Package 'signatureSurvival'

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Type Package

Title Signature survival analysis

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Description Package ``signatureSurvival'' is composed of multiple R functions and used to implement single or multiple univariate or multivariate Cox proportional hazard regression analyses and make one or multiple ``Kaplan-Meier'' survival curve plots. When multiple Cox proportional hazard models are performed with a set of genes,the result outputted can be used to screen genes for up and down signatures by using Hazard risk values, ``z-scores'' and ``p-values'' of genes,to calculate weights and expression values of up or down signature in all patients in a cohort. Univariate or multivariate Cox proportional hazard survival analysis on the patients with death or recurrence status in one cohort can be performed using the created up or down signature.

License GPL(>=3)

Depends R(>= 3.5.0)

Imports stats, utils,graphics,grDevices,dplyr,forestplot, gplots, gtools, survival,survminer,ggplot2

Suggests Rmisc

LazyLoad yes

NeedsCompilation no

Encoding UTF-8

LazyData true

R topics documented:

`signatureSurvival-package`
Signature survival analysis

Description

Package "signatureSurvival" is composed of multiple R functions and used to implement single or multiple univariate or multivariate Cox proportional hazard regression analyses and make one or multiple "Kaplan-Meier" survival curve plots. When multiple Cox proportional hazard models are performed with a set of genes,the result outputted can be used to screen genes for up and down signatures by using Hazard risk values, "z-scores" and "p-values" of genes,to calculate weights and expression values of up or down signature in all patients in a cohort. Univariate or multivariate Cox proportional hazard survival analysis on the patients with death or recurrence status in one cohort can be performed using the created up or down signature.

Details

The DESCRIPTION file: This package was not yet installed at build time.

Index: This package was not yet installed at build time.
This package is used to create up and down signatures,do univariate or multivariate survival analysis and make forest plot for the results of multivariate Cox proportional hazard survival analysis. The steps for screening signature are as following: At step1, users should perform differential expression analysis of genes in one or multiple microarray datasets or RNA-seq count datasets or the other expression datasets and then mark these differentally expressed (DE) genes selected with "up" and "down" using negative or positive t-values. At step2, retrieve survival (or clinical data) using these DE genes and construct a new survival data(age, sex, stages/smoking, month, status, and DE genes in column and patients in row). Note that expression data ofthe DE genes are listed in the right side in the survival data. At step 3, perform musvtest.R (multiple univariate survival tests) or mvstest (multiple multivariate survival tests) with covariates age, sex and/smoking ect. Use p-value to select

genes in big difference between low and high-survival probalities and use HR and up and down-regulation to classify genes selected into up and down groups in multiple cohorts. At step 4,use weight.R to calculate weight values of each gene in signature and use signatureExp.R to caculate expression values of signature in all patients and move the expression values to the last column in survival data. At step 5, perform MUKMplot.R or MMKMplot.R on signature in the survival data to plot Kaplan-Meier survival curves.

Author(s)

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Examples

```
data(GSE50081)
res<-musvtest(sdata=GSE50081,stn=3500,gn=3506,time="month",status="status",
quant=c("no",-0.2,0.2))
```

GSE50081 *Survival data from cohort GSE50081*

Description

This dataset was derived from cohort GSE50081. It contains observation of 129 patients and 3577 probeids (without gene names),two signaturs "up" and "down" and 17 clinical variables suchas sex, age, smoking, stages, status(death, relapse, moth). 3577 probeids listgene expression values in 129 patients.

Usage

```
data("GSE50081")
```

Format

A data frame with 129 observations on the following 3596 variables.

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`n.stage` a numeric vector

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`stage` a character vector

`status1` a numeric vector

`age` a numeric vector

`smoking` a character vector

`month1` a numeric vector

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`month` a numeric vector

`recurrence` a character vector

`X.Sample_characteristics_ch1` a character vector

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X233903_s_at a numeric vector
X209169_at a numeric vector
X204894_s_at a numeric vector
X205978_at a numeric vector

X204731_at a numeric vector
X222885_at a numeric vector
X226950_at a numeric vector
X209220_at a numeric vector
X201540_at a numeric vector
X205019_s_at a numeric vector
X235489_at a numeric vector
X205237_at a numeric vector
X1552326_a_at a numeric vector
X205609_at a numeric vector
X230132_at a numeric vector
X1556003_a_at a numeric vector
X202760_s_at a numeric vector
X226228_at a numeric vector
X227197_at a numeric vector
X225078_at a numeric vector
X209897_s_at a numeric vector
X212713_at a numeric vector
X205725_at a numeric vector
X205206_at a numeric vector
X207302_at a numeric vector
X204154_at a numeric vector
X239349_at a numeric vector
X206167_s_at a numeric vector
X226769_at a numeric vector
X205819_at a numeric vector
X206069_s_at a numeric vector
X213715_s_at a numeric vector
X204677_at a numeric vector
X229973_at a numeric vector
X229308_at a numeric vector
X236085_at a numeric vector
X220646_s_at a numeric vector
X219059_s_at a numeric vector
X229529_at a numeric vector
X219719_at a numeric vector
X218723_s_at a numeric vector

X219436_s_at a numeric vector
X220269_at a numeric vector
X213316_at a numeric vector
X206159_at a numeric vector
X230130_at a numeric vector
X238206_at a numeric vector
X206283_s_at a numeric vector
X238062_at a numeric vector
X204271_s_at a numeric vector
X38691_s_at a numeric vector
X209167_at a numeric vector
X219529_at a numeric vector
X202242_at a numeric vector
X209170_s_at a numeric vector
X1556325_at a numeric vector
X228915_at a numeric vector
X1555216_a_at a numeric vector
X203548_s_at a numeric vector
X205433_at a numeric vector
X209614_at a numeric vector
X236359_at a numeric vector
X205935_at a numeric vector
X212097_at a numeric vector
X231001_at a numeric vector
X220266_s_at a numeric vector
X235108_at a numeric vector
X219597_s_at a numeric vector
X234996_at a numeric vector
X226462_at a numeric vector
X209616_s_at a numeric vector
X209793_at a numeric vector
X206701_x_at a numeric vector
X241782_at a numeric vector
X229641_at a numeric vector
X219230_at a numeric vector
X1556711_at a numeric vector
X203980_at a numeric vector

`X206488_s_at` a numeric vector
`X235228_at` a numeric vector
`X228504_at` a numeric vector
`X206702_at` a numeric vector
`X203571_s_at` a numeric vector
`X238332_at` a numeric vector
`X209555_s_at` a numeric vector
`X227874_at` a numeric vector
`X206208_at` a numeric vector
`X204396_s_at` a numeric vector
`X1552509_a_at` a numeric vector
`X202524_s_at` a numeric vector
`X203323_at` a numeric vector
`X228698_at` a numeric vector
`X225207_at` a numeric vector
`X220994_s_at` a numeric vector
`X235568_at` a numeric vector
`X226028_at` a numeric vector
`X203065_s_at` a numeric vector
`X228568_at` a numeric vector
`X237020_at` a numeric vector
`X235649_at` a numeric vector
`X215918_s_at` a numeric vector
`X235670_at` a numeric vector
`X1556579_s_at` a numeric vector
`X236029_at` a numeric vector
`X204482_at` a numeric vector
`X230250_at` a numeric vector
`X224061_at` a numeric vector
`X209841_s_at` a numeric vector
`X224013_s_at` a numeric vector
`X228885_at` a numeric vector
`X238116_at` a numeric vector
`X228268_at` a numeric vector
`X204273_at` a numeric vector
`X239650_at` a numeric vector
`X243924_at` a numeric vector

X204931_at a numeric vector
X229012_at a numeric vector
X209840_s_at a numeric vector
X222717_at a numeric vector
X210299_s_at a numeric vector
X228766_at a numeric vector
X205200_at a numeric vector
X227848_at a numeric vector
X209613_s_at a numeric vector
X213317_at a numeric vector
X241672_at a numeric vector
X229542_at a numeric vector
X209612_s_at a numeric vector
X223836_at a numeric vector
X205982_x_at a numeric vector
X211735_x_at a numeric vector
X230469_at a numeric vector
X206742_at a numeric vector
X214387_x_at a numeric vector
X209904_at a numeric vector
X205952_at a numeric vector
X217046_s_at a numeric vector
X214135_at a numeric vector
X209074_s_at a numeric vector
X206651_s_at a numeric vector
X209469_at a numeric vector
X215454_x_at a numeric vector
X205866_at a numeric vector
X213456_at a numeric vector
X230560_at a numeric vector
X206209_s_at a numeric vector
X210081_at a numeric vector
X232578_at a numeric vector
X209470_s_at a numeric vector
up a numeric vector
down a numeric vector

Source

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE50081

References

Der SD, Sykes J, Pintilie M, Zhu CQ et al. Validation of a histology-independent prognostic gene signature for early-stage, non-small-cell lung cancer including stage IA patients. J Thorac Oncol 2014 Jan;9(1):59-64. PMID: 24305008.

Examples

```
data(GSE50081)
```

`MKMplot` *Multivariate Kaplan-Meier survival curve plot*

Description

Function MKMplot plots the outcome of multivariate survival analysis of patients in a cohort. Independent variable is specified as a gene or a signature. Covariates are sex, age, stage, genotype etc. If user needs one or multiple covariates, for example,smoking, tumor stage, etc., user can use X to specify the covariates.

Usage

```
MKMplot(data, mol, X = NULL, HR="hazard risk",time = "month", status = "status",
sml="hv",quant=c("No",-0.2,0.2),plotmethod="plot",adjx)
```

Arguments

`data`	survival data including clinical data such as status, month, age, sex and/or smoking and expression data of genes or signatures.
`mol`	char value specified a gene symbol or a gene id or a signature existed in data or int value for a column number of a specified gene or a signature in data.
`X`	a string or string vector for one or multiple specified covariates. For example, X="smoking" or X=c("age","sex",smoking","genotype"). 10 covariates are limited in the current version. All covariates should be listed in the data.
`HR`	a string to specify hazard risk or hazard rate. If HR="Hazard risk" or "Hazard_risk", then plot would show coefficient, which has negative, zero, or positive value. The domain is ($-\infty$,∞). The Negative value indicates reduction of hazard risk while the positive value suggests increment of risk. Zero suggests no change of hazard risk. If HR = "hazard rate" or "hazard_rate", then plot would show exp(coefficient), which the value is from 0 to ∞ and HR < 1 indicates that hazard risk is reduced and HR > 1 means that hazard risk is increased. The default is "hazard risk". HR is only used in plot.

time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
status	string to specify status name in the input survival data. For example, status may be "death", "relapse", or "status", depending on user's data. The default value is "status".
sml	surv.median.line: character vector for drawing a horizontal/vertical line at median survival. Allowed values include one of c("none", "hv", "h", "v"). v: vertical, h:horizontal. The value of sml is used in only ggsurvplot. The default is "hv".
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose qunatile or no quantile according to the data. The default values are c("no",-0.2,0.2).
plotmethod	string value: choose a method to plot Kaplan-Meier survival curves. In current version, we have two methods for chose: plot and ggsurvplot. The defauld is plot method. In plot method, we show p-value for result of Ward t-test but in ggsurvplot, we show p-value for the result of log-rank test.
adjx	numeric value used to adjust x-axis position of p-value and HR in only plot.

Details

survival data contain clinical data such as status, month, age, sex and/or smoking and expression of gene or protein. The status may be death, recurrence or relapse and must be a binary variable: 1 for an event (such as death) or 0 for no event (such as alive). The month, age, and gene are numeric continuous variables but sex is a binary variable. The other covariates may be numeric continuous or binary variables. They are listed in column and patients or observations are listed in row.

Value

output a survival curve plot of multivariate survival analysis.

Note

To plot outcome of univariate survival, user can use UKMplot. All inputting parametes are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

UKMplot,MUKMplot,MMKMplot

Examples

```
require(survival)
require(ggplot2)
data(GSE50081)
MKMplot(data=GSE50081,mol=56,X=c("t.stage","n.stage","m.stage"),time="month",
status="status1",sml="none",quant=c("No",-0.2,0.2),plotmethod="ggsurvplot",
adjx = 5)
```

MMKMplot *Multiple multivariate Kaplan-Meier survival curve plots*

Description

Function MMKMplot plots outcomes of multivariate survival analyses of patients with covariates age and sex in a cohort with a specified set of genes. Each gene has a plot and each plot takes a page.

Usage

```
MMKMplot(sdata, stn, gn, X = NULL, HR="hazard risk", status = "status",
time = "month", sml="hv",quant=c("No",-0.2,0.2),plotmethod="plot",adjx,
outdir = "NULL", file)
```

Arguments

sdata	survival data including clinical data such as status, month, age, sex, and expressions of genes or expressions of proteins. Status such as death, recurrence or relapse must be 1 for event (such as death) or 0 for no event (such as alive), month is numeric data, age is numeric data, sex is binary data and genes are numeric data. They are listed in columns and patients are listed in rows.
stn	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the first gene in survival data.
gn	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the last gene in survival data.
X	string vector for covariate(s), an option with inputting names of one, two, three or more covariates. For example, X="smoking", X=c("age","sex","smoking","stage_n"). The number of covariates is limited to 10. All covariates should be listed in the data.

HR	a string for specifying hazard risk or hazard rate. If HR="Hazard risk" or "Hazard_risk", then plot would show coefficient, which has negative, zero, or positive value. The domain is (-∞,∞). The Negative value indicates reduction of hazard risk while the positive value suggests increment of risk. Zero suggests no change of hazard risk. If HR = "hazard rate" or "hazard_rate", then plot would show exp(coefficient), which the value is from 0 to ∞ and HR < 1 indicates that hazard risk is reduced and HR > 1 means that hazard risk is increased. The default is "hazard risk". HR is only used in plot.
status	string for a specifying status name. For example, status may be death, relapse or recurrence. User can set status="death", "relapse" or "recurrence" or "status", depending on the data.
time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
sml	surv.median.line: character vector for drawing a horizontal/vertical line at median survival. Allowed values include one of c("none", "hv", "h", "v"). v: vertical, h:horizontal.The value of sml is used in only ggsurvplot. The default is "hv".
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).
plotmethod	string value: choose a method to plot Kaplan-Meier survival curves. In current version, we have two methods for choice: plot and ggsurvplot. The defauld is plot method. In plot method, we show p-value for result of Ward t-test but in ggsurvplot, we show p-value for the result of log-rank-sum test.
adjx	numeric value used to adjust x-axis position of p-value and HR in only plot.
outdir	string, a path to save a file. If user uses setwd to set a dir for saving file, the outdir can be set "NULL", MMKMplot can automatically save pdf file in this dir folder in user local computer.
file	string for file name. If user sets a path with setwd or a path to outdir, then file just sets file name. The file is a pdf file containing all plot pages.

Value

output multiple pdf pages for multiple survival curve plots.

Note

User may not perform this function if unnecessary.

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

UKMplot,MKMplot,MUKMplot

Examples

```
#require(survival)
#require(ggplot2)
#require(survminer)
data(GSE50081)
XX=c("age","sex","t.stage","n.stage","m.stage")
hr="hazard rate"
MMKMplot(sdata=GSE50081,stn=3593, gn=3596,X=XX,HR=hr,status="status1",
time="month", plotmethod="plot",adjx = 3.5,
file ="GSE50081_ADC_multivariate_survplot")

MMKMplot(sdata=GSE50081,stn="X232578_at", gn="down",X=XX,HR=hr,status="status1",
time="month", quant=c("yes",0.25,0.75),plotmethod="plot",adjx = 3.5,
file ="GSE50081_ADC_multivariate_survplot")

#MMKMplot(sdata=GSE50081,stn=3593, gn=3596,X=XX,HR="hazard rate",status="status1",
#time="month", sml="none",plotmethod="ggsurvplot",adjx = 3.5,file =
#"GSE50081_ADC_multivariate_ggsurvplot")
```

MUKMplot *Function Multiple univariate Kaplan-Meier survival curve plots*

Description

MUKMplot plots the outcomes of univariate survival analyses of patients in a cohort using all selected genes.

Usage

```
MUKMplot(svdata, stn, gn,HR="hazard risk",time = "month", status = "status",
         sml="hv",quant=c("No",-0.2,0.2),plotmethod="plot",adjx, outdir =
         "NULL", file)
```

Arguments

svdata	survival data including clinical data such as status, month, and expressions of genes or proteins. Status such as death, recurrence or relapse must be 1 for event (such as death) or 0 for no event (such as alive). Genes or signatures are numeric continuous variables. They are listed in columns and patients or observations are listed in rows.
stn	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the first gene in survival data.
gn	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the first gene in survival data.
HR	a string for specifying hazard risk or hazard rate. If HR="Hazard risk" or "Hazard_risk", then plot would show coefficient, which has negative, zero, or positive value. The domain is (-∞,∞). The Negative value indicates reduction of hazard risk while the positive value suggests increment of risk. Zero suggests no change of hazard risk. If HR = "hazard rate" or "hazard_rate", then plot would show exp(coefficient), which the value is from 0 to ∞ and HR < 1 indicates that hazard risk is reduced and HR > 1 means that hazard risk is increased. The default is "hazard risk".
time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
status	string for a specifying status name. For example, status may be death, relapse or recurrence. User can set status="death", "relapse" or "recurrence" or "status", depending on the data.
sml	surv.median.line: character vector for drawing a horizontal/vertical line at median survival. Allowed values include one of c("none", "hv", "h", "v"). v: vertical, h:horizontal.The value of sml is used in only ggsurvplot. The default is "hv".
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).
plotmethod	string value: choose a method to plot Kaplan-Meier survival curves. In current version, we have two methods for choice: "plot" and "ggsurvplot". The defauld is plot method. In plot method, we show p-value for result of Ward-test but in ggsurvplot, we show p-value for the result of log-rank test.
adjx	numeric value used to adjust x-axis position of p-value and HR in only plot.
outdir	string for a folder path to save the image file. If user uses setwd to set a path to save the image file, then outdir is not necessary to be given. The default outdir is "NULL".
file	string for a file name or path and file name. If user sets a path with setwd or set path to outdir, then file just contain file name. The file is pdf file containing all plot pages.

Note

User can use MKMplot to plot all signatures and gives a plot file name to save all signature suvival curve plots.

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

UKMplot,MMKMplot,MKMplot

Examples

```
#require(survival)
#require(ggplot2)
data(TCGA_survivalData)
MUKMplot(svdata =TCGA_survivalData,stn=157,gn=160,time ="month", status="status",
plotmethod="plot",adjx = 170,file="TCGA_ADC_univariate_survivalplot")

#MUKMplot(svdata =TCGA_survivalData,stn="157"ARHGEF15"",gn="RPS28",time ="month",
#status="status",sml="hv",quant=c("Yes",-0.2,0.2),plotmethod="ggsurvplot",adjx = 170,
#file="TCGA_ADC_univariate_ggsurvplot")
```

---

musvtest *Multiple univariate suvival tests with a set of genes*

Description

Function musvtest performs SKMCresult by an iteration from the specified first gene to the specified last gene. The output of musvtest is used to build a weight vector for signature survival analysis.

Usage

```
musvtest(sdata,stn,gn,time="month",status="status",quant=c("No",-0.2,0.2))
```

Arguments

sdata	survival and gene-expression data containing patients in row, survival status for death or recurrence or relapse, survival time such as month, day or year and a set of genes in columns.
stn	character value specifying the first gene symbol or gene id existed in sdata or int value specifying column number for the first gene in survival data.
gn	character value specifying the last gene symbol or gene id existed in sdata or int value specifying column number for the last gene in survival data.
time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
status	string for survival status which is binary variable: 1 for event occurrence and 0 for no event occurrence. status may be "death","relapse" or "recurrence", depending on clinical data.
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).

Details

Patient survival status is a binary variable with 1 for an event (such as death) and 0 for no event(such as alive). Genes have expression values(numeric values), which are used to calculate z-scores for classifying patients into two groups: high-expression patients and low-expression patients. SKMCresult performs univariate Cox proportional hazard survival analyses of patients with expression values of a specified gene and outputs hazard risk (HR), z-score and p-value of this specified gene. At first, user can run this function by performing musvtest to screen genes for prognostic signature by using HRs, z-scores, and p-values. Once getting a set of genes for signature, user can perform this function to build a weight vector using

$$w_i = \frac{log_{10}(p_i)}{\sum_{i=1}^{g} log_{10}(p_i)}$$

where p_i is p-value for Ward-test of gene i. For a patient, the signature score or expression value is given by weighting expression values of genes in the signature:

$$y_j = \sum_{i}^{g} w_i x_{ij}$$

where x_{ij} is expression of gene i in patient j.

Value

output a matrix with n rows for gene name and hazard risk, hazard rate, standard error, z-value and p-value of each gene.

Note

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

SKMCresult

Examples

```
data(GSE50081)
res<-musvtest(sdata=GSE50081,stn=3500,gn=3506,time="month",status="status")
#res
#              Gene Hazad risk hazard rate standard error    z-value     p-value
#3500  X209170_s_at -0.6510414   0.5215024      0.3133664 -2.0775721 0.037748792
#3501   X1556325_at -0.6041918   0.5465159      0.3507459 -1.7225913 0.084962455
#3502    X228915_at -0.4992865   0.6069636      0.3394520 -1.4708606 0.141328818
#3503 X1555216_a_at -0.5465844   0.5789238      0.3143044 -1.7390290 0.082029656
#3504  X203548_s_at -0.2004345   0.8183751      0.3018504 -0.6640193 0.506677970
#3505    X205433_at -1.3528063   0.2585138      0.4134465 -3.2720229 0.001067809
#3506    X209614_at -0.8389441   0.4321666      0.3905470 -2.1481262 0.031703733
```

MVKMresult *Multivariate survival analysis with multiple specified independent variables*

Description

Function MVKMresult performs multivariate Cox proportional hazard survival analysis with a set of patients and an independent variable (a specified gene or a feature) and a set of covariates (age, sex and/or smoking or stage) and outputs hazard risks (HR), z-scores, and p-values of the gene and these covariates.

Usage

```
MVKMresult(data,X=NULL,mol, status="status",time="month",quant=c("No",-0.2,0.2))
```

Arguments

data	survival data containing p patients in row, s survival variables such as survival status for death, recurrence or relapse, survival time such as day, month,or year, covariates age, sex and/or smoking, etc. and a set of genes in column.
X	string for covariate(s), number of covariates is limited to 10. If X=NULL, then MVKMresult would be stopped.
mol	int value for column number of the first gene specified.
status	string for survival status of patients, may be "relapse" or "recurrence" or "death". User can set status="death", "relapse" or "recurrence","status" depending on user's survival data. The default value is "status".
time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).

Details

Function MVKMresult performs multivariate Cox proportional hazard survival analyses with p patients and a specified gene and a set of covariates specified and outputs hazard risk (HR),z-score and p-value for the specified gene or signature and covariates.

Value

output a matrix with one row and multiple columns for gene name, Hazard risk, hazard rate, standard error, z-value, p-value of gene and covariates.

Note

User can also use SKMCresult to screen a prognostic signature and a weight vector without covariates.

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

Author(s)

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See Also

SKMCresult,musvtest,mvstest

Examples

```
data(GSE50081)
res<-MVKMresult(data=GSE50081,X=c("t.stage","n.stage","m.stage"),mol=3500,
status="status",time="month",quant=c("no",-0.2,0.2))
```

`mvstest` *Multivariate Cox proportional hazard survival analyses with multiple genes*

Description

Function mvstest performs MVKMresult by iteration from the first gene to the last gene. The output result of musvtest is used to build a vector of weights for screening genes as prognostic signature or doing signature survival analysis.

Usage

```
mvstest(sdata,X=NULL,stn,gn, status,time,quant=c("No",-0.2,0.2))
```

Arguments

`sdata`	survival data containing p patients in row, survival status for death or recurrence or relapse, survival time such as day, month, or year, and covariates age, sex and/or smoking, tumor stage, or chemotherapy, and a set of genes in column.
`X`	string specifying one or multiple covariates such as age, sex, smoking, or tumor stage or genotype. The number of covariates in X is limited to 10.
`stn`	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the first gene in survival data.
`gn`	character value specifying gene symbol or gene id existed in sdata or int value specifying column number for the last gene in survival data.
`status`	string for survival status which must be binary variable: 1 for event occurrence and 0 for no event occurrence. status may be "death", "relapse" or "recurrence", depending on clinical data.
`time`	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
`quant`	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).

Details

Patient survival status is binary variable with 1 for event (such as death) and 0 for no event (such as alive). Genes have expression values(numeric values), which are used to calculate z-scores for classifying patients into two groups: high-expression patients and low-expression patients. SKMCresult performs univariate Cox proportional hazard survival analyses of patients with expression values of a specified gene and outputs hazard risk (HR), z-score and p-value of this specified gene. At first, user can run this function by performing msvtest to screen genes for prognostic signature by using HRs, z-scores, and p-values. Once getting a set of genes for signature, user can perform this function to build a weight vector using

$$w_i = \frac{log_{10}(p_i)}{\sum_{i=1}^{g} log_{10}(p_i)}$$

where p_i is p-value for Ward-test of gene i. For a patient, the signature score or expression value is given by weighting expression values of g genes in the signature:

$$y_j = \sum_{i}^{g} w_i x_{ij}$$

where x_{ij} is expression of gene i in patient j.

Value

output a matrix with n rows for n genes, m+1 columns for Hazard risk, hazard rate, standard error, z-value, p-value of gene name and m covariates.

Note

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

MVKMresult

Examples

```
data(GSE50081)

res<-mvstest(sdata=GSE50081,X=c("t.stage","n.stage"),stn=3550,gn=3555,
status="status",time="month",quant=c("No",-0.2,0.2))
```

`results` *results of univariate Cox proportional hazard analysis of patients with ADC in three cohorts.*

Description

The "results" is a list consisting of three results generated by performing univariate Cox proportional hazard survival analysis in three different cohorts. Each result has four columns gene(gene symbol or geneid), zahard.ratio, zscore, and p.value for each gene. The results list is used to construct weight vector in the signature.

Usage

```
data("results")
```

Format

The format is: List of 3 $:'data.frame': 28 obs. of 4 variables: ..$ Gene : chr [1:28] "CDKN1C" "CDKN2B" "DAB2IP" "DCC" ... ..$ Hazard.ratio: num [1:28] 1.027 0.685 0.663 0.494 0.634 ... ..$ zscore : num [1:28] 0.0734 -1.162 -1.4084 -1.9798 -1.4282 ... ..$ p.value : num [1:28] 0.9415 0.2452 0.159 0.0477 0.1532 ... $:'data.frame': 26 obs. of 4 variables: ..$ Gene : chr [1:26] "201335_s_at" "201621_at" "203185_at" "203525_s_at" ... ..$ Hazard.ratio: num [1:26] 2.712 0.849 0.742 0.99 0.402 ... ..$ zscore : num [1:26] 1.7257 -0.3047 -0.6031 -0.0198 -1.6817 ... ..$ p.value : num [1:26] 0.0844 0.7606 0.5464 0.9842 0.0926 ... $:'data.frame': 34 obs. of 4 variables: ..$ Gene : chr [1:34] "age" "gender" "sex" "cell_type" ... ..$ Hazard.ratio: num [1:34] NA NA NA NA NA ... ..$ zscore : num [1:34] NA NA NA NA NA ... ..$ p.value : num [1:34] NA NA NA NA NA ...

Examples

```
data(results)
```

`signatureExp` *signature expression or signature score*

Description

Function signatureExp.R is used to give signature expression or score across all patients in a cohort data by using weight vector of a signature.

Usage

```
signatureExp(svdata,weight)
```

Arguments

svdata	a survival dataset containing clinic data such as death or relapse status, month, covariates age, sex and/smoking, stages, therapy etc. and a set of genes containing subset of genes in the signature in column.
weight	a matrix that contains gene and/or gene_id and weight columns.

Details

a matrix with $g \times (2 or 3)$. If weight contains two columns, then first column must be gene or gene_id and the second column must be weight. If weight has three columns, then the first two columns are gene and gene_id but the third column must be weight. Gene name or gene_id in weigth must be matched with gene name or gene_id in the survival data.

Value

a survival dataset with signature scores of patients.

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See Also

weight

Examples

```
data(TCGA_survivalData)
data(signature_weight)
res1<-signatureExp(svdata=TCGA_survivalData,weight=signature_weight)
```

---

signature_weight *Weights of genes in a signature*

Description

Weights of genes in a signature were estimated by using the following equation

$$w_i = \frac{log_{10}(p_i)}{\sum_{i=1}^{g} log_{10}(p_i)}$$

where p_i is p-value for Ward-test of gene i in survival analysis.

Usage

```
data("signature_weight")
```

Format

A data frame with 84 observations on the following 2 variables.

`stage3_down` a character vector

`weight.7` a numeric vector

Details

signature_weight is a matrix with g$\times$ 2 or 3 where g is number of genes in a signature and there are two or three columns for gene id or gene name and weights.

Examples

```
data(signature_weight)
```

SKMCresult *Univariate Cox proportional hazard survival analysis with a specified independent variable*

Description

Function SKMCresult performs univariate Cox proportional hazard survival analysis of patients with a specified independent variable or a gene without covariates and outputs hazard risk (HR), z-score, and p-value of this specified gene.

Usage

```
SKMCresult(data,mol, time="month", status="status",quant=c("No",-0.2,0.2))
```

Arguments

`data`	survival and gene-expression data containing patients in row, survival status for death, recurrence or relapse, survival time and a set of genes in column.
`mol`	char value specified a gene symbol or a gene id or a signature existed in data or int value for a column number of a specified gene or a signature in data.
`time`	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".
`status`	string for survival status of patients, may be "relapse" or "recurrence" or "death". User can set status="death", "relapse" or "recurrence","status" depending on user's survival data. The default value is "status".
`quant`	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).

Details

Patient survival status is binary variable with 1 for event (such as death) and 0 for no event(such as alive). Genes have expression values(numeric values), which are used to calculate z-scores for classifying patients into two groups: high-expression patients and low-expression patients. SKMCresult performs univariate Cox proportional hazard survival analyses of patients with expression values of a specified gene and outputs hazard risk (HR), z-score and p-value of this specified gene.

Value

output a matrix with one row and 6 columns for gene name, Hazard risk, hazard rate, standard error, z-value, p-value of the specified gene.

Note

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

MVKMresult,musvtest,mvstest

Examples

```
data(GSE50081)
res<-SKMCresult(data=GSE50081,mol=350, time="month", status="status")
```

---

survivalForest *Forestplot for result of multivariate Cox proportional hazard survival analysis*

Description

This function provides a publishable forestplot figure that shows results of multivariate Cox proportional hazard regression analysis of patients in a cohort.

Usage

```
survivalForest(sdata,xtick)
```

Arguments

sdata	results of multivariate survival analyses,outputted by performing MKMplot.
xtick	x-coordinate size in forestplot. For example, user can set xtick=c(-2,-1,0,1,2)

Details

The data includes column "model" and/or stage", "variable","HR","SE", and "p_value". In inputing data, stage may be stage IA, stageIB, stageII, stageIIA, stageIIB, stageIII, etc. The Variable may contain signature, sex, age, smoking, genotype,etc.. The variable column may be named with "Variate","variate", "Variable","variable", "factor" or "category" word. "HR" is hazard risk, also called coefficient or beta of Cox proportional hazard regression. So, HR column may be named with "HR","hazard risk", "coefficient","beta" or "Beta" word. "SE" is standard error and may be named with "se","SE" or "standard error". "p_value" is p-value for Ward test/ranksum test, may be named with "pvalue","p_value", "p-value","p value","PV" or "pv" word. The rows include signature (gene or biomarker), age, sex and covariate(s).

Value

output a plot figure.

Note

sdata may contain multiple models such as model1, model2, model3. Model1: signature, age,sex. Model2: signature, age, sex, smoking. Model 3: signature, age, sex, smoking, and genotype. User can use empty row to separate these models.

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See Also

forestplot

Examples

```
#library(forestplot)
data(TCGA_forestplt)
xtick=c(-1,-0.5,0,0.5,1)
pdf(file="TCGA_survival_forestplot.pdf")
survivalForest(sdata=TCGA_forestplt,xtick=xtick)
dev.off()
```

TCGA_forestplt *Data for forestplot*

Description

The data are derived from results of performing multivariate Cox proportional hazard survival analysis on patients with ADC in TCGA lung cancer.

Usage

```
data("TCGA_forestplt")
```

Format

A data frame with 28 observations on the following 5 variables.

`stage` a character vector

`variate` a character vector

`beta` a numeric vector

`se` a numeric vector

`p_value` a numeric vector

Details

The dataset was constructed with 28 observations for up and down signatures, sex and age in stages 1A, 1B, stage2 and stage3 and 5 variables stage, variate, beta, se and p_value.

Examples

```
data(TCGA_forestplt)
```

TCGA_survivalData *TCGA data for survival analysis*

Description

TCGA data is a clinical and microarray dataset consisting of 572 samples (observations) in row and 162 variables (20 clinical variables such as age, sex month, status,race, genotype and 142 DE genes)

Usage

```
data("TCGA_survivalData")
```

Format

A data frame with 572 observations on the following 162 variables.

`sample` a character vector

`sampleID` a numeric vector

`status` a numeric vector

`vital_status.demographic` a character vector

`day` a numeric vector

`month` a numeric vector

`age` a numeric vector

`geneder` a character vector

`sex` a numeric vector

`race.demographic` a character vector

`race` a numeric vector

`year_of_birth.demographic` a numeric vector

`year_of_death.demographic` a numeric vector

`age_at_diagnosis.diagnoses` a numeric vector

`days_to_death.demographic` a numeric vector

`egfr_mutation_performed` a character vector

`eml4_alk_translocation_performed` a character vector

`followup_treatment_success` a character vector

`additional_pharmaceutical_therapy` a character vector

`additional_radiation_therapy` a character vector

`SLC25A13` a numeric vector

`PSMC4` a numeric vector

`MRE11A` a numeric vector

`PTCD2` a numeric vector

`STYK1` a numeric vector

`GOLGA5` a numeric vector

`IARS2` a numeric vector

`KIF2A` a numeric vector

`HLTF` a numeric vector

`C14orf166` a numeric vector

`GEMIN2` a numeric vector

`CDC6` a numeric vector

`MSH2` a numeric vector

`FKBP3` a numeric vector

`PSMC6` a numeric vector

PSMB5 a numeric vector

CSNK2A1 a numeric vector

KNOP1 a numeric vector

AVL9 a numeric vector

DNAJC2 a numeric vector

RPA3 a numeric vector

TMEM106B a numeric vector

COA1 a numeric vector

GAPDH a numeric vector

FAF2 a numeric vector

UCHL5 a numeric vector

CBX3 a numeric vector

HNRNPA2B1 a numeric vector

CALU a numeric vector

GAD1 a numeric vector

PDLIM4 a numeric vector

TIMM17A a numeric vector

NAA35 a numeric vector

GOLM1 a numeric vector

SULF1 a numeric vector

FANCI a numeric vector

CLTC a numeric vector

SDHC a numeric vector

MRPL9 a numeric vector

ACP1 a numeric vector

FBXO28 a numeric vector

PDIA6 a numeric vector

SIGMAR1 a numeric vector

ADAM12 a numeric vector

XRCC4 a numeric vector

PLOD2 a numeric vector

TMEM87B a numeric vector

BUB3 a numeric vector

DPY19L4 a numeric vector

HLCS a numeric vector

PSMC2 a numeric vector

SLBP a numeric vector

ORC5 a numeric vector

SGPL1 a numeric vector

GREM1 a numeric vector

VKORC1 a numeric vector

ZNF146 a numeric vector

CHAF1A a numeric vector

TK1 a numeric vector

FEN1 a numeric vector

FRMD5 a numeric vector

DPY19L1 a numeric vector

CKAP5 a numeric vector

ZNF93 a numeric vector

SEMA4B a numeric vector

PRMT3 a numeric vector

ERO1L a numeric vector

DNAJC9 a numeric vector

FMO3 a numeric vector

FHL1 a numeric vector

DAPK2 a numeric vector

PREX2 a numeric vector

VPS13D a numeric vector

TGFBR3 a numeric vector

NDST1 a numeric vector

LIMS2 a numeric vector

GLI2 a numeric vector

ACACB a numeric vector

PIK3C3 a numeric vector

PCM1 a numeric vector

RUNX1T1 a numeric vector

NCOA1 a numeric vector

TTC28 a numeric vector

CBX7 a numeric vector

CPED1 a numeric vector

PTGDS a numeric vector

SPOCK2 a numeric vector

GAB1 a numeric vector

FOXP1 a numeric vector

RAP1A a numeric vector

TCF21 a numeric vector

WDR35 a numeric vector

WBP4 a numeric vector

SORBS3 a numeric vector

TBX2 a numeric vector

ITIH5 a numeric vector

PZP a numeric vector

ATP1B2 a numeric vector

CBFA2T3 a numeric vector

GSTM5 a numeric vector

GSTM3 a numeric vector

ADAMTS8 a numeric vector

GYPC a numeric vector

ARHGAP24 a numeric vector

PDE5A a numeric vector

FBLN5 a numeric vector

IQSEC1 a numeric vector

SNCA a numeric vector

HMBOX1 a numeric vector

NFIB a numeric vector

PAMR1 a numeric vector

SAP18 a numeric vector

IGSF10 a numeric vector

ANGPT1 a numeric vector

JAM2 a numeric vector

PTH1R a numeric vector

NFASC a numeric vector

DLC1 a numeric vector

FIGF a numeric vector

PKNOX2 a numeric vector

NDRG2 a numeric vector

FRAT1 a numeric vector

ANAPC16 a numeric vector

TNXB a numeric vector

SFTPC a numeric vector

KCNK3 a numeric vector

SYNPO a numeric vector

ID4 a numeric vector

PER1 a numeric vector

SLIT3 a numeric vector

FOXO4 a numeric vector

GJA4 a numeric vector

PCBP2 a numeric vector

ADARB1 a numeric vector

PARVA a numeric vector

CFD a numeric vector

ARHGEF15 a numeric vector

GPR20 a numeric vector

HSBP1 a numeric vector

RPS28 a numeric vector

TNXA a numeric vector

FXYD1 a numeric vector

Source

https://www.cancer.gov/ccg/access-data

Examples

```
data(TCGA_survivalData)
```

TS_signature *A signature constructed with a set of tumor suppressor genes*

Description

TS_signature was constructed with a set of 26 tumor suppressor genes screened from microarray data GSE19804 and cohorts GSE18842, GSE40419, and GSE21933 using differential analysis and bioinformatics methods.

Usage

```
data("TS_signature")
```

Format

A data frame with 28 observations on the following 2 variables.

probeid a character vector

gene a character vector

Details

TS signature has 26 tumor suppressor genes (26 probeids). These genes are normally expressed but repressed in cancer or tumor cells. Therefore, a TS signature also has low expression in normal tissues but high expression in cancer cells of patients.

References

Zhang, C., Jiang, M., Zhou, N. et al. Use tumor suppressor genes as biomarkers for diagnosis of non-small cell lung cancer. Sci Rep 11, 3596 (2021). https://doi.org/10.1038/s41598-020-80735-x.

Examples

```
data(ST_signature)
```

UKMplot *Univariate Kaplan-Meier survival curve plot*

Description

Function UKMplot is used to plot outcome of survival analysis of patients in a cohort using a specified gene or a signature.

Usage

```
UKMplot(data,mol,HR="hazard risk", time="month",status="status", sml="hv",
      quant=c("No",-0.2,0.2), plotmethod="plot",adjx)
```

Arguments

data	survival data in which columns contain patient survival data such as survival status, survival month, age, sex,cell type and genes and rows list all patients. Status and sex are binary data. In status, 1 is defined as an event occurrece (such as death) and 0 as no event occurrence (such as alive). Month, age, and genes, signature are numeric and continuous data.
mol	char value specified a gene symbol or a gene id or a signature existed in data or int value for a column number of a specified gene or signature in data.
HR	a string for specifying hazard risk or hazard rate. If HR="Hazard risk" or "Hazard_risk", then plot would show coefficient, which has negative, zero, or positive value. The domain is (-∞,∞). The Negative value indicates reduction of hazard risk while the positive value suggests increment of risk. Zero suggests no change of hazard risk. If HR = "hazard rate" or "hazard_rate", then plot would show exp(coefficient), which the value is from 0 to ∞ and HR < 1 indicates that hazard risk is reduced and HR > 1 means that hazard risk is increased. The default is "hazard risk". HR is only used in plot.
time	string for survival time and may be one of c("day", "month", "year"), depending on the clinical data. The default value is "month".

status	string for survival status of patients, may be "relapse" or "recurrence" or "death". User can set status="death", "relapse" or "recurrence","status" depending on user's survival data. The default value is "status".
sml	surv.median.line: character vector for drawing a horizontal/vertical line at median survival. Allowed values include one of c("none", "hv", "h", "v"). v: vertical, h:horizontal.The value of sml is used in ggsurvplot, not in plot. The default is "hv".
quant	vector for quantile, low and high values. the low and high values are used to define or classify low and high expression groups. If quantile is "yes" or "YES", then the low and high are non-negative precent values, for example, quant=c("yes",0.25,0.75). If quantile is "no", then the low and high values are z-scores, the low value may be negative. For example, quant=c("no",-0.2, 0.2). The quantile = "yes" or = "No" may produce different results of survival analysis. User should carefully choose quantile or no quantile according to the data. The default values are c("no",-0.2,0.2).
plotmethod	string value: choose a method to plot Kaplan-Meier survival curves. In current version, we have two methods for chose: plot and ggsurvplot. The defauld is plot method
adjx	a numeric value used to adjust x-axis position of p-value and HR in plot.

Details

UKMplot is a function invoked by MKMplot. By invoking UMKplot, MKMplot can make a set of survival plots for a set of genes or a set of signatures.

Value

UMKplot outputs a survival curve plot of a specified gene.

Note

For a multivariate survival analysis, user can use MVKMplot to plot survival outcome.

All inputting parameters are not sensitive to upper or lower. That is, user can input upper or lower string or letter. For example, both time ="MONTH" or time = "month" work.

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See Also

MKMplot,MMKMplot,MUKMplot

Examples

```
require(survival)
require(ggplot2)
data(TCGA_survivalData)
UKMplot(data=TCGA_survivalData,mol=78,time="month", status="status",
quant=c("No",-0.2,0.2),adjx=100)
UKMplot(data=TCGA_survivalData,mol="RPS28",time="month", status="status",adjx=100)
```

---

weight *Caculation of Weights for signature genes*

Description

Weights for signature genes are calculated from the results obtained by performing Cox proportional hazard regression on the training survival datasets.

Usage

```
weight(results,signature)
```

Arguments

results	a list of multiple results obtained by performing survival analysis on the training datasets.
signature	a vector or matrix of genes screened by a method from survival data and expression data.

Details

The results file is a list of multiple results obtained by performing Cox proportional hazard survival analysis based on univariate models in multiple datasets. User can create this list by using results<-list(result1,result2,..., resultn). Signature may be a matrix with two columns and n rows. One column may be gene id(such as probe id or Ensembl id or NCBI Entrez id) and the other is gene symbol or gene name. Signature may be a vector(a set of genes or gene ids).

Value

Output a matrix where gene and/or gene id and weight in column and gene names and/or gene id values and weight values.

Note

Sum of weights may not be equal to 1 if some genes in results are lost.

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Examples

```
data(TS_signature)
data(results)
res<-weight(results = results,signature = TS_signature)
```