Package 'Fletcher2013b'

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Title Master regulators of FGFR2 signalling and breast cancer risk

Version 1.17.0

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Description This package reproduces the systems biology analysis for the data in package Fletcher2013a using RTN.

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Imports RColorBrewer

License GPL (>= 2)

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R topics documented:

`Fletcher2013b.gsea.regulons` *Supplementary GSEA analyses to reproduce results for Fletcher et al. 2013.*

Description

Supplementary functions to reproduce results for Fletcher et al. 2013.

Usage

```
Fletcher2013gsea.regulons(what = "Exp1", timepoint = 6, verbose = TRUE)
```

Arguments

`what`	a single character value specifying one of the experimental systems implemented in the study (Options: 'Exp1','Exp2' and 'Exp3').
`timepoint`	a single integer value specifying a timepoint of the experimental system (Options: 6 or 24).
`verbose`	a single logical value specifying to display detailed messages (when verbose=TRUE) or not (when verbose=FALSE).

Value

All results will be saved in the current work directory.

Author(s)

Mauro Castro <mauro.a.castro@gmail.com>

Source

Michael NC Fletcher, Mauro AA Castro, Suet-Feung Chin, Oscar Rueda, Xin Wang, Carlos Caldas, Bruce AJ Ponder, Florian Markowetz, Kerstin B Meyer. Master regulators of FGFR2 signalling and breast cancer risk. Nature Communications, 4:2464, 2013.

Examples

```
## Not run:
Fletcher2013gsea.regulons(what="Exp1")

## End(Not run)
```

Fletcher2013b.pipelines

A pipeline to reproduce results for Fletcher et al. 2013.

Description

Pipeline functions to reproduce results for Fletcher et al. 2013.

Usage

```
Fletcher2013pipeline.mra1st(hits, minRegulonSize=20, idtype="probeid",
  pAdjustMethod="holm",tnet="dpi", eps=0, pValueCutoff=1e-4, verbose=TRUE, ...)
Fletcher2013pipeline.mra2nd(hits, minRegulonSize=20, idtype="probeid",
  pAdjustMethod="holm",tnet="dpi", eps=0, pValueCutoff=1e-4, verbose=TRUE, ...)
Fletcher2013pipeline.mraNormals(hits, minRegulonSize=20, idtype="probeid",
  pAdjustMethod="holm",tnet="dpi", eps=0, pValueCutoff=1e-4, verbose=TRUE, ...)
Fletcher2013pipeline.mraTALL(hits, minRegulonSize=20, idtype="probeid",
  pAdjustMethod="holm", tnet="dpi", eps=0, pValueCutoff=0.01, verbose=TRUE, ...)
Fletcher2013pipeline.synergyShadow()
Fletcher2013pipeline.consensusnet()
Fletcher2013pipeline.enrichmap()
```

Arguments

hits	a character vector of gene identifiers for those considered as hits (see TNA-class).
minRegulonSize	a single integer or numeric value specifying the minimum number of elements in a regulon that must map to elements of the gene universe (see tna.mra).
idtype	a single character value specifying the inpute gene id (Options: 'probeid' or 'entrez').
pAdjustMethod	a single character value specifying the p-value adjustment method to be used (see p.adjust for details).
tnet	a single character value specifying which transcriptional network should to used to compute the MRA analysis. Options: "dpi" and "ref".
eps	a single numeric value specifying the threshold under which Aracne algorithm should apply the dpi filter (see tni.dpi.filter).
pValueCutoff	a single numeric value specifying the cutoff for p-values considered significant.
verbose	a single logical value specifying to display detailed messages (when verbose=TRUE) or not (when verbose=FALSE).
...	other arguments passed to the RTN package.

Value

All results will be saved in the current work directory.

Author(s)

Mauro Castro <mauro.a.castro@gmail.com>

Source

Michael NC Fletcher, Mauro AA Castro, Suet-Feung Chin, Oscar Rueda, Xin Wang, Carlos Caldas, Bruce AJ Ponder, Florian Markowetz, Kerstin B Meyer. Master regulators of FGFR2 signalling and breast cancer risk. Nature Communications, 4:2464, 2013.

Examples

```
## Not run:
hits <- Fletcher2013pipeline.deg(what="Exp1")
mra1 <- Fletcher2013pipeline.mra1st(hits=hits$E2FGF10)

## End(Not run)
```

`miscellaneous` *Miscellaneous datasets.*

Description

Different data sets used to produce a variety of analyses and figures in Fletcher et al., 2013.

Usage

```
data(miscellaneous)
```

Format

A set of `miscellaneous` data objects:

- `risksites`: a data.frame with top 1385 risk SNPs derived from UK2 GWAS study for breast cancer (mapped to genome assembly NCBI36/hg18).
- `randsites`: a data.frame with random SNPs derived from Affy SNP-6 array (sites mapped to hg19).
- `chromlen`: a vector listing human chromosome length (genome assembly NCBI36/hg18).
- `ESR1bdsites`: a data.frame listing ChIP-seq ESR1 binding sites in MCF-7 cells (mapped to genome assembly NCBI36/hg18).
- `FOXA1bdsites`: a data.frame listing ChIP-seq FOXA1 binding sites in MCF-7 cells (mapped to genome assembly NCBI36/hg18).
- `GATA3bdsites`: a data.frame listing ChIP-seq GATA3 binding sites in MCF-7 cells (mapped to genome assembly NCBI36/hg18).
- `SPDEFbdsites`: a data.frame listing ChIP-seq SPDEF binding sites in MCF-7 cells (mapped to genome assembly NCBI36/hg18).
- `fimoESR1`: a list with ESR1 motifs mapped across the human genome.TRANSFAC PWM was used as input for the FIMO DNA motif identification tool, Grant et al., 2011 (mapped to hg19).
- `fimoFOXA1`: a list with FOXA1 motifs mapped across the human genome.TRANSFAC PWM was used as input for the FIMO DNA motif identification tool, Grant et al., 2011 (mapped to hg19).
- `fimoGATA3`: a list with GATA3 motifs mapped across the human genome.TRANSFAC PWM was used as input for the FIMO DNA motif identification tool, Grant et al., 2011 (mapped to hg19).

- `metaPCNA`: a vector listing genes from the metaPCNA proliferation-based gene signature (Venet, D. et al., 2011).
- `consensus`: a list with consensus breast cancer master regulators described in Fletcher et a., 2013.
- `tfs`: a vector listing the transcription factors used to compute the transcriptional networks `rtni1st`,`rtni2nd`, `rtniNormals` and `rtniTALL`.

Details

ChIP-seq datasets are represetative of 3 independent experiments, with peaks overlapping in at least 2 out of 3 replicates (taking one as reference). All peaks are provided related to the summit positions (+- 35 bp), including peak height and significance (in the form of -10*log10(pvalue)). Additional details about this and the other datasets are provided in the vignette.

Source

Michael NC Fletcher, Mauro AA Castro, Suet-Feung Chin, Oscar Rueda, Xin Wang, Carlos Caldas, Bruce AJ Ponder, Florian Markowetz, Kerstin B Meyer. Master regulators of FGFR2 signalling and breast cancer risk. Nature Communications, 4:2464, 2013.

Grant CE, Bailey TL, Noble WS: FIMO: scanning for occurrences of a given motif. Bioinformatics, 27(7):1017-1018, 2011.

Venet, D., Dumont, J.E. & Detours, V. Most random gene expression signatures are significantly associated with breast cancer outcome. PLoS Comput Biol, 7:e1002240, 2011.

Examples

```
data(miscellaneous)
```

`rtni.data` *Transcriptional network datasets.*

Description

The datasets consist of a transcriptional networks computed by the package RTN.

Usage

```
data(rtni1st)
data(rtni2nd)
data(rtniNormals)
data(rtniTALL)
```

Format

A set of `TNI` objects:

- `rtni1st`: A TF-centric network based on 2000 breast cancer gene expression profiles - Cohort I (Curtis, C. et al).
- `rtni2nd`: A TF-centric network based on 2000 breast cancer gene expression profiles - Cohort II (Curtis, C. et al).

- `rtniNormals`: A TF-centric network based on normal breast gene expression profiles (Curtis, C. et al).
- `rtniTALL`: A TF-centric network based non-breast cancer gene expression profiles, derived from T-cell acute l ymphoblastic leukaemia (Van Vlierberghe, P. et al.).
- `rtniIDs`: A `data.frame` with gene ids.

Source

Michael NC Fletcher, Mauro AA Castro, Suet-Feung Chin, Oscar Rueda, Xin Wang, Carlos Caldas, Bruce AJ Ponder, Florian Markowetz, Kerstin B Meyer. Master regulators of FGFR2 signalling and breast cancer risk. Nature Communications, 4:2464, 2013.

Curtis, C. et al. The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. Nature, 486:346-52, 2012.

Van Vlierberghe, P. et al. ETV6 mutations in early immature human T cell leukemias. J Exp Med, 208:2571-9, 2011.

Examples

```
data(rtni1st)
```

---

siRNA *Dataset from siRNA experiments used to reproduce results in Fletcher et al., 2012.*

Description

The data consists of differentially expressed genes in MCF-7 cells after knockdown experiments.

Usage

```
data(siRNA)
```

Format

A `list` object:

- `siRNA$ESR1`: differentially expressed genes in MCF-7 cells after knocking down ESR1 gene.
- `siRNA$SPDEF`: differentially expressed genes in MCF-7 cells after knocking down SPDEF gene.
- `siRNA$PTTG1`: differentially expressed genes in MCF-7 cells after knocking down PTTG1 gene.

Note

The differential expression analysis is documented in the package 'Fletcher2013a', and row gene expression data is available at `siOTHERS` and `siESR1`.

Source

Michael NC Fletcher, Mauro AA Castro, Suet-Feung Chin, Oscar Rueda, Xin Wang, Carlos Caldas, Bruce AJ Ponder, Florian Markowetz, Kerstin B Meyer. Master regulators of FGFR2 signalling and breast cancer risk. Nature Communications, 4:2464, 2013.

Examples

```
data(siRNA)
```

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