# Pancreatic Cancer Analysis

Bravo, Williams, and Acharjee 19 Sept 2018

#Libraries

##### Begin Block 1

setwd("~/AnimeshReview/LauraPaper/Journal of Translational Medicine /LauraFinal/") library(readxl) library(data.table) library(tidyverse) library(dplyr) library(devtools) library(ggcorrplot) library(car) library(ggpubr) library(glmnet) library(summarytools) library(knitr) library(htmltools) library(corrplot) library(caret) library(factoextra) library(Metrics) library(readr) library(gplots) library(dplyr) library(stringr) library(readxl) library(plotly) library(e1071) library(ggplot2) library(reshape2) library(multtest) library(ROCR) library(gridExtra) library(MLmetrics) #### Begin Load Laura's Functions doubleAUCfun <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre> yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k]) model3<-glm(Outcome~Predictor+Predictor2,data=yy3, family=binomial(link='logit'))</pre> new3<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre> p3<-predict(model3,new3,type="response")</pre> new5<-data.frame(Outcome=ytest)</pre> pr3 <- prediction(p3, new5)</pre>

```
prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
}
doubleAUCfunNB <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    model4<-naiveBayes(Outcome~Predictor+Predictor2,data=yy3)</pre>
    new4<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    p4<-predict(model4,new4,type="raw")
    #without raw write confusion matrix directly
    prob2<-NULL
    for (i in 1:dim(p4)[1]){
        prob2[i]<-p4[i,2]/p4[i,1]
    }
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(prob2, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
}
doubleAUCfunRFCross <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    control <- trainControl(method="repeatedcv", number=10, repeats=3) #Is this the only thing needed f
    seed <- 7
    metric <- "Accuracy"</pre>
    set.seed(seed)
    #mtry <- 2
    tunegrid <- expand.grid(.mtry=c(1:6))</pre>
    set.seed(seed)
    rf_default <- train(Outcome~Predictor+Predictor2,data=yy3, method="rf", metric=metric, tuneGrid=tun
    #print(rf_default)
    new4<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    pred=predict(rf_default, new4,type="prob")
    pred2=predict(rf_default, new4)
    prob2<-NULL
    for (i in 1:dim(pred)[1]){
        prob2[i] <-pred[i,2]/pred[i,1]</pred[i,1]
    }
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(prob2, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
}
```

```
2
```

```
doubleAUCfunSVM <- function(xtrain, ytrain,xtest,ytest,s,k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    seed <-7
    set.seed(seed)
    model3<-svm(Outcome~Predictor+Predictor2,data=yy3)</pre>
    new3<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    p3<-predict(model3,new3,decision.values = TRUE)
    p4<-attr(p3,"decision.values")
    new5<-data.frame(Outcome=ytest)</pre>
    pr3<- prediction(p4, new5)</pre>
    #table(p3, new5)
    #confusionMatrix(p3, new5)
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
}
doubleAUCfunSVMCross <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    seed <- 7
    set.seed(seed)
    model4<-svm(Outcome~Predictor+Predictor2,data=yy3,method="C-classification",</pre>
                 kernel="radial", gamma = 0.01, cost = 100, cross=10, probability=TRUE)
    new4<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    p4<-predict(model4,new4,decision.values = TRUE)</pre>
    p5<-attr(p4,"decision.values")</pre>
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(p5, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc30y.values[[1]]</pre>
    result2<-auc3
}
doublePlusfun <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    model3<-glm(Outcome~Predictor+Predictor2,data=yy3, family=binomial(link='logit'))</pre>
    new3<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    p3<-predict(model3,new3,type="response")</pre>
    new5<-data.frame(Outcome=ytest)</pre>
    pr <- prediction(p3, new5)</pre>
    Acc <- performance(pr, measure="acc")</pre>
    AccV<-Acc@y.values[[1]] [max(which(Acc@x.values[[1]] >= 0.5))]
    Sens <- performance(pr, measure= "sens")</pre>
    SensV<-Sens@y.values[[1]][max(which(Sens@x.values[[1]] >= 0.5))]
    Spec <- performance(pr, measure= "spec")</pre>
    SpecV<-Spec@y.values[[1]][max(which(Spec@x.values[[1]] >= 0.5))]
    Prec <- performance(pr, measure= "prec")</pre>
    PrecV<-Prec@y.values[[1]][max(which(Prec@x.values[[1]] >= 0.5))]
```

```
AllV<-data.frame(Vector=c(AccV, SensV, SpecV, PrecV))</pre>
    return(AllV)
}
doubleROCfun <- function(xtrain, ytrain, xtest, ytest, s, k) {</pre>
    yy3<-data.frame(Outcome=ytrain, Predictor=xtrain[,s],Predictor2=xtrain[,k])
    model3<-glm(Outcome~Predictor+Predictor2,data=yy3, family=binomial(link='logit'))</pre>
    new3<-data.frame(Predictor=xtest[,s],Predictor2=xtest[,k])</pre>
    p3<-predict(model3,new3,type="response")</pre>
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(p3, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    result<-prf3
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    return(result)
}
MeansNames <- function(doubleAUCR,trial){</pre>
    doubleAUCR<-as.data.frame(doubleAUCR)</pre>
    doubleAUCR<-mutate(doubleAUCR, Means=rowMeans(doubleAUCR))</pre>
    row.names(doubleAUCR)<-trial</pre>
    return(doubleAUCR)
}
multipleAUCfun <- function(xtrain,ytrain,xtest,ytest) {</pre>
    yy3<-data.frame(Outcome=ytrain,xtrain)</pre>
    model3<-glm(Outcome~.,data=yy3, family=binomial(link='logit'))</pre>
    new3<-data.frame(xtest)</pre>
    p3<-predict(model3,new3,type="response")</pre>
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(p3, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
    return(result2)
}
multipleAUCfunNB <- function(xtrain, ytrain, xtest, ytest) {</pre>
    yy3<-data.frame(Outcome=ytrain,xtrain)</pre>
    model4<-naiveBayes(Outcome~.,data=yy3)</pre>
    new3<-data.frame(xtest)</pre>
    p4<-predict(model4,new3,type="raw")
    #without raw write confusion matrix directly
    prob2<-NULL
    for (i in 1:dim(p4)[1]){
        prob2[i]<-p4[i,2]/p4[i,1]
```

```
}
    new5<-data.frame(Outcome=vtest)</pre>
    pr3 <- prediction(prob2, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
    return(result2)
}
multipleROCfun <- function(xtrain,ytrain,xtest,ytest) {</pre>
    yy3<-data.frame(Outcome=ytrain,xtrain)</pre>
    model3<-glm(Outcome~.,data=yy3, family=binomial(link='logit'))</pre>
    new3<-data.frame(xtest)
    p3<-predict(model3,new3,type="response")</pre>
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(p3, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
    return(prf3)
}
multipleROCfunNB <- function(xtrain, ytrain, xtest, ytest) {</pre>
    yy3<-data.frame(Outcome=ytrain,xtrain)</pre>
    model4<-naiveBayes(Outcome~.,data=yy3)</pre>
    new3<-data.frame(xtest)
    p4<-predict(model4,new3,type="raw")
    #without raw write confusion matrix directly
    prob2<-NULL
    for (i in 1:dim(p4)[1]){
        prob2[i]<-p4[i,2]/p4[i,1]
    }
    new5<-data.frame(Outcome=ytest)</pre>
    pr3 <- prediction(prob2, new5)</pre>
    prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
    auc3 <- performance(pr3, measure = "auc")</pre>
    auc3 <- auc3@y.values[[1]]</pre>
    result2<-auc3
    return(prf3)
}
singleAUCfun <- function(xtrain, ytrain, xtest, ytest, s) {</pre>
    yy2<-data.frame(Outcome=ytrain, Predictor=xtrain[,s])</pre>
    model2<-glm(Outcome~Predictor,data=yy2,family=binomial(link='logit'))</pre>
    new2<-data.frame(Predictor=xtest[,s])</pre>
    p<-predict(model2,new2,type = "response")</pre>
    new4<-data.frame(Outcome=ytest)</pre>
```

```
pr <- prediction(p, new4)</pre>
    prf <- performance(pr, measure = "tpr", x.measure = "fpr")</pre>
    auc <- performance(pr, measure = "auc")</pre>
    auc <- auc@y.values[[1]]</pre>
    return(auc)
}
singlePlusfun <- function(xtrain, ytrain, xtest, ytest, s) {</pre>
    yy2<-data.frame(Outcome=ytrain, Predictor=xtrain[,s])</pre>
    model2<-glm(Outcome~Predictor,data=yy2,family=binomial(link='logit'))</pre>
    new2<-data.frame(Predictor=xtest[,s])</pre>
    p<-predict(model2,new2,type = "response")</pre>
    new4<-data.frame(Outcome=ytest)</pre>
    pr <- prediction(p, new4)</pre>
    Acc <- performance(pr, measure="acc")</pre>
    AccV<-Acc<sup>0</sup>y.values[[1]][max(which(Acc<sup>0</sup>x.values[[1]] >= 0.5))]
    Sens <- performance(pr, measure= "sens")</pre>
    SensV<-Sens@y.values[[1]] [max(which(Sens@x.values[[1]] >= 0.5))]
    Spec <- performance(pr, measure= "spec")</pre>
    SpecV<-Spec@y.values[[1]] [max(which(Spec@x.values[[1]] >= 0.5))]
    Prec <- performance(pr, measure= "prec")</pre>
    PrecV<-Prec@y.values[[1]] [max(which(Prec@x.values[[1]] >= 0.5))]
    AllV<-data.frame(Vector=c(AccV, SensV, SpecV, PrecV))</pre>
    return(AllV)
}
singleROCfun <- function(xtrain, ytrain, xtest, ytest, s) {</pre>
    yy2<-data.frame(Outcome=ytrain, Predictor=xtrain[,s])</pre>
    model2<-glm(Outcome~Predictor,data=yy2,family=binomial(link='logit'))</pre>
    new2<-data.frame(Predictor=xtest[,s])</pre>
    p<-predict(model2,new2,type = "response")</pre>
    new4<-data.frame(Outcome=ytest)</pre>
    pr <- prediction(p, new4)</pre>
    prf <- performance(pr, measure = "tpr", x.measure = "fpr")</pre>
    resultU2<-prf
    tomeany<-as.data.frame(prf@y.values)</pre>
    tomeanx<-as.data.frame(prf@x.values)</pre>
    auc <- performance(pr, measure = "auc")</pre>
    auc <- auc@y.values[[1]]</pre>
    return(resultU2)
}
```

set.seed(132)

```
### Load Pancreatic Cancer Dta
setwd("/Users/j.williams/AnimeshReview/LauraPaper/Journal of Translational Medicine /LauraFinal/Sept18_
All2 <- readRDS("All2.Pancreatic.rds"); savee <- readRDS("savee.Pancreatic.rds")
#TRAIN
### set n to 10 for now to make quicker
n<-100 #Number of LASSO and EN loops. Per loop a model with features selected. The 80% most popular fea
#N and nn control the number of models created for combinatorial analysis to help in further feature se
N < -10
nn <-25
ErrorsFinEN<-vector(mode="double", length=n)</pre>
BetasFinEN<-vector(mode="character", length=n)</pre>
LambdaFinEN<-vector(mode="double", length=n)</pre>
BNumFinEN<-vector(mode="double", length=n)</pre>
see2EN<-data.frame(All="All")</pre>
LauCoef1<-data.frame(Coeff="See",stringsAsFactors=FALSE)</pre>
BetasTodo<-data.frame(Features="Name",Coefficients=1)</pre>
ListError<-vector(mode="double", length=n)</pre>
BetasFin<-vector(mode="character", length=n)</pre>
LambdaFin<-vector(mode="double", length=n)</pre>
BNumFin<-vector(mode="double", length=n)</pre>
see2<-data.frame(All="All")</pre>
LauCoef1L<-data.frame(Coeff="See",stringsAsFactors=FALSE)</pre>
BetasTodoL<-data.frame(Features="Name",Coefficients=1)</pre>
##### End Block 1
##### Begin Block 2
for (i in 1:n){
  smp_size = floor(0.75 * nrow(All2))
  train_ind <- caret::createDataPartition(All2$Label, p = 0.75, list = FALSE, times = 1)</pre>
  #Training set
  train = All2[train_ind, ]
  #Test set
  test = All2[-train_ind, ]
  #Creates matrices for independent and dependent variables.
  xtrain <- train[ , !(names(train) %in% "Label")] %>% as.matrix()
  ytrain = train$Label
```

```
xtest <- test[ , !(names(test) %in% "Label")] %>% as.matrix()
ytest = test$Label
#Choose lambda value that minimize missclassification error.
#0.5 as elastic nets, all variables with EN are based on ElasticNets analysis. 100 lambdas sampled wi
CVEN=cv.glmnet(xtrain,ytrain,family="binomial",type.measure="class",alpha=0.5,nlambda=100)
attach(CVEN)
Lambda.BestEN<-CVEN$lambda.min #can be either minimum or 1 standard deviation
print(Lambda.BestEN)
CVFinEN=glmnet(xtrain,ytrain,family="binomial",alpha=0.5,lambda=Lambda.BestEN)
CoefEN<-coef(CVFinEN) #Beta coefficients obtained from here
InterceptEN<-CoefEN@x[1]</pre>
BetasEN<-CVFinEN$beta
Betas2EN<-data.frame(Features=BetasEN@Dimnames[[1]][BetasEN@i+1], Coefficients=BetasEN@x) #Beta coeff
CVPred1EN = predict(CVFinEN, family="binomial", s=Lambda.BestEN, newx = xtest,type="class") #predict
#Calculate error for categorical values
ytest2<-as.factor(ytest)</pre>
ResultsEN<-table(CVPred1EN,ytest)</pre>
confusionMatrix(as.factor(CVPred1EN),ytest)
AccuracyEN<-(ResultsEN[1]+ResultsEN[4])/sum(ResultsEN[1:4])
ErrorEN<-1-AccuracyEN
LauCoef <- Betas 2EN $Coefficients
LauCoefEN<-data.frame(Coeff=LauCoef,stringsAsFactors=FALSE)</pre>
LauCoef1<-rbind(LauCoef1,LauCoefEN)
BetasTodo<-rbind(BetasTodo,Betas2EN) #store coefficients and store betas
seeEN<-Betas2EN$Features</pre>
seeEN1<-data.frame(All=seeEN)</pre>
see2EN<-rbind(see2EN,seeEN1) #all beta names stored</pre>
mEN<-count(see2EN, All) #frequency of the betas stored counted
see3EN<-toString(seeEN)</pre>
ErrorsFinEN[i] <- ErrorEN #error of the model stored</pre>
BetasFinEN[i] <- see3EN #name of features the model used</pre>
BNumFinEN[i]<-length(seeEN) #number of features the model used</pre>
LambdaFinEN[i] <- Lambda.BestEN #lambda chosen for model
detach(CVEN)
#Change between Lasso and EN, alpha=1 (*)
CV=cv.glmnet(xtrain,ytrain,family="binomial",type.measure="class",alpha=1,nlambda=100)
attach(CV)
Lambda.Best<-CV$lambda.min
CVFin=glmnet(xtrain,ytrain,family="binomial",alpha=1,lambda=Lambda.Best)
Coef<-coef(CVFin)
Intercept<-Coef@x[1]</pre>
Betas<-CVFin$beta
```

```
Betas2<-data.frame(Features=Betas@Dimnames[[1]][Betas@i+1], Coefficients=Betas@x)
CVPred1 = predict(CVFin, family="binomial", s=Lambda.Best, newx = xtest,type="class")</pre>
```

```
#Calculate error for categorical values
ytest2<-as.factor(ytest)
confusionMatrix(as.factor(CVPred1),ytest)
Results<-table(CVPred1,ytest)
Accuracy<-(Results[1]+Results[4])/sum(Results[1:4])
Error<-1-Accuracy</pre>
```

#### #visual display of for

```
BetasTodoL<-rbind(BetasTodoL,Betas2)
see<-Betas2$Features
see1<-data.frame(All=see)
see2<-rbind(see2,see1)
m<-count(see2, All)</pre>
```

```
see3<-toString(see)
ListError[i]<-Error
BetasFin[i]<-see3
BNumFin[i]<-length(see)
LambdaFin[i]<-Lambda.Best
detach(CV)</pre>
```

```
}
```

```
## [1] 0.6689277
## [1] 0.6303686
## [1] 0.7294298
## [1] 0.2883708
## [1] 0.4733006
## [1] 0.5943159
## [1] 0.235993
## [1] 0.6584265
## [1] 0.1317309
## [1] 0.395802
## [1] 0.6748829
## [1] 0.6907273
## [1] 0.4808845
## [1] 0.2339522
## [1] 0.6926208
## [1] 0.4017377
## [1] 0.6815938
## [1] 0.3682275
## [1] 0.6878564
## [1] 0.5334466
## [1] 0.25522
## [1] 0.7062928
## [1] 0.5021274
## [1] 0.2454332
## [1] 0.3415769
## [1] 0.1445318
```

##	[1]	0.2492792
##	[1]	0.7286193
##	[1]	0.4040431
##	[1]	0.5608647
##	[1]	0.4575239
##	[1]	0.639378
##	[1]	0.1181126
##	[1]	0.194737
##	[1]	0.1059382
##	[1]	0.4479945
##	[1]	0.3634272
##	[1]	0.4787447
##	[1]	0.5555517
##	[1]	0.5364108
##	[1]	0.1343051
##	[1]	0.4800724
##	[1]	0.3865033
##	[1]	0.6247686
##	[1]	0.2318932
##	[1]	0.1884252
##	[1]	0.6696531
##	[1]	0.5132077
##	[1]	0.502099
##	[1]	0.629618
##	[1]	0.06499661
##	[1]	0.6696552
##	[1]	0.3857286
##	[1]	0.2742923
##	[1]	0.2977953
##	[1]	0.607225
##	[1]	0.2129634
##	[1]	0.4963329
##	[1]	0.4782131
##	[1]	0.2843202
##	[1]	0.3724457
##	[1]	0.4973665
##	[1]	0.6293572
##	[1]	0.251071
##	[1]	0.7596586
##	[1]	0.4509715
##		0.4194573
##		0.2410539
## ##		0.6456791
## ##		0.7355681
## ##		0.031905
## ##	L⊥J [1]	0.09030
π# ##	∟⊥」 [1]	0 4760281
##	[1]	0.642023
##	[1]	0.36937
 ##	[1]	0.4357793
##	[1]	0.2766556
##	[1]	0.5132012
##	[1]	0.1636617

## [1] 0.7393992 ## [1] 0.4958403 ## [1] 0.172681 ## [1] 0.6463179 ## [1] 0.5903157 ## [1] 0.393137 ## [1] 0.7239418 ## [1] 0.3621122 ## [1] 0.6498011 ## [1] 0.2339883 ## [1] 0.5483706 ## [1] 0.2081683 ## [1] 0.5177668 ## [1] 0.6192567 ## [1] 0.609796 ## [1] 0.2968183 ## [1] 0.6362316 ## [1] 0.4532429 ## [1] 0.6682868 ## [1] 0.4565895

#Visualizing data from LASSO and EN ####

#obtain in a data frame all error, betas names, number and lamda for the N models for each lasso and EN
All\_info<-data.frame(Error=ListError, BetasNames=BetasFin, BetasNum=BNumFin, Lambda=LambdaFin)
All\_infoEN<-data.frame(Error=ErrorsFinEN, BetasNames=BetasFinEN, BetasNum=BNumFinEN, Lambda=LambdaFinEN</pre>

m<-m[-1,] mEN<-mEN[-1,]

Final\_LASSO<-m[order(-m\$n),] #order highest frequencies above and filter with those that appear more th
Final\_LASSO1<-filter(Final\_LASSO,n>40) #threshold selected - 80%

Final\_EN<-mEN[order(-mEN\$n),]
Final\_EN1<-filter(Final\_EN,n>40)
Final\_Plot\_Names<-filter(Final\_EN,n>40)

outputVenn2<-venn(list(EN= Final\_EN\$All, LASSO = Final\_LASSO\$All))</pre>



outputVenn<-venn(list(EN= Final\_EN1\$All, LASSO = Final\_LASSO1\$All))</pre>



Freqs<-m[order(-m\$n),]
num<-length(Freqs\$All)</pre>

Freqs\$All <- factor(Freqs\$All, levels = Freqs\$All[order(-Freqs\$n)]) #plot in a bar graph the frequencie
ggplot(Freqs, aes(All, n))+geom\_bar(stat="identity")+theme(axis.text.x = element\_text(size=8, angle=90)</pre>



```
FreqsEN$All <- factor(FreqsEN$All, levels = FreqsEN$All[order(-FreqsEN$n)])
ggplot(FreqsEN, aes(All, n))+geom_bar(stat="identity")+theme(axis.text.x = element_text(size=8, angle=9)</pre>
```



#plot of how many times each feature appears. Most important will appear in all models = N.

#### #Boxplot with Betas and its coefficients

Boxplot1<-BetasTodo[BetasTodo\$Features %in% Final\_EN1\$All,] #see which features appear in the filtered ggplot(Boxplot1,aes(Boxplot1\$Features,Boxplot1\$Coefficients))+geom\_boxplot()+geom\_jitter()



Boxplot1["Method"] <-as.factor("EN")</pre>

Boxplot2<-BetasTodoL[BetasTodoL\$Features %in% Final\_LASS01\$All,]
ggplot(Boxplot2,aes(Boxplot2\$Features,Boxplot2\$Coefficients))+geom\_boxplot()+geom\_jitter()</pre>



Boxplot2["Method"] <-as.factor("LASSO")</pre>

Fin\_Boxplot<-rbind(Boxplot1,Boxplot2) #Unite both boxplots LASSO and EN
ggplot(Fin\_Boxplot,aes(Fin\_Boxplot\$Features,Fin\_Boxplot\$Coefficients))+geom\_boxplot(aes(color=Method))+</pre>

### Beta coefficients EN and LASSO



```
# Test set
test<-Betas_select[-train_ind, ]</pre>
xtrain <- train[ , !(names(train) %in% "Label")] %>% as.matrix()
xtest <- test[ , !(names(test) %in% "Label")] %>% as.matrix()
ytrain<-train$Label
ytest <- test $Label
xtest<-data.frame(xtest)</pre>
xtrain<-data.frame(xtrain)</pre>
y<-Betas_select[,NumVar]</pre>
X<-Betas_select[,1:(NumVar-1)]
levels(ytrain)[1]<-"0"</pre>
levels(ytrain)[2]<-"1"</pre>
levels(ytest)[1]<-"0"</pre>
levels(ytest)[2]<-"1"</pre>
for (k in 1:nn){
  columns<-c(1:dim(xtrain)[2])</pre>
  columns<-sample(columns)</pre>
  d<-xtrain[,columns]
  for (i in 1:dim(xtrain)[2]){
    for (j in 1:dim(xtrain)[2]){
      yy3<-data.frame(Outcome=ytrain,d[i:j])</pre>
      model3<-glm(Outcome~.,data=yy3, family=binomial(link='logit'))</pre>
      dd<-xtest[,columns]
      new3<-data.frame(dd[i:j])</pre>
      p3<-predict(model3,new3,type="response")</pre>
      new5<-data.frame(Outcome=ytest)</pre>
      pr3 <- prediction(p3, new5)</pre>
      prf3 <- performance(pr3, measure = "tpr", x.measure = "fpr")</pre>
      auc3 <- performance(pr3, measure = "auc")</pre>
      auc3 <- auc3@y.values[[1]]</pre>
      result2<-auc3
      if (auc3>auc3max){
        if (i>j){
           maxComb<-data.frame(Name=toString(names(d)[j:i]),AUC=auc3)</pre>
           auc3max<-auc3
           cont<-cont+1
        }
        else{
           maxComb<-data.frame(Name=toString(names(d)[i:j]),AUC=auc3)</pre>
           auc3max<-auc3
           cont<-cont+1
        }
      }
```

```
else{
           cont2<-cont2+1
         }
      }
    }
  }
  maxCombF<-rbind(maxCombF,maxComb)</pre>
  auc3max<-0
}
maxCombF2<-maxCombF[order(maxCombF$AUC),]</pre>
names<-maxCombF2$Name[dim(maxCombF2)[1]]</pre>
names1<-as.character(names)</pre>
names1<-strsplit(names1,", ")</pre>
names<-as.data.frame(names1)</pre>
Betas_select2<-All2[,colnames(All2[,intersect(gsub("`", "", names[,1]), colnames(All2))])]</pre>
Betas_select2["Label"]<-savee</pre>
Betas_select2<-as.data.frame(Betas_select2)</pre>
##### End Block 3
##### Begin Block 4
```

#Random mix between variables and AUC value obtained through GLM model, rough approximation of future p
#Betas\_select2, final features selected.

```
NumVar<-length(Betas_select2)</pre>
```

N<-1000 #number of models produced (both permuted (random) and real) – for all univariate (Each featur #Real program runs with 1000 – Takes 12 hours.

```
multipleAUC<-matrix(rnorm(2),1,N)
multipleAUCR<-matrix(rnorm(2),1,N)
multipleAUCNB<-matrix(rnorm(2),1,N)
multipleAUCNBR<-matrix(rnorm(2),1,N)</pre>
```

```
multipleROC<-matrix(as.list(rnorm(2)),1,N)
multipleROCR<-matrix(as.list(rnorm(2)),1,N)
multipleNBROC<-matrix(as.list(rnorm(2)),1,N)
multipleNBROCR<-matrix(as.list(rnorm(2)),1,N)</pre>
```

```
singleROC<-list()
doubleROC<-list()
singleROCR<-list()
doubleROCR<-list()</pre>
```

doublePlus<-list()
singlePlus<-list()</pre>

```
singleAUC<-matrix(rnorm(2),NumVar-1,N)</pre>
doubleAUC<-matrix(rnorm(2),(NumVar-1),N)</pre>
singleAUCR<-matrix(rnorm(2),NumVar-1,N)</pre>
doubleAUCR<-matrix(rnorm(2), (NumVar-1),N)</pre>
doubleAUCSVMR<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCSVM<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCSVMCrossR<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCSVMCross<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCRFCross<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCRFCrossR<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCNBR<-matrix(rnorm(2),(NumVar-1),N)</pre>
doubleAUCNB<-matrix(rnorm(2),(NumVar-1),N)</pre>
MatsingleROC<-matrix(as.list(rnorm(2)),NumVar-1,N)</pre>
MatsingleROCR<-matrix(as.list(rnorm(2)),NumVar-1,N)</pre>
MatdoubleROC<-matrix(as.list(rnorm(2)),(NumVar-1),N)</pre>
MatdoubleROCR<-matrix(as.list(rnorm(2)),(NumVar-1),N)</pre>
MatsinglePlus<-matrix(as.list(rnorm(2)),NumVar-1,N)</pre>
MatdoublePlus<-matrix(as.list(rnorm(2)),(NumVar-1),N)</pre>
MatsinglePlusR<-matrix(as.list(rnorm(2)),NumVar-1,N)</pre>
MatdoublePlusR<-matrix(as.list(rnorm(2)),(NumVar-1),N)</pre>
##### End Block 4
##### Begin Block 5
for (j in 1:N){ #N different measurements of AUC values, mean done at the end.
  smp_size<-floor(0.65 * nrow(Betas_select2))</pre>
  train_ind <- caret::createDataPartition(All2$Label, p = 0.65, list = FALSE, times = 1)</pre>
  # Training set
  train<-Betas_select2[train_ind, ]</pre>
  # Test set
  test<-Betas_select2[-train_ind, ]</pre>
  xtrain <- train[ , !(names(train) %in% "Label")] %>% as.matrix()
  xtest <- test[ , !(names(test) %in% "Label")] %>% as.matrix()
  ytrain<-train$Label</pre>
  ytest<-test$Label
  xtest<-data.frame(xtest)</pre>
  xtrain<-data.frame(xtrain)</pre>
  y<-Betas_select2[,NumVar]</pre>
  X<-Betas_select2[,1:(NumVar-1)]</pre>
  levels(ytrain)[1]<-"0"</pre>
```

```
levels(ytrain)[2]<-"1"
levels(ytest)[1]<-"0"
levels(ytest)[2]<-"1"</pre>
```

# source('AUCFun29-3.R')

```
## multiple, good
multipleAUCNB[1,j]<-multipleAUCfunNB(xtrain, ytrain,xtest,ytest)
multipleAUC[1,j]<-multipleAUCfun(xtrain, ytrain,xtest,ytest)</pre>
```

```
multipleNBROC[[j]]<-multipleROCfunNB(xtrain, ytrain,xtest,ytest)
multipleROC[[j]]<-multipleROCfun(xtrain, ytrain,xtest,ytest)</pre>
```

# separate

```
## single, should be good
for (s in (1:(NumVar-1))){
    s<-as.numeric(s)
    singleAUC[s,j]<-singleAUCfun(xtrain, ytrain,xtest,ytest,s)
    singleROC[[s]]<-singleROCfun(xtrain, ytrain,xtest,ytest,s)
    MatsinglePlus[s,j]<-singlePlusfun(xtrain, ytrain,xtest,ytest,s)
}
</pre>
```

```
MatsingleROC[,j]<-matrix(singleROC)</pre>
```

# Training set

train\$Label<-sample(train\$Label)
test\$Label<-sample(test\$Label)
#Permuted data, will make sure that are models are really valid as randomizing the label should yield</pre>

# Test set

```
xtrain <- train[, !(names(train) %in% "Label")] %>% as.matrix()
xtest <- test[, !(names(test) %in% "Label")] %>% as.matrix()
ytrain<-train$Label
ytest<-test$Label
xtest<-data.frame(xtest)
xtrain<-data.frame(xtrain)
y<-Betas_select2[,NumVar]</pre>
```

```
X<-Betas_select2[,1:(NumVar-1)]</pre>
```

```
levels(ytrain)[1]<-"0"</pre>
  levels(ytrain)[2]<-"1"</pre>
  levels(ytest)[1]<-"0"</pre>
  levels(ytest)[2]<-"1"</pre>
  multipleAUCNBR[1,j]<-multipleAUCfunNB(xtrain, ytrain, xtest, ytest)</pre>
  multipleAUCR[1,j]<-multipleAUCfun(xtrain, ytrain,xtest,ytest)</pre>
  multipleNBROCR[[j]]<-multipleROCfunNB(xtrain, ytrain, xtest, ytest)</pre>
  multipleROCR[[j]]<-multipleROCfun(xtrain, ytrain, xtest, ytest)</pre>
  for (s in (1:(NumVar-1))){
    s<-as.numeric(s)</pre>
    singleAUCR[s,j]<-singleAUCfun(xtrain, ytrain,xtest,ytest,s)</pre>
    singleROCR[[s]]<-singleROCfun(xtrain, ytrain, xtest, ytest, s)</pre>
    MatsinglePlusR[s,j]<-singlePlusfun(xtrain, ytrain,xtest,ytest,s)</pre>
  }
  MatsingleROCR[,j]<-matrix(singleROCR)</pre>
  #
}
##### End Block 5
##### Begin Block 6
  names2<-sapply(1:(NumVar-1), function(i){paste0("NISS/",names(xtrain)[i])})</pre>
trial<-NULL
h=1
for (b in (2:NumVar-1)) {
  print(b)
  trial[b] <-names2[h]</pre>
  h=h+1
}
## [1] 1
## [1] 2
## [1] 3
## [1] 4
## [1] 5
## [1] 6
## [1] 7
## [1] 8
## [1] 9
```

```
23
```

```
## [1] 10
## [1] 11
## [1] 12
## [1] 13
## [1] 14
singleAUC<-as.data.frame(singleAUC)</pre>
singleAUC<-mutate(singleAUC, Means=rowMeans(singleAUC))</pre>
row.names(singleAUC)<-names(xtrain)</pre>
singleAUCR<-as.data.frame(singleAUCR)</pre>
singleAUCR<-mutate(singleAUCR, Means=rowMeans(singleAUCR))</pre>
row.names(singleAUCR)<-names(xtrain)</pre>
multipleAUCNBR<-as.data.frame(multipleAUCNBR)</pre>
multipleAUCNBR["Means"] <- rowMeans(multipleAUCNBR)</pre>
multipleAUCR<-as.data.frame(multipleAUCR)</pre>
multipleAUCR["Means"] <- rowMeans(as.data.frame(multipleAUCR))</pre>
multipleAUCNB<-as.data.frame(multipleAUCNB)</pre>
```

```
multipleAUCNB["Means"]<-rowMeans(as.data.frame(multipleAUCNB))
multipleAUC<-as.data.frame(multipleAUC)
multipleAUC["Means"]<-rowMeans(as.data.frame(multipleAUC))</pre>
```

Final<-data.frame(MultiNB=t(multipleAUCNB),MultiNBRand=t(multipleAUCNBR),Multi=t(multipleAUC),MultiRand FinalMeans<-data.frame(MultiNB=multipleAUCNB\$Means,MultiNBRand=multipleAUCNBR\$Means,Multi=multipleAUC\$M</pre>

```
#sacar ROC CURVES #####
```

```
print("here")
## [1] "here"
for (g in 1:(NumVar-1)){
    plot(MatsingleROC[[g,1]],lwd=3,main=paste("ROC curve of", names(xtrain)[g]))
    for (b in 1:N){
        plot(MatsingleROCR[[g,b]],col=b,lty=3,add=TRUE)
    }
}
```

**ROC curve of GPRC5A** 



**ROC curve of CAPG** 



**ROC curve of INHBA** 



**ROC curve of COL8A1** 







**ROC curve of RASAL2** 



**ROC curve of SLPI** 



**ROC curve of ADAMTS12** 



**ROC curve of THBS2** 



**ROC curve of VCAN** 



**ROC curve of LTBP1** 



**ROC curve of AEBP1** 



**ROC curve of MIR34AHG** 



## **ROC curve of KRT7**



```
plot(multipleROC[[1]],lwd=3,main=paste("ROC curve of", trial[1]))
for (b in 1:N){
    plot(multipleNBROCR[[b]],col=b,lty=3,add=TRUE)
}
```

## **ROC curve of NISS/GPRC5A**





### 







### 







### 

















## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



range : 4 grobs	(2) ar	LeGrob (2 2		Ιċ	##
grob	name	cells	z		##
<pre>gtable[layout]</pre>	arrange	(1-1,1-1)	1	1	##
<pre>gtable[layout]</pre>	arrange	(1-1,2-2)	2	2	##
<pre>gtable[layout]</pre>	arrange	(2-2,1-1)	3	3	##
gtable[layout]	arrange	(2-2, 2-2)	4	4	##



##	Τa	ab]	LeGrob (2 :	x 2) "arı	range": 4 grobs
##		z	cells	name	grob
##	1	1	(1-1,1-1)	arrange	gtable[layout]
##	2	2	(1-1,2-2)	arrange	gtable[layout]
##	3	3	(2-2,1-1)	arrange	gtable[layout]
##	4	4	(2-2, 2-2)	arrange	gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



##	Τa	abl	LeGrob (2 :	x 2) "arı	range": 4 grobs
##		z	cells	name	grob
##	1	1	(1-1,1-1)	arrange	gtable[layout]
##	2	2	(1-1,2-2)	arrange	gtable[layout]
##	3	3	(2-2,1-1)	arrange	gtable[layout]
##	4	4	(2-2, 2-2)	arrange	gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



##	15	abl	LeGrob (2 :	x 2) "arı	cange": 4 grobs
##		z	cells	name	grob
##	1	1	(1-1,1-1)	arrange	gtable[layout]
##	2	2	(1-1,2-2)	arrange	<pre>gtable[layout]</pre>
##	3	3	(2-2,1-1)	arrange	gtable[layout]
##	4	4	(2-2, 2-2)	arrange	gtable[layout]



## TableGrob (2 x 2) "arrange": 4 grobs
## z cells name grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
## 3 3 (2-2,1-1) arrange gtable[layout]
## 4 4 (2-2,2-2) arrange gtable[layout]



			100100 (1 1	. 2) ari	
##		z	cells	name	grob
##	1	1	(1-1,1-1)	arrange	gtable[layout]
##	2	2	(1-1,2-2)	arrange	gtable[layout]
##	3	3	(2-2,1-1)	arrange	<pre>gtable[layout]</pre>
##	4	4	(2-2, 2-2)	arrange	gtable[layout]





Mono<-rbind(MA,MAR)

pp<-ggdensity(Mono, x = "Mono", fill = "Label", palette = "jco")+geom\_vline(xintercept=Meanq[1,1],linet print(pp+geom\_vline(xintercept=Meanq[1,2],linetype = 2,color="black",show.legend = TRUE))



```
## NOX4
## THBS2
## ADAMTS12
## RASAL2
## CAPG
## FAP
## CTHRC1
## VCAN
## WISP1
## TIMP1
## LTBP1
## SLPI
## GPRC5A
## MIR34AHG
## AEBP1
## KRT7
cat("Beta_Select_Threshold")
## Beta_Select_Threshold
cat("\n")
cat(genes_to_networkStrict, sep = "\n")
## GPRC5A
## CAPG
## INHBA
## COL8A1
## SULF1
## RASAL2
## SLPI
## ADAMTS12
## THBS2
## VCAN
## LTBP1
## AEBP1
## MIR34AHG
## KRT7
sink()
```