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

Cancer Gene expression data of 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
MAcancer

Format
This describes the format of MAcancer.

Source
This gives the source of MAcancer

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

MAcancer_CDH1

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

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


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


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.
MethylMix_PlotModel

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

```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)

# 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.
METnormal_CDH1

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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