Package 'HD2013SGI'

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Type Package

Title Mapping genetic interactions in human cancer cells with RNAi and multiparametric phenotyping

Version 1.46.0

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Description This package contains the experimental data and a complete executable transcript (vignette) of the analysis of the HCT116 genetic interaction matrix presented in the paper ``Mapping genetic interactions in human cancer cells with RNAi and multiparametric phenotyping" by C. Laufer, B. Fischer, M. Billmann, W. Huber, M. Boutros; Nature Methods (2013) 10:427-31. doi: 10.1038/nmeth.2436.

License Artistic-2.0

LazyLoad true

Depends R (>= 2.10.0), RColorBrewer, gplots, geneplotter, splots, limma, vcd, LSD,EBImage

Suggests BiocStyle

SystemRequirements GNU make

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`HD2013SGI-package` *Experimental Data and Analysis of the HCT116 Genetic Interaction Matrix*

Description

Experimental Data and Analysis of the HCT116 Genetic Interaction Matrix. This package contains the data and source code for the paper Laufer, Fischer, Billmann, Huber, Boutros, HD2013SGI, 2013.

Details

Package:	HD2013SGI
Type:	Package
Version:	0.0.3
License:	Artistic-2.0
LazyLoad:	true
Imports:	
Depends:	rhdf5, RColorBrewer, gplots, geneplotter, MASS, grid, hwriter, splots, igraph, abind, limma, vcd,
SystemRequirements:	GNU make
biocViews:	Infrastructure
Built:	R 2.15.1; ; 2013-02-14 12:08:09 UTC; unix

The interaction matrix can be loaded by `data(Interactions, package="HD2013SGI")`. Type `?Interactions` to see a documentation of the interaction data.

The vignette of the package can be seen by typing >library("HD2013SGI") >vignette("HD2013SGI") It contains the complete documentation and R-code for the analysis of the data published in the original publication.

All intermediate results are precomputed and can be loaded. the following datasets are available:

`featuresPerWell`	The screen data in screen order
`datamatrixfull`	The phenotype data of all pairwise g
`QueryAnnotation`	Annotation of all the query genes in
`TargetAnnotation`	Annotation of all target genes in the
`stabilitySelection`	Results from the feature selection ste
`datamatrix`	The phenotype data of all pairwise g
`mainEffects`	

estimated main effects (single knock down effects)	`nrOfInteractionsPerTarget` number of interactions per target ger
`Interactions`	The genetic interaction data (pi-scor

A number of helper functions are defined in the package and used in the vignette.

`HD2013SGIorderDim`	hclust on one out of three dimensions of an interaction matrix
`HD2013SGIHeatmapHuman`	plotting a heatmap of a three dimensional array of pi-scores (target genes x query gene
`HD2013SGImaineffects`	estimation main effects
`HD2013SGIselectByStability`	feature selection to select features most stable between replicated experiments

Author(s)

Bernd Fischer

Maintainer: Bernd Fischer <bernd.fischer@embl.de>

References

Laufer, Fischer, Billmann, Huber, Boutros, HD2013SGI, 2013.

Examples

```
data(Interactions, package="HD2013SGI")
```

`datamatrix` *Phenotypic data after quality control and feature selection*

Description

Phenotypic features of pairwise genetic perturbation experiments **after** selection of non-redundant features and quality control. `D` is the 6-dimensional array of experimental measurements. Its dimensions are target genes x target siRNA designs x query genes x query siRNA designs x features x replicates. The array has a dimnames attribute, but there exists a more comprehensive annotation of target genes, query genes, and phenotypes in `Anno`.

Usage

```
data(datamatrix)
```

Format

The format is: List of 2 $ D : num [1:289, 1:2, 1:20, 1:2, 1:11, 1:2] -0.05334 -0.20294 -0.10123 0.33203 0.00638 ... ..- attr(*, "dimnames")=List of 6 .. ..$ targetGene : chr [1:289] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ targetDesign: chr [1:2] "1" "2" .. ..$ queryGene : chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... .$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... .$ replicate : chr [1:2] "1" "2" $ Anno:List of 3 ..$ target :'data.frame': 289 obs. of 4 variables: .. ..$ ID : chr [1:289] "B1" "B2" "B3" "B4" ... .$ Symbol: chr [1:289] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ Well : chr [1:289] "B1" "B2" "B3" "B4" ... .$ group : chr [1:289] "sample" "sample" "sample" "sample" ... ..$ query :'data.frame': 20 obs. of 2 variables: .. ..$ ID : chr [1:20] "01" "02" "03" "04" ... .$ Symbol: chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... ..$ phenotype: chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ...

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(datamatrix, package="HD2013SGI")
plot(datamatrix$D[,1,1,1,1,1])
```

`datamatrixfull` *Phenotypic data before quality control and feature selection*

Description

Phenotypic features of pairwise genetic perturbation experiments **before** selection of non-redundant features and quality control. `D` is the 6-dimensional array of experimental measurements. Its dimensions are target genes x target siRNA designs x query genes x query siRNA designs x features x replicates. The array has a dimnames attribute.

Usage

```
data(datamatrixfull)
```

Format

The format is: List of 1 $ D: num [1:345, 1:2, 1:20, 1:2, 1:353, 1:2] 2686 2573 2650 3000 2733 ... ..- attr(*, "dimnames")=List of 6 .. ..$ targetGene : chr [1:345] "B1" "B2" "B3" "B4" ... .$ targetDesign: chr [1:2] "1" "2" .. ..$ queryGene : chr [1:20] "01" "02" "03" "04" ... .$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:353] "count" "nuc.0.m.cx" "nuc.0.m.cy" "nuc.0.m.majoraxis" ... .$ replicate : chr [1:2] "1" "2"

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(datamatrixfull, package="HD2013SGI")
plot(datamatrixfull$D[,1,1,1,1,1])
```

featuresPerWell *Original phenotypic measurements in screen order*

Description

Original phenotypic features in screen order. `Anno` contains the annotation for each experiment including the plate name, row, col, and field. `data` is a `data.frame` with a column for each phenotypic feature and rows as much as there are experiments in the screen.

Usage

```
data(featuresPerWell)
```

Format

The format is: List of 2 $ Anno:'data.frame': 231840 obs. of 4 variables: ..$ plate: chr [1:231840] "001CIQ01IRI" "001CIQ01IRI" "001CIQ01IRI" "001CIQ01IRI" ... ..$ row : chr [1:231840] "B" "B" "B" "B" ... ..$ col : chr [1:231840] "1" "1" "1" "1" ... ..$ field: chr [1:231840] "1" "2" "3" "4" ... $ data: num [1:231840, 1:353] 2780 3120 2242 2603 2170 ... ..- attr(*, "dimnames")=List of 2 .. ..$: NULL .. ..$: chr [1:353] "count" "nuc.0.m.cx" "nuc.0.m.cy" "nuc.0.m.majoraxis" ...

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(featuresPerWell, package="HD2013SGI")
plot(log2(featuresPerWell$data[,1]),pch=".")
```

HD2013SGIHeatmapHuman *Plotting heatmaps of genetic interaction scores*

Description

Plotting heatmaps of three-dimensional arrays of interaction scores. Two dimensions of the array will be flattened.

Usage

```
HD2013SGIHeatmapHuman(x, cuts, col, colnames = TRUE, rownames = FALSE, mrow = 10, mcol = 10, cexrow =
```

Arguments

x	A three dimensional array to be plotted as a heatmap.
cuts	cuts on the values of x for color coding. length(cuts) has be one larger than length(col).
col	Values of x are mapped on color definitions as defined in col using the cuts argument.
colnames	Gene names for columns of the matrix.
rownames	Gene names for rows of the matrix.
mrow	row margin for printing gene names..
mcol	column margin for printing gene names.
cexrow	cex for the row names.
cexcol	cex for the column names.
border	line width of the border.
space	spacing between elements of the third array dimension of x after flattening.

Value

Nothing is returned.

Author(s)

Bernd Fischer

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

HD2013SGImaineffects *Estimation of main effects*

Description

A function to estimate main effects (single knock-down effects) in genetic interaction screens.

Usage

```
HD2013SGImaineffects(x, TP, TargetNeg, QueryNeg, eps = 1e-04, maxiter = 100, na.rm = TRUE)
```

Arguments

x	Two dimensional array.
TP	Assignment of target genes to target plates. Used to compute target main effects for each target plate separately.
TargetNeg	Negative controls within the set of target genes.
QueryNeg	Negative controls within the set of query genes.
eps	real number greater than 0. A tolerance for convergence.
maxiter	the maximum number of iterations
na.rm	logical. Should missing values be removed?

Value

neg	Effect of the negative control.
targetMainEffect	target main effects
queryMainEffect	query main effects
pi	Pairwise interaction scores (pi-scores)

Author(s)

changes applied by Bernd Fischer to the implementation of R stats functionmedpolish

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

HD2013SGIorderDim *hclust on one out of three dimensions of an interaction matrix*

Description

hclust on one out of three dimensions of a three-dimensional array of interaction scores (target genes x query genes x features)

Usage

```
HD2013SGIorderDim(x, i)
```

Arguments

x	A three dimensional array to be clustered.
i	The dimension of the array along which the data is clustered.

Value

Returns a cluster hierarchy of class `hclst`.

Author(s)

Bernd Fischer

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

`HD2013SGIselectByStability`
Feature selection method

Description

A function to select features that are most stable across replicated experiments

Usage

```
HD2013SGIselectByStability(subsample, preselect = "count", Rdim = 40, verbose = TRUE)
```

Arguments

`subsample`	This is the input data. Usually a subsample of the complete screen is enough to select the non-redundant features. `subsample` is a list with three elements: `D` is a three-dimensional array with dimensions samples x features x replicates. As samples usually 1000 to 5000 experiments are randomly selected. The function needs two replicates.
`preselect`	Names of the features that should be preselected, e.g. count is preselected in this screen, because of its biological interpretability and comparability to other viability-based genetic interaction screens.
`Rdim`	The maximum number of features to be selected.
`verbose`	If TRUE information about the progress and the quality of the selected features is printed.

Value

(selected = selected, correlation = correlation, ratioPositive = ratioPositive, correlationAll = correlationAll)

`selected`	The names of the selected features in the order as selected.
`correlation`	The correlation of the residual features after fitting a linear function on the previously selected features. Correlations are in same order as `selected`.
`ratioPositive`	The fraction of positively correlated features among all candidate features in each step. In same order as `selected`.
`correlationAll`	The correlation of the residual features of all candidate features in each step of the selection process.

Author(s)

Bernd Fischer

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

`Interactions` *The genetic interaction data.*

Description

The genetic interaction data. Pairwise interaction scores (`piscore`) are presented in a 6-dimensional array with dimensions target genes x target siRNA designs x query genes x query siRNA designs x features x replicates. BH-corrected p-values (padj) are presented in a 5-dimensional array with dimensions target genes x target siRNA designs x query genes x query siRNA designs x features. An annotation of target and query genes and of phenotypes can be found in (`Anno`). `scale` is the standard deviation measure used for normalization. At first standard deviations were computed between replicates for each experiment and afterwards the median of standard deviations was computed.

Usage

```
data(Interactions)
```

Format

The format is: List of 4 $ piscore: num [1:282, 1:2, 1:20, 1:2, 1:11, 1:2] -1.814 -2.457 -3.094 -1.448 -0.142 ... ..- attr(*, "dimnames")=List of 6 .. ..$ targetGene : chr [1:282] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ targetDesign: chr [1:2] "1" "2" .. ..$ queryGene : chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... .$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... .$ replicate : chr [1:2] "1" "2" $ scale : num [1:11] 0.214 0.125 0.139 0.193 0.207 ... $ padj : num [1:282, 1:2, 1:20, 1:2, 1:11] 0.6838 0.4167 0.0949 0.5786 0.7933 ... ..- attr(*, "dimnames")=List of 5 .. ..$ targetGene : chr [1:282] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ targetDesign: chr [1:2] "1" "2" .. ..$ queryGene : chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... .$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... $ Anno :List of 3 ..$ target :'data.frame': 282 obs. of 4 variables: .. ..$ ID : chr [1:282] "B1" "B2" "B3" "B4" ... .$ Symbol: chr [1:282] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ Well : chr [1:282] "B1" "B2" "B3" "B4" ... .$ group : chr [1:282] "sample" "sample" "sample" "sample" ... ..$ query :'data.frame': 20 obs. of 2 variables: .. ..$ ID : chr [1:20] "01" "02" "03" "04" ... .$ Symbol: chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... ..$ phenotype: chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ...

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(Interactions, package="HD2013SGI")
plot(Interactions$piscore[,1,"SUV39H1",1,"cell.act.m.majoraxis",1])
print(names(which(Interactions$padj[,1,"SUV39H1",1,
                                    "cell.act.m.majoraxis"] <= 0.01)))
```

---

mainEffects *Estimated main effects*

Description

Estimated main effects (single knock-down effects) for target and query genes. Additional overall effects for each phenotype are contained. The dataset contains an annotation of target genes, query genes, and phenotypes.

Usage

```
data(mainEffects)
```

Format

The format is: List of 4 $ target: num [1:289, 1:2, 1:2, 1:11, 1:2] -0.31065 -0.32253 -0.08466 -0.00367 -0.60867 ... ..- attr(*, "dimnames")=List of 5 .. ..$ targetGene : chr [1:289] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ targetDesign: chr [1:2] "1" "2" .. ..$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... .$ replicate : chr [1:2] "1" "2" $ query : num [1:2, 1:20, 1:2, 1:11, 1:2] 0.277 0.265 0.235 0.226 1.165 ... ..- attr(*, "dimnames")=List of 5 .. ..$ targetDesign: chr [1:2] "1" "2" .. ..$ queryGene : chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... .$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... .$ replicate : chr [1:2] "1" "2" $ overall : num [1:2, 1:2, 1:11, 1:2] 0.3685 0.4638 0.3331 0.487 -0.0985 ... ..- attr(*, "dimnames")=List of 4 .. ..$ targetDesign: chr [1:2] "1" "2" .. ..$ queryDesign : chr [1:2] "1" "2" .. ..$ features : chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... .$ replicate : chr [1:2] "1" "2" $ Anno :List of 3 ..$ target :'data.frame': 289 obs. of 4 variables: .. ..$ ID : chr [1:289] "B1" "B2" "B3" "B4" ... .$ Symbol: chr [1:289] "TDRD6" "PRDM11" "KDM1B" "INTS12" ... .$ Well : chr [1:289] "B1" "B2" "B3" "B4" ... .$ group : chr [1:289] "sample" "sample" "sample" "sample" ... ..$ query :'data.frame': 20 obs. of 2 variables: .. ..$ ID : chr [1:20] "01" "02" "03" "04" ... .$ Symbol: chr [1:20] "DPF2" "SMARCA1" "SMARCC1" "SMARCD2" ... ..$ phenotype: chr [1:11] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ...

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(mainEffects, package="HD2013SGI")
print(dim(mainEffects$target))
plot(mainEffects$target[,1,1,1,1])
```

`nrOfInteractionsPerTarget` *Number of interactions per target gene*

Description

Number of genetic interactions per target gene.

Usage

```
data(nrOfInteractionsPerTarget)
```

Format

The format is: int [1:282] 1 3 0 2 0 3 1 1 0 1 ...

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(nrOfInteractionsPerTarget, package="HD2013SGI")
plot(nrOfInteractionsPerTarget)
```

`QueryAnnotation` *Annotation of all query genes in the screen*

Description

Annotation of all query genes in the screen.

Usage

```
data(QueryAnnotation)
```

Format

A data frame with 20 observations on the following 2 variables.

`ID` a character vector

`Symbol` a character vector

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(QueryAnnotation, package="HD2013SGI")
print(QueryAnnotation$Symbol)
```

`stabilitySelection` *Results from the feature selection method*

Description

Results from the feature selection method.

Usage

```
data(stabilitySelection)
```

Format

The format is: List of 4 $ selected : chr [1:25] "count" "cell.act.m.majoraxis" "nuc.nuc.b.q001" "nuc.0.m.eccentricity" ... $ correlation : num [1:25] 0.917 0.972 0.938 0.928 0.896 ... $ ratioPositive : num [1:25] 1 1 0.947 0.942 0.937 ... $ correlationAll: List of 25 ..$: Named num [1:227] 0.917 0.884 0.93 0.897 0.882 ... .- attr(*, "names")= chr [1:227] "count" "nuc.0.m.majoraxis" "nuc.0.m.eccentricity" "nuc.0.s.area" ... ..$: Named num [1:226] 0.884 0.931 0.899 0.887 0.9 ... .- attr(*, "names")= chr [1:226] "nuc.0.m.majoraxis" "nuc.0.m.eccentricity" "nuc.0.s.area" "nuc.0.s.perimeter" ... ..$: Named num [1:225] 0.884 0.934 0.884 0.882 0.883 ... .- attr(*, "names")= chr [1:225] "nuc.0.m.majoraxis" "nuc.0.m.eccentricity" "nuc.0.s.area" "nuc.0.s.perimeter" ... ...

Details

`selected` is a vector of the selected feature namess. `correlation` are the Pearson correlation coefficients of the residual features. `ratioPositive` is the fraction of positively correlated features among all candidate features for selection. `correlationAll` contains a vector of correlations of the residual features of all candidate features for each step in the selection process.

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(stabilitySelection, package="HD2013SGI")
barplot(stabilitySelection$correlation,
        names.arg=stabilitySelection$selected,las=2)
barplot(stabilitySelection$ratioPositive-0.5, offset=0.5,
        names.arg=stabilitySelection$selected,las=2)
```

TargetAnnotation *Annotation of all target genes in the screen*

Description

Annotation of the target genes on one target plate. It includes an ENSEMBL gene identifier, the HUGO name, the position on the plate (well), and the group of the target siRNA (sample or control).

Usage

```
data(TargetAnnotation)
```

Format

A data frame with 345 observations on the following 4 variables.

`ID` a character vector

`Symbol` a character vector

`Well` a character vector

`group` a character vector

References

Laufer, Fischer et al., 2013

See Also

HD2013SGI

Examples

```
data(TargetAnnotation, package="HD2013SGI")
print(TargetAnnotation$Symbol)
```

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