Package 'Fletcher2013b'

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Title Master regulators of FGFR2 signalling and breast cancer risk

Version 1.44.0

Author Mauro Castro, Michael Fletcher, Florian Markowetz and Kerstin Meyer.

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

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

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`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.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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