Package 'TSEA'

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Type Package

Title Tissue-Specific Enrichment Analysis

Version 1.0

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Author Guangsheng Pei

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Imports pheatmap, RColorBrewer

Description Tissue-specific enrichment analysis to assess lists of candidate genes or RNA-Seq expression profiles.

License GPL (>= 2)

NeedsCompilation no

Depends R (>= 2.10)

R topics documented:

`TSEA-package`	*Tissue-Specific Enrichment Analysis Tissue-Specific Enrichment Analysis*

Description

Tissue-specific enrichment analysis to assess lists of candidate genes and tissue-specific expression decode analysis for RNA-seq data to decode RNA expression matrices tissue heterogeneity.

Details

Since disease and physiological condition are often associated with a specific tissue, understanding the tissue-specific genes (TSG) expression patterns will substantially reduce false discoveries in biomedical research. However, due to cell complexity in human system, heterogeneous tissues are frequently collected. Making it difficult to distinguish gene expression variability and mislead result interpretation. Here, we present TSEA, an R package that conducts Tissue-Specific Enrichment Analysis (TSEA) using two built-in reference panels: the Genotype-Tissue Expression (GTEx) data and the ENCyclopedia Of DNA Elements (ENCODE) data. We implemented two major functions in TSEA to assess lists of candidate genes or expression matrices.

The DESCRIPTION file:

Package:	TSEA
Type:	Package
Title:	Tissue-Specific Enrichment Analysis
Version:	1.0
Date:	2018-08-20
Author:	Guangsheng Pei
Maintainer:	Guangsheng Pei <peiguangsheng@gmail.com>
Imports:	pheatmap, RColorBrewer
Description:	Tissue-specific enrichment analysis to assess lists of candidate genes or RNA-Seq expression profiles.
License:	GPL (>= 2)

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Author(s)

Guangsheng Pei

Maintainer: Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(GTEx_t_score)
#data(ENCODE_z_score)
#library(pheatmap)

#====================================================================
#Example 1: Lists of candidate genes for single sample.
#data(GWAS_gene)
#query_gene_list = GWAS_gene

#TSEA in GTEx panel
#tsea_t = tsea.analysis(query_gene_list, GTEx_t_score, 0.05,
#p.adjust.method = "bonferroni")
#write.csv(tsea_t,"1.1.GWAS_TSEA_in_GTEx_panel.csv")
#pdf ("1.2.GWAS_TSEA_in_GTEx_panel.pdf", 5, 9, onefile = FALSE)
#tsea.plot(tsea_t, 0.05)
#dev.off()
#tsea_t_summary = tsea.summary(tsea_t)
#write.csv(tsea_t_summary,"1.3.GWAS_summary_in_GTEx_panel.csv")

#TSEA in ENCODE panel
#tsea_z = tsea.analysis(query_gene_list, ENCODE_z_score, 0.05,
#p.adjust.method = "bonferroni")
#write.csv(tsea_z,"1.4.GWAS_TSEA_in_ENCODE_panel.csv")
#pdf ("1.5.GWAS_TSEA_in_ENCODE_panel.pdf", 5, 9, onefile = FALSE)
#tsea.plot(tsea_z, 0.05)
#dev.off()
#tsea_z_summary = tsea.summary(tsea_z)
#write.csv(tsea_z_summary,"1.6.GWAS_summary_in_ENCODE_panel.csv")

#====================================================================
```

```
#Example 2: Lists of candidate genes for multiple samples.
#data(GWAS_gene_multiple)
#query_gene_list = GWAS_gene_multiple

#TSEA in GTEx panel
#tsea_t_multi = tsea.analysis.multiple(query_gene_list,
#GTEx_t_score, 0.05, p.adjust.method = "BH")
#write.csv(tsea_t_multi,"2.1.GWAS_multi_TSEA_in_GTEx_panel.csv")
#pdf ("2.2.GWAS_multi_TSEA_in_GTEx_panel.pdf", 6, 6, onefile = FALSE)
#tsea.plot(tsea_t_multi, 0.05)
#dev.off()
#tsea_t_multi_summary = tsea.summary(tsea_t_multi)
#write.csv(tsea_t_multi_summary,"2.3.GWAS_multi_summary_in_GTEx_panel.csv")

#TSEA in ENCODE panel
#tsea_z_multi = tsea.analysis.multiple(query_gene_list,
#ENCODE_z_score, 0.05, p.adjust.method = "BH")
#write.csv(tsea_z_multi,"2.4.GWAS_multi_TSEA_in_ENCODE_panel.csv")
#pdf ("2.5.GWAS_multi_TSEA_in_ENCODE_panel.pdf", 7, 7, onefile = FALSE)
#tsea.plot(tsea_z_multi, 0.2)
#dev.off()
#tsea_z_multi_summary = tsea.summary(tsea_z_multi)
#write.csv(tsea_z_multi_summary,"2.6.GWAS_multi_summary_in_ENCODE_panel.csv")

#====================================================================
#Example 3: RNA expression profiles TSEA in ENCODE panel.
#data(query_GTEx)
#query_matrix = query_GTEx

#data(correction_factor)
#RNA expression profiles z-score normalization
#query_mat_zscore_nor = tsea.expression.normalization(query_matrix,
#correction_factor, normalization = "z-score")

#RNA expression profiles TSEA in ENCODE panel
#tseaed_in_ENCODE = tsea.expression.decode(query_mat_zscore_nor,
#ENCODE_z_score, 0.05, p.adjust.method = "BH")
#write.csv(tseaed_in_ENCODE,"3.1.RNAseq_TSEA_in_ENCODE_panel.csv")
#pdf ("3.2.RNAseq_TSEA_in_ENCODE_panel.pdf", 10, 9, onefile = FALSE)
#tsea.plot(tseaed_in_ENCODE, 0.05)
#dev.off()
#tseaed_in_ENCODE_summary = tsea.summary(tseaed_in_ENCODE)
#write.csv(tseaed_in_ENCODE_summary,"3.3.RNAseq_summary_in_ENCODE_panel.csv")

#====================================================================
#Example 4: RNA expression profiles TSEA in GTEx panel.
#data(query_ENCODE)
#query_matrix = query_ENCODE

#RNA expression profiles abundance normalization
#query_mat_abundance_nor = tsea.expression.normalization(query_matrix,
#correction_factor, normalization = "abundance")

#RNA expression profiles TSEA in GTEx panel
#tseaed_in_GTEx = tsea.expression.decode(query_mat_abundance_nor,
#GTEx_t_score, 0.05, p.adjust.method = "BH")
#write.csv(tseaed_in_GTEx,"4.1.RNAseq_TSEA_in_GTEx_panel.csv")
```

```
#pdf ("4.2.RNAseq_TSEA_in_GTEx_panel.pdf", 10, 9, onefile = FALSE)
#tsea.plot(tseaed_in_GTEx, 0.05)
#dev.off()
#tseaed_in_GTEx_summary = tsea.summary(tseaed_in_GTEx)
#write.csv(tseaed_in_GTEx_summary,"4.3.RNAseq_summary_in_GTEx_panel.csv")
```

---

correction_factor   *Gene average expression level and standard deviation in GTEx data*

Description

Gene average expression level and standard deviation in GTEx data

Usage

```
data("correction_factor")
```

Format

A data frame with 14725 observations on the following 2 variables.

`avg.all` a factor with levels `0 0.0001121405301674170.000114315778302239`

`sd.all` a factor with levels `0 0.0001013747943874760.000114808260468376`

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(correction_factor)
```

ENCODE_z_score   *ENCODE z-score to define tissue-specific genes*

Description

ENCODE z-score matrix to define tissue-specific genes

Usage

```
data("ENCODE_z_score")
```

Format

The format is: num [1:14031, 1:44] -0.6738 -0.0779 -0.0929 3.0283 -0.6371 ... - attr(*, "dim-names")=List of 2 ..$: chr [1:14031] "C1orf112" "FGR" "CFH" "FUCA2" ... ..$: chr [1:44] "Adrenal Gland" "Body of Pancreas" "Breast Epithelium" "Camera-type Eye" ...

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(ENCODE_z_score)
```

GTEx_t_score   *GTEx t-score to define tissue-specific genes*

Description

GTEx t-score matrix to define tissue-specific genes

Usage

```
data("GTEx_t_score")
```

Format

The format is: num [1:14725, 1:47] -0.524 -9.921 -6.812 -7.785 -7.113 ... - attr(*, "dimnames")=List of 2 ..$: chr [1:14725] "OR4F5" "SAMD11" "KLHL17" "PLEKHN1" ... ..$: chr [1:47] "Adipose - Subcutaneous" "Adipose - Visceral (Omentum)" "Adrenal Gland" "Artery - Aorta" ...

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(GTEx_t_score)
```

GWAS_gene   *Gene symbol query data for single sample*

Description

An example of input gene symbol query data for single sample tissue-specific enrichment analysis

Usage

```
data("GWAS_gene")
```

Format

The format is: chr [1:21729] "A1BG" "A1BG-AS1" "A1CF" "A2M" "A2M-AS1" "A2ML1" "A2MP1" "A3GALT2" "A4GALT" "A4GNT" "AA06" "AAAS" "AACS" "AACSP1" "AADAC" "AADACL2" ...

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(GWAS_gene)
```

GWAS_gene_multiple *Gene symbol query data for multiple samples*

Description

An example of input gene symbol query data for multiple samples tissue-specific enrichment analysis

Usage

```
data("GWAS_gene_multiple")
```

Format

A data frame with 21729 observations on the following 26 variables.

ALZ a numeric vector

ADHD a numeric vector

ASD a numeric vector

BD a numeric vector

MDD a numeric vector

SCZ a numeric vector

BMI a numeric vector

'FN-BMD' a numeric vector

'LS-BMD' a numeric vector

EDU a numeric vector

HEIGHT a numeric vector

WHR a numeric vector

CD a numeric vector

IBD a numeric vector

RA a numeric vector

UC a numeric vector

AAM a numeric vector

CAD a numeric vector

FG a numeric vector

FI a numeric vector

HDL a numeric vector

LDL a numeric vector

TC a numeric vector

TG a numeric vector

T1D a numeric vector

T2D a numeric vector

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(GWAS_gene_multiple)
```

`query_ENCODE`	*ENCODE raw query data*

Description

An example of RNA-Seq query data from ENCODE data for tissue-specific enrichment analysis

Usage

```
data("query_ENCODE")
```

Format

A data frame with 18661 observations on the following 44 variables.

'`Adrenal Gland`' a numeric vector

'`Body of Pancreas`' a numeric vector

'`Breast Epithelium`' a numeric vector

'`Camera-type Eye`' a numeric vector

`Cerebellum` a numeric vector

`Diencephalon` a numeric vector

'`Esophagus Muscularis Mucosa`' a numeric vector

'`Esophagus Squamous Epithelium`' a numeric vector

'`Frontal Cortex`' a numeric vector

'`Gastrocnemius Medialis`' a numeric vector

'`Gastroesophageal Sphincter`' a numeric vector

`Heart` a numeric vector

'`Heart Left Ventricle`' a numeric vector

`Liver` a numeric vector

'`Lower Leg Skin`' a numeric vector

`Lung` a numeric vector

`Metanephros` a numeric vector

'`Occipital Lobe`' a numeric vector

'`Omental Fat Pad`' a numeric vector

`Ovary` a numeric vector

'`Parietal Lobe`' a numeric vector

'`Peyer's Patch`' a numeric vector

'`Prostate Gland`' a numeric vector

'`Right Atrium Auricular Region`' a numeric vector

'`Right Lobe of Liver`' a numeric vector

'`Sigmoid Colon`' a numeric vector

'`Skeletal Muscle Tissue`' a numeric vector

'`Skin of Body`' a numeric vector

'`Spinal Cord`' a numeric vector

`Spleen` a numeric vector

`Stomach` a numeric vector

'`Subcutaneous Adipose Tissue`' a numeric vector

'`Suprapubic Skin`' a numeric vector

'`Temporal Lobe`' a numeric vector

`Testis` a numeric vector

'`Thoracic Aorta`' a numeric vector

'`Thyroid Gland`' a numeric vector

'`Tibial Nerve`' a numeric vector

`Tongue` a numeric vector

'`Transverse Colon`' a numeric vector

'`Umbilical Cord`' a numeric vector

'`Upper Lobe of Left Lung`' a numeric vector

'`Urinary Bladder`' a numeric vector

`Uterus` a numeric vector

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(query_ENCODE)
```

---

query_GTEx   *GTEx raw query data*

Description

An example of RNA-Seq query data from GTEx data for tissue-specific enrichment analysis

Usage

```
data("query_GTEx")
```

Format

The format is: num [1:18067, 1:49] 0.0317 0.4451 21.9084 4.1406 0.4531 ... - attr(*, "dim-names")=List of 2 ..$: chr [1:18067] "OR4F5" "SAMD11" "NOC2L" "KLHL17" ... ..$: chr [1:49] "Adipose - Subcutaneous" "Adipose - Visceral (Omentum)" "Adrenal Gland" "Artery - Aorta" ...

Details

nothing

Source

nothing

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

Examples

```
data(query_GTEx)
```

---

tsea.analysis   *Tissue-specific enrichment analysis for query gene list*

Description

Tissue-specific enrichment analysis by Fisher's Exact Test for given gene list.

Usage

```
tsea.analysis(query_gene_list, score, ratio = 0.05,
p.adjust.method = "BH")
```

Arguments

query_gene_list
>   a gene symbol list object.

score
>   a gene tissue-specific score matrix, c("GTEx_t_score" or "ENCODE_z_score"), can be loaded by data(GTEx) or data(ENCODE), the default value is recommended "GTEx_t_score".

ratio
>   the threshold to define tissue-specific genes (with top t-score or z-score), the default value is 0.05.

p.adjust.method
>   p.adjust.method, c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")

Details

Tissue-specific enrichment analysis by Fisher's Exact Test for given gene list.

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(GWAS_gene)
#query_gene_list = GWAS_gene
#tsea_t = tsea.analysis(query_gene_list, GTEx_t_score, 0.05,
#p.adjust.method = "bonferroni")
```

tsea.analysis.multiple

Tissue-specific enrichment analysis for multi query gene lists

Description

Tissue-specific enrichment analysis by Fisher's Exact Test for multiple gene list.

Usage

```
tsea.analysis.multiple(query_gene_list, score, ratio = 0.05,
p.adjust.method = "BH")
```

Arguments

query_gene_list
    a 0~1 gene~sample table object, row should be gene symbol, column should be sample name. In the table, gene labeled with 1 indicated it is target gene for a given sample, while 0 indicated it is not target in a given sample.

score
    a gene tissue-specific score matrix, c("GTEx_t_score" or "ENCODE_z_score"), can be loaded by data(GTEx) or data(ENCODE), the default value is recommended "GTEx_t_score".

ratio
    the threshold to define tissue-specific genes (with top t-score or z-score), the default value is 0.05.

p.adjust.method
    p.adjust.method, c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")

Details

Tissue-specific enrichment analysis by Fisher's Exact Test for multiple gene list.

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(GWAS_gene_multiple)
#query_gene_list = GWAS_gene_multiple
#tsea_t_multi = tsea.analysis.multiple(query_gene_list,
#GTEx_t_score, 0.05, p.adjust.method = "BH")
```

---

tsea.expression.decode
Tissue-specific enrichment analysis for RNA-Seq expression profiles

---

Description

Tissue-specific enrichment analysis to decode whether a given RNA-seq sample (RPKM) with potential confounding effects based on expression profiles.

Usage

```
tsea.expression.decode(query_mat_normalized_score, score,
ratio = 0.05, p.adjust.method = "BH")
```

Arguments

query_mat_normalized_score
> a normalized RNA-seq RPKM object, which produced by "tsea.expression.normalization".

score
> a gene tissue-specific score matrix, c("GTEx_t_score" or "ENCODE_z_score"), can be loaded by data(GTEx) or data(ENCODE), the default value is recommended "GTEx_t_score".

ratio
> the threshold to define tissue-specific genes (with top t-score or z-score), the default value is 0.05.

p.adjust.method
> p.adjust.method, c("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none")

Details

Tissue-specific enrichment analysis for RNA-Seq expression profiles.

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(query_GTEx)
#query_matrix = query_GTEx
#data(correction_factor)
#RNA expression profiles z-score normalization
#query_mat_zscore_nor = tsea.expression.normalization(query_matrix,
#correction_factor, normalization = "z-score")

#RNA expression profiles TSEA in ENCODE panel
#tseaed_in_ENCODE = tsea.expression.decode(query_mat_zscore_nor,
#ENCODE_z_score, 0.05, p.adjust.method = "BH")
```

```
tsea.expression.normalization
```
RNA-Seq expression profiles normalization

Description

To avoid the data bias and adapt better data heterogeneity, before tsea.expression.decode() analysis, the raw discrete RPKM value have to normalized to continuous variable meet the normal distribution before t-test.

Usage

```
tsea.expression.normalization(query_mat,
correction_factor, normalization = "abundance")
```

Arguments

query_mat   a RNA-seq RPKM object, row name should be gene symbol, and column name should be sample name.

correction_factor

correction_factor, a gene table object contain genes average expression level and standard variance in GTEx database, can be loaded by data(correction_factor).

normalization

normalization methods, c("z-score", "abundance")

Details

As RNA-Seq samples are often heterogeneous, before in-depth analysis, it is necessary to decode tissue heterogeneity to avoid samples with confounding effects. However, the raw discrete RPKM value have to normalized to continuous variable meet the normal distribution before t-test.

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(query_GTEx)
#query_matrix = query_GTEx
#data(correction_factor)
#RNA expression profiles z-score normalization
#query_mat_zscore_nor = tsea.expression.normalization(query_matrix,
#correction_factor, normalization = "z-score")

#RNA expression profiles TSEA in ENCODE panel
#tseaed_in_ENCODE = tsea.expression.decode(query_mat_zscore_nor,
#ENCODE_z_score, 0.05, p.adjust.method = "BH")
```

---

tsea.plot	*Tissue-specific enrichment analysis result heatmap plot*

Description

Heat map plot for tissue-specific enrichment analysis result.

Usage

```
tsea.plot(tsea_result, threshold = 0.05)
```

Arguments

tsea_result   the result of tissue-specific enrichment analysis, which produced by "tsea.analysis",
               "tsea.analysis.multiple" or "tsea.expression.decode".

threshold   the p-value threshold to define if the gene list or RNA-seq data enriched in a
               given tissue, p-value greater than threshold will not be labeled in the plot. The
               default value is 0.05.

Details

Heat map plot for tissue-specific enrichment analysis result

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(GWAS_gene_multiple)
#query_gene_list = GWAS_gene_multiple

#TSEA in GTEx panel
#tsea_t_multi = tsea.analysis.multiple(query_gene_list,
#GTEx_t_score, 0.05, p.adjust.method = "BH")
#tsea.plot(tsea_t_multi, 0.05)
```

---

tsea.summary   *Tissue-specific enrichment analysis result summary*

Description

Tissue-specific enrichment analysis result summary (list the top 3 most enriched tissues) from the given gene list or RNA-seq expression profiles.

Usage

```
tsea.summary(tsea_result)
```

Arguments

tsea_result   the result of tissue-specific enrichment analysis, which produced by "tsea.analysis", "tsea.analysis.multiple" or "tsea.expression.decode".

Details

Tissue-specific enrichment analysis result summary

Value

nothing

Note

nothing

Author(s)

Guangsheng Pei

References

Pei G., Dai Y., Zhao Z. Jia P. (2018) Tissue-Specific Enrichment Analysis (TSEA) to decode tissue heterogeneity. Bioinformatics, In submission.

See Also

https://github.com/bsml320/TSEA/

Examples

```
#data(query_GTEx)
#query_matrix = query_GTEx
#data(correction_factor)
#RNA expression profiles z-score normalization
#query_mat_zscore_nor = tsea.expression.normalization(query_matrix,
#correction_factor, normalization = "z-score")

#RNA expression profiles TSEA in ENCODE panel
#tseaed_in_ENCODE = tsea.expression.decode(query_mat_zscore_nor,
#ENCODE_z_score, 0.05, p.adjust.method = "BH")
#tseaed_in_ENCODE_summary = tsea.summary(tseaed_in_ENCODE)
```

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