

# Package ‘Fletcher2013b’

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**Title** Master regulators of FGFR2 signalling and breast cancer risk.

**Version** 1.1.1

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

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**Depends** R (>= 2.15), Fletcher2013a, biomaRt, VennDiagram, RTN (>= 1.1.2), RedeR (>= 1.8.1)

**Imports** RColorBrewer, corrgram

**License** GPL (>= 2)

**biocViews** ExperimentData, RNAExpressionData, Cancer

**URL** <http://dx.doi.org/10.1038/ncomms3464>

**InstallableEverywhere** yes

## R topics documented:

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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 Markowitz, 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.mra.supplements

*Supplementary MRA analyses to reproduce results for Fletcher et al. 2013.*

---

### **Description**

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

### **Usage**

```
Fletcher2013mra.agreement.cohort1()  
Fletcher2013mra.agreement.exp1()  
Fletcher2013mra.agreement.exp2()  
Fletcher2013mra.agreement.exp3()  
Fletcher2013mra.heatmap1()  
Fletcher2013mra.heatmap2()  
Fletcher2013mra.consensus()
```

### **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.

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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.siRNA(what="siESR1")
Fletcher2013pipeline.chipseq(what="SPDEF")
Fletcher2013pipeline.masters()
Fletcher2013pipeline.synergyShadow()
Fletcher2013pipeline.consensusnet()
Fletcher2013pipeline.enrichmap()
Fletcher2013pipeline.motifs()

```

**Arguments**

hits	a character vector of gene identifiers for those considered as hits (see <a href="#">TNA-class</a> ).
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 <a href="#">tna.mra</a> ).
idtype	a single character value specifying the input gene id (Options: 'probeid' or 'entrez').
pAdjustMethod	a single character value specifying the p-value adjustment method to be used (see <a href="#">p.adjust</a> for details).
tnet	a single character value specifying which transcriptional network should be 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 <a href="#">tni.dpi.filter</a> ).
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).
what	a single character value specifying which data should be used in the pipeline. Options for Fletcher2013pipeline.siRNA: 'siESR1', 'siSPDEF', and 'siPTTG1'. Options for Fletcher2013pipeline.chipseq: 'ESR1', 'SPDEF', 'FOXA1', and 'GATA3'.
...	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 al., 2013.
- `tfs`: a vector listing the transcription factors used to compute the transcriptional networks `rtni1st`, `rtni2nd`, `rtniNormals` and `rtniTALL`.

### Details

ChIP-seq datasets are representative 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  $-10 \cdot \log_{10}(\text{pvalue})$ ). 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 lymphoblastic 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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