oncoClassSurv

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### Introduction

In the era of precision medicine, the molecular characteristics of patients are increasingly valued for precise management and scientific research. I developed this R package because it will be useful for molecular classifications and individualized prognosis evaluation.

The current R package involves two main fields: classifier for molecular characteristics, and survival risk over time. The function also provides useful visual output. I also noticed that different datasets have batch effects, which increases the difficulty of accurate evaluation. To simplify this process, I optimized the function. When this function is executed, the batch effects between different datasets will be automatically removed. In addition, we initially used this R package for hepatocellular carcinoma (HCC), but actually, other kind of tumors or even non-tumor disease can also benefit from it based on the user’s customized training data.

The evaluation of tumor molecular classifications is a prerequisite for achieving precise medical management. Based on pre-analyzed or learned sub-types with diverse clinical features (response to drugs, survival outcomes, etc.) and sub-type-specific marker genes, machine learning algorithms could be used for classification training, and thereafter personalized typing prediction could be achieved for any new-diagnosed patients. This classification can be used to guide clinical treatment and further scientific research.

The prognosis evaluation of tumor patients is a key concern for patients and clinical researchers. So far, there have been many nomograms based on gene expression for every type of tumor, which are dazzling. Although some of them are excellent, many nomograms lack external validation and are not convenient for external clinical practice validation. To address this practicality issue, we provide a calculation tool based on customized prognostic features, where users can use gene expression data or choose to add additional clinical covariates such as age, gender, stage, etc. This function can calculate the prognostic risk of each patient at different time points and plot a survival curve for each patient.

Any questions or tips, please don’t hesitate to let me know!

### Installation

1. Online

if(!require(devtools))install.packages("devtools")  
if(!require(oncoClassSurv))devtools::install\_github("OliveryYL/oncoClassSurv",  
upgrade = FALSE,dependencies = TRUE)

1. Local

#Click the green button "code" on this page, then click "Download ZIP" to download   
it to your R working directory. Install it with:  
devtools::install\_local("oncoClassSurv-master.zip",upgrade = F,dependencies = T)

### Functions

The oncoClassSurv() provides three optional tasks based on two training and predicting processes: (1) classifier; and (2) survival risk over time. Users can select one task from the three tasks. Among them, "task=1" means only calculating the classifications for patients; "task=2" means only calculating the survival risk over time for patients; "task=3" means calculating the classifications and survival risk over time for patients. When the function of classification is being performed, there are two available machine learning algorithms: random forest (RF) and support vector machine (SVM). Notably, for the prediction of HCC, we found high consistency between the RF and SVM algorithms, and have set the optimal parameter of predicting HCC as the default value of the R package. For other cancers, it is recommended to validate the accuracy and consistency of prediction before conducting large-scale predictions.

In addition, to overcome the tedious steps of programming and make it friendly for ordinary users, we developed an interactive application based on Shiny. Users only need to use the command oncoClassSurv\_RunShiny() to visit it.

### Data prepare

The training and input data can all be customized.

1. For tables of expression matrix, they should be “TPM” or “FPKM” normalized, without log() conversion, and without negative values. The first column name should be a customized label for features or genes, and the other column names should be sample names.

#training expression matrix:  
train.tumor.exp<-data.table::fread(file = system.file("extdata",   
 "train.tumor.exp.fpkm.txt",package = "oncoClassSurv"),  
 data.table = F,showProgress = T)  
train.tumor.exp[1:6,1:3]  
#> Features TCGA-DD-AAVS-01A-11R-A41C-07 TCGA-DD-AAE3-01A-11R-A41C-07  
#> 1 LAPTM5 18.4255100 18.9946800  
#> 2 ITGB2 3.5492310 3.4017280  
#> 3 ARHGDIB 26.1084025 25.7679609  
#> 4 COTL1 3.3672073 6.2691545  
#> 5 GBP5 0.5242262 0.2610244  
#> 6 HLA\_DQA1 1.6251020 3.9560500  
  
#input expression matrix:  
input.tumor.exp<-data.table::fread(  
 file = system.file("extdata", "icgc.tumor.exp.fpkm.txt",  
 package = "oncoClassSurv"),  
 data.table = F,showProgress = T)  
input.tumor.exp[1:6,1:3]  
#> Features SA560642 SA560673  
#> 1 LAPTM5 22.513485 42.872559  
#> 2 ITGB2 11.986753 9.630085  
#> 3 ARHGDIB 32.644188 47.843265  
#> 4 COTL1 9.996586 15.076860  
#> 5 GBP5 7.466073 1.116859  
#> 6 HLA\_DQA1 44.956461 43.881046

1. For tables of clinical data, the format could be “.rds” or “.csv”, “.txt”, “.xlsx”, etc., which could be imported by the function of data.table::fread(). The first column name should be named “sample\_name”. Additional description for the clinical training data: If users need to train a classifier and perform prediction, please include the pre-prepared classification information of the samples in the clinical training data. The column name of the classification should be “Cluster”. In addition, the survival data is necessary if users want to train a Cox regression model. Other columns in the clinical training data should include at least the status (or event), and survival time, whose labels should be consistent with the parameters of “event” and “time” in the oncoClassSurv() function.  
   If users want to explore additional clinical factors, such as age, stage, gender, etc., please include the corresponding information. Additional description for the clinical input data: The survival data is not necessary. In addition, clinical factors are not always necessary depending on demands. However, if users want to explore additional clinical factors, please include the corresponding clinical factors in the clinical input data.

#For the training clinical data:  
train.tumor.clin.surv=readRDS(system.file("extdata",   
 "train.cluster.surv.rds",package = "oncoClassSurv"))  
head(train.tumor.clin.surv)  
#> Cluster status OS Stage  
#> TCGA-DD-AAVS-01A-11R-A41C-07 C1 0 60.8 Stage I  
#> TCGA-DD-AAE3-01A-11R-A41C-07 C2 0 18.9 Stage I  
#> TCGA-DD-A4NS-01A-11R-A311-07 C3 1 81.9 Stage I  
#> TCGA-5R-AA1D-01A-11R-A38B-07 C3 0 15.0 Stage III  
#> TCGA-BW-A5NO-01A-11R-A27V-07 C2 0 0.7 Stage III  
#> TCGA-DD-AADL-01A-11R-A41C-07 C2 0 21.2 Stage I  
  
#For the input clinical data:  
input.clinsurv<-data.table::fread(file = system.file("extdata",   
 "input\_clinsurv.txt",package = "oncoClassSurv"),  
 data.table = F)  
head(input.clinsurv)  
#> sample\_name status OS Stage  
#> 1 SA560642 1 44 Stage II  
#> 2 SA560673 1 40 Stage IV  
#> 3 SA560695 1 24 Stage II  
#> 4 SA560702 0 55 Stage III  
#> 5 SA594207 0 54 Stage II  
#> 6 SA594223 1 43 Stage II

1. The demands of the file format are the same as the clinical data file. The input data (expression matrix) should include all genes same as the marker genes used for training.

cluster\_markergenes=readRDS(system.file("extdata",   
 "train\_cluster.features.rds",package = "oncoClassSurv"))  
head(cluster\_markergenes)  
#> [1] "LAPTM5" "ITGB2" "ARHGDIB" "COTL1" "GBP5" "HLA\_DQA1"

1. The demands of the file format are the same as the clinical data file. The input data (expression matrix and/ or clinical data) should include all features (significant survival genes and/ or additional clinical factors) same as features for training.

prog.signif.features<-readRDS(system.file("extdata",   
 "train\_survival.features.rds",package = "oncoClassSurv"))  
head(prog.signif.features)  
#> [1] "PCK2" "G6PD" "FTCD" "ADH4" "ALDH1L1" "PON1"

### Example

1. This is an example for predicting classifications when task=1 using "RF":

library(oncoClassSurv)  
results<-oncoClassSurv(input.exp.path = system.file("extdata",   
 "icgc.tumor.exp.fpkm.txt",package = "oncoClassSurv"),  
 miss\_go.on=T,task=1,rm.batch.effect=TRUE,  
 plot.combatch=TRUE,print.combat.plots=FALSE,  
 cluster.method="SVM",show.message=FALSE)  
#> Input data is performing log2(expression+1)...  
#> log2(expression+1) finished.  
#> Found2batches  
#> Adjusting for0covariate(s) or covariate level(s)  
#> Standardizing Data across genes  
#> Fitting L/S model and finding priors  
#> Finding parametric adjustments  
#> Adjusting the Data  
results$original\_combat.plots

head(results$svm.cluster$svm.cluster.pred)  
#> ID svm.cluster.pred  
#> SA560642 SA560642 C2  
#> SA560673 SA560673 C1  
#> SA560695 SA560695 C4  
#> SA560702 SA560702 C3  
#> SA594207 SA594207 C2  
#> SA594223 SA594223 C2

1. This is an example for predicting classifications when task=1 using "SVM":

library(oncoClassSurv)  
results<-oncoClassSurv(input.exp.path = system.file("extdata",   
 "icgc.tumor.exp.fpkm.txt",package="oncoClassSurv"),task=1,  
 rm.batch.effect=TRUE,plot.combatch=TRUE,  
 print.combat.plots=FALSE,cluster.method="RF",  
 show.message=FALSE)  
#> Input data is performing log2(expression+1)...  
#> log2(expression+1) finished.  
#> Found2batches  
#> Adjusting for0covariate(s) or covariate level(s)  
#> Standardizing Data across genes  
#> Fitting L/S model and finding priors  
#> Finding parametric adjustments  
#> Adjusting the Data  
head(results$rf.cluster$rf.cluster.pred)  
#> ID rf.cluster.pred  
#> SA560642 SA560642 C2  
#> SA560673 SA560673 C1  
#> SA560695 SA560695 C4  
#> SA560702 SA560702 C2  
#> SA594207 SA594207 C2  
#> SA594223 SA594223 C2

1. This is an example for predicting survival risk over time when task=2:

library(oncoClassSurv)  
results<-oncoClassSurv(  
train\_survival.feature.path=system.file("extdata",  
"train\_survival.features.rds",package = "oncoClassSurv"),  
input.exp.path = system.file("extdata", "icgc.tumor.exp.fpkm.txt",  
package = "oncoClassSurv"),  
input.clin.path = system.file("extdata", "input\_clinsurv.txt",  
package = "oncoClassSurv"),  
task=2,rm.batch.effect=TRUE,plot.combatch=TRUE,  
print.combat.plots=FALSE,  
surv.t.custom=NULL,plot.surv.curve=TRUE,  
survcurve.break.x.by = 12,print.survplot = FALSE,  
plot.samples=c(1:10),show.message=FALSE)  
#> Input data is performing log2(expression+1)...  
#> log2(expression+1) finished.  
#> Found2batches  
#> Adjusting for0covariate(s) or covariate level(s)  
#> Standardizing Data across genes  
#> Fitting L/S model and finding priors  
#> Finding parametric adjustments  
#> Adjusting the Data  
#> Warning: `gather\_()` was deprecated in tidyr 1.2.0.  
#> ℹ Please use `gather()` instead.  
#> ℹ The deprecated feature was likely used in the survminer package.  
#> Please report the issue at <https://github.com/kassambara/survminer/issues>.  
#> This warning is displayed once every 8 hours.  
#> Call `lifecycle::last\_lifecycle\_warnings()` to see where this warning was  
#> generated.  
results$surv.probablity[1:6,1:5]  
#> Time SurvivalProbablity.SA560642 SurvivalProbablity.SA560673  
#> 1 0.3 0.9993512 0.9942816  
#> 2 0.4 0.9980315 0.9827386  
#> 3 0.5 0.9967081 0.9712832  
#> 4 0.6 0.9960414 0.9655569  
#> 5 0.9 0.9953614 0.9597480  
#> 6 1.0 0.9946740 0.9539069  
#> SurvivalProbablity.SA560695 SurvivalProbablity.SA560702  
#> 1 0.9956199 0.9991132  
#> 2 0.9867604 0.9973100  
#> 3 0.9779439 0.9955027  
#> 4 0.9735276 0.9945924  
#> 5 0.9690413 0.9936644  
#> 6 0.9645237 0.9927265  
results$ggsurv.curve$ggsurv.curve$plot

1. This is an example for predicting classifications and survival risk over time when task=3:

library(oncoClassSurv)  
results<-oncoClassSurv(train\_survival.feature.path=system.file("extdata",  
 "train\_survival.features.rds",package = "oncoClassSurv"),  
 input.exp.path = system.file("extdata", "icgc.tumor.exp.fpkm.txt",  
 package = "oncoClassSurv"),  
 input.clin.path = system.file("extdata", "input\_clinsurv.txt",  
 package = "oncoClassSurv"),  
 task=3,rm.batch.effect=TRUE,plot.combatch=TRUE,  
 print.combat.plots=FALSE,cluster.method="SVM",  
 surv.t.custom=NULL,plot.surv.curve=TRUE,  
 survcurve.break.x.by = 12,print.survplot = FALSE,  
 plot.samples=c(1:10),show.message=FALSE)  
#> Input data is performing log2(expression+1)...  
#> log2(expression+1) finished.  
#> Found2batches  
#> Adjusting for0covariate(s) or covariate level(s)  
#> Standardizing Data across genes  
#> Fitting L/S model and finding priors  
#> Finding parametric adjustments  
#> Adjusting the Data  
head(results$svm.cluster$svm.cluster.pred)  
#> ID svm.cluster.pred  
#> SA560642 SA560642 C2  
#> SA560673 SA560673 C1  
#> SA560695 SA560695 C4  
#> SA560702 SA560702 C3  
#> SA594207 SA594207 C2  
#> SA594223 SA594223 C2  
results$surv.probablity[1:6,1:5]  
#> Time SurvivalProbablity.SA560642 SurvivalProbablity.SA560673  
#> 1 0.3 0.9993512 0.9942816  
#> 2 0.4 0.9980315 0.9827386  
#> 3 0.5 0.9967081 0.9712832  
#> 4 0.6 0.9960414 0.9655569  
#> 5 0.9 0.9953614 0.9597480  
#> 6 1.0 0.9946740 0.9539069  
#> SurvivalProbablity.SA560695 SurvivalProbablity.SA560702  
#> 1 0.9956199 0.9991132  
#> 2 0.9867604 0.9973100  
#> 3 0.9779439 0.9955027  
#> 4 0.9735276 0.9945924  
#> 5 0.9690413 0.9936644  
#> 6 0.9645237 0.9927265  
results$ggsurv.curve$ggsurv.curve$plot

### Interactive ShinyAPP

Run ShinyAPP by oncoClassSurv\_RunShiny():

library(oncoClassSurv)  
oncoClassSurv\_RunShiny()

Description: All .pdf or .csv files can be downloaded to the local disk.

1. Run oncoClassSurv\_RunShiny() using the default settings.
2. Run oncoClassSurv\_RunShiny() to predict the classifications for a customized cohort.
3. Run oncoClassSurv\_RunShiny() to predict the prognosis for a customized cohort.
4. The output tables. Classification table is in the left. Prognosis table is in the right.
5. Users can select interesting samples for further research.
6. Analyses for curated samples and genes.
7. Survival curves and the process to remove batch effect.

Follow us for updates (<https://github.com/OliveryYL/oncoClassSurv>).