Package ‘MethylMix’

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Type Package
Title MethylMix: Identifying methylation driven cancer genes.
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Description MethylMix is an algorithm implemented to identify hyper and hypomethylated genes for a disease. MethylMix is based on a beta mixture model to identify methylation states and compares them with the normal DNA methylation state. MethylMix uses a novel statistic, the Differential Methylation value or DM-value defined as the difference of a methylation state with the normal methylation state. Finally, matched gene expression data is used to identify, besides differential, functional methylation states by focusing on methylation changes that effect gene expression.
License GPL-2
LazyLoad yes
Depends R (>= 3.1.1)
Imports foreach, parallel, doParallel, RColorBrewer, optimx, RPMM
biocViews
  DNA Methylation, Statistical Method, Differential Methylation, Gene Regulation, Gene Expression, Methylation Array, Differential Expression, Pathways, Network
Suggests BiocStyle
NeedsCompilation no

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**MAcancer_CDH1**

**Description**

Cancer Gene expression data for the gene CDH1 of breast cancer patients from the TCGA project.

**Usage**

MAcancer_CDH1

**Format**

This describes the format of MAcancer.

**Source**

This gives the source of MAcancer
**References**


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**METcancer**

*DNA methylation data from cancer tissue from glioblastoma patients from the TCGA project.*

**Description**

Cancer Gene expression data of glioblastoma patients from the TCGA project. A set of 14 genes that have been shown in the literature to be involved in differential methylation in glioblastoma were selected as an example to try out MethylMix.

**Usage**

METcancer

**Format**

This describes the format of METcancer.

**Source**

This gives the source of METcancer

**References**


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**METcancer_CDH1**

*DNA methylation data for CDH1 from the breast cancer TCGA project.*

**Description**

Raw DNA methylation data for CDH1 from the 450k Infinium platform from breast cancer patients from the TCGA project.

**Usage**

METcancer_CDH1
MethylMix

Format
This describes the format of METcancer.

Source
This gives the source of METcancer.

References

MethylMix

Mixture model for DNA methylation data in cancer.

Description
MethylMix identifies DNA methylation driven genes by modeling DNA methylation data in cancer vs. normal and looking for homogeneous subpopulations. In addition matched gene expression data (e.g. from microarray technology or RNA sequencing) is used to identify functional DNA methylation events by requiring a negative correlation between methylation and gene expression of a particular gene.

Usage
MethylMix(METcancer,METnormal,MAcancer,OutputRoot,Parallel)

Arguments
- METcancer: This a matrix with the methylation data of cancer tissue with genes in rows and samples in columns.
- METnormal: This is a matrix with the normal methylation data of the same genes as in METcancer. Again genes in rows and samples in columns. The samples do not have to match with the cancer data.
- MAcancer: This is the matched gene expression data for the same samples as in METcancer.
- OutputRoot: Path to store the MethylMix results object.
- Parallel: If true MethylMix will be run using parallel processing.

Value
MethylMixResults is a list with the following components:

- MethylationStates: Matrix with for all genes the Methylation states using DM-value (i.e. Differential methylation values) that are defined as the methylation value with respect to the average normal methylation for a gene.
- NrComponents: The number of methylation states for each gene.
- Models: Beta mixture model parameters for each gene.
MethylationDrivers
Genes identified as functional and differential by MethylMix.

MixtureStates
A list with the DM-values for each gene that is functional and differential.

Examples

```r
# load the three data sets needed for MethylMix
data(METcancer)
data(METnormal)
data(MAcancer)

# run methylmix on a small set of example data
MethylMixResults=MethylMix(METcancer,METnormal,MAcancer)

# try the parallel toolbox to speed up MethylMix modeling
MethylMixResults=MethylMix(METcancer,METnormal,MAcancer,Parallel=TRUE)
```

MethylMix_PlotModel
Plotting a mixture model for a gene.

Description

MethylMix identifies DNA methylation driven genes by modeling DNA methylation data in cancer vs. normal and looking for homogeneous subpopulations. In addition matched gene expression data (e.g. from microarray technology or RNA sequencing) is used to identify functional DNA methylation events by requiring a negative correlation between methylation and gene expression of a particular gene.

Usage

```r
MethylMix_PlotModel(GeneName,METdata,MixtureModelResults,MAdata=0,
METnormal=0,FileName="")
```

Arguments

- **GeneName**: Name of the gene for which to create a MethylMix plot.
- **METdata**: This a matrix with the methylation data of cancer tissue with genes in rows and samples in columns.
- **MixtureModelResults**: The results object from a MethylMix run.
- **METnormal**: This is a matrix with the normal methylation data of the same genes as in METcancer. Again genes in rows and samples in columns. The samples do not have to match with the cancer data.
- **MAdata**: This is the matched gene expression data for the same samples as in METcancer.
- **FileName**: Filename to export the figure. If empty figure is shown in console.
Examples

# load the three data sets needed for MethylMix
data(METcancer)
data(METnormal)
data(MAcancer)

# run methylmix on a small set of example data
MethylMixResults=MethylMix(METcancer,METnormal,MAcancer)

# Plot the most famous methylated gene for glioblastoma
MethylMix_PlotModel('MGMT',METcancer,MethylMixResults)

# plot MGMT also with its normal methylation variation
MethylMix_PlotModel('MGMT',METcancer,MethylMixResults,MAdata=0,METnormal)

# plot a MethylMix model for another gene
MethylMix_PlotModel('ZNF217',METcancer,MethylMixResults,MAdata=0,METnormal)

# also plot the inverse correlation with gene expression
# this creates two separate plots
MethylMix_PlotModel('MGMT',METcancer,MethylMixResults,MAdata=MAcancer)

# plot all functional and differential genes
for (i in 1:length(MethylMixResults$MethylationDrivers)) {
  MethylMix_PlotModel(MethylMixResults$MethylationDrivers[i],METcancer,
                      MethylMixResults,MAdata=0,METnormal)
}

METnormal

DNA methylation data from normal tissue from glioblastoma patients.

Description

Normal tissue DNA methylation data of glioblastoma patients. These normal tissue samples were run on the same platform and are described in the publication referenced below.

Usage

METnormal

Format

This describes the format of METnormal.

Source

This gives the source of METnormal
References


METnormal_CDH1

DNA methylation data for CDH1 from the breast cancer TCGA project.

Description

Raw DNA methylation data for CDH1 from the 450k Infinium platform from breast cancer patients from the TCGA project.

Usage

METnormal_CDH1

Format

This describes the format of METcancer.

Source

This gives the source of METcancer

References


Also see TCGA: The Cancer Genome Atlas: http://cancergenome.nih.gov/
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