

Package ‘PATHChange’

June 17, 2016

Type Package

Title A Tool for Identification of Differentially Expressed Pathways
using Multi-Statistic Comparison

Version 1.0

Date 2016-05-18

Author Fontoura, C.A.R.S. and Mombach, J.C.M.

Maintainer Carla Fontoura <carladriani@yahoo.com.br>

Description

An R tool suited to Affymetrix microarray data that combines three different statistical tests (Bootstrap, Fisher exact and Wilcoxon signed rank) to evaluate genetic pathway alterations.

Imports stringr, rlist, VennDiagram, grDevices, stats, utils, grid

LazyData true

License GPL-2

NeedsCompilation no

Repository CRAN

Date/Publication 2016-06-17 08:18:35

R topics documented:

PATHChange-package	2
PATHChange	3
PATHChangeDat	4
PATHChangeList	5
PATHChangeVenn	6

Index	8
--------------	----------

PATHChange-package	<i>A Tool for Identification of Differentially Expressed Pathways using Multi-Statistic Comparison</i>
--------------------	--

Description

An R tool suited to Affymetrix microarray data that combines three different statistical tests (Bootstrap, Fisher exact and Wilcoxon signed rank) to evaluate genetic pathway alterations.

Details

The DESCRIPTION file:

```

Package:      PATHChange
Type:         Package
Title:        A Tool for Identification of Differentially Expressed Pathways using Multi-Statistic Comparison
Version:      1.0
Date:         2016-05-18
Author:       Fontoura, C.A.R.S. and Mombach, J.C.M.
Maintainer:   Carla Fontoura <carladriani@yahoo.com.br>
Description:  An R tool suited to Affymetrix microarray data that combines three different statistical tests (Bootstrap, Fisher
Imports:      stringr, rlist, VennDiagram, grDevices, stats, utils, grid
LazyData:    true
License:      GPL-2

```

Index of help topics:

PATHChange	Determination of differentially expressed pathways using multi-statistic comparison
PATHChange-package	A Tool for Identification of Differentially Expressed Pathways using Multi-Statistic Comparison
PATHChangeDat	PATHChangeDat
PATHChangeList	PATHChangeList
PATHChangeVenn	PATHChangeVenn

PATHChange is a multi-statistic approach designed to improve the detection of differentially expressed pathways in transcriptomic studies. The script was designed to perform the analysis over experimental data that include control samples.

The program uses four functions. The first is the data pre-processing called PATHChangeDat, which comprises the download of Matrix Series Files from GEO, average over the expression values of repeated genes and histology combinations steps. The next process is PATHChangeList, which is basically the selection of the pathways. After this, PATHChange performs the main function in the PATHChange package. The PATHChange function perform the statistical analysis, which involves calculating pathway activity, application of the bootstrap, Wilcoxon and Fisher tests, and determination of the false discovery rate (FDR) correction. Finally, the last function PATHChangeVenn

generates the presentation of the results in the form of a Venn diagram of the differentially expressed pathways consensus.

The program uses two input files: 'Genes', all genes present in the database where the pathways were obtained and 'filePathway' with the pathways to be evaluated.

Author(s)

Fontoura, C.A.R.S. and Mombach, J.C.M.

Maintainer: Carla Fontoura <carladriani@yahoo.com.br>

References

Efron, B.(1979) Bootstrap methods: another look at the jackknife. *The Annals of Statistics* **7**.

Wilcoxon, F. (1945) Individual comparisons by ranking methods. *Biometrics bulletin* **1(6)**, 80–83.

Fisher, R.A. (1934) Statistical methods for research workers. In: Crew, F.A.E., Cutler, D.W. (eds.) *Biological Monographs and Manuals*. Oliver And Boyd Tweeddale Court ; Edinburgh ; Paternoster Row ; London

Benjamini, Y. and Hochberg, Y. (1995) Controlling the false discovery rate: a practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society, Series B (Methodological)* **57(1)**, 289–300

PATHChange	<i>Determination of differentially expressed pathways using multi-statistic comparison</i>
------------	--

Description

This is the main function of the PATHChange package. It applies to each histological comparison selected that the three non-parametric tests (Bootstrap, Fisher's exact and Wilcoxon signed-rank).

Usage

```
PATHChange(path, MeanData, writeCSV, writeRDS, destDIR)
```

Arguments

path	List of pathways previously generated by the function PATHChangeList.
MeanData	List of the results of the histological comparisons chosen by the user (It can be calculated by the function PATHChangeDat).
writeCSV	TRUE for write a .csv file result
writeRDS	TRUE for write a .rds file result
destDIR	Destination folder for .csv and .rds files.

Details

The approach is a multiple comparison experiment since it involves several pathways, then PATHChange corrects the false discovery rate (FDR) based on Benjamini-Hochberg algorithm.

Value

p.value Results

Author(s)

Carla A. R. S. Fontoura

See Also

[PATHChangeList](#), [PATHChangeDat](#)

Examples

```
require(rlist)
path<-list.load(system.file("extdata", "path.rds", package = "PATHChange"))[c(1:10)]
MeanData<-list.load(system.file("extdata", "MeanData.rds", package = "PATHChange"))

## Not run: PATHChange(path=path, MeanData=MeanData, writeCSV=FALSE, writeRDS=FALSE)
## Not run: p.value <- list.load(file.path(tempdir(), "pValue.rds"))
```

PATHChangeDat

PATHChangeDat

Description

PATHChangeDat is the first step of the PATChange package. This function performs a array information step. For this, PATHChangeDat download the Matrix Series Files from GEO database.

Usage

```
PATHChangeDat(eDat, DataSet, NumbSample, Genes, HistComp, hc, writeRDS, destDIR)
```

Arguments

eDat	Input dataset file name (tab delimited (*.csv) format) containing the expression data for the probes and symbols from the samples.
DataSet	GEO dataset series (e.g. 'GSE4186').
NumbSample	Number of samples in dataset.
Genes	Genes file.
HistComp	TRUE for more than one histological comparison. You may want to set this to FALSE if you already know which histological comparison you wish to do.

hc	Is a character string required if histComparison argument is set to FALSE defining the specific histological comparison (e.g. hc=c('colon normal', 'colon adenoma')).
writeRDS	TRUE for write a .rds file result.
destDIR	Destination folder for .rds file.

Details

In the case of repeated genes in the array, the PATHChangeDat performs an average over their expression values. This ensures that the probability of choosing each gene in the Bootstrap is the same. Many GEO series contains more than a single combination of tissues to be studied, using PATHChangeDat, the user will be prompted to choose different histological comparisons in the study.

Value

MeanData Tables with all histological comparisons.

Author(s)

Carla A. R. S. Fontoura

References

<http://www.ncbi.nlm.nih.gov/geo>

Examples

```
# For Ontocancro pathways, you can download a file with all genes from
# http://ontocancro.inf.ufsm.br/download/genes_ontocancro.zip

require(rlist)
eDat<-system.file("extdata", "eDat.csv", package = "PATHChange")
genes<-system.file("extdata", "genes.txt", package="PATHChange")

## Not run: PATHChangeDat(eDat=eDat, DataSet="GSE35972", NumbSample=6, Genes=genes,
                        HistComp=FALSE, hc=c("untreated", "treated with"), writeRDS=FALSE)
## End(Not run)
## Not run: MeanData <- list.load(file.path(tempdir(),"MeanData.rds"))
```

PATHChangeList

PATHChangeList

Description

This function reads the file 'filePath.txt' to organize the pathways separately in lists.

Usage

```
PATHChangeList(filePath, writeRDS, destDIR)
```

Arguments

filePath	The 'filePath.txt' file.
writeRDS	TRUE for write a .rds file result
destDIR	Destination folder for .rds file.

Value

path An object of class "list" is returned and saved in "rds" format.

Author(s)

Carla A. R. S. Fontoura

Examples

```
# For Ontocancro pathways, you can download a file with all pathways from
# http://ontocancro.inf.ufsm.br/download/BigPathways.zip

filePath<-system.file("extdata", "BigPathways.txt", package = "PATHChange")

PATHChangeList(filePath = filePath, writeRDS = FALSE)
require(rlist)
path <- list.load(file.path(tempdir(),"path.rds"))
```

PATHChangeVenn

PATHChangeVenn

Description

The results of PATHChange are presented through Venn diagrams that provide the consensus of differentially expressed pathways using the statistical tests for the chosen significance level.

Usage

```
PATHChangeVenn(p.value, p, writePDF, destDIR)
```

Arguments

p.value	The result of the PATChange function.
p	Significance level
writePDF	TRUE for write a .pdf file result
destDIR	Destination folder for .pdf file.

Value

VennDiagram A venn diagram with the consensus of the statistical tests.

Author(s)

Carla A. R. S. Fontoura

See Also

[PATHChange](#)

Examples

```
pval <- list(data.frame(Pathway=paste("Path", 1:10, sep="_"),
  Activity=c(0.50478,0.5019,0.49059,0.49056,0.48591,0.49457,
    0.49228,0.49628,0.48908,0.48698),
  Bootstrap=c(0.06911578,0.11415555,0.98059024,0.30543333,
    0.02051875,0.00098,0.12326666,0.578624,0.01206153,
    0.86294),
  Fisher=c(0.32619656,0.00310826,0.26249225,0.26389102,0.00060358,
    0.00015427,0.01796717,0.00069173,8.22E-06,0.00310826),
  Wilcoxon=c(0.11862404,0.00502450,0.00543268,1.32E-10,0.22675787,
    8.45E-06,0.46767425,4.51E-17,9.11E-08,0.00467674)))
PATHChangeVenn(p.value=pval, p=0.05, writePDF=FALSE)
```

Index

*Topic **package**

PATHChange-package, 2

PATHChange, 3, 7

PATHChange-package, 2

PATHChangeDat, 4, 4

PATHChangeList, 4, 5

PATHChangeVenn, 6