Package 'ASpediaFI'

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Type Package

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Description This package provides functionalities for a systematic and integrative analysis of alternative splicing events and their functional interactions.

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`analyzeFI` *Functional interaction analysis of AS events*

Description

Analyze functional interactions of AS events using Discriminative Random Walk with Restart (DRaWR). It runs a DRaWR on a heterogeneous network containing genes, AS events, and pathways. It then performs GSEA on gene sets related to query genes.

Usage

```
analyzeFI(object, query, expr, ppi = NULL, pathways = NULL,
    restart = 0.7, num.folds = 5, num.feats = 100, low.expr = 1,
    low.var = NULL, prop.na = 0.05, prop.extreme = 1,
    cor.threshold = 0.3)
```

Arguments

`object`	Object of class ASpediaFI
`query`	a character vector or a data frame containing query genes
`expr`	a `SummarizedExperiment` object or matrix containing gene expression profiles (FPKM)
`ppi`	an `igraph` object containing known interactions between genes. If NULL, an `igraph` object containing human gene-gene interactions will be used.
`pathways`	a GMT file or a named list of pathway gene sets. If NULL, a combined list of HALLMARK, KEGG, and REACTOME pathway gene sets will be used.
`restart`	a restart probability
`num.folds`	the number of folds for cross-validation
`num.feats`	the number of feature nodes to be retained in the final subnetwork
`low.expr`	Genes with mean expression below low.expr are excluded. AS events for corresponding genes are also excluded.

low.var	AS events with variance below low.var are excluded. If NULL, top 10,000 variable events are used for analysis.
prop.na	AS events with the higher proportion of missing values than prop.na are excluded.
prop.extreme	AS events with the higher proportion of extreme values (0 or 1) than prop.extreme are excluded.
cor.threshold	a pair of AS event and gene with Spearman's correlation greather than cor.threshold are connected in a heterogeneous network.

Value

ASpediaFI object with results of functional interaction analysis

References

Blatti, C. et al. (2016). Characterizing gene sets using discrminative random walks with restart on heterogeneous biological networks. *Bioinformatics*, 32.

Examples

```
library(limma)
data(GSE114922.fpkm)
data(GSE114922.psi)
design <- cbind(WT = 1, MvsW = colData(GSE114922.psi)$condition == 'MUT')
fit <- lmFit(log2(GSE114922.fpkm + 1), design = design)
fit <- eBayes(fit, trend = TRUE)
tt <- topTable(fit, number = Inf, coef = 'MvsW')
query <- rownames(tt[tt$logFC > 1 & tt$P.Value < 0.1, ])
head(query)
## Not run:
GSE114922.ASpediaFI <- analyzeFI(
    GSE114922.ASpediaFI, query,
    GSE114922.fpkm
)

## End(Not run)
```

---

annotateASevents *AS event annotation*

Description

Detect and annotate AS events from GTF. This function borrows code from the IVAS package.

Usage

```
annotateASevents(object, gtf.file, num.cores = 1)
```

Arguments

object	Object of class ASpediaFI
gtf.file	an input GTF file
num.cores	the number of cores for parallel processing

Value

ASpediaFI object with a list of AS event annotations

References

Han, S. et al. (2017). Genome wide discovery of genetic variants affecting alternative splicing patterns in human using bioinformatics method. *Genes & Genomics*, 39.

Examples

```
fi <- new('ASpediaFI')
gtf <- system.file('extdata/GRCh38.subset.gtf', package = 'ASpediaFI')
fi <- annotateASevents(fi, gtf.file = gtf, num.cores = 1)
sapply(events(fi), length)
head(events(fi)$SE)
```

ASpediaFI-class *ASpediaFI class*

Description

ASpediaFI class is a wrapper of ASpediaFI functionalities and a container of inputs and outputs.

Usage

```
ASpediaFI(sample.names, bam.files, conditions)
```

Arguments

sample.names	a character vector of sample names (or IDs)
bam.files	a character vector of paths to RNA-Seq BAM files
conditions	a vector of sample conditions (e.g. mutation status)

Value

ASpediaFI object

Slots

`samples`: a data frame containing information about samples. The first three columns should be names, BAM file paths, and conditions.

`events`: a list of AS events extracted from a GTF file.

`gtf`: a `GRanges` object containing genomic features extracted from a GTF file.

`psi`: a `SummarizedExperiment` object containing AS event quantification

`network`: an `igraph` object containing a query-specific subnetwork as a result of DRaWR.

`gene.table`, `as.table`, `pathway.table`: data frames containing gene nodes, AS event nodes, and pathway nodes.

Accessors

In the following, 'x' represents a `ASpediaFI` object:

`samples(x)`, `samples(x) <- value`: get or set sample information. value must be a data frame containing sample information.

`events(x)`, `events(x) <- value`: get or set AS event annotations. value must be a list of annotations.

`gtf(x)`, `gtf(x) <- value`: get or set a `GRanges` object containing GTF. value must be a `GRanges` object.

`psi(x)`, `psi(x) <- value`: get or set PSI values. value must be a `SummarizedExperiment` object.

`network(x)`, `network(x) <- value`: get or set final subnetwork. value must be an `igraph` object.

`gene.table(x)`, `gene.table(x) <- value`: get or set gene node tables. value must be a data frame containing information about gene nodes.

`as.table(x)`, `as.table(x) <- value`: get or set AS node tables. value must be a data frame containing information about AS nodes.

`pathway.table(x)`, `pathway.table(x) <- value`: get or set pathway node tables. value must be a data frame containing information about pathway nodes.

Examples

```
bamWT <- system.file('extdata/GSM3167290.subset.bam', package = 'ASpediaFI')
GSE114922.ASpediaFI <- ASpediaFI(
    sample.names = 'GSM3167290',
    bam.files = bamWT, conditions = 'WT'
)
```

exportNetwork *Export network to GML format*

Description

Export a subnetwork pertaining to the given pathway to GML format which can be used in Cytoscape. If no pathway is given, the entire final subnetwork is exported.

Usage

```
exportNetwork(object, node = NULL, file)
```

Arguments

object	Object of class ASpediaFI
node	the name of pathway. If NULL, the entire subnetwork is exported.
file	the file name to export the network

Value

a GML file containing a subnetwork

Examples

```
library(igraph)
fi <- new('ASpediaFI', network = make_empty_graph(n = 0))
exportNetwork(fi, node = NULL, file = 'empty.gml')
```

GSE114922.fpkm *Example gene expression dataset*

Description

A matrix containing gene expression values. We downloaded RNA-Seq reads of 82 MDS patients from GEO database (GSE114922), aligned with STAR, and obtained FPKM values using RSEM.

Usage

```
GSE114922.fpkm
```

Format

An object of class `matrix` with 6275 rows and 40 columns.

References

Pellagatti, A. et al. (2018). Impact of spliceosome mutations on RNA splicing in myelodysplasia: dysregulated genes/pathways and clinical associations. *Blood*, 132.

Examples

```
data(GSE114922.fpkm)
```

`GSE114922.psi` *Example dataset containing PSI values*

Description

A SummarizedExperiment containing PSI values of 5,000 AS events. We downloaded RNA-Seq reads of 82 MDS patients from GEO database (GSE114922), aligned with STAR, and computed PSI values using rMATS. AS events with a lot of missing values or extreme values, or those on genes with low expression were filtered out and 5,000 most variable AS events were selected.

Usage

```
GSE114922.psi
```

Format

An object of class `SummarizedExperiment` with 10000 rows and 40 columns.

References

Pellagatti, A. et al. (2018). Impact of spliceosome mutations on RNA splicing in myelodysplasia: dysregulated genes/pathways and clinical associations. *Blood*, 132.

Examples

```
data(GSE114922.psi)
```

quantifyPSI *AS event quantification*

Description

Compute PSI values of AS events. This function borrows code from the IMAS package.

Usage

```
quantifyPSI(object, read.type = "paired", read.length, insert.size,
    min.reads, num.cores = 1)
```

Arguments

object	Object of class ASpediaFI
read.type	a type of RNA-seq reads ('single' or 'paired')
read.length	read length
insert.size	insert size
min.reads	a minimum number of reads mapped to a given exon
num.cores	the number of cores for parallel processing

Value

ASpediaFI object with PSI values

References

Han, S. et al. (2017). IMAS: Integrative analysis of Multi-omics data for Alternative Splicing. R package version 1.8.0.

Examples

```
bamWT <- system.file('extdata/GSM3167290.subset.bam', package = 'ASpediaFI')
GSE114922.ASpediaFI <- ASpediaFI(
    sample.names = 'GSM3167290',
    bam.files = bamWT, conditions = 'WT'
)
## Not run:
GSE114922.ASpediaFI <- quantifyPSI(GSE114922.ASpediaFI,
    read.type = 'paired',
    read.length = 100, insert.size = 300,
    min.reads = 3, num.cores = 1
)

## End(Not run)
```

samples *ASpediaFI accessors*

Description

ASpediaFI accessors

Usage

```
samples(object, ...)

## S4 method for signature 'ASpediaFI'
samples(object)

samples(object) <- value

## S4 replacement method for signature 'ASpediaFI'
samples(object) <- value

events(object, ...)

## S4 method for signature 'ASpediaFI'
events(object)

events(object) <- value

## S4 replacement method for signature 'ASpediaFI'
events(object) <- value

psi(object, ...)

## S4 method for signature 'ASpediaFI'
psi(object)

psi(object) <- value

## S4 replacement method for signature 'ASpediaFI'
psi(object) <- value

gtf(object, ...)

## S4 method for signature 'ASpediaFI'
gtf(object)

gtf(object) <- value

## S4 replacement method for signature 'ASpediaFI'
```

```
gtf(object) <- value

network(object, ...)

## S4 method for signature 'ASpediaFI'
network(object)

network(object) <- value

## S4 replacement method for signature 'ASpediaFI'
network(object) <- value

gene.table(object, ...)

## S4 method for signature 'ASpediaFI'
gene.table(object)

gene.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
gene.table(object) <- value

as.table(object, ...)

## S4 method for signature 'ASpediaFI'
as.table(object)

as.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
as.table(object) <- value

pathway.table(object, ...)

## S4 method for signature 'ASpediaFI'
pathway.table(object)

pathway.table(object) <- value

## S4 replacement method for signature 'ASpediaFI'
pathway.table(object) <- value
```

Arguments

object	an ASpediaFI object
...	additional arguments to be passed
value	a value to replace. For details, please see help(ASpediaFI).

Value

Slots of the ASpediaFI object

Examples

```
fi <- new('ASpediaFI')

data('GSE114922.psi')
psi(fi) <- GSE114922.psi

psi(fi)
```

`visualize` *AS event and pathway visualization*

Description

Visualize AS event or pathway. If an AS event node is given, the function modified from the `plotTranscripts` function in the `maser` package is used to visualize the event. If a pathway node is given, a subnetwork pertaining to the pathway is visualized.

Usage

```
visualize(object, node, zoom = NULL, n = NULL)
```

Arguments

`object`	Object of class ASpediaFI
`node`	the name of AS event or pathway
`zoom`	a logical to determine if genomic coordinates are zoomed (for AS event visualization)
`n`	the number of genes and AS events to be shown (for pathway visualization)

Value

a plot demonstrating AS event or pathway

References

Veiga, D. (2019). maser: Mapping Alternative Splicing Events to pRoteins. R package version 1.2.0. https://github.com/DiogoVeiga/maser

Examples

```
## Not run:
# Visualize AS event
visualize(GSE114922.ASpediaFI,
    node = as.table(GSE114922.ASpediaFI)$EventID[1],
    zoom = FALSE
)

# Visualize pathway
visualize(GSE114922.ASpediaFI, node = 'HALLMARK_HEME_METABOLISM', n = 10)

## End(Not run)
```

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