## Messina E3: Messina vs? on APGI

March 22, 2015

## 1 Preparation

```
library(plyr)
library(ggplot2)

## Loading required package: methods

library(messina)

## Loading required package: survival

## Loading required package: splines

library(maxstat)
library(doMC)

## Loading required package: foreach

## Loading required package: iterators

## Loading required package: parallel

paropts = list(.options.multicore = list(preschedule = FALSE))
```

## 2 Data preparation

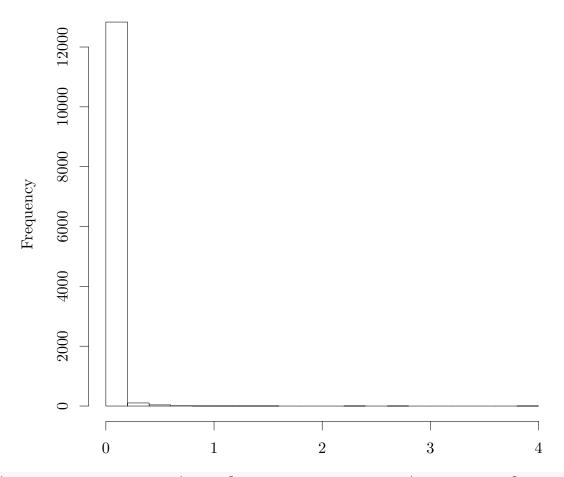
```
load("../biosurv/data/07_data_for_SIS.rda")
APGI.x = x.diag_dsd
APGI.y = y.diag_dsd
APGI.samps = samps.diag_dsd
APGI.feats = data.frame(symbol = rownames(APGI.x))

temp = NA
temp = ls()
rm(list = temp[!(temp %in% c("APGI.x", "APGI.y", "APGI.samps", "APGI.feats"))])

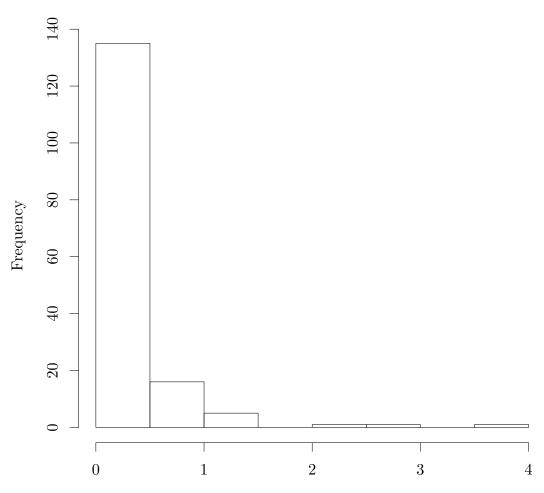
load("../biosurv/data/15_validation.rda")
rm(GSE28735.lingex, GSE21501.lingex)
GSE28735.x = GSE28735.gex
GSE21501.x = GSE21501.gex
GSE28735.feats = GSE28735.feat
GSE21501.feats = GSE21501.feat
rm(GSE28735.gex, GSE21501.feat
rm(GSE28735.gex, GSE21501.gex, GSE21501.feat)
```

```
load("../biosurv/data/validation/tcga-clin-gex.20141118.rda")
TCGA.x = data.merged$paad$gex$illuminahiseq_rnaseqv2
rownames(TCGA.x) = gsub("\\|.*", "", rownames(TCGA.x))
TCGA.x = TCGA.x[rownames(TCGA.x) != "?",]
TCGA.x = log2(TCGA.x + 1)
temp.time = as.numeric(as.character(data.merged$paad$clin$days_to_death))
temp.time[is.na(temp.time)] = as.numeric(as.character(data.merged$paad$clin$days_to_last_followup[is.na
TCGA.y = Surv(temp.time, data.merged$paad$clin$vital_status == "Dead")
TCGA.feats = data.frame(symbol = rownames(TCGA.x))
rm(data.merged)
keepMostVariableGeneMeasurement = function(gex, feats, ids)
        sds = apply(gex, 1, sd, na.rm = TRUE)
        perm = order(-sds)
        gex = gex[perm,,drop = FALSE]
        feats = feats[perm,,drop = FALSE]
        ids = ids[perm]
        drop = duplicated(ids) | is.null(ids)
        gex = gex[!drop,,drop = FALSE]
        feats = feats[!drop,,drop = FALSE]
        ids = ids[!drop]
        list(gex = gex, feats = feats, ids = ids)
# Now moved to the validation function
\# regularizeX = function(x)
# {
# require(robustbase)
\# location = apply(x, 1, median, na.rm = TRUE)
\# scale = apply(x, 1, scaleTau2, na.rm = TRUE)
\# (x - location) / scale
# }
temp = keepMostVariableGeneMeasurement(APGI.x, APGI.feats, APGI.feats$symbol)
APGI.x = temp\$gex
APGI.feats = temp$feats
temp = keepMostVariableGeneMeasurement(GSE28735.x, GSE28735.feats, GSE28735.feats$Gene.symbol)
GSE28735.x = temp\$gex
GSE28735.feats = temp$feats
temp = keepMostVariableGeneMeasurement(GSE21501.x, GSE21501.feats, GSE21501.feats$Gene.symbol)
GSE21501.x = temp\$gex
GSE21501.feats = temp$feats
GSE28735.y = Surv(GSE28735.samp$time, GSE28735.samp$event)
GSE21501.y = Surv(GSE21501.samp$time, GSE21501.samp$event)
\# APGI.xreg = regularizeX(APGI.x)
\# GSE28735.xreg = regularizeX(GSE28735.x) \# This one validated for surviges
\# GSE21501.xreq = regularizeX(GSE21501.x)
```

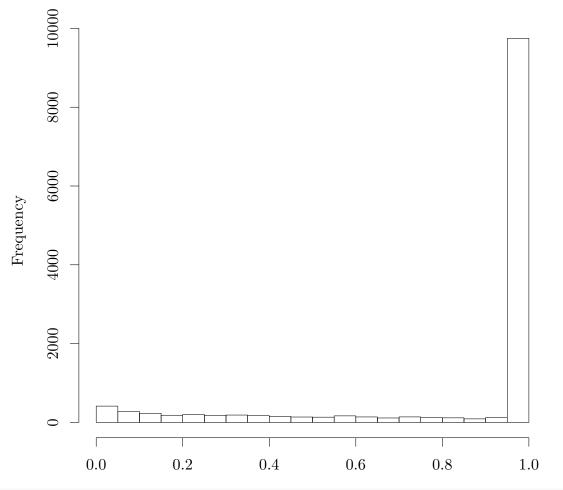
```
# Temporary testing measure. Probably will be used in real application, but somewhat defeats
# the whole purpose of Messina for testing, so should be removed when comparing us other methods.
\# temp.sel = apply(APGI.x, 1, sd) >= 1 \& grepl("^D", rownames(APGI.x))
\# APGI.x = APGI.x[temp.sel,,drop = FALSE]
# APGI.feats = APGI.feats[temp.sel,,drop = FALSE]
\# messinaSurv(APGI.x, APGI.y, messinaSurvObj.CoxCoef(round(log(2), 3)), parallel = TRUE, silent = FALSE
\# messinaSurv(APGI.x, APGI.y, messinaSurvObj.Tau(0.6), parallel = TRUE, silent = FALSE, seed = 20150321.
\# messinaSurv(APGI.x, APGI.y, messinaSurvObj.RelTau(0.7), parallel = TRUE, silent = FALSE, seed = 20150.
registerDoMC(32)
library(plyr)
APGI.messina.cc2 = messinaSurv(APGI.x, APGI.y, messinaSurvObj.CoxCoef(round(log(2), 3)), parallel = TRU
## Performance bootstrapping...
## Final training...
APGI.messina.cc3 = messinaSurv(APGI.x, APGI.y, messinaSurvObj.CoxCoef(round(log(3), 3)), parallel = TRU
## Performance bootstrapping...
## Final training...
APGI.messina.tau6 = messinaSurv(APGI.x, APGI.y, messinaSurvObj.Tau(0.6), parallel = TRUE, silent = FALSI
## Performance bootstrapping...
## Final training...
APGI.messina.tau7 = messinaSurv(APGI.x, APGI.y, messinaSurvObj.Tau(0.7), parallel = TRUE, silent = FALSI
## Performance bootstrapping...
## Final training...
APGI.messina = APGI.messina.cc2
APGI.maxstat = alply(APGI.x, 1, function(x1) {
        data = data.frame(time = APGI.y[,1], event = APGI.y[,2], x = x1)
        test = try(maxstat.test(Surv(time, event) ~ x, data = data, smethod = "LogRank", pmethod = "HL"]
        result = list(p.value = NA, threshold = NA)
        if (class(test) != "try-error")
                result$p.value = test$p.value
                result$threshold = test$estimate
        result
}, .parallel = TRUE)
print(dim(APGI.x))
## [1] 13000
               110
hist(APGI.messinaOfitsOsummarySmargin, main = "", xlab = "")
```



hist(APGI.messina@fits@summary\$margin[APGI.messina@fits@summary\$passed == TRUE], main = "", xlab = "")



```
sum(APGI.messina@fits@summary$passed == TRUE)
## [1] 159
mean(APGI.messina@fits@summary$passed == TRUE)
## [1] 0.01223
sum(APGI.messina@fits@summary$margin >= 1)
## [1] 11
mean(APGI.messina@fits@summary$margin >= 1)
## [1] 0.0008462
sum(APGI.messina@fits@summary$margin >= 1 & APGI.messina@fits@summary$passed == TRUE)
## [1] 8
mean(APGI.messina@fits@summary$margin >= 1 & APGI.messina@fits@summary$passed == TRUE)
## [1] 0.0006154
hist(sapply(APGI.maxstat, function(x) x$p.value), main = "", xlab = "")
```



hist(log10(sapply(APGI.maxstat, function(x) x\$p.value)), main = "", xlab = "")

```
Frequency
                   -5
                                -4
                                             -3
                                                          -2
                                                                       -1
                                                                                    0
sum(sapply(APGI.maxstat, function(x) x$p.value) < 0.05, na.rm = TRUE)</pre>
## [1] 413
sum(sapply(APGI.maxstat, function(x) x$p.value) < 0.05, na.rm = TRUE) / length(APGI.maxstat)</pre>
## [1] 0.03177
doValidation = function(train.features, train.x, train.threshold, train.merit, min_merit, test.features
        require(robustbase)
        sel.merit = train.merit >= min_merit
        sel.val_avail = train.features %in% test.features
        sel = sel.merit & sel.val_avail
        print(fisher.test(table(sel.merit, sel.val_avail)))
        val.train.features = train.features[sel]
        val.train.x = train.x[sel,,drop=FALSE]
        val.train.threshold = train.threshold[sel]
        val.train.merit = train.merit[sel]
        val.perm = match(val.train.features, test.features)
        val.test.features = test.features[val.perm]
        val.test.x = test.x[val.perm,,drop=FALSE]
        stopifnot(val.test.features == val.train.features)
```

```
# Translate the threshold on the training x to an approximate equivalent
        \# on the test x, by normalization
        locscale.train = apply(val.train.x, 1, function(x) scaleTau2(x[!is.na(x)], mu.too = TRUE))
        loc.train = locscale.train[1,]
        scale.train = locscale.train[2,]
        locscale.test = apply(val.test.x, 1, function(x) scaleTau2(x[!is.na(x)], mu.too = TRUE))
        loc.test = locscale.test[1,]
        scale.test = locscale.test[2,]
        val.test.threshold = (val.train.threshold - loc.train) / scale.train * scale.test + loc.test
        val.chisq = mapply(function(row_index, threshold) {
                x = val.test.x[row_index,]
                xd = x > threshold
                if (all(xd) || all(!xd))
                                                { return(NA) }
                fit = survdiff(test.y ~ xd)
                fit$chisq
        }, 1:length(val.test.threshold), val.test.threshold)
        result = data.frame(merit = val.train.merit, threshold.train = val.train.threshold, threshold.te
        rownames(result) = val.test.features
        result = result[order(-result$merit),]
        result
val.GSE28735.messina = doValidation(as.character(APGI.feats$symbol), APGI.x, APGI.messina@fits@summary$
## Loading required package: robustbase
## Attaching package: 'robustbase'
## The following object is masked from 'package:survival':
##
##
      heart
##
## Fisher's Exact Test for Count Data
##
## data: table(sel.merit, sel.val_avail)
## p-value = 0.003805
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 1.552 28.453
## sample estimates:
## odds ratio
        6.109
##
val.GSE28735.maxstat = doValidation(as.character(APGI.feats$symbol), APGI.x, sapply(APGI.maxstat, funct:
##
## Fisher's Exact Test for Count Data
##
## data: table(sel.merit, sel.val_avail)
```

```
## p-value < 2.2e-16
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 2.431 3.653
## sample estimates:
## odds ratio
##
        2.982
val.GSE21501.messina = doValidation(as.character(APGI.feats$symbol), APGI.x, APGI.messina@fits@summary$
##
## Fisher's Exact Test for Count Data
## data: table(sel.merit, sel.val_avail)
## p-value = 1.561e-05
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
    3.835 176.208
## sample estimates:
## odds ratio
       18.54
##
val.GSE21501.maxstat = doValidation(as.character(APGI.feats$symbol), APGI.x, sapply(APGI.maxstat, funct:
##
## Fisher's Exact Test for Count Data
##
## data: table(sel.merit, sel.val_avail)
## p-value = 1.805e-10
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 1.649 2.540
## sample estimates:
## odds ratio
        2.051
val.TCGA.messina = doValidation(as.character(APGI.feats$symbol), APGI.x, APGI.messina@fits@summary$thres
##
## Fisher's Exact Test for Count Data
##
## data: table(sel.merit, sel.val_avail)
## p-value = 1
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.2236
             Inf
## sample estimates:
## odds ratio
          Inf
val.TCGA.maxstat = doValidation(as.character(APGI.feats$symbol), APGI.x, sapply(APGI.maxstat, function(
## Fisher's Exact Test for Count Data
```

```
## data: table(sel.merit, sel.val_avail)
## p-value = 0.08234
## alternative hypothesis: true odds ratio is not equal to 1
## 95 percent confidence interval:
## 0.961 2.318
## sample estimates:
## odds ratio
        1.46
## Error in if (all(xd) || all(!xd)) {: missing value where TRUE/FALSE needed
val.GSE28735.messina
##
          merit threshold.train threshold.test
                                               chisq
## KRT6A
          3.999
                 9.503
                                4.754 1.638186
## ANGPTL4 2.716
                         8.900
                                       3.754 0.670894
## DHRS9 1.468
                         8.965
                                       4.404 0.007037
## FGG
          1.365
                         8.585
                                      13.796
                                                   NA
## PPY
          1.098
                                       4.068 2.536840
                         11.931
## LOX
         1.051
                        7.686
                                       6.841 0.494314
## IL20RB 1.043
                         6.971
                                       4.060 0.435502
val.GSE21501.messina
          merit threshold.train threshold.test chisq
## KRT6A 3.999 9.503 3.3849 0.2333
## ANGPTL4 2.716
                         8.900
                                      0.7529 0.1246
## KRT6C 2.333
                         7.458
                                      40.3387 NA
## IGFBP1 1.474
                         7.070
                                      -4.0458 2.3645
## DHRS9 1.468
                         8.965
                                      1.9614 3.9596
## FGG
          1.365
                                      9.7976 NA
                         8.585
## PPY
          1.098
                        11.931
                                      3.8380 0.3419
## LOX
        1.051
                         7.686
                                     -0.5062 0.1867
## IL20RB 1.043
                         6.971
                                      1.7140 0.6682
val.GSE28735.maxstat
##
             merit threshold.train threshold.test
                                                    chisq
## ANGPTL4
             4.835
                            8.356
                                        3.527 1.217e+00
## KRT6A
             4.450
                            8.915
                                          4.503 2.180e+00
## LOX
             4.225
                            7.502
                                           6.609 5.419e-01
## PYGL
                                           7.074 2.251e+00
             3.837
                            8.829
## ST6GAL1
             3.803
                            9.542
                                           6.145 1.230e+00
## FAM189A2 3.630
                                          4.052 3.197e-03
                            6.455
## KLHL5
             3.511
                            8.978
                                          6.464 2.728e+00
## ADM
                                          4.730 1.088e+00
             3.394
                            8.820
## E2F7
             3.373
                            6.507
                                          3.854 4.938e+00
## SMOX
             3.165
                            7.190
                                          4.852 2.650e-02
## KIF20A
                                           3.584 2.396e+00
             3.123
                            7.250
## CAPN6
             3.073
                            6.516
                                          4.094 7.537e-01
## IL20RB
             2.994
                            6.505
                                          3.492 6.901e-01
## P4HA1
             2.882
                            9.080
                                           7.426 3.618e-02
## FYN
             2.854
                            8.079
                                           6.086 5.064e-01
## AURKA
                                           3.628 5.199e-01
             2.850
                            7.727
## TCEA3 2.791 8.955
                                      4.898 3.547e+00
```

IIII TOXT 4	0 770	7 200	0.005 4.050 00
## LOXL4	2.778	7.628	3.985 4.353e-03
## LDHA	2.744	11.922	9.716 6.056e-01
## CKAP2L	2.693	7.047	3.898 3.238e+00
## PPY	2.628	11.966	4.074 2.537e+00
## TREM1	2.588	6.546	5.146 3.641e-01
## PLOD1	2.541	10.492	5.802 6.070e-02
## CDC20	2.506	8.806	4.385 7.903e-01
## PFKP	2.483	9.183	5.636 7.701e-02
## ERRFI1	2.364	10.222	8.463 2.657e-02
## RGS5	2.303	8.665	6.941 1.157e-01
## TPX2	2.283	7.213	4.613 2.342e+00
## P4HA2	2.267	9.209	6.579 2.345e+00
## SLC15A1	2.242	6.716	5.053 4.828e-01
## DPY19L1	2.227	9.183	6.364 3.403e-02
## MME	2.227	6.441	4.645 1.425e-01
## ATF7IP2	2.212	7.139	5.793 4.623e-02
## PAEP	2.186	6.304	5.022 2.214e-01
## EPHX2	2.173	7.223	3.637 7.331e-01
## KYNU	2.169	7.161	5.370 9.540e-04
## FOXM1	2.166	6.884	4.573 5.998e+00
## NAMPT	2.159	7.988	10.049 3.699e-01
## PLOD2	2.155	10.451	7.593 3.300e+00
## UPP1	2.130	9.094	4.411 1.248e+00
## KCTD10	2.119	7.907	6.094 3.352e-04
## ZNF185	2.105	7.420	3.933 1.060e+00
## EDIL3	2.105	6.400	8.217 5.409e-03
## NEK2	2.103	8.167	4.426 5.032e-01
## LCP1	2.100	8.702	6.629 6.413e+00
## GAPDH	2.086	11.336	9.814 1.951e+00
## ARSD	2.085	9.970	6.440 2.866e+00
## KIF2C	2.080	6.839	3.953 3.629e+00
## ENO2	2.069	7.557	5.422 3.748e-02
## COL12A1	2.052	8.689	8.314 5.723e-02
## VSNL1	2.052	6.712	4.221 2.337e-03
## ENTHD1	2.044	6.345	3.130 1.851e-01
## CADPS2	2.043	7.892	5.795 3.026e+00
## ASPM	1.993	7.916	5.271 9.366e-02
## ASAP1	1.993	9.917	7.260 4.509e-02
## SPATA18	1.952	7.197	5.264 2.207e+00
## KRT18	1.943	12.487	7.917 6.325e-01
## POLQ	1.938	6.758	3.609 5.093e+00
## FAM3D	1.933	9.474	6.136 2.076e+00
## CD109	1.929	6.370	5.959 2.207e-01
## UBE2C	1.927	9.305	5.228 1.843e+00
## OCLN	1.922	7.722	7.186 5.277e-01
## WNK2	1.915	6.293	3.922 2.774e+00
## TGFBI	1.912	12.180	8.229 2.750e+00
## SPOCK1	1.903	8.915	5.387 7.009e+00
## CD300A	1.885	6.707	5.248 1.331e-01
## RAVER2	1.856	7.583	5.856 7.799e-01
## P2RY8	1.856	7.349	4.024 1.079e-02
## A4GNT	1.846	6.439	3.549 1.023e+00
## RIMKLB	1.825	7.221	6.093 7.238e-03
## ADAM23	1.824	6.394	4.155 7.598e-03

	TOT	4 000	7 455	4 557	4 000 .00	
	FST	1.820	7.155		1.088e+00	
	CA8	1.819	6.429		1.650e+00	
	CEP55	1.819	7.985		1.431e+00	
	IL1A	1.813	6.266		1.460e-01	
##	ANLN	1.811	7.020		3.439e+00	
##	DCBLD2	1.806	10.689	8.544	7.788e+00	
##	PLA2G10	1.795	9.726	4.000	4.374e+00	
##	KLHL13	1.791	6.430	3.543	6.677e-01	
##	STAG3L4	1.784	6.532	4.970	3.087e-01	
##	GOLM1	1.777	6.547	8.986	NA	
##	F3	1.770	9.228	7.930	4.135e-02	
##	NTS	1.760	6.317	2.643	1.702e+00	
##	TPI1	1.759	10.890	6.342	4.913e-01	
##	PTGES	1.757	7.540		7.838e-06	
	IGKV1ORY-1		11.809		2.201e-03	
	SNAI2	1.753	8.469		7.687e-02	
	NFIA	1.727	7.914		1.255e+00	
	COL7A1	1.726	8.066		2.645e+00	
	FGD6	1.724	6.426		9.292e-01	
	MCM4	1.724	7.948		1.214e+00	
	TUBA1C	1.721	11.899		1.285e-02	
	MELK	1.713	7.288		2.117e+00	
	C5orf46	1.700	6.858	2.836	NA	
		1.700				
	COL17A1		10.742		7.886e-01	
	PDLIM7	1.691	8.030		6.057e-01	
	PTTG1	1.674	9.067		1.004e+00	
	DSG2	1.663	10.999		6.084e+00	
	COL1A2	1.658	12.989		1.470e+00	
	SYNE2	1.657	8.782		1.589e-01	
	SERPINH1	1.646	10.187		2.134e+00	
	PHLDA1	1.643	9.269		1.132e+00	
	CTSE	1.642	11.677		1.154e+00	
	ADH1A	1.635	8.432		3.482e+00	
	WEE1	1.635	7.480		1.675e+00	
	CHEK1	1.623	6.501		2.718e+00	
	GSDMC	1.618	6.409		4.329e+00	
	SLC2A1	1.615	10.218		3.749e-03	
	SERPINB3	1.614	6.324		1.020e-02	
	DHRS9	1.609	8.430		2.091e-01	
	PPP1R3C	1.597	8.282		3.812e+00	
	FLRT3	1.596	9.224		3.404e+00	
	CCNB2	1.594	7.685		1.338e+00	
##	CORO1A	1.593	8.375		4.792e-03	
	RHOF	1.591	6.800	4.881	5.617e-01	
##	GRAMD3	1.587	7.707		7.763e-03	
##	IL33	1.583	7.299	4.397	2.122e-03	
	AQP1	1.577	7.146	5.848	7.817e-02	
##	VEGFA	1.573	7.090	6.212	1.095e-02	
##	ANGPTL2	1.563	9.897	5.866	1.308e+00	
##	SEMA4A	1.562	7.304	4.697	1.226e-01	
##	GCNT1	1.562	8.263	6.462	2.802e-01	
##	CCL19	1.560	9.155	6.111	2.032e-01	
##	CACHD1	1.555	6.709	5.075	4.289e-03	
##	NCAPG	1.544	7.323	5.149	4.495e-01	

## FCGR2E 1.536 7.007 4.506 2.784e-02 ## BDC 1.528 6.805 5.509 3.207e+00 ## CNIH3 1.513 6.461 4.149 9.764e-01 ## ILIR2 1.508 8.252 5.522 3.305e+00 ## ITM2A 1.505 8.100 5.330 7.701e-02 ## ITM2A 1.504 9.660 5.222 7.935e-01 ## SLC9A9 1.502 7.348 6.777 2.790e-02 ## TM4SF19 1.496 6.269 4.532 1.245e+00 ## FN1 1.488 9.130 8.263 4.872e+00 2 ## FN1 1.488 9.130 8.263 4.872e+00 2 ## RNP2 1.484 6.606 8.615 NA ## TM12 1.480 6.303 4.497 3.223e-01 ## APOL1 1.469 6.456 7.103 6.062e-02 ## KRNK4 1.468 7.979 4.247 2.105e-01 ## BDSC 1.458 6.704 7.468 8.154e+00 ## FN1 1.445 8.324 5.413 2.803e+00 ## FNC1 1.438 8.691 6.250 2.768e+00 ## KKIF18A 1.440 6.472 3.550 1.717e+00 ## SEMAS 1.426 6.622 7.091 3.126e+00 ## RGSA 1.432 7.328 6.924 1.541e+00 ## RGSA 1.432 7.328 6.924 1.551e+00 ## RGSA 1.432 7.328 7.328 6.924 1.551e+00 ## RGSA 1.432 7.338 7.364 6.225 2.303e+00 ## RGSA 1.432 7.338 7.364 6.225 2.303e+00 ##		TOOROR	4 500	7 007	4 = 4 =	0.704
## CNIH3						
## ILIR2						
## ITGA5						
## ITM2A						
## SLC9A9	##	ITGA5	1.505	8.100	5.330	7.701e-02
## TM4SF19	##	ITM2A	1.504	9.660	5.222	7.935e-01
## JAG1	##	SLC9A9	1.502	7.348	6.777	2.790e-02
## JAG1	##	TM4SF19	1.496	6.269	4.532	1.245e+00
## FN1	##	JAG1	1.488		8.263	4.872e+00
## NRP2			1.486			
## TNNI2						
## APOL1						
## KANK4						
## RFX2						
## DSC2						
## KRT17						
## ANKLE2						
## PRC1						
## PPP2R2C						
## KIF18A						
## NDRG2						
## LONRF2						
## SEMA3A						
## ARHGAP26	##	LONRF2	1.437	6.411	4.445	4.865e-01
## ZBED2	##	SEMA3A	1.432	7.328	6.924	1.541e+00
## PCF11	##	ARHGAP26	1.426	6.622	7.091	3.126e+00
## PCF11	##	ZBED2	1.424	6.267	4.047	1.361e+00
## TGJ	##	PCF11			5.972	5.690e+00
## RGS16						
## HRASLS2						
## AHCYL2						
## TLE4						
## CDA						
## DNASE1 1.415 6.346 3.864 6.021e-01 ## DKK1 1.413 9.728 5.287 1.032e+00 ## CD38 1.405 7.104 6.298 7.484e-01 ## MALL 1.405 10.388 6.245 3.778e-01 ## GPC3 1.399 7.457 6.106 8.675e-01 ## SH3RF1 1.391 8.535 6.363 4.798e+00 ## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SDD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## DKK1						
## CD38						
## MALL 1.405 10.388 6.245 3.778e-01 ## GIMAP2 1.400 7.313 5.276 2.303e+00 ## GPC3 1.399 7.457 6.106 8.675e-01 ## SH3RF1 1.391 8.535 6.363 4.798e+00 ## DUOXA2 1.384 7.261 4.065 3.746e+00 ## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SDD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## GIMAP2 1.400 7.313 5.276 2.303e+00 ## GPC3 1.399 7.457 6.106 8.675e-01 ## SH3RF1 1.391 8.535 6.363 4.798e+00 ## DUOXA2 1.384 7.261 4.065 3.746e+00 ## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SDD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## GPC3						
## SH3RF1 1.391 8.535 6.363 4.798e+00 ## DUOXA2 1.384 7.261 4.065 3.746e+00 ## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## DUOXA2 1.384 7.261 4.065 3.746e+00 ## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00	##	GPC3	1.399	7.457		
## FRMD6 1.379 9.411 7.018 1.674e+00 ## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00	##	SH3RF1	1.391	8.535	6.363	4.798e+00
## KNTC1 1.365 7.209 5.133 2.333e+00 ## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00	##	DUOXA2	1.384	7.261	4.065	3.746e+00
## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00	##	FRMD6	1.379	9.411	7.018	1.674e+00
## TMSB10 1.364 13.721 10.239 9.794e-01 ## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00	##	KNTC1	1.365		5.133	2.333e+00
## KPNA2 1.356 6.543 6.121 6.968e-01 ## CST6 1.354 8.451 4.027 1.272e+00 ## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## CST6						
## CCNB1 1.353 7.364 5.563 3.176e-01 ## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## CD79A 1.350 7.991 4.204 1.653e+00 ## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## RAP1GAP 1.346 9.590 3.821 2.320e-01 ## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## CENPF 1.346 7.209 5.142 5.130e-01 ## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## SOD2 1.341 8.755 7.349 NA ## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## MIF 1.334 12.328 7.195 2.992e-01 ## GBE1 1.331 7.564 6.499 1.296e+00						
## GBE1 1.331 7.564 6.499 1.296e+00						
## MEOX1 1.331 6.748 4.334 3.263e-02						
	##	MEOX1	1.331	6.748	4.334	3.263e-02

```
## KIF14 1.322
                   6.914 3.835 3.222e+00
## TRNP1
           1.319
                          10.665
                                         5.963 4.984e-03
                                        10.996 NA
## FGG
             1.319
                           8.010
                                          3.937 1.296e-01
## MUC16
            1.312
                            6.930
## DYNC2H1 1.312
                            7.510
                                         6.309 4.117e+00
## MMP10
                           6.412
                                         2.984 6.057e-01
           1.307
## LETM2
             1.306
                            6.642
                                         4.413 6.681e-01
val.GSE21501.maxstat
          merit threshold.train threshold.test chisa
## ANGPTL4 4.835 8.356 0.19587 6.865e-01
## KRT6A
        4.450
                         8.915
                                     2.97484 2.615e-02
           4.225
                                     -0.79221 1.058e+00
## LOX
                          7.502
## KRT6C
          4.215
                         6.392
                                     5.59238
## ST6GAL1 3.803
                         9.542
                                     0.78319 5.739e-01
## FAM189A2 3.630
                         6.455
                                     0.28808 7.248e-01
## ADM
           3.394
                          8.820
                                     -1.66023 7.681e+00
## E2F7
                         6.507
                                     -2.26972 1.101e+01
           3.373
## CAPN6
         3.073
                         6.516
                                     0.58777 1.934e+00
## IL20RB 2.994
                         6.505
                                     0.27819 2.890e+00
## FGF13
           2.837
                          6.400
                                     -0.33980 2.197e+00
## TCEA3
           2.791
                         8.955
                                     0.67789 4.561e+00
           2.778
                         7.628
                                     0.96728 4.499e-01
## LOXL4
## TMEM26
                                      0.77037 4.695e-02
           2.688
                         6.692
## BIRC5
                          7.334
                                     -1.61111 4.021e+00
           2.643
## CD70
                         6.748
                                     -0.60306 5.035e-01
           2.632
## PPY
           2.628
                        11.966
                                     3.85564 7.804e-01
                                     2.12235 4.167e+00
## TREM1
           2.588
                         6.546
## IGFBP1
           2.466
                          7.076
                                     -4.02812 1.675e+00
## ERRFI1 2.364
                         10.222
                                     0.59119 1.790e+01
## RGS5
           2.303
                         8.665
                                     4.26999 5.369e+00
## PHACTR3 2.275
                         6.884
                                      1.98393 1.343e+00
## MME
           2.227
                         6.441
                                     -1.58576 2.189e-01
## PRDM16
           2.206
                         6.605
                                     3.97296 1.839e+00
## PAEP
                                     0.77117 4.242e-01
           2.186
                         6.304
## EPHX2
           2.173
                          7.223
                                      0.03016 4.564e-01
                          7.161
## KYNU
           2.169
                                     -1.99673 3.795e-01
## NAMPT
           2.159
                         7.988
                                     0.11528 1.970e+00
## PLOD2
           2.155
                                     0.06961 8.655e-02
                         10.451
## EDIL3
                                      4.24471 1.304e+00
           2.105
                          6.400
                                     -1.80395 4.750e+00
## NEK2
                         8.167
           2.103
## LCP1
                                     -1.84614 2.896e+00
           2.100
                         8.702
## COL12A1 2.052
                         8.689
                                     1.83301 3.053e-01
## VSNL1
           2.052
                          6.712
                                     -1.64740 1.529e-01
## ENTHD1
           2.044
                         6.345
                                     1.75682 2.632e-01
## PCDH20 2.003
                          7.551
                                     3.99419 1.354e+00
## ASPM
           1.993
                         7.916
                                     -0.07079 1.759e+00
## CATSPER1 1.956
                         6.371
                                      0.89696 1.486e+00
## KRT18 1.943
                         12.487
                                     0.25249 1.552e+00
         1.933
## FAM3D
                         9.474
                                     5.30834 6.346e+00
## CD109
         1.929
                         6.370
                                     -0.49431 4.737e-01
## UBE2C
         1.927
                          9.305
                                     -1.15748 2.006e+00
## OCLN 1.922
                    7.722
                                   2.27334 3.056e+00
```

```
## TGFBI
         1.912
                            12.180
                                         1.17508 7.810e-02
## SPOCK1
            1.903
                            8.915
                                         -0.07385 3.241e-02
## P2RY2
            1.899
                             6.885
                                          2.53729 5.626e-01
## RAVER2
            1.856
                            7.583
                                          0.05711 4.701e-01
## P2RY8
            1.856
                            7.349
                                          0.52845 1.882e+00
## A4GNT
                            6.439
                                          3.40057 8.431e-01
            1.846
## APOA4
            1.823
                             6.333
                                         -1.04560 3.747e-01
## CEP55
            1.819
                            7.985
                                         -0.77283 1.442e-03
## IL1A
            1.813
                            6.266
                                         -0.13329 2.483e-02
## ANLN
            1.811
                            7.020
                                         -2.66571 1.547e-01
## DCBLD2
                                          0.63766 4.607e+00
            1.806
                            10.689
## PLA2G10 1.795
                            9.726
                                          3.52033 1.519e-01
## GOLM1
            1.777
                            6.547
                                          4.36321 3.484e+00
## F3
                                          3.33470 7.961e-01
            1.770
                            9.228
                                         -5.02906 1.450e+00
## NTS
            1.760
                            6.317
## SNAI2
            1.753
                            8.469
                                          0.96462 2.333e+00
## COL7A1
            1.726
                            8.066
                                         -0.65725 1.243e+00
## FGD6
            1.724
                            6.426
                                          1.00560 2.874e-02
## NFIX
            1.713
                            9.904
                                          1.57937 1.036e+00
## C5orf46 1.700
                            6.858
                                          1.16807 5.466e+00
## COL17A1 1.700
                            10.742
                                          4.24593 2.682e-01
## VSTM2L
            1.679
                                          2.67464 2.975e-01
                            7.078
## COL1A2
            1.658
                            12.989
                                          3.96788 4.629e-03
## SERPINH1 1.646
                            10.187
                                          0.16779 4.575e+00
                                          7.26038 3.184e+00
## CTSE
            1.642
                            11.677
## TNFRSF6B 1.638
                            7.634
                                          3.32680 6.004e-01
## ADH1A
          1.635
                            8.432
                                          2.32552 1.282e+00
## CHEK1
            1.623
                            6.501
                                         -3.47669 7.154e-02
## SLC2A1
            1.615
                            10.218
                                         -0.52907 5.130e-01
## SERPINB3 1.614
                            6.324
                                          0.71096 4.767e-01
            1.609
                                          1.56562 2.307e+00
## DHRS9
                            8.430
## PPP1R3C 1.597
                                          0.52826 8.428e-05
                            8.282
## FLRT3
            1.596
                            9.224
                                          3.15856 2.789e+00
## CCNB2
            1.594
                            7.685
                                         -0.56249 1.099e+00
## CXCR5
            1.589
                            6.681
                                          7.98854
## IL33
            1.583
                            7.299
                                          4.11799 2.212e-02
                                          3.32621 1.330e-01
## AQP1
            1.577
                            7.146
## TNFRSF17 1.573
                            7.032
                                         12.81828
                                                          NA
## VEGFA
            1.573
                            7.090
                                         -0.39754 2.750e-01
## GCNT1
            1.562
                            8.263
                                          1.40450 6.109e-02
## CCL19
            1.560
                            9.155
                                          5.98546 9.945e-01
## ADRA1B
                                          0.12758 3.060e+00
            1.546
                            6.285
## CAV2
            1.540
                            8.562
                                          1.61441 2.749e+00
## FCGR2B
            1.536
                            7.007
                                          1.56740 9.048e-01
## MRAP2
            1.532
                            7.684
                                          0.29126 2.912e-01
## CCL3L3
            1.524
                            6.799
                                          1.79960 1.696e+00
## CNIH3
            1.513
                            6.461
                                          0.57543 1.041e+00
## IL1R2
            1.508
                                          3.85019 2.006e-01
                             8.252
                                         -0.78323 1.336e+00
## ITM2A
            1.504
                            9.660
## SLC9A9
            1.502
                            7.348
                                          3.46665 9.579e-02
## FN1
            1.486
                            6.406
                                          0.04531 3.830e-01
## SOX8
            1.486
                             7.496
                                          0.79012 5.370e-03
## NRP2
            1.484
                            6.606
                                          5.28797
                                                          NΑ
## TNNI2 1.480
                                         -1.30119 7.253e+00
                            6.303
```

```
## HES1 1.479
                                  1.10294 4.000e-01
                           8.112
## KCNH2
         1.476
                           6.778
                                        0.69336 2.375e+00
                                        0.79884 2.381e-02
## APOL1
           1.469
                           6.456
## KANK4
           1.468
                           7.979
                                        1.54307 1.052e-01
                          10.862
## KRT17
           1.449
                                        1.84873 3.034e+00
## PPP2R2C 1.443
                           6.859
                                       -0.11054 1.115e-01
## KIF18A
            1.440
                           6.472
                                        -2.19452 1.770e-01
## LONRF2
            1.437
                           6.411
                                       -1.25358 1.612e+00
## SEMA3A
           1.432
                           7.328
                                        0.13548 6.067e-01
## ARHGAP26 1.426
                           6.622
                                        1.86500 5.095e-01
## ZBED2
           1.424
                           6.267
                                        2.24266 7.387e-01
                                        1.25823 5.807e+00
## SPOCD1
           1.422
                           6.904
## IGJ
           1.420
                           9.761
                                        1.21379 3.078e-01
## RGS16
            1.419
                           6.813
                                        1.94034 2.366e-01
## HRASLS2 1.418
                           7.346
                                        4.41621 2.843e-01
## AHCYL2
           1.417
                           8.620
                                        1.74374 4.884e+00
## DNASE1
           1.415
                           6.346
                                        0.03199 5.313e-02
## DKK1
           1.413
                           9.728
                                        0.52018 1.947e+00
## CD38
           1.405
                           7.104
                                        2.18938 7.635e-01
## MALL
           1.405
                          10.388
                                        3.83833 5.231e-01
## FGF18
         1.397
                           6.280
                                        1.94601 3.342e-03
## ZNF365
          1.390
                           7.180
                                        2.32667 3.166e-01
## FRMD6
           1.379
                           9.411
                                        1.01822 1.170e-02
## TK1
           1.375
                           8.114
                                       -1.37859 4.348e+00
## CST6
            1.354
                           8.451
                                        4.65564 2.530e-01
## CD79A
            1.350
                           7.991
                                        2.33695 7.925e-02
## RAP1GAP 1.346
                                        0.53578 8.878e-03
                           9.590
## CENPF
          1.346
                           7.209
                                       -2.07887 2.536e+00
           1.341
## SOD2
                           8.755
                                       -0.40747 6.928e-01
## MEOX1
           1.331
                           6.748
                                        0.96369 5.732e-01
## KIF14
           1.322
                           6.914
                                       -1.85459 3.210e-01
           1.319
                                        3.20514 9.527e-04
## TRNP1
                          10.665
           1.319
## FGG
                           8.010
                                        6.42581
                                                 NA
## CBX1
           1.317
                           6.644
                                        0.09649 4.679e-01
## MUC16
          1.312
                           6.930
                                       -1.13833 1.513e-01
## DYNC2H1 1.312
                           7.510
                                        0.47423 6.089e-03
                                        3.72622 2.664e+00
## GATA6
            1.310
                           6.470
## MMP10
           1.307
                           6.412
                                        1.44298 3.202e-02
val.TCGA.messina
          merit threshold.train threshold.test chisq
## KRT6A
          3.999
                          9.503
                                         3.656 1.4483
## ANGPTL4 2.716
                          8.900
                                         3.336 0.2310
## KRT6C 2.333
                          7.458
                                        16.773
## CIDEC
                                         3.192 2.0245
          2.269
                          8.021
## IGFBP1 1.474
                          7.070
                                         3.788 NA
                                         3.203 0.1557
## DHRS9
         1.468
                          8.965
## FGG
          1.365
                          8.585
                                       10.219
                                                  NA
## LYNX1
           1.344
                          7.020
                                         3.998
                                                   NA
## PPY
           1.098
                                         3.969 0.3139
                          11.931
## LOX
          1.051
                          7.686
                                         3.602 0.3011
## IL20RB 1.043
                          6.971
                                        2.975 4.0928
val.TCGA.maxstat
```

## Error in eval(expr, envir, enclos): object 'val.TCGA.maxstat' not found