Package 'SLAPenrich'

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Type Package

Title Sample-population Level Analysis of Pathway enrichments

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Description SLAPenrich implements a statistical framework to identify pathways that tend to be recurrently genomically altered across a the samples of a genomic dataset. Differently from traditional over-recurrence analyses, SLAPenrich does not require the genes belonging to a given pathway to be statistically enriched among those altered in the individual samples. Consistently with the mutual exclusivity principle, and differently from other proposed computational tools, our approach assumes that the functionality of a given pathway might be altered in an individual sample if at least one of its genes is genomically altered. The method accounts for the differences in the mutation rates between samples and the exonic lengths of the genes in the pathways. It statistically tests against the null hypothesis that no associations between a pathway and the disease population under study does exist, assessing analytically the divergence of the total number of samples with alterations in a given pathway from its expectation. Moreover, the used formalism allows SLAPenrich to perform differential enrichment analysis of pathway alterations across different clinically relevant sub-populations of samples. SLAPenrich also includes function to visualise the identified enriched pathway implementing a heuristic sorting to highlight mutual exclusivity trends among the pattern of alterations of the composing genes.

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Depends HGNChelper, igraph, pheatmap, poibin, stringr, qvalue, biomaRt

R topics documented:

LUAD_CaseStudy	*Genomic event matrix derived from variants found in a cohort of 188 lung adenocarcinoma patients*

Description

A sparse integer matrix where column names are sample identifiers, and the row names official HUGO gene symbols. A non-zero entry in position i, j of this matrix indicates the number of somatic point mutations harbored by the $j-$sample in the $i-$gene. This matrix summarizes the somatic variants of a cohort of 188 lung adenocarcinoma patients of a public available dataset (see source).

Format

A named integer matrix with HUGO official gene symbols as row names and sample identifiers as column names: i.e. format: num [1:356, 1:163] 1 0 0 0 0 0 0 0 0 0 ...

- attr(*, "dimnames")=List of 2

..$: chr [1:356] "ABL1" "ABL2" "ACVR1B" "ACVR1C" ... ..$: chr [1:163] "16770" "16646" "17741" "16915" ...

Source

The dataset from which this matrix was derived has been studied in Ding et al, 2008. The variant annotations used to assemble this matrix are in Supplementary Table 2 of this publication (available at http://genome.wustl.edu/pub/supplemental/tsp_nature_2008/)

References

Ding L, Getz G, Wheeler DA, Mardis ER, McLellan MD, Cibulskis K, et al. Somatic mutations affect key pathways in lung adenocarcinoma. Nature. 2008;455:1069-75.

See Also

LUAD_CaseStudy_updatedGS

LUAD_CaseStudy_updatedGS
Genomic event matrix derived from variants found in a cohort of 188 lung adenocarcinoma patients, with updated gene names.

Description

A sparse integer matrix where column names are sample identifiers, and the row names official HUGO gene symbols. A non-zero entry in position i, j of this matrix indicates the number of somatic point mutations harbored by the $j-$sample in the $i-$gene. This matrix summarizes the somatic variants of a cohort of 188 lung adenocarcinoma patients of a public available dataset (see source). In this matrix the gene names are updated to recent HUGO nomenclatures.

Format

A named integer matrix with HUGO official gene symbols as row names and sample identifiers as column names: i.e. format: num [1:356, 1:163] 1 0 0 0 0 0 0 0 0 0 ...

- attr(*, "dimnames")=List of 2

..$: chr [1:356] "ABL1" "ABL2" "ACVR1B" "ACVR1C" ... ..$: chr [1:163] "16770" "16646" "17741" "16915" ...

Source

The dataset from which this matrix was derived has been studied in Ding et al, 2008. The variant annotations used to assemble this matrix are in Supplementary Table 2 of this publication (available at http://genome.wustl.edu/pub/supplemental/tsp_nature_2008/)

References

Ding L, Getz G, Wheeler DA, Mardis ER, McLellan MD, Cibulskis K, et al. Somatic mutations affect key pathways in lung adenocarcinoma. Nature. 2008;455:1069-75.

See Also

LUAD_CaseStudy

SLAPE.all_genes_exonic_lengths_ensemble
Genome-wide exone attributes and genomic coordinates

Description

A data frame containing attributes and chromosomal coordinate of all the gene exones

Format

A data frame with 553609 rows (one for each exone) and the following columns

ensembl_gene_id String vector containing ensemble gene identifiers;

external_gene_name String vector containing gene names;

exon_chrom_start Numerical vector containing chromosomal start positions;

exon_chrom_end Numerical vector containing chromosomal end positions

Variable name: GEA.

Details

This list has been assembled by using functions from the biomaRt package and can be updated using the SLAPE.update_exon_attributes.

Note

This object is used by the SLAPE.compute_gene_exon_content_block_lengths and SLAPE.gene_ecbl_length function to compute the genome-wide total exonic block lengths or the total exonic block length of a given gene, respectively.

See Also

SLAPE.update_exon_attributes, SLAPE.compute_gene_exon_content_block_lengths SLAPE.gene_ecbl_length

---

SLAPE.check_and_fix_gs_Dataset
                              Check and fix gene symbol names in a genomic event dataset

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Description

This function checks that the row names of a genomic dataset are actually updated official gene symbols approved by the HUGO Gene Nomenclature Committee (HGNC) (http://www.genenames.org).

Usage

```
SLAPE.check_and_fix_gs_Dataset(Dataset, updated.hgnc.table)
```

Arguments

Dataset   An integer matrix modeling a genomic event dataset where row names are gene
                   symbols and column names are sample identifiers. A non-null entry in the i, j
                   position indicates the presence of a somatic mutation hosted by the i-th gene in
                   the j-th sample (if the matrix is binary) or the number of point mutations hosted
                   by the i-th gene in the j-th sample (if the matrix contains integers).

updated.hgnc.table
                   A data frame containing up-to-date approved HGNC symbols (Approved.Symbol
                   variable) and their synonyms (Symbol variable). This is availalbe in the SLAPE.hgnc.table
                   data object or can be created by downloading updated relevant information from
                   the HUGO Gene Nomenclature Committee web-portal (http://www.genenames.org),
                   using the function SLAPE.update_HGNC_Table.

Value

The integer matrix provided in input but with row names updated to the most recent approved gene symbol and rows with not found gene synonyms as names removed.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.update_HGNC_Table, SLAPE.hgnc.table

Examples

```
data(LUAD_CaseStudy)
data(SLAPE.hgnc.table)
updatedGeneSymbolsDataset<-SLAPE.check_and_fix_gs_Dataset(LUAD_CaseStudy,hgnc.table)
```

SLAPE.check_and_fix_path_collection

Check and fix gene symbol names in a collection of pathway gene sets.

Description

This function checks that gene identifiers contained in a pathway gene set collection are actually updated official gene symbols approved by the HUGO Gene Nomenclature Committee (HGNC) (http://www.genenames.org).

Usage

```
SLAPE.check_and_fix_path_collection(pathColl, updated.hgnc.table)
```

Arguments

pathColl   A list containing pathway gene-sets and annotations.

updated.hgnc.table

A data frame containing up-to-date approved HGNC symbols (Approved.Symbol variable) and their synonyms (Symbol variable). This is availalbe in the SLAPE.hgnc.table data object or can be created by downloading updated relevant information from the HUGO Gene Nomenclature Committee web-portal (http://www.genenames.org), using the function SLAPE.update_HGNC_Table.

Value

Pathway collection provided in input but with gene identifiers updated to the most recent approved gene symbols and not approved symbols removed.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.update_HGNC_Table, SLAPE.hgnc.table

Examples

```
data(SLAPE.PATHCOM_HUMAN)
data(SLAPE.hgnc.table)
updatedGeneSymbolsDataset<-
SLAPE.check_and_fix_path_collection(PATHCHOM_HUMAN,hgnc.table)
```

SLAPE.compute_gene_exon_content_block_lengths
Computing genome-wide total exonic block lengths

Usage

```
SLAPE.compute_gene_exon_content_block_lengths(ExonAttributes)
```

Arguments

ExonAttributes   Dataframe containing genomic coordinates of all the exon for all the genes in the
                  genome. This is available in the SLAPE.all_genes_exonic_lengths_ensemble
                  data object.

Value

A genome-wide named vector containing the total exonic block lengths for all the genes. Names of
this vector are offical HUGO gene symbols.

Note

The genome-wide exonic block lengths are precomputed and available in the SLAPE.all_genes_exonic_content_bloc
data object, this function can be used to update this data object with the most-up-to-date information
from Ensemble (using biomaRt functions).

See Also

SLAPE.all_genes_exonic_content_block_lengths_ensemble, SLAPE.all_genes_exonic_lengths_ensemble,
SLAPE.compute_gene_exon_content_block_lengths,

SLAPE.gene_ecbl_length

Computing the total exonic block length of a given gene

Usage

```
SLAPE.gene_ecbl_length(ExonAttributes, GENE)
```

Arguments

ExonAttributes Dataframe containing genomic coordinates of all the exon for all the genes in the genome. This is available in the SLAPE.all_genes_exonic_lengths_ensemble data object.

GENE   A official HUGO gene symbol.

Value

An integer value specifying the total exonic block length of the genes specified in GENE.

Note

All the genome-wide exonic block lengths are precomputed and available in the SLAPE.all_genes_exonic_content_bl data object. This data object can be updated using the SLAPE.update_exon_attributes function.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.all_genes_exonic_lengths_ensemble, SLAPE.all_genes_exonic_content_block_lengths_ensemble

---

SLAPE.hgnc.table   *HUGO gene symbols and their previous synonyms (up to February 2016)*

Usage

```
data("SLAPE.hgnc.table")
```

Format

A data frame with approved HUGO gene symbols in one column Approved.Symbol and their previously approved synonyms Symbol in another column (up to February 2016). Variable Name: hgnc.table.

Note

This object can be updated to a more recent version using the SLAPE.update_HGNC_Table function.

Source

HUGO Gene Nomenclature Committee web-portal (http://www.genenames.org)

See Also

SLAPE.update_HGNC_Table

Examples

```
data(SLAPE.hgnc.table)
## maybe str(SLAPE.hgnc.table_20160210) ; plot(SLAPE.hgnc.table_20160210) ...
```

SLAPE.PATHCOM_HUMAN   *Collection of pahtway gene-sets from Pathway-Commons*

Description

A list containing pathway gene-sets from multiple public resources, downloaded from Pathway-Commons.

Format

A list containing the following items:

PATHWAY A string vector in which the i-th entry contains the Pathway-Commons name of the i-th pathway;

SOURCE A string vector in which the i-th entry contains the Pathway-Commons description of the source of the i-th pathway;

UNIPROTID A list in which the i-th element is a string vector containing the uniprot identifiers of the genes belonging to the i-th pathway;

HGNC_SYMBOL A list in which the i-th element is a string vector containing the official HUGO symbols of the genes belonging to the i-th pathway;

Ngenes An integer vector in which the i-th element is the number of genes belonging to the i-th pathway;

backGround A string vector containing the HUGO symbols of all the genes belonging to at least one pathway

miniSOURCE A string vector in which the i-th entry contains the name of the source of the i-th pathway (panther, humancyc, pid or reactome);

includesTP53 A boolean vector whose i-th is TRUE if the i-th pathway contains TP53.

Please note that the name of this list is PATHCOM_HUMAN.

Source

This list was assembled from the collection of pathway gene sets from the Pathway-Commons data portal (v4-201311) (Cerami et al, 2011) (http://www.pathwaycommons.org/archives/PC2/v4-201311/).

References

Cerami EG, Gross BE, Demir E, Rodchenkov I, Babur O, Anwar N, et al. Pathway Commons, a web resource for biological pathway data. Nucleic Acids Res. 2011;39:D685-90

SLAPE.PATHCOM_HUMAN_nr_i_hu_2014

Collection of pahtway gene-sets from Pathway-Commons (v2014) post-processed for redundancy reduction and to update composing gene name to recent HUGO gene symbols

Description

A list containing pathway gene-sets from multiple public resources, downloaded from Pathway-Commons and post-processed to reduce their overlaps (see details) and update gene names.

Format

A list containing the following items:

PATHWAY A string vector in which the i-th entry contains the Pathway-Commons name, or multiple Pathway-Commons name joined (separated by '//'), for the i-th pathway gene-set (or gene-set resulting from merging multiple pathways, see details);

SOURCE A string vector in which the i-th entry contains the Pathway-Commons description of the source of the i-th pathway, or sources of multiple merged pathways;

UNIPROTID A list in which the i-th element is a string vector containing the uniprot identifiers of the genes belonging to the i-th pathway;

HGNC_SYMBOL A list in which the i-th element is a string vector containing the official HUGO symbols of the genes belonging to the i-th pathway or multiple merged pathways, differently from SLAPE.20140608_PATHCOM_HUMAN_nonredundant_intersection_hugoUpdated in this object these symbols are updated to recent nomenclature;

Ngenes An integer vector in which the i-th element is the number of genes belonging to the i-th pathway;

backGround A string vector containing the HUGO symbols of all the genes belonging to at least one pathway;

miniSOURCE A string vector in which the i-th entry contains the name of the source of the i-th pathway (panther, humancyc, pid or reactome);

includesTP53 A boolean vector whose i-th is TRUE if the i-th pathway contains TP53.

Please note that the name of this list is PATHCOM_HUMAN.

Details

This object was assembled from a collection of pathway gene sets from the Pathway Commons data portal. From this collection gene sets containing less than 4 genes were discarded. Additionally, in order to remove redundancies those gene sets i) corresponding to the same pathway across different resources or ii) with a large overlap (Jaccard index (J) > 0.8, as detailed below) were merged together by intersecting them. The gene sets resulting from these compressions were then added to the collection (with a joint pathway label) and those participating in at least one of these merging were discarded. The final collection resulting from this pre-processing is composed by 1,636 gene sets, for a total amount of 8,056 unique genes included in at least one gene set. Given two gene sets P_1 and P_2 the corresponding $J(P_1, P_2)$ is defined as:

$$J(P_1, P_2) = \frac{|P_1 \cap P_2|}{|P_1 \cup P_2|}$$

.

Additionally, all the pathway gene sets contained in this object are updated to recent official HUGO gene nomenclatures, using the informations contained in the `SLAPE.hgnc.table_20160210` data object (which can be itself updated using the dedicated function `SLAPE.update_HGNC_Table`).

Source

This list was assembled from the collection of pathway gene sets from the Pathway-Commons data portal (v4-201311) (Cerami et al, 2011) (http://www.pathwaycommons.org/archives/PC2/v4/).

References

Cerami EG, Gross BE, Demir E, Rodchenkov I, Babur O, Anwar N, et al. Pathway Commons, a web resource for biological pathway data. Nucleic Acids Res. 2011;39:D685-90

See Also

SLAPE.PATHCOM_HUMAN, SLAPE.update_HGNC_Table

SLAPE.PATHCOM_HUMAN_nr_i_hu_2016

Collection of pahtway gene-sets from Pathway-Commons (v2016) post-processed for redundancy reduction and to update composing gene name to recent HUGO gene symbols

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Description

A list containing pathway gene-sets from multiple public resources, downloaded from Pathway-Commons and post-processed to reduce their overlaps (see details) and update gene names.

Format

A list containing the following items:

PATHWAY A string vector in which the i-th entry contains the Pathway-Commons name, or multiple Pathway-Commons name joined (separated by '//'), for the i-th pathway gene-set (or gene-set resulting from merging multiple pathways, see details);

SOURCE A string vector in which the i-th entry contains the Pathway-Commons description of the source of the i-th pathway, or sources of multiple merged pathways;

UNIPROTID A list in which the i-th element is a string vector containing the uniprot identifiers of the genes belonging to the i-th pathway;

HGNC_SYMBOL A list in which the i-th element is a string vector containing the official HUGO symbols of the genes belonging to the i-th pathway or multiple merged pathways, differently from `SLAPE.20140608_PATHCOM_HUMAN_nonredundant_intersection_hugoUpdated` in this object these symbols are updated to recent nomenclature;

Ngenes An integer vector in which the i-th element is the number of genes belonging to the i-th pathway;

backGround A string vector containing the HUGO symbols of all the genes belonging to at least one pathway;

miniSOURCE A string vector in which the i-th entry contains the name of the source of the i-th pathway (panther, humancyc, pid or reactome);

includesTP53 A boolean vector whose i-th is TRUE if the i-th pathway contains TP53.

Please note that the name of this list is PATHCOM_HUMAN.

Details

This object was assembled from a collection of pathway gene sets from the Pathway Commons data portal. From this collection gene sets containing less than 4 genes were discarded. Additionally, in order to remove redundancies those gene sets i) corresponding to the same pathway across different resources or ii) with a large overlap (Jaccard index (J) > 0.8, as detailed below) were merged together by intersecting them. The gene sets resulting from these compressions were then added to the collection (with a joint pathway label) and those participating in at least one of these merging were discarded. The final collection resulting from this pre-processing is composed by 1,636 gene sets, for a total amount of 8,056 unique genes included in at least one gene set. Given two gene sets P_1 and P_2 the corresponding $J(P_1, P_2)$ is defined as:

$$J(P_1, P_2) = \frac{|P_1 \cap P_2|}{|P_1 \cup P_2|}$$

.

Additionally, all the pathway gene sets contained in this object are updated to recent official HUGO gene nomenclatures, using the informations contained in the SLAPE.hgnc.table_20160210 data object (which can be itself updated using the dedicated function SLAPE.update_HGNC_Table).

Source

This list was assembled from the collection of pathway gene sets from the Pathway-Commons data portal (v4-201311) (Cerami et al, 2011) (http://www.pathwaycommons.org/archives/PC2/v8/).

References

Cerami EG, Gross BE, Demir E, Rodchenkov I, Babur O, Anwar N, et al. Pathway Commons, a web resource for biological pathway data. Nucleic Acids Res. 2011;39:D685-90

See Also

SLAPE.20140608_PATHCOM_HUMAN, SLAPE.update_HGNC_Table

SLAPE.pathvis   *Generatig a heatmap of the alteration matrix of a SLAPenriched pathway and barplots with statistical scores*

Description

This function generates a pdf file containing a heatmap of the alteration matrix of a SLAPenriched pathway across the samples of the analysed dataset, after permuting rows and columns to highlight trend of mutual exclusivity in the alteration-patterns.

Additionally, it generates, a pdf file with three barplots indicating, respectively: (i) the number of mutated genes across samples; (ii) the probabilities of the pathway under consideration to be altered across samples, together with the expected number of samples with alteration in the pathway under consideration; (iii) The observed pathway alteration status across samples, together with the observed total number of samples with alteration in the pathway under consideration.

Usage

```
SLAPE.pathvis(EM, PFP, Id, i = NULL, PATH = "./", PATH_COLLECTION)
```

Arguments

EM   A sparse binary matrix, or a sparse matrix with integer non-null entries. In this matrix the column names are sample identifiers, and the row names official HUGO gene symbols. A non-zero entry in position i, j of this matrix indicates the presence of a somatic mutations harbored by the $j-$sample in the $i-$gene. This matrix must be the same that has been inputted to the SLAPE.analyse function to produce the results in the PFP list.

PFP   A list containing the SLAPenrich analysis results outputted by the SLAPE.analyse function while analysing the genomic dataset summarised by the EM genomic event matrix.

Id   The index of the pathway for which the pdf files should be produced in the vectors/lists of the pathway collection set specified in PATH_COLLECTION

prefName   A string containing the prefix that should be added to the pdf file name.

PATH   String specifiying the path of the pdf file to be created (including its name).

PATH_COLLECTION
                The pathway collection that has been tested against the EM dataset with the SLAPE.analyse function to produce the PFP list of results.

Note

This function makes use of the SLAPE.heuristic_mut_ex_sorting function to realise the mutual exclusivity sorting of the pathway alteration matrix, and it is iteratively used by SLAPE.serialPathVis to generate pdf files with heatmaps and barplots for all the SLAPenriched pathways found in a list of results generated by SLAPE.analyse.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.analyse, SLAPE.serialPathVis

Examples

```
#Loading the Genomic Event data object derived from variants annotations
#identified in 188 Lung Adenocarcinoma patients (Ding et al, 2008)
data(LUAD_CaseStudy_updatedGS)

#Loading KEGG pathway gene-set collection data object
data(SLAPE.MSigDB_KEGG_hugoUpdated)

#Loading genome-wide total exonic block lengths
data(SLAPE.all_genes_exonic_content_block_lengths_ensemble)

#Running SLAPenrich analysis
PFPw<-SLAPE.analyse(EM = LUAD_CaseStudy_ugs,
                PATH_COLLECTION = KEGG_PATH,
                BACKGROUNDpopulation = rownames(LUAD_CaseStudy_ugs),
                GeneLenghts = GECOBLenghts)

#Generating a pdf file containing a heatmap of the mutual-exclusivity
#sorted pathway alteration matrix, for an SLAPenriched pathway with
#an exclusive coverage > 80%, and barplots with statistical scores.
#The pdf is saved in a file with \code{Example_} as prefix in its name,
#in the current working directory.
SLAPE.pathvis(EM = LUAD_CaseStudy_ugs,PFP = PFPw,
    Id = PFPw$pathway_id[which(PFPw$pathway_exclusiveCoverage>80)[1]],
    prefName = 'Example_',
    PATH = './',PATH_COLLECTION = KEGG_PATH)
```

SLAPE.readDataset   *Reading genomic evant dataset*

Description

This function reads a genomic dataset from a csv file and it stores it into an integer matrix. Row names of this matrix are official gene symbols and column names are sample identifiers. A non-zero entry in the i, j position indicates the presence of somatic mutation hosted by the i-th gene in the j-th sample (if the matrix is binary) or the number of point mutations hosted by the i-th gene in the j-th sample (if the matrix contains integers).

Usage

```
SLAPE.readDataset(filename)
```

Arguments

filename   The path of the csv file to be read and stored in the genomic event matrix.

Value

An integer matrix modeling a genomic event dataset. Row names of this matrix are official gene symbols and column names are sample identifiers. A non-zero entry in the i, j position indicates the presence of a somatic mutation hosted by the i-th gene in the j-th sample (if the matrix is binary) or the number of point mutations hosted by the i-th gene in the j-th sample (if the matrix contains integers).

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

SLAPE.serialPathVis	*Systematic generation of heatmaps of the alteration matrices for SLAPenriched pathways and barplots with statistical scores*

Description

This function generates pdf files containing heatmaps of the alteration matrices for SLAPenriched pathways (with user-defined enrichment FDR and exclusive coverage) across the samples of the analysed dataset, after permuting rows and columns to highlight trend of mutual exclusivity in the alteration-patterns.

Additionally, it generates, a pdf files with three barplots indicating, for each pathway, respectively: (i) the number of mutated genes across samples; (ii) the probabilities of the pathway under consideration to be altered across samples, together with the expected number of samples with alteration in the pathway under consideration; (iii) The observed pathway alteration status across samples, together with the observed total number of samples with alteration in the pathway under consideration.

Usage

```
SLAPE.serialPathVis(EM, PFP, fdrth = 5, exCovTh = 50, PATH = "./", PATH_COLLECTION)
```

Arguments

EM	A sparse binary matrix, or a sparse matrix with integer non-null entries. In this matrix the column names are sample identifiers, and the row names official HUGO gene symbols. A non-zero entry in position i, j of this matrix indicates the presence of a somatic mutations harbored by the $j-$sample in the $i-$gene. This matrix must be the same that has been inputted to the SLAPE.analyse function to produce the results in the PFP list.
PFP	A list containing the SLAPenrich analysis results outputted by the SLAPE.analyse function while analysing the genomic dataset summarised by the EM genomic event matrix.
fdrth	The false discovery rate threshold that should be used to select SLAPenriched pathways from the PFP list (percentage). By default in the PFP with an FDR < 5% are selected.
exCovTh	The mutual exclusivity coverage threshold that should be used to select SLAPenriched pathways from the PFP list (percentage). By default in the PFP with an exclusive coverage > 50% are selected.
PATH	String specifiying the path of the directory where the pdf file shoud be created.
PATH_COLLECTION	The pathway collection that has been tested against the EM dataset with the SLAPE.analyse function to produce the PFP list of results.

Note

This function calls iteratively the SLAPE.pathvis function.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.analyse, SLAPE.pathvis

Examples

```
#Loading the Genomic Event data object derived from variants annotations
#identified in 188 Lung Adenocarcinoma patients (Ding et al, 2008)
data(LUAD_CaseStudy_updatedGS)

#Loading KEGG pathway gene-set collection data object
data(SLAPE.MSigDB_KEGG_hugoUpdated)

#Loading genome-wide total exonic block lengths
data(SLAPE.all_genes_exonic_content_block_lengths_ensemble)

#Running SLAPenrich analysis
PFPw<-SLAPE.analyse(EM = LUAD_CaseStudy_ugs,
                    PATH_COLLECTION = KEGG_PATH,
                    BACKGROUNDpopulation = rownames(LUAD_CaseStudy_ugs),
                    GeneLenghts = GECOBLenghts)

#Generating pdf files containing heatmaps of the mutual-exclusivity
#sorted pathway alteration matrices, for an SLAPenriched pathway with
#an exclusive coverage > 80%, and barplots with statistical scores.
#The pdf files are saved in the current working directory.
SLAPE.serialPathVis(EM = LUAD_CaseStudy_ugs,PFP = PFPw,
                    exCovTh = 80,fdrth = 5,
                    PATH = './',PATH_COLLECTION = KEGG_PATH)
```

SLAPE.update_exon_attributes

Creating an updated gene exon attributes data object

Usage

```
SLAPE.update_exon_attributes()
```

Value

A dataframe containing updated genomic coordinates of all the exon for all the genes in the genome, from Ensemble.

Note

A dataframe containing genomic coordinates of all the exon for all the genes in the genome, from Ensemble is precomputed and available in the SLAPE.all_genes_exonic_lengths_ensemble data object.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.all_genes_exonic_content_block_lengths_ensemble, SLAPE.all_genes_exonic_lengths_ensemble,
SLAPE.compute_gene_exon_content_block_lengths, SLAPE.gene_ecbl_length

---

SLAPE.update_HGNC_Table

Updating the R data object containing a HUGO approved catalogue
of gene symbols and synomyms

Description

This function creates a data frame containing up-to-date HUGO Gene Nomenclature Committee
(HGNC) approved symbols and their synonyms downloading updated relevant information from the
HUGO Gene Nomenclature Committee web-portal (http://www.genenames.org). This table is
used by the SLAPE.check_and_fix_gs_Dataset and SLAPE.check_and_fix_path_collection
functions to check and update the gene symbol identifiers of a integer genomic event matrix. A
precomputed data frame (created on February 2016) is available in the SLAPE.hgnc.table data
object.

Usage

```
SLAPE.update_HGNC_Table()
```

Value

A data frame with updated approved HUGO gene symbols in one column and their previously
approved synonyms in another column.

Author(s)

Francesco Iorio - iorio@ebi.ac.uk

See Also

SLAPE.hgnc.table

SLAPE.check_and_fix_path_collection

SLAPE.check_and_fix_gs_Dataset

SLAPE.write.table   *Writing SLAPenrich results in a csv file*

Description

This function takes in input a list of results outputted by the [SLAPE.analyse](), selects enriched pathways according to user-defined significance and mutual exclusivity coverage thresholds and creates an easy to explore csv file with selected enriched pathways.

Usage

```
SLAPE.write.table(PFP,
                  EM,
                  filename = "",
                  fdrth = Inf,
                  exclcovth = 0,
                  PATH_COLLECTION,
                  GeneLenghts)
```

Arguments

PFP	A list containing the SLAPenrich analysis results outputted by the [SLAPE.analyse]() function while analysing the genomic dataset summarised by the EM genomic event matrix.
EM	A sparse binary matrix, or a sparse matrix with integer non-null entries. In this matrix the column names are sample identifiers, and the row names official HUGO gene symbols. A non-zero entry in position i, j of this matrix indicates the presence of a somatic mutations harbored by the $j-$sample in the $i-$gene. This matrix must be the same that has been inputted to the [SLAPE.analyse]() function to produce the results in the PFP list.
filename	String specifiying the path of the csv file to be created (including its name).
fdrth	The false discovery rate threshold that should be used to select SLAPenriched pathways from the PFP list (percentage). By default all the pathway included in the PFP list are selected.
exclcovth	The mutual exclusivity coverage threshold that should be used to select SLAPenriched pathways from the PFP list (percentage). By default all the pathway included in the PFP list are selected.
PATH_COLLECTION	
	The pathway collection that has been tested against the EM dataset with the [SLAPE.analyse]() function to produce the PFP list of results.
GeneLenghts	The named vector containing the genome-wide total exonic block lengths that has been used by the [SLAPE.analyse]() function to produce the PFP list of results.

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See Also

[SLAPE.analyse]()

Examples

```
#Loading the Genomic Event data object derived from variants annotations
#identified in 188 Lung Adenocarcinoma patients (Ding et al, 2008)
data(LUAD_CaseStudy_updatedGS)

#Loading KEGG pathway gene-set collection data object
data(SLAPE.MSigDB_KEGG_hugoUpdated)

#Loading genome-wide total exonic block lengths
data(SLAPE.all_genes_exonic_content_block_lengths_ensemble)

#Running SLAPenrich analysis
PFPw<-SLAPE.analyse(EM = LUAD_CaseStudy_ugs,
              PATH_COLLECTION = KEGG_PATH,
              BACKGROUNDpopulation = rownames(LUAD_CaseStudy_ugs),
              GeneLenghts = GECOBLenghts)

#Selecting pathway enriched at a 5% FDR,
#that have a 50% mutual exclusivity coverage and writing them
#in a csv file
SLAPE.write.table(PFP = PFPw,
                  EM = LUAD_CaseStudy_ugs,
                  filename = "./LungDS_KEGG_enrichments.csv",
                  fdrth=5, exclcovth = 50, PATH_COLLECTION = KEGG_PATH,
                  GeneLenghts = GECOBLenghts)
```

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