

Package ‘COPDSexualDimorphism’

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Type Package

Title Sexual dimorphic and COPD differential analysis for gene expression and methylation.

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Description Sexual dimorphic and COPD differential (SDCD) analysis contrasts regression coefficients from two stratified analysis. Stratification can be done in two ways: by COPD status or by sex. For COPD-stratified analysis, SDCD analysis contrasts sexual dimorphism between cases and controls, while sex-stratified SDCD analysis contrasts COPD differential expression pattern between males and females. The package is meant to be used in conjunction with the package limma.

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LazyLoad yes

Depends COPDSexualDimorphism.data, NCBI2R, RColorBrewer, beeswarm, limma, GenomicRanges, gplots, gtools

biocViews Software, AssayDomain, Microarray, GeneExpression, DNAMethylation, DifferentialExpression

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COPDSexualDimorphism-package

Sexual Dimorphic and COPD Differential Analysis

Description

Sexual dimorphic and COPD differential (SDCD) analysis contrasts regression coefficients from two stratified analysis. Stratification can be done in two ways: by COPD status or by sex. For COPD-stratified analysis, SDCD analysis contrasts sexual dimorphism between cases and controls, while sex-stratified SDCD analysis contrasts COPD differential expression pattern between males and females. The package is meant to be used in conjunction with the package limma.

Details

Package: COPDSexualDimorphism
Type: Package
Version: 1.0
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License: LGPL-2.1

Data and main methods to accompany "Integrative Genomics of Sexual Dimorphism in COPD." The main functions are `sdcd`, which contrasts regression coefficients from sex-stratified and COPD-stratified analyses.

Author(s)

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References

Sathirapongsasuti JF, Glass K, Huttenhower C, Quackenbush J, DeMeo DL. Integrative Genomics of Sexual Dimorphism in COPD. (In Prep).

www.lung-genomics.org

Examples

```
data(lgrc.expr.meta)
data(lgrc.expr)
data(lgrc.genes)

library(limma)

## Sex-stratified
design.mtx = cbind(ctrl=1,
```

```

copd=as.integer(grepl("COPD",colnames(expr))),
age=expr.meta$age,
pkyr=expr.meta$pkyrs)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & (expr.meta$gender == "1-Male")
male.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
male.fit = eBayes(male.fit)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & (expr.meta$gender == "2-Female")
female.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
female.fit = eBayes(female.fit)

male.female.copd.beta.diff.genes = sdcd(male.fit, female.fit, "copd", lgrc.genes, fdr.cutoff=0.25, file.prefix="n

## COPD-stratified
design.mtx = cbind(ctrl=1,
gender=expr.meta$gender,
age=expr.meta$age,
pkyr=expr.meta$pkyrs)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & grepl("COPD",colnames(expr))
copd.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
copd.fit = eBayes(copd.fit)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & grepl("CTRL",colnames(expr))
ctrl.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
ctrl.fit = eBayes(ctrl.fit)

copd.ctrl.gender.beta.diff.genes = sdcd(copd.fit, ctrl.fit, "gender", lgrc.genes, fdr.cutoff=0.25, file.prefix="n

## Combine
sdcd.genes = merge(copd.ctrl.gender.beta.diff.genes, male.female.copd.beta.diff.genes, by=setdiff(intersect(names(male.female.copd.beta.diff.genes),names(male.female.copd.beta.diff.genes))))
sdcd.genes = unique(sdcd.genes)
print(paste("There are", nrow(sdcd.genes),"SDCD genes"))

```

do.sdcd.boxplot

Represent sexual dimorphic data as boxplots.

Description

Stratify and plot data by gender and by disease status.

Usage

```
do.sdcd.boxplot(marker, data, copd.bool, male.bool, symbol = marker, filename = paste(marker, ".pdf", sep = ""))
```

Arguments

marker Character string representing the name of the marker (e.g. Ensembl gene, VMR) to plot.

data	Data to be plot. E.g. gene expression or percent methylation.
copd.bool	Boolean array corresponding to the COPD subject columns of data.
male.bool	Boolean array corresponding to the male subject columns of data.
symbol	Gene symbol associated with the marker.
filename	File name. If NA, display plot on screen.
take.log	Boolean. If true, plot in log scale.

Author(s)

J Fah Sathirapongsausti

References

Sathirapongsausti JF, Glass K, Huttenhower C, Quackenbush J, DeMeo DL. Integrative Genomics of Sexual Dimorphism in COPD. (In Prep).

Examples

```
data(lgrc.sdcd.genes)
data(lgrc.expr.meta)
data(lgrc.expr)
copd.bool = (expr.meta$diagmaj == "2-COPD/Emphysema")
male.bool = (expr.meta$gender == "1-Male")
do.sdcd.boxplot("ENSG00000182472", expr, copd.bool, male.bool, symbol="CAPN12", filename=NA)
```

lgrc.sdcd.genes *Sexual dimorphic and COPD differential genes*

Description

A list of 959 genes whose expressions were significantly different between males and females and between COPD and controls. These were identified by the function `sdcd`.

Usage

```
data(lgrc.sdcd.genes)
```

Format

The format is: num [1:14557, 1:229] 10.45 1.88 12 9.02 8.81 ... - attr(*, "dimnames")=List of 2 ..\$:
chr [1:14557] "ENSG00000000003" "ENSG00000000005" "ENSG00000000419" "ENSG00000000457"
... ..\$: chr [1:229] "LT001098RU_COPD" "LT001796RU_CTRL" "LT005419RU_COPD" "LT007392RU_COPD"
...

References

Sathirapongsausti JF, Glass K, Huttenhower C, Quackenbush J, DeMeo DL. Integrative Genomics of Sexual Dimorphism in COPD. (In Prep).

Examples

```
data(lgrc.sdcd.genes)
head(sdcd.genes)
```

sdcd

Sexual dimorphic and COPD differential analysis

Description

Given linear models (limma) from a stratified analysis, `sdcd` compares the coefficients of the main effects across sexes. It then reports on the markers with significant differences in the coefficients. Typically used in conjunction with `limma`.

Usage

```
sdcd(male.fit, female.fit, coeff, genes, fdr.cutoff = 0.25, stat = c("z", "t"), file.prefix = "male.fem
sdcd.vmr(male.fit, female.fit, coeff, genes, fdr.cutoff = 0.25, stat = c("z", "t"), annotate = FALSE, an
sdcd.core(male.fit, female.fit, coeff, stat = c("z", "t"))
```

Arguments

<code>male.fit</code> , <code>female.fit</code>	Objects of type <code>limma</code> , as generated by the function <code>eBayes</code> . OR a list with fields: <code>coefficients</code> (matrix), <code>stdev.unscaled</code> (matrix), <code>sigma</code> (numeric vector), <code>df.residual</code> (numeric), and <code>df.prior</code> (numeric).
<code>coeff</code>	Coefficients of the main effect of interest. <code>sex</code> for COPD-stratified analysis and COPD for sex-stratified analysis. This should correspond to a column name of the matrices <code>coefficients</code> and <code>stdev.unscaled</code> in <code>male.fit</code> and <code>female.fit</code> .
<code>genes</code>	Annotation of the gene expression probes.
<code>fdr.cutoff</code>	Numeric cutoff for FDR q-values
<code>stat</code>	Choices between "z" and "t". For "z", a z-test is used to assess significance of the difference between the regression coefficients. For "t", the t-statistics, as opposed to the coefficients themselves, are contrasted.
<code>annotate</code>	For SDCD methylation analysis, a boolean to determin if the methylated regions (VMRs) should be annotated by genes within 10kb or not.
<code>annotate.with</code>	For SDCD methylation analysis, when <code>annotate == TRUE</code> this option indicates how to annotate the methylated regions. The "genes" option uses the input object while the "NCBI" option uses function <code>GetNeighGenes</code> in the package <code>NCBI2R</code> .
<code>file.prefix</code>	Prefix for output file name.
<code>class.names</code>	An array of character strings of length two representing the two strata.
<code>write.file</code>	A boolean that determined weather the results should be written out as files.

Details

This is to be used in conjunction with the package `limma`. Linear model fits are passed to the `sdcd` function. The main function is for gene expression data while the function `sdcd.vmr` is for methylation data. The main functionality is the same between the two, but the data annotation and output are slightly different. See intended usage in the vignette.

Value

A data frame with gene information and the following columns:

<code>*.beta</code>	Coefficients of the main effects in the two strata
<code>*.sd</code>	Standard deviation of the coefficients of the main effects in the two strata
<code>*.t</code>	T-statistics associated with the coefficients of the main effects in the two strata
<code>*.p.value</code>	P-value associated with the coefficients of the main effects in the two strata
<code>beta.diff</code>	The difference between the coefficients in the two strata
<code>beta.diff.pooled.sd</code>	Standard deviation of <code>beta.diff</code>
<code>stratum1.stratum2.p</code>	P-value associated with <code>beta.diff</code>
<code>stratum1.stratum2.p.adj</code>	Benjamini-Hochberg FDR corrected p-value

Author(s)

J Fah Sathirapongsasuti

References

Sathirapongsasuti JF, Glass K, Huttenhower C, Quackenbush J, DeMeo DL. Integrative Genomics of Sexual Dimorphism in COPD. (In Prep).

See Also

[lgrc.expr](#)

Examples

```
data(lgrc.expr.meta)
data(lgrc.expr)
data(lgrc.genes)

## Sex-stratified
design.mtx = cbind(ctrl=1,
  copd=as.integer(grepl("COPD", colnames(expr))),
  age=expr.meta$age,
  pkyr=expr.meta$pkyrs)

good.idx = apply(design.mtx, 1, function(x){!any(is.na(x))}) & (expr.meta$gender == "1-Male")
male.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
```

```
male.fit = eBayes(male.fit)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & (expr.meta$gender == "2-Female")
female.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
female.fit = eBayes(female.fit)

male.female.copd.beta.diff.genes = sdcd(male.fit, female.fit, "copd", lgrc.genes, fdr.cutoff=0.25, file.prefix="r

## COPD-stratified
design.mtx = cbind(ctrl=1,
gender=expr.meta$gender,
age=expr.meta$age,
pkyr=expr.meta$pkyrs)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & grepl("COPD",colnames(expr))
copd.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
copd.fit = eBayes(copd.fit)

good.idx = apply(design.mtx,1,function(x){!any(is.na(x))}) & grepl("CTRL",colnames(expr))
ctrl.fit = lmFit(log(expr)[,good.idx], design.mtx[good.idx,])
ctrl.fit = eBayes(ctrl.fit)

copd.ctrl.gender.beta.diff.genes = sdcd(copd.fit, ctrl.fit, "gender", lgrc.genes, fdr.cutoff=0.25, file.prefix="c

## Combine
sdcd.genes = merge(copd.ctrl.gender.beta.diff.genes, male.female.copd.beta.diff.genes, by=setdiff(intersect(names(male.female.copd.beta.diff.genes), names(male.female.copd.beta.diff.genes))), all=TRUE)
sdcd.genes = unique(sdcd.genes)
print(paste("There are ", nrow(sdcd.genes), " SDCD genes"))
```

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