```r
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)

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

---

**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: 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
```r
data(dataURA)
dataDual <- PRA(dataURA = dataURA,
BPname = c("apoptosis","proliferation of cells"),
thres.role = 0)
TSGsgenes <- names(dataDual$TSG)
OCGsgenes <- names(dataDual$OCG)
plotURA(dataURA = dataURA[c(TSGsgenes, OCGsgenes),], additionalFilename = ".example")```

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)

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**

```r
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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