SIS NMF Final: Diagnosis to DSD

January 26, 2015

1 Preparation

```
options(java.parameters = "-Xmx4G")
library(survival)
## Loading required package: splines
library(energy)
library(NMF)
## Loading required package: methods
## Loading required package: pkgmaker
## Loading required package: registry
## Loading required package: rngtools
## Loading required package: cluster
## NMF - BioConductor layer [OK] | Shared memory capabilities [OK] | Cores 2/2
library(nnls)
library(bnlearn)
## Attaching package: 'bnlearn'
## The following object is masked from 'package:NMF':
##
##
      compare
library(glmulti)
## Loading required package: rJava
## Attaching package: 'glmulti'
## The following object is masked from 'package:NMF':
##
##
      consensus
library(glmnet)
## Loading required package: Matrix
## Loaded glmnet 1.9-8
library(RColorBrewer)
library(gplots)
```

```
##
## Attaching package: 'gplots'
##
## The following object is masked from 'package:stats':
##
## lowess
library(xtable)
library(stargazer)
##
## Please cite as:
##
## Hlavac, Marek (2014). stargazer: LaTeX code and ASCII text for well-formatted regression and summary statistics tables.
## R package version 5.1. http://CRAN.R-project.org/package=stargazer
load("image.rda")
```

2 Cohort characteristics

```
cpvs.diag_dsd$Path.TumourLocation[cpvs.diag_dsd$Path.TumourLocation == ""] = NA
cpvs.diag_dsd$Path.Nodes.Regional.Involved.Fraction = cpvs.diag_dsd$Path.Nodes.Regional.Involved / cpvs
cpvs.diag_dsd$Treat.Surgery.ExcisionStatus.Coarse = ordered(ifelse(cpvs.diag_dsd$Treat.Surgery.ExcisionStatus.Coarse = ordered(ifelse(cpvs.diag_dsd)).
cpvs.diag_dsd$Path.Grade.Coarse = ordered(ifelse(cpvs.diag_dsd$Path.Grade %in% c("1", "2"), "1or2", "3ordered(ifelse(cpvs.diag_dsd$Path.Grade %in% c("1", "2"), "3ordered(ifelse(cpvs.diag_dsd$Path.Grade %in% c("1"), "3ordered(ifelse(cpvs.diag_dsd"), "3ordered(ifelse(cpvs.diag
cpvs.diag_dsd$Path.TumourLocation.Coarse = factor(ifelse(cpvs.diag_dsd$Path.TumourLocation %in% c("Head
summary(cpvs.diag_dsd)
             Patient.ID
                                                                             Patient.Gender
                                                                                                                                                                                                        Patient. Ethnicity
## Length:110
                                                                            Female:50
                                                                                                                            Asian
                                                                                                                                                                                                                                       : 5
## Class :character Male :60
                                                                                                                               Asian, White/Caucasian
                                                                                                                                                                                                                                        : 0
          Mode :character
                                                                                                                                Black/African
##
##
                                                                                                                                 Black/African, White/Caucasian: 0
                                                                                                                                 White/Caucasian
##
                                                                                                                                                                                                                                       :104
##
                                                                                                                                 NA's
##
                                                                   Patient.Country History.LastFollowup.Date
##
                                                                                                                        Min.
                                                                                                                                              :2007-06-29
## Australia
                                                                                              :110
##
          Italy
                                                                                                                         1st Qu.:2011-08-19
## New Zealand
                                                                                             : 0
                                                                                                                        Median :2013-03-12
## Puerto Rico
                                                                                             : 0 Mean :2012-10-16
## United Kingdom
                                                                                                                          3rd Qu.:2014-04-24
                                                                                             : 0
## United States of America: 0
                                                                                                                          Max. :2014-09-23
##
                                                                                                                          NA's :1
## History.Smoking.PackYears History.Diagnosis.Date
## Min. : 0.75
                                                                                                    Min.
                                                                                                                           :2007-06-04
## 1st Qu.: 9.00
                                                                                                     1st Qu.:2010-01-28
## Median :22.50
                                                                                                   Median :2011-01-04
## Mean :26.89
                                                                                                     Mean :2011-01-14
## 3rd Qu.:43.75
                                                                                                     3rd Qu.:2012-02-15
## Max. :70.00
                                                                                     Max. :2012-10-17
```

```
## NA's :68
## History.Diagnosis.AgeAtYears History.Surgery.Date
## Min. :36.0
                           Min. :2007-05-29
## 1st Qu.:61.0
                             1st Qu.:2010-01-22
## Median :67.0
                            Median :2011-01-01
## Mean :66.4
                            Mean :2011-01-13
                             3rd Qu.:2012-02-13
## 3rd Qu.:73.0
## Max. :87.0
                            Max. :2012-10-17
##
##
                                          Treat.Surgery.Procedure
## Classic Whipple
## Splenectomy, Subtotal Panc/L sided Panc or distal Panc: 6
## Cholecystectomy, Classic Whipple
                                                    : 4
## Subtotal Panc/L sided Panc or distal Panc
## Classic Whipple, Exploratory laparotomy
## PPPD
                                                     : 3
## Treat.Surgery.ExcisionStatus Treat.Surgery.Margin.Pancreatic
## R0:69
                              <2 mm : 4
## R1:35
                              Clear :88
## R2: 6
                              Involved: 9
##
                              NA's : 9
##
##
##
## Treat.Surgery.MarginSizeMm.Pancreatic Treat.Surgery.Margin.Periunc
## Min. : 0.0
                                      <2 mm :20
## 1st Qu.: 5.0
                                      Clear :52
## Median :10.0
                                      Involved:15
## Mean :10.6
                                      NA's :23
## 3rd Qu.:10.2
## Max. :40.0
## NA's :30
## Treat.Surgery.MarginSizeMm.Periunc Treat.Surgery.Margin.PVGroove
## Min. : 0.00
                                  <2 mm :23
## 1st Qu.: 1.00
                                   Clear :55
## Median : 3.00
                                   Involved:12
## Mean : 6.21
                                   NA's :20
## 3rd Qu.:10.00
## Max. :40.00
## NA's :43
## Treat.Surgery.MarginSizeMm.PVGroove Treat.Surgery.Margin.Retrop
## Min. : 0.00
                                    <2 mm :21
## 1st Qu.: 1.00
                                    Clear :68
## Median : 3.00
                                    Involved: 9
## Mean : 4.08
                                    NA's :12
## 3rd Qu.: 5.00
## Max. :30.00
## NA's
## Treat.Surgery.MarginSizeMm.Retrop Treat.Surgery.Margin.CBD
## Min. : 0.10
                                 <2 mm : 1
## 1st Qu.: 1.75
                                  Clear :83
## Median : 3.00
                                  Involved: 0
## Mean : 5.62
                               NA's :26
```

```
## 3rd Qu.:10.00
## Max. :25.00
## NA's :31
## Treat.Surgery.MarginSizeMm.CBD Treat.Surgery.Margin.Duodenal
## Min. : 1.0
                              Clear :60
## 1st Qu.:11.8
                              Involved: 1
## Median :20.0
                             NA's :49
## Mean :23.6
## 3rd Qu.:32.5
## Max. :55.0
## NA's :47
## Treat.Surgery.MarginSizeMm.Duodenal Treat.Surgery.Margin.Gastric
## Min. : 10.0
                                 Clear:59
## 1st Qu.: 40.0
                                  NA's :51
## Median: 80.0
## Mean : 86.2
## 3rd Qu.:132.5
## Max. :190.0
## NA's :102
## Treat.Surgery.MarginSizeMm.Gastric Treat.Surgery.Margin.Comments
## Min. : 10.0
                                Length:110
## 1st Qu.: 50.0
                                 Class :character
## Median : 70.0
                                Mode :character
## Mean : 67.9
## 3rd Qu.: 97.5
## Max. :100.0
## NA's :103
##
                        Path.HistoType
## Pancreatic Ductal Adenocarcinoma:110
## Acinar Cell Carcinoma : 0
## Ampullary Adenocarcinoma
## Carcinoid Tumour
                              : 0
## Cholangiocarcinoma
## Clear Cell Carcinoma
## (Other)
                              : 0
                  Path.HistoType.Subtype Path.Grade
## Gastric
                            : 0 1: 8
## Intestinal
                            : 0
                                      2:71
## Mixed
                                     3:30
                            : 0
## Not otherwise Specified (NOS):31
                                     4: 1
## Pancreatobiliary
                            :13
## Squamous
                            : 0
## NA's
                            :66
##
       Path.TumourLocation Path.TumourSizeMm Path.Invasion.PN
                    Min. :10.0 Absent :13
## Head
         :83
## Head (Uncinate):10
                       1st Qu.:28.0
                                      Present:96
         : 9
## Tail
                       Median:35.0
                                      NA's : 1
               : 7
                       Mean :37.6
## Body
               : 0
                        3rd Qu.:45.0
## (Other)
               : 0
                       Max. :90.0
               : 1
                       NA's :1
## Path.Invasion.VS Path.Nodes.Regional.Total Path.Nodes.Regional.Involved
                               Min. : 0.00
## Absent :34 Min. : 0.0
## Present:72 1st Qu.:11.0 1st Qu.: 1.00
```

```
NA's : 4
                   Median :16.0
                                            Median: 2.00
##
                    Mean :18.1
                                            Mean : 3.18
##
                    3rd Qu.:24.0
                                             3rd Qu.: 4.00
##
                    Max. :46.0
                                            Max. :18.00
##
## Path.Nodes.SepRec.Total Path.Nodes.SepRec.Involved
                          Min. : 0.00
## Min. : 0.0
## 1st Qu.:11.0
                          1st Qu.: 1.00
## Median :16.0
                         Median: 2.00
## Mean :18.1
                         Mean : 3.18
## 3rd Qu.:24.0
                          3rd Qu.: 4.00
## Max. :46.0
                          Max. :18.00
##
##
                                    Staging. Version Staging.pM Staging.pN
##
  pTNM AJCC 6th Ed 2002
                                            :14
                                                   MO : 2
                                                            NO :25
## pTNM AJCC 7th Ed 2010
                                            :96
                                                   M1 : 6
                                                             N1 :84
## pTNM AJCC 7th Ed 2010 (Ampulla)
                                           : 0
                                                   NA's:102
                                                             NA's: 1
## pTNM AJCC 7th Ed 2010 (Cholangiocarcinoma): 0
##
   pTNM AJCC 7th Ed 2010 (Neuroendocrine)
##
##
##
   Staging.pT Staging.Stage
                              History.Recurrence History.Recurrence.Date
## Tis : 0
              IA : O
                           Not observed:24
                                                Min. :2007-10-14
## T1 : 0
             IB : 3
                           Suspected : 4
                                                1st Qu.:2010-12-11
## T2 : 6 IIA:20
                           Confirmed
                                     :78
                                                Median :2012-02-22
## T3 :102 IIB:80
                                                Mean :2012-01-21
                           NA's
                                      : 4
## T4 : 1 III: 1
                                                3rd Qu.:2012-12-29
## NA's: 1 IV: 6
                                                Max. :2014-08-27
##
                                                NA's
                                                       :29
## History.Recurrence.Site.Stomach History.Recurrence.Site.Peritoneum
## Mode :logical
                                  Mode :logical
## FALSE:110
                                  FALSE:94
                                  TRUE:16
## NA's :0
                                  NA's :0
##
##
##
## History.Recurrence.Site.PancRemnant History.Recurrence.Site.PancBed
## Mode :logical
                                     Mode :logical
## FALSE: 106
                                      FALSE:91
                                      TRUE :19
## TRUE:4
##
   NA's :0
                                      NA's :0
##
##
##
## History.Recurrence.Site.Other History.Recurrence.Site.Omentum
## Mode :logical
                               Mode :logical
## FALSE:102
                                FALSE: 109
## TRUE:8
                                TRUE:1
## NA's :0
                                NA's :0
##
##
##
## History.Recurrence.Site.Mesentery History.Recurrence.Site.LymphNodes
```

```
## Mode :logical
                                   Mode :logical
## FALSE:108
                                   FALSE:88
## TRUE :2
                                   TRUE:22
## NA's :0
                                   NA's :0
##
##
##
## History.Recurrence.Site.Lung History.Recurrence.Site.Liver
## Mode :logical
                  Mode :logical
## FALSE:88
                             FALSE:72
                              TRUE:38
   TRUE:22
## NA's :0
                              NA's :0
##
##
##
## History.Recurrence.Site.Brain History.Recurrence.Site.Bone
                              Mode :logical
## Mode :logical
## FALSE:109
                               FALSE: 104
## TRUE :1
                               TRUE :6
## NA's :0
                               NA's :0
##
##
##
##
                      History.Status History.Death.Date
## Alive - With Disease
                       :15 Min. :2007-11-21
                            :22
                                 1st Qu.:2011-01-14
Median :2012-03-07
                                   1st Qu.:2011-01-14
## Alive - Without Disease
## Deceased - Of Disease
                           :70
## Deceased - Of Other Cause : 3 Mean :2012-02-21
                                 3rd Qu.:2013-03-17
## Deceased - Of Unknown Cause: 0
##
                                    Max. :2014-06-17
##
                                   NA's :37
##
                       History.Death.Cause Surv.Event.Death
## Cancer Death (Pancreatic) :69 Min. :0.000
## Cancer Death (Other) - Lung ca : 1
                                          1st Qu.:0.000
                                      1st Qu.:0.000
Median :1.000
## Died of Treatment Complication : 1
## Other (please specify) : 1
                                          Mean :0.664
## Other (please specify) - Suicide: 1
                                          3rd Qu.:1.000
## (Other)
                                 : 0
                                          Max. :1.000
## NA's
                                 :37
## Surv.EventTimeFromDiag.Death Surv.EventTimeFromSurg.Death
## Min. : 36
                              Min. : 36
## 1st Qu.: 402
                              1st Qu.: 406
## Median : 632
                              Median: 634
## Mean : 674
                              Mean : 676
##
   3rd Qu.: 912
                              3rd Qu.: 917
## Max. :1778
                              Max. :1779
##
## Surv.EventTimeFromRec.Death Surv.Event.DSDeath
## Min. : 7
                  Min. :0.000
## 1st Qu.: 68
                             1st Qu.:0.000
## Median: 183
                            Median :1.000
## Mean : 250
                            Mean :0.636
## 3rd Qu.: 338
                             3rd Qu.:1.000
## Max. :1333
                     Max. :1.000
```

```
## NA's :29
## Surv.EventTimeFromDiag.DSDeath Surv.EventTimeFromSurg.DSDeath
## Min. : 36
                               Min. : 36
## 1st Qu.: 402
                               1st Qu.: 406
## Median: 632
                               Median: 634
## Mean : 673
                               Mean : 675
## 3rd Qu.: 912
                              3rd Qu.: 917
## Max. :1778
                               Max. :1779
##
## Surv.EventTimeFromRec.DSDeath Surv.Event.Recurrence
## Min. : 7
                             Min. :0.000
                              1st Qu.:0.000
## 1st Qu.: 68
## Median : 183
                             Median :1.000
## Mean : 250
                              Mean :0.736
## 3rd Qu.: 338
                              3rd Qu.:1.000
## Max. :1333
                              Max. :1.000
                              NA's :4
## Surv.EventTimeFromDiag.Recurrence Surv.EventTimeFromSurg.Recurrence
## Min. : 34
                                  Min. : 34
## 1st Qu.: 240
                                  1st Qu.: 240
## Median: 392
                                  Median: 398
## Mean : 511
                                  Mean : 512
                                  3rd Qu.: 699
## 3rd Qu.: 697
## Max. :1778
                                  Max. :1779
## NA's :6
                                 NA's :6
## Path.Nodes.Regional.Involved.Fraction Treat.Surgery.ExcisionStatus.Coarse
## Min. :0.0000
                                    Clear :69
## 1st Qu.:0.0435
                                     Involved:41
## Median: 0.1667
## Mean :0.2026
## 3rd Qu.:0.2727
## Max. :1.0000
## NA's :1
## Path.Grade.Coarse Path.TumourLocation.Coarse
## 1or2:79 Head :93
## 3or4:31
                 Other:17
##
##
##
##
##
sort(apply(is.na(cpvs.diag_dsd), 2, sum))
##
                           Patient.ID
##
##
                       Patient.Gender
##
##
                      Patient.Country
##
                History.Diagnosis.Date
##
##
##
          History.Diagnosis.AgeAtYears
```

```
##
                    History.Surgery.Date
##
                 Treat.Surgery.Procedure
            Treat.Surgery.ExcisionStatus
##
##
##
           Treat.Surgery.Margin.Comments
##
##
                           Path.HistoType
##
##
                               Path.Grade
##
               Path.Nodes.Regional.Total
##
##
##
            Path.Nodes.Regional.Involved
##
                                         0
##
                 Path.Nodes.SepRec.Total
##
##
              Path.Nodes.SepRec.Involved
##
##
                          Staging. Version
##
##
                            Staging.Stage
##
##
         History.Recurrence.Site.Stomach
##
##
      History.Recurrence.Site.Peritoneum
##
##
     History.Recurrence.Site.PancRemnant
##
##
         History.Recurrence.Site.PancBed
##
##
           History.Recurrence.Site.Other
##
         History.Recurrence.Site.Omentum
##
##
       History.Recurrence.Site.Mesentery
##
      History.Recurrence.Site.LymphNodes
##
##
            History.Recurrence.Site.Lung
##
           History.Recurrence.Site.Liver
##
##
##
           History.Recurrence.Site.Brain
##
            History.Recurrence.Site.Bone
##
##
                                         0
##
                           History.Status
##
                         Surv. Event. Death
##
##
            Surv.EventTimeFromDiag.Death
```

```
##
            Surv.EventTimeFromSurg.Death
##
##
                       Surv.Event.DSDeath
          Surv.EventTimeFromDiag.DSDeath
##
          Surv.EventTimeFromSurg.DSDeath
##
##
##
     Treat.Surgery.ExcisionStatus.Coarse
##
                        Path.Grade.Coarse
##
##
##
              Path.TumourLocation.Coarse
##
                       Patient. Ethnicity
##
               History.LastFollowup.Date
##
##
                      Path.TumourLocation
                       Path.TumourSizeMm
##
                         Path.Invasion.PN
##
##
                               Staging.pN
##
##
                               Staging.pT
   Path.Nodes.Regional.Involved.Fraction
##
                        Path.Invasion.VS
##
##
                      History.Recurrence
##
                   Surv. Event. Recurrence
##
##
       Surv.EventTimeFromDiag.Recurrence
##
       Surv.EventTimeFromSurg.Recurrence
##
##
         Treat.Surgery.Margin.Pancreatic
##
             Treat.Surgery.Margin.Retrop
##
##
           Treat.Surgery.Margin.PVGroove
##
            Treat.Surgery.Margin.Periunc
##
##
                Treat.Surgery.Margin.CBD
##
                 History.Recurrence.Date
##
##
             Surv.EventTimeFromRec.Death
```

```
##
           Surv.EventTimeFromRec.DSDeath
##
   Treat.Surgery.MarginSizeMm.Pancreatic
##
##
##
       Treat.Surgery.MarginSizeMm.Retrop
##
##
                       History.Death.Date
##
                                        37
##
                      History.Death.Cause
##
      Treat.Surgery.MarginSizeMm.Periunc
##
##
##
     Treat.Surgery.MarginSizeMm.PVGroove
##
          Treat.Surgery.MarginSizeMm.CBD
##
##
##
           Treat.Surgery.Margin.Duodenal
##
##
            Treat.Surgery.Margin.Gastric
##
                  Path.HistoType.Subtype
##
##
               History.Smoking.PackYears
##
##
##
     {\tt Treat.Surgery.MarginSizeMm.Duodenal}
##
                                       102
##
                               Staging.pM
##
##
      Treat.Surgery.MarginSizeMm.Gastric
##
```

3 Probe selection

```
table(cpss.sis$sel)
##
## FALSE TRUE
## 12639 361

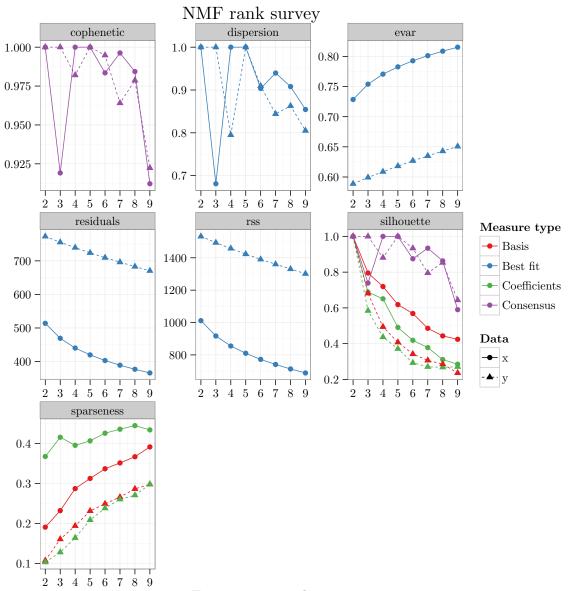
mean(cpss.sis$sel)
## [1] 0.02777

apply(cpss.sis.permuted, 2, sum)
## [1] 37 175 92 32 298 49 47 138 43 173 98 86 207 102 147 41 28
## [18] 160 75 273 154 124 415 109 41 141 50 63 107 63 64 237 84 52
## [35] 40 203 88 55 98 87 57 231 54 48 81 186 114 43 58 347

median(apply(cpss.sis.permuted, 2, sum))
## [1] 87.5
```

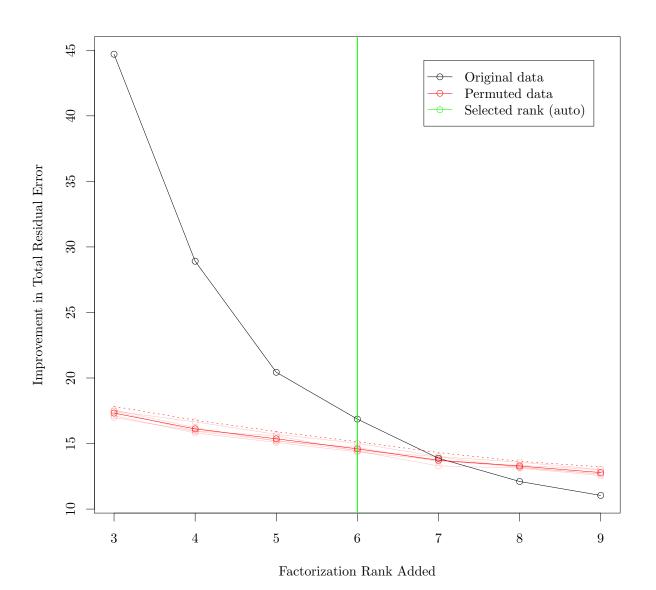
4 Factorization

```
plot(nmf.runs.rank, nmf.runs.rank.random[[1]])
```

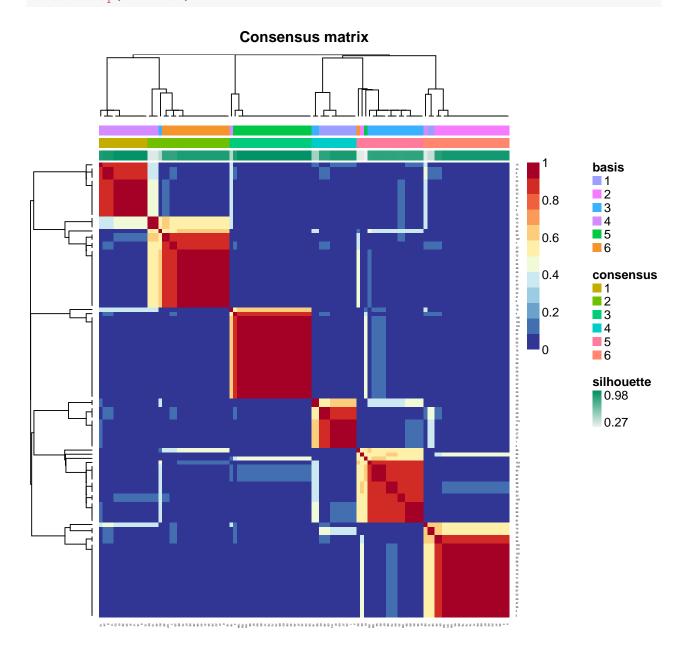


Factorization rank

```
if (nmf.rank.wasauto == TRUE)
{
        temp.col = "green"
} else {
        temp.col = "blue"
}
abline(v = nmf.rank, col = temp.col, lwd = 2)
legend("topright", legend = c("Original data", "Permuted data", sprintf("Selected rank (%s)", ifelse(nm:)
```

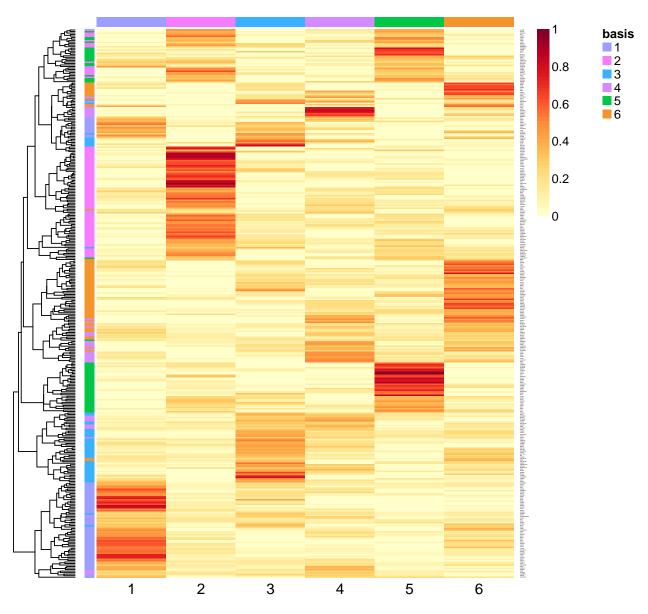


4.1 Fit



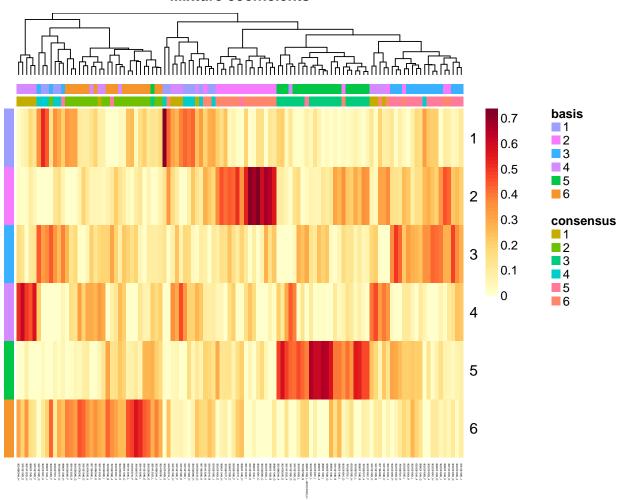
basismap(nmf.final)

Basis components



coefmap(nmf.final)

Mixture coefficients



```
coefs.diag_dsd = apply(xlin.diag_dsd.sel, 2, function(xcol) nnls(basis(nmf.final), xcol)$x)
coefs.diag_rec = apply(xlin.diag_rec.sel, 2, function(xcol) nnls(basis(nmf.final), xcol)$x)
coefs.recr_dsd = apply(xlin.recr_dsd.sel, 2, function(xcol) nnls(basis(nmf.final), xcol)$x)
coefs.pdac_au = apply(xlin.pdac_au.sel, 2, function(xcol) nnls(basis(nmf.final), xcol)$x)
axis_coefs.diag_dsd = as.matrix(cbind(axis1 = coefs.diag_dsd[1,] - coefs.diag_dsd[5,], axis2 = coefs.diag_dsd[1,]
```

```
library(MASS)
W_plus = ginv(basis(nmf.final))

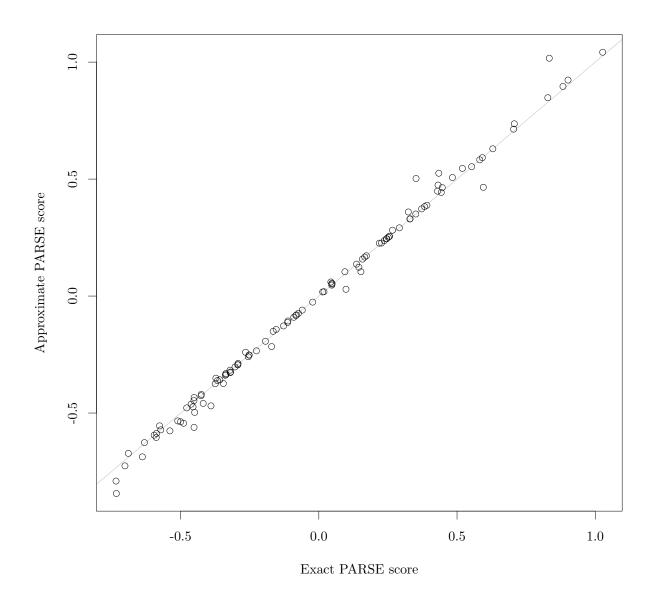
A1 = W_plus[1,] - W_plus[5,]
A2 = W_plus[6,] - W_plus[2,]
PARSE_approx = matrix(1.354*A1 + 1.548*A2, ncol = 1)
```

```
rownames(PARSE_approx) = rownames(basis(nmf.final))

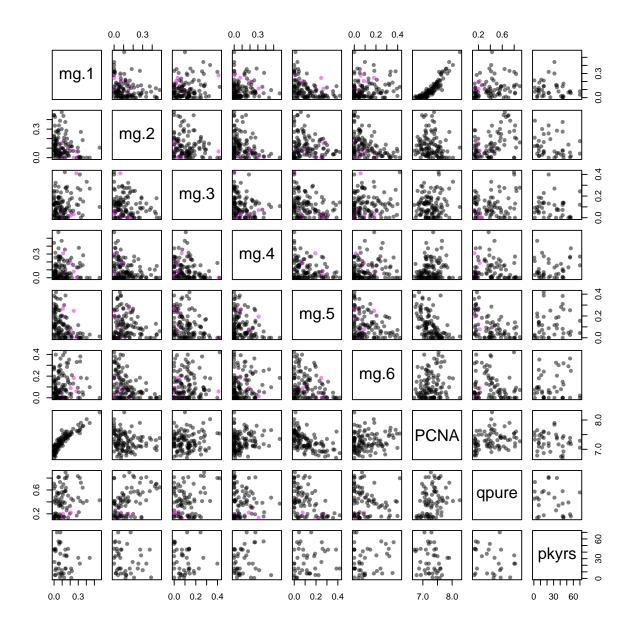
PARSE_approx_scores = t(xlin.diag_dsd.sel) %*% PARSE_approx

PARSE_exact_scores = 1.354*(coefs.diag_dsd[1,] - coefs.diag_dsd[5,]) + 1.548*(coefs.diag_dsd[6,] - coefs.

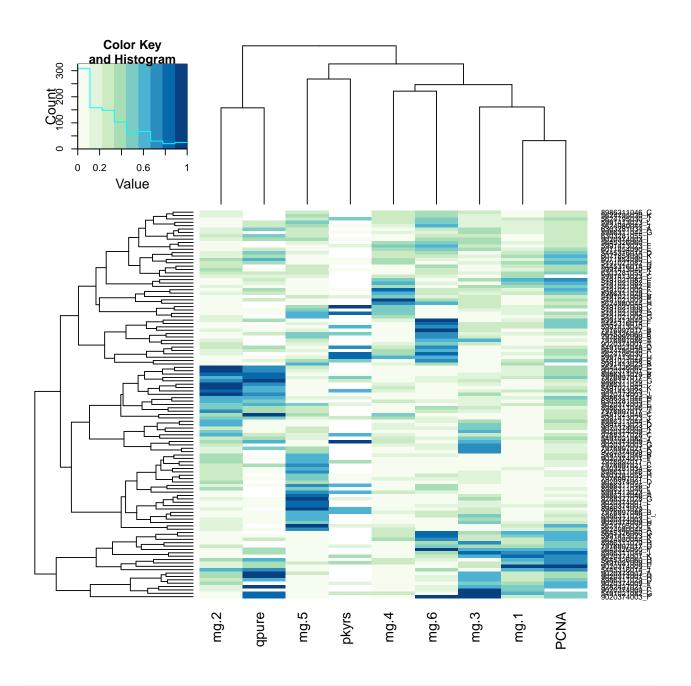
plot(PARSE_exact_scores, PARSE_approx_scores, xlab = "Exact PARSE score", ylab = "Approximate PARSE score abline(0, 1, col = rgb(0, 0, 0, 0.25))
```



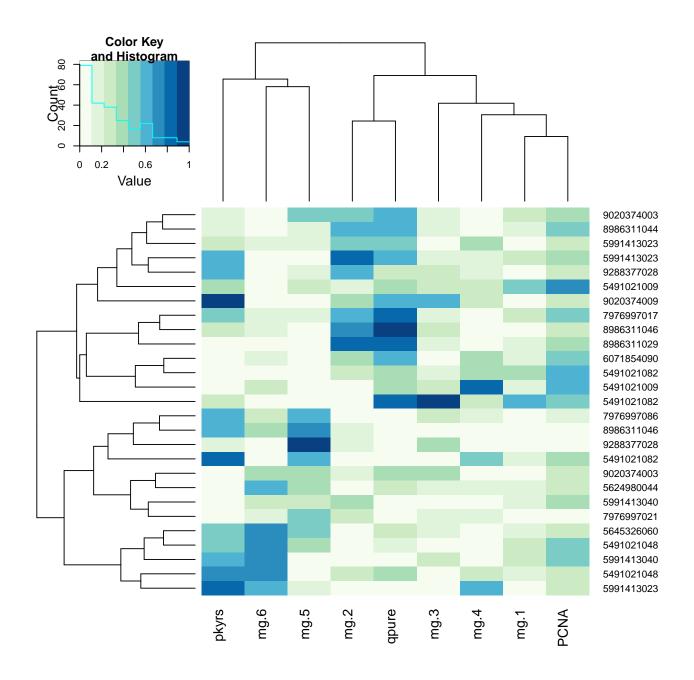
```
temp.pred.pairs = t(rbind(coefs.pdac_au, metapcna.scores[colnames(coefs.pdac_au)]))
colnames(temp.pred.pairs) = paste("mg", 1:ncol(temp.pred.pairs), sep = ".")
colnames(temp.pred.pairs)[ncol(temp.pred.pairs)] = "PCNA"
temp.pred.pairs = cbind(temp.pred.pairs, qpure = samps.pdac_au$purity_qpure, pkyrs = cpvs.pdac_au$Histor
pairs(temp.pred.pairs, pch = 16, cex = 1, col = ifelse(rownames(temp.pred.pairs) %in% colnames(xlin.diag)
```



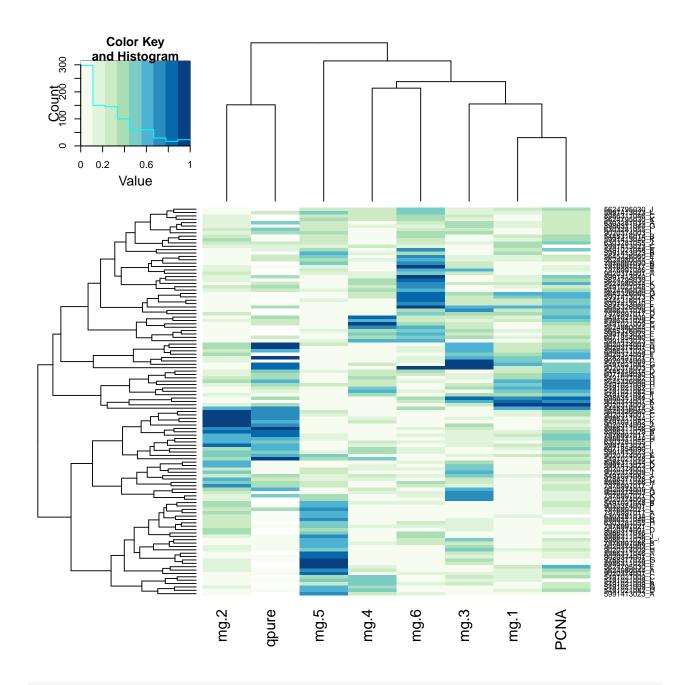
temp.pred.pairs.rescaled = t((t(temp.pred.pairs) - apply(temp.pred.pairs, 2, min, na.rm = TRUE)) / (appl heatmap.2(temp.pred.pairs.rescaled, trace = "none", scale = "none", col = brewer.pal(9, "GnBu"))



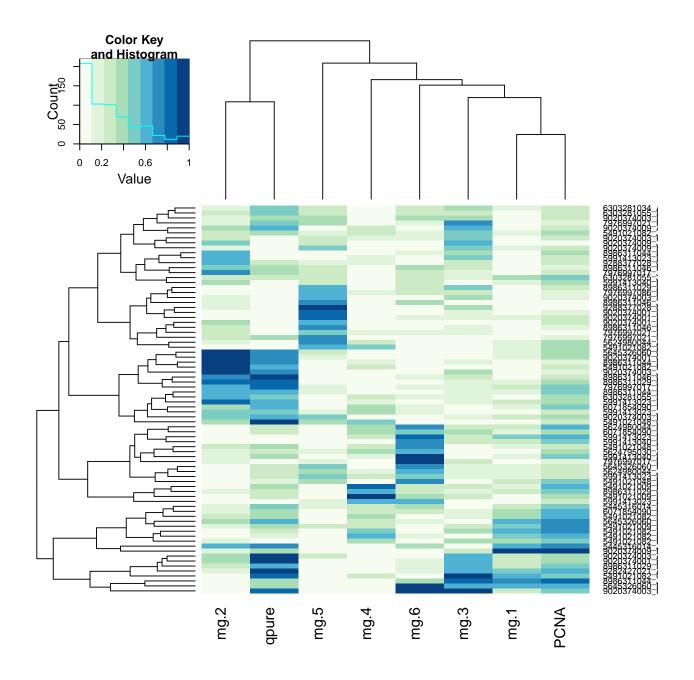
heatmap.2(temp.pred.pairs.rescaled[apply(!is.na(temp.pred.pairs.rescaled), 1, all),], trace = "none", se



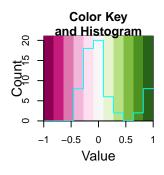
temp.pred.pairs.rescaled2 = temp.pred.pairs.rescaled[,colnames(temp.pred.pairs.rescaled) != "pkyrs"]
heatmap.2(temp.pred.pairs.rescaled2, trace = "none", scale = "none", col = brewer.pal(9, "GnBu"))

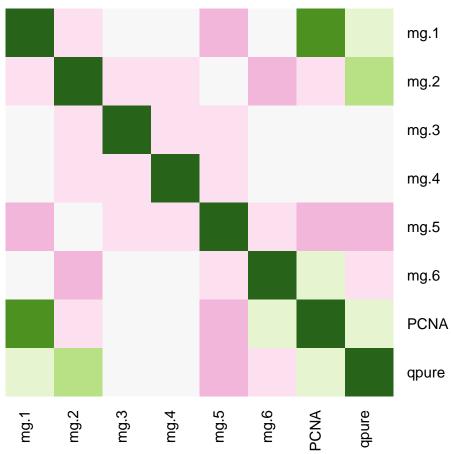


heatmap.2(temp.pred.pairs.rescaled2[apply(!is.na(temp.pred.pairs.rescaled2), 1, all),], trace = "none",

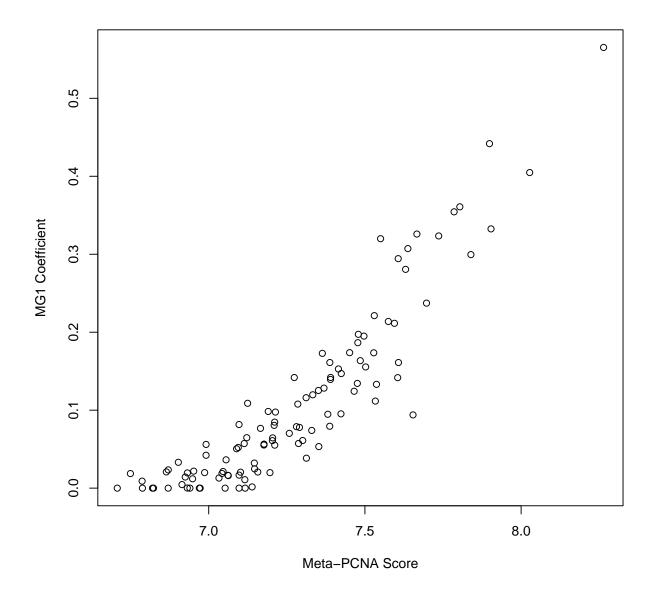


temp.cors = apply(temp.pred.pairs[,colnames(temp.pred.pairs) != "pkyrs"], 2, function(x) apply(temp.pred
#diag(temp.cors) = NA
heatmap.2(temp.cors, trace = "none", Rowv = FALSE, Colv = FALSE, col = brewer.pal(11, "PiYG"), dendrogrammer.

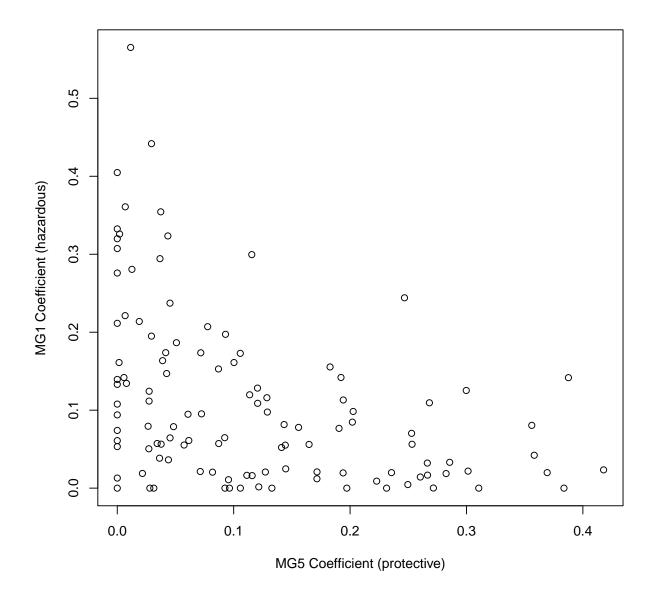




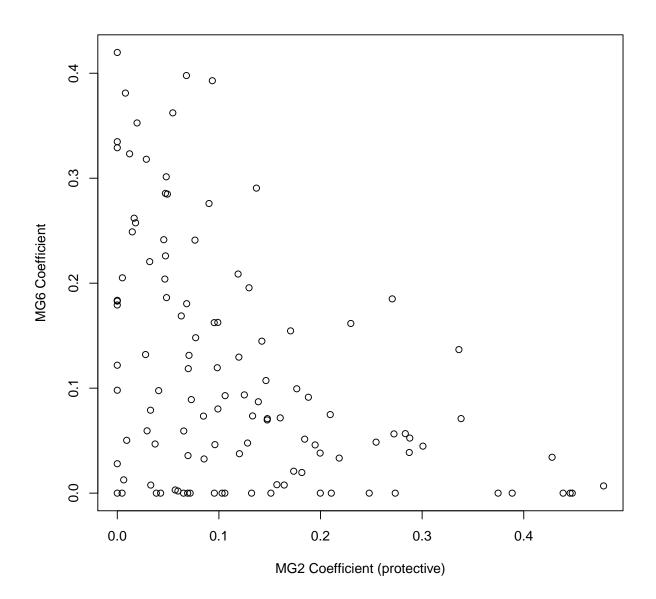
plot(temp.pred.pairs[,"mg.1"] ~ temp.pred.pairs[,"PCNA"], col = ifelse(rownames(temp.pred.pairs) %in% col



plot(temp.pred.pairs[,"mg.5"], temp.pred.pairs[,"mg.1"], xlab = "MG5 Coefficient (protective)", ylab = "



plot(temp.pred.pairs[,"mg.2"], temp.pred.pairs[,"mg.6"], xlab = "MG2 Coefficient (protective)", ylab = "

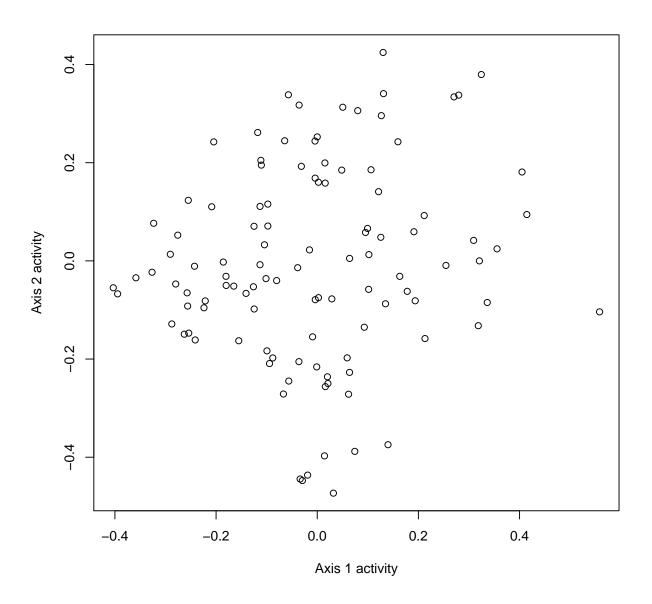


#scatter.smooth(temp.pred.pairs[, "mg.5"], temp.pred.pairs[, "mg.1"], xlab = "MG5 Coefficient (protective,
#scatter.smooth(temp.pred.pairs[, "mg.2"], temp.pred.pairs[, "mg.6"], xlab = "MG2 Coefficient (protective,
#smoothScatter(temp.pred.pairs[, "mg.5"], temp.pred.pairs[, "mg.1"], xlab = "MG5 Coefficient (protective)
#smoothScatter(temp.pred.pairs[, "mg.2"], temp.pred.pairs[, "mg.6"], xlab = "MG2 Coefficient (protective)

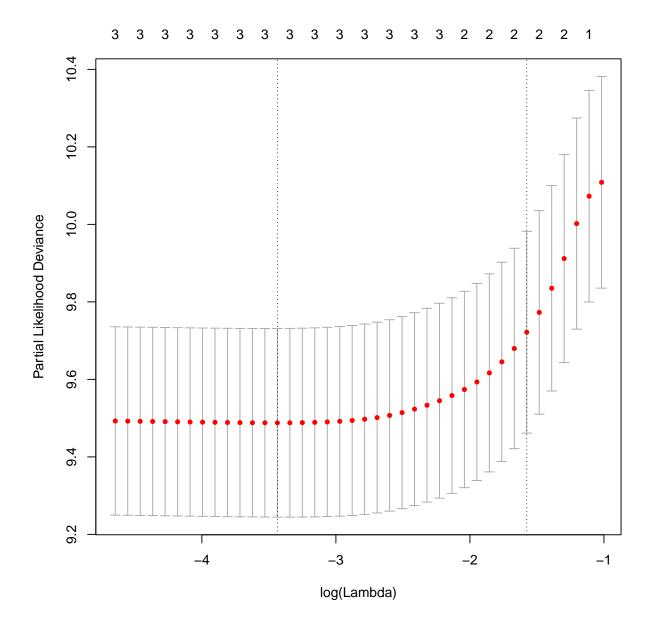
temp.coefs.pdcor = apply(coefs.diag_dsd, 1, function(x1) apply(coefs.diag_dsd, 1, function(x2) dcov.test
temp.coefs.pfisher = apply(coefs.diag_dsd, 1, function(x1) apply(coefs.diag_dsd, 1, function(x2) fisher
diag(temp.coefs.pdcor) = NA
temp.coefs.pdcor[lower.tri(temp.coefs.pdcor)] = NA
temp.coefs.pfisher[lower.tri(temp.coefs.pfisher)] = NA
temp.coefs.pdcor.holm = matrix(p.adjust(temp.coefs.pdcor, "holm"), nrow = nrow(temp.coefs.pfisher))
temp.coefs.pdcor.holm

```
[,1]
             [,2] [,3] [,4] [,5] [,6]
## [1,]
         NA 0.2016 0.4500 1.0000 0.0015 1.0000
## [2,]
         NA
                NA 0.3066 0.0130 0.1800 0.0015
## [3,]
                NA
                       NA 0.0336 0.0451 1.0000
        NA
## [4,]
                              NA 0.0480 1.0000
         NA
                NA
                       NA
## [5,]
         NA
                NA
                       NA
                              NA
                                     NA 0.0480
## [6,]
         NA
                NA
                       NA
                              NA
                                     NA
temp.coefs.pfisher.holm
        [,1] [,2] [,3] [,4]
                               [,5]
## [1,]
              1 1.0000
                         1 0.03203 1.00000
         NA
## [2,]
         NA
              NA 0.7286
                           1 1.00000 0.03203
## [3,]
         NA
              NA
                     NA
                          1 1.00000 1.00000
## [4,]
         NA
              NA
                     NA
                         NA 0.72858 1.00000
## [5,]
                                  NA 1.00000
         NA
              NA
                     NA
                          NA
## [6,]
        NA
              NA
                     NA
                          NA
                                  NA
                                          NA
dcov.test(coefs.diag_dsd[5,], coefs.diag_dsd[1,], R = 19999)
##
##
   dCov test of independence
##
## data: index 1, replicates 19999
## nV^2 = 0.1291, p-value = 5e-05
## sample estimates:
##
      dCov
## 0.03426
dcov.test(coefs.diag_dsd[2,], coefs.diag_dsd[6,], R = 19999)
##
## dCov test of independence
## data: index 1, replicates 19999
## nV^2 = 0.1396, p-value = 5e-05
## sample estimates:
##
   dCov
## 0.03562
cor.test(coefs.diag_dsd[5,], coefs.diag_dsd[1,], method = "kendall")
##
   Kendall's rank correlation tau
##
## data: coefs.diag_dsd[5, ] and coefs.diag_dsd[1, ]
## z = -4.97, p-value = 6.694e-07
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
##
      tau
## -0.3243
cor.test(coefs.diag_dsd[2,], coefs.diag_dsd[6,], method = "kendall")
```

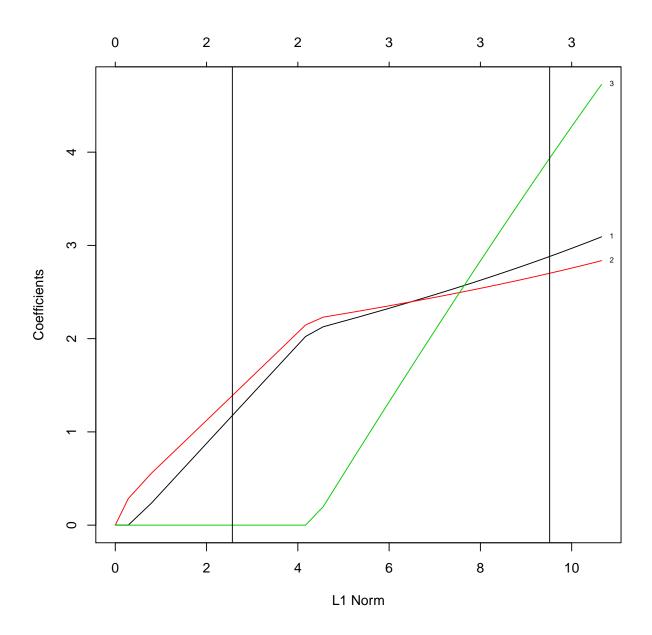
```
##
## Kendall's rank correlation tau
## data: coefs.diag_dsd[2, ] and coefs.diag_dsd[6, ]
## z = -4.931, p-value = 8.195e-07
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
##
      tau
## -0.3236
temp.axis1 = coefs.diag_dsd[1,] - coefs.diag_dsd[5,]
temp.axis2 = coefs.diag_dsd[6,] - coefs.diag_dsd[2,]
dcov.test(temp.axis1, temp.axis2, R = 19999)
##
## dCov test of independence
##
## data: index 1, replicates 19999
## nV^2 = 0.1074, p-value = 0.0197
## sample estimates:
## dCov
## 0.03124
cor.test(temp.axis1, temp.axis2, method = "kendall")
## Kendall's rank correlation tau
##
## data: temp.axis1 and temp.axis2
## z = 1.253, p-value = 0.2103
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
## tau
## 0.0809
plot(temp.axis2 ~ temp.axis1, xlab = "Axis 1 activity", ylab = "Axis 2 activity")
```



```
coxph(y.diag_dsd ~ temp.axis1 * temp.axis2)
## Call:
## coxph(formula = y.diag_dsd ~ temp.axis1 * temp.axis2)
##
##
                         coef exp(coef) se(coef)
##
                                                     Z
                         3.19
                                    24.2
                                            0.676 4.72 2.4e-06
## temp.axis1
## temp.axis2
                         2.89
                                    18.0
                                            0.657 4.40 1.1e-05
                                   153.1
                                            4.189 1.20 2.3e-01
## temp.axis1:temp.axis2 5.03
## Likelihood ratio test=48 on 3 df, p=2.12e-10 n= 110, number of events= 70
temp = cv.glmnet(cbind(temp.axis1, temp.axis2, temp.axis1*temp.axis2), y.diag_dsd, family = "cox", nfold
plot(temp)
```



```
plot(temp$glmnet.fit, label = TRUE)
abline(v = sum(abs(coef(temp$glmnet.fit, s = temp$lambda.1se))))
abline(v = sum(abs(coef(temp$glmnet.fit, s = temp$lambda.min))))
```



```
coef(temp$glmnet.fit, s = temp$lambda.1se)

## 3 x 1 sparse Matrix of class "dgCMatrix"

## 1

## temp.axis1 1.176

## temp.axis2 1.390

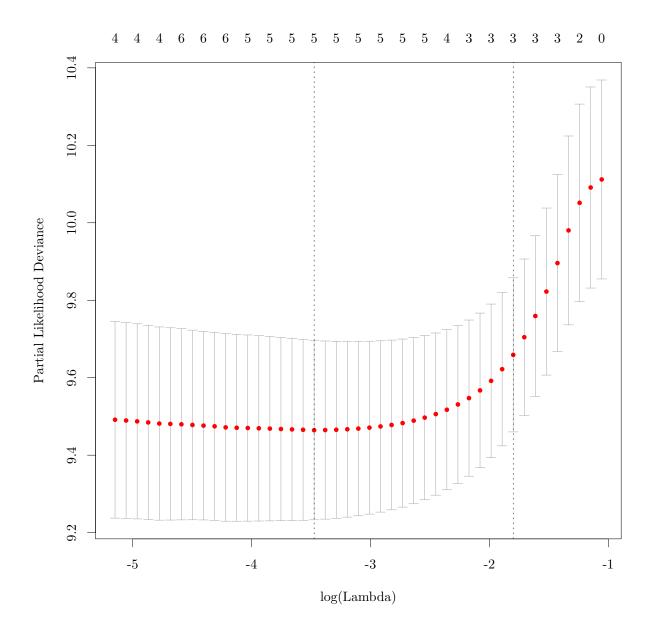
## .
```

4.2 LASSO on training set

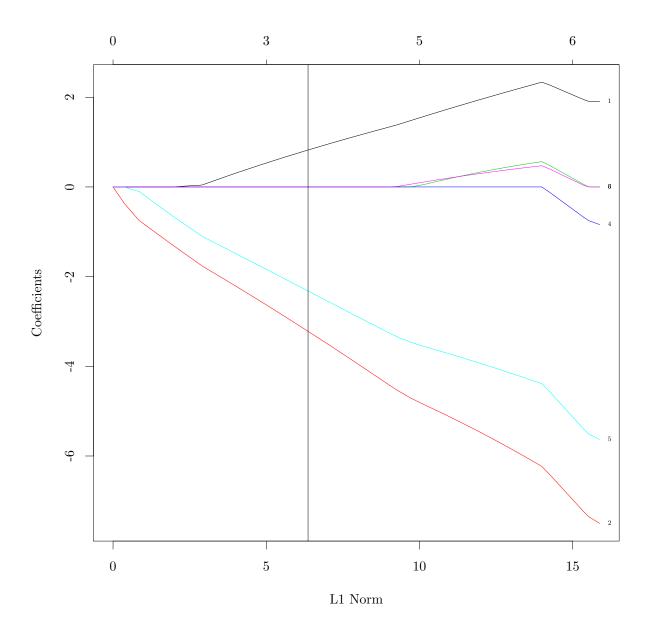
```
glmnet.fit.cv.diag_dsd = cv.glmnet(t(coefs.diag_dsd), y.diag_dsd, family = "cox", nfolds = 10)
glmnet.fit.cv.diag_rec = cv.glmnet(t(coefs.diag_rec), y.diag_rec, family = "cox", nfolds = 10)
```

```
glmnet.fit.cv.recr_dsd = cv.glmnet(t(coefs.recr_dsd), y.recr_dsd, family = "cox", nfolds = 10)
```

plot(glmnet.fit.cv.diag_dsd)



```
plot(glmnet.fit.cv.diag_dsd$glmnet.fit, label = TRUE)
abline(v = sum(abs(coef(glmnet.fit.cv.diag_dsd$glmnet.fit, s = glmnet.fit.cv.diag_dsd$lambda.1se))))
```



```
#abline(v = sum(abs(coef(glmnet.fit.cv.diag_dsdfglmnet.fit, s = glmnet.fit.cv.diag_dsdflambda.min))))
coef(glmnet.fit.cv.diag_dsd$glmnet.fit, s = glmnet.fit.cv.diag_dsd$lambda.1se)

## 6 x 1 sparse Matrix of class "dgCMatrix"

## 1

## V1 0.8238

## V2 -3.2195

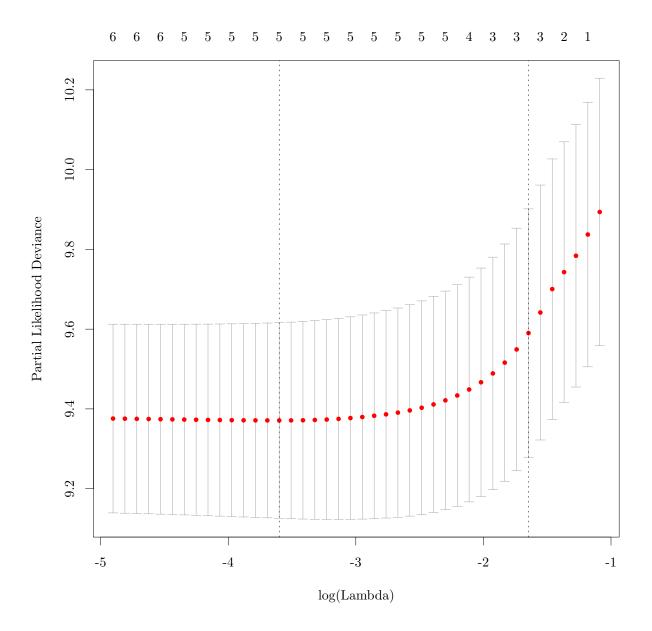
## V3 .

## V4 .

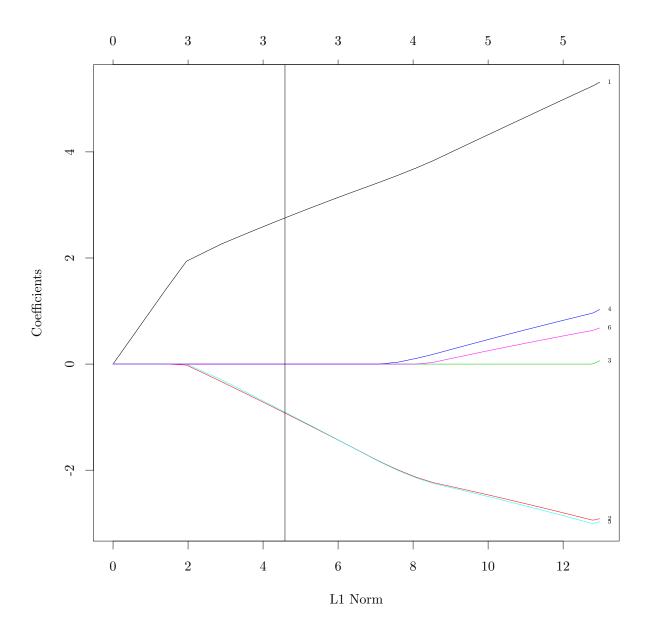
## V5 -2.3208

## V6 .

plot(glmnet.fit.cv.diag_rec)
```



```
plot(glmnet.fit.cv.diag_rec$glmnet.fit, label = TRUE)
abline(v = sum(abs(coef(glmnet.fit.cv.diag_rec$glmnet.fit, s = glmnet.fit.cv.diag_rec$lambda.1se))))
```



```
#abline(v = sum(abs(coef(glmnet.fit.cv.diag_recfglmnet.fit, s = glmnet.fit.cv.diag_recflambda.min))))
coef(glmnet.fit.cv.diag_rec$glmnet.fit, s = glmnet.fit.cv.diag_rec$lambda.1se)

## 6 x 1 sparse Matrix of class "dgCMatrix"

## 1

## V1 2.7555

## V2 -0.9230

## V3 .

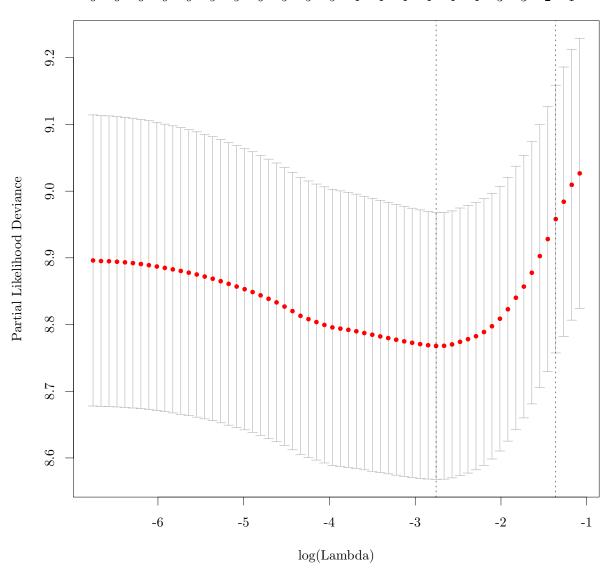
## V4 .

## V5 -0.9055

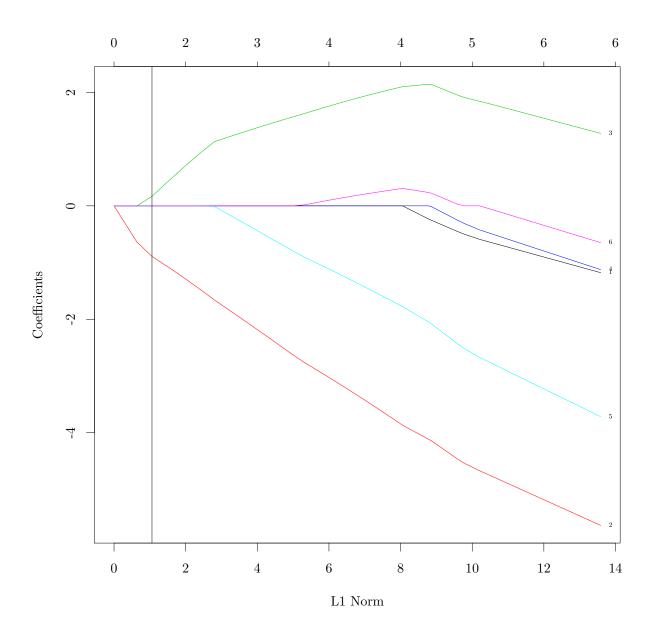
## V6 .

plot(glmnet.fit.cv.recr_dsd)
```





```
plot(glmnet.fit.cv.recr_dsd$glmnet.fit, label = TRUE)
abline(v = sum(abs(coef(glmnet.fit.cv.recr_dsd$glmnet.fit, s = glmnet.fit.cv.recr_dsd$lambda.1se))))
```



```
#abline(v = sum(abs(coef(glmnet.fit.cv.recr_dsdfglmnet.fit, s = glmnet.fit.cv.recr_dsdflambda.min))))
coef(glmnet.fit.cv.recr_dsd$glmnet.fit, s = glmnet.fit.cv.recr_dsd$lambda.1se)

## 6 x 1 sparse Matrix of class "dgCMatrix"

## 1

## V1 .

## V2 -0.8920

## V3 0.1676

## V4 .

## V5 .

## V6 .
```

4.3 Prediction on validation sets

load("../../data/15_validation.rda")

##

```
val.basis = basis(nmf.final)
rownames(GSE21501.lingex) = GSE21501.feat$Gene.symbol
rownames(GSE28735.lingex) = GSE28735.feat$Gene.symbol
GSE21501.lingex.for_basis = GSE21501.lingex[match(rownames(val.basis), rownames(GSE21501.lingex)),]
GSE28735.lingex.for_basis = GSE28735.lingex[match(rownames(val.basis), rownames(GSE28735.lingex)),]
GSE21501.lingex.for_basis[is.na(GSE21501.lingex.for_basis)] = 0
GSE28735.lingex.for_basis[is.na(GSE28735.lingex.for_basis)] = 0
GSE21501.coefs = apply(GSE21501.lingex.for_basis, 2, function(xcol) nnls(val.basis, xcol)$x)
GSE28735.coefs = apply(GSE28735.lingex.for_basis, 2, function(xcol) nnls(val.basis, xcol)$x)
GSE21501.axis1 = GSE21501.coefs[1,] - GSE21501.coefs[5,]
GSE21501.axis2 = GSE21501.coefs[6,] - GSE21501.coefs[2,]
GSE28735.axis1 = GSE28735.coefs[1,] - GSE28735.coefs[5,]
GSE28735.axis2 = GSE28735.coefs[6,] - GSE28735.coefs[2,]
GSE21501.score = 1.354*GSE21501.axis1 + 1.548*GSE21501.axis2
GSE28735.score = 1.354*GSE28735.axis1 + 1.548*GSE28735.axis2
GSE21501.pcna = apply(GSE21501.gex[match(metapcna.sig, GSE21501.feat$Gene.symbol),], 2, median, na.rm =
GSE28735.pcna = apply(GSE28735.gex[match(metapcna.sig, GSE28735.feat$Gene.symbol),], 2, median, na.rm =
temp = coxph(Surv(GSE21501.samp$time, GSE21501.samp$event) ~ GSE21501.score)
summary(temp)
## Call:
## coxph(formula = Surv(GSE21501.samp$time, GSE21501.samp$event) ~
      GSE21501.score)
##
##
   n= 102, number of events= 66
##
                 coef exp(coef) se(coef) z Pr(>|z|)
## GSE21501.score 1.81
                       6.13
                                   1.14 1.59
                                                0.11
##
##
                 exp(coef) exp(-coef) lower .95 upper .95
## GSE21501.score
                     6.13
                               0.163
                                         0.655
                                                 57.3
## Concordance= 0.577 (se = 0.042)
## Rsquare= 0.024 (max possible= 0.993 )
## Likelihood ratio test= 2.49 on 1 df, p=0.115
                                        p=0.112
## Wald test
                       = 2.52 on 1 df,
## Score (logrank) test = 2.54 on 1 df, p=0.111
temp = coxph(Surv(GSE28735.samp$time, GSE28735.samp$event) ~ GSE28735.score)
summary(temp)
## coxph(formula = Surv(GSE28735.samp$time, GSE28735.samp$event) ~
      GSE28735.score)
##
```

```
##
##
                  coef exp(coef) se(coef)
                                             z Pr(>|z|)
## GSE28735.score 1.867 6.471
                                    0.752 2.48 0.013
##
                 exp(coef) exp(-coef) lower .95 upper .95
##
## GSE28735.score
                     6.47
                                0.155
                                          1.48
##
## Concordance= 0.655 (se = 0.064)
## Rsquare= 0.132 (max possible= 0.981)
## Likelihood ratio test= 5.92 on 1 df,
                                         p=0.0149
             = 6.17 on 1 df,
                                        p=0.013
## Wald test
## Score (logrank) test = 6.46 on 1 df, p=0.011
anova(coxph(Surv(GSE21501.samp$time, GSE21501.samp$event) ~ GSE21501.axis1 + GSE21501.axis2))
## Analysis of Deviance Table
## Cox model: response is Surv(GSE21501.samp$time, GSE21501.samp$event)
## Terms added sequentially (first to last)
                 loglik Chisq Df Pr(>|Chi|)
##
## NULL
                   -255
## GSE21501.axis1
                   -254 1.44 1
                                       0.23
## GSE21501.axis2 -254 1.09 1
                                       0.30
anova(coxph(Surv(GSE28735.samp$time, GSE28735.samp$event) ~ GSE28735.axis1 + GSE28735.axis2))
## Analysis of Deviance Table
## Cox model: response is Surv(GSE28735.samp$time, GSE28735.samp$event)
## Terms added sequentially (first to last)
##
                 loglik Chisq Df Pr(>|Chi|)
## NULL
                  -83.1
## GSE28735.axis1 -81.4 3.43 1
                                      0.064
## GSE28735.axis2 -80.2 2.51 1
                                      0.113
load("../../data/validation/tcga-clin-gex.20141118.rda")
doValForSingleCancer = function(cancer_id)
        # nevents, ntotal, score_p, anova_pcna, anova_score, anova_axis1, anova_axis2
       message(cancer_id)
       cancer_data = data.merged[[cancer_id]]
       if (!"illuminahiseq_rnaseqv2" %in% names(cancer_data$gex)) { return(c(0, 0, NA, NA, NA, NA
       gex = cancer_data$gex$illuminahiseq_rnaseqv2
       clin = cancer_data$clin
       days_to_death = clin$days_to_death
       days_to_death[days_to_death == "[Not Applicable]"] = NA
       days_to_death = as.numeric(as.character(days_to_death))
       days_to_initial_pathologic_diagnosis = clin$days_to_initial_pathologic_diagnosis
```

n= 42, number of events= 29

##

```
days_to_initial_pathologic_diagnosis[days_to_initial_pathologic_diagnosis == "[Not Applicable]"]
days_to_initial_pathologic_diagnosis = as.numeric(as.character(days_to_initial_pathologic_diagnosis)
days_to_last_followup = clin$days_to_last_followup
days_to_last_followup[days_to_last_followup == "[Not Applicable]"] = NA
days_to_last_followup = as.numeric(as.character(days_to_last_followup))
time_event = days_to_death - days_to_initial_pathologic_diagnosis
time_lfu = days_to_last_followup - days_to_initial_pathologic_diagnosis
time_obs = time_event
time_obs[is.na(time_obs)] = time_lfu[is.na(time_obs)]
time_obs[!is.na(time_obs) & !is.na(time_lfu)] = pmin(time_obs[!is.na(time_obs) & !is.na(time_lfu)]
event = (time_event <= time_lfu & !is.na(time_event) & !is.na(time_lfu)) | (!is.na(time_event) &
y = Surv(time_obs, event)
gex = gex[!grepl("^\\?\\|", rownames(gex)),]
rownames(gex) = gsub("\\|.*", "", rownames(gex))
pcna = apply(log2(gex[rownames(gex) %in% metapcna.sig,] + 1), 2, median)
gex.axes = gex[match(rownames(val.basis), rownames(gex)),]
gex.axes[apply(is.na(gex.axes), 1, all),] = 0
gex.axes = gex.axes - apply(gex.axes, 1, min, na.rm = TRUE)
gex.axes = gex.axes / apply(gex.axes, 1, max, na.rm = TRUE)
gex.axes[is.na(gex.axes)] = 0
coefs = apply(gex.axes, 2, function(xcol) nnls(val.basis, xcol)$x)
axis1 = coefs[1,] - coefs[5,]
axis2 = coefs[6,] - coefs[2,]
score = 1.354*axis1 + 1.548*axis2
valid = !is.na(score) & !is.na(pcna) & !is.na(y[,1]) & !is.na(y[,2])
axis1 = axis1[valid]
axis2 = axis2[valid]
score = score[valid]
pcna = pcna[valid]
y = y[valid,]
nevents = sum(y[,2])
ntotal = nrow(y)
score_p = pchisq(2*diff(coxph(y ~ score)$loglik), 1, lower.tail = FALSE)
anova_pcna = anova(coxph(y ~ pcna + score))[,"Pr(>|Chi|)"][2]
anova_score = anova(coxph(y ~ pcna + score))[,"Pr(>|Chi|)"][3]
anova_axis1 = anova(coxph(y ~ axis1 + axis2))[,"Pr(>|Chi|)"][2]
anova_axis2 = anova(coxph(y ~ axis1 + axis2))[,"Pr(>|Chi|)"][3]
c(nevents, ntotal, score_p, anova_pcna, anova_score, anova_axis1, anova_axis2)
```

```
val_pvals = sapply(names(data.merged), doValForSingleCancer)
## acc
## blca
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## brca
## cesc
## coad
## dlbc
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, : Loglik converged
before variable 1,2; beta may be infinite.
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, : Loglik converged
before variable 1,2; beta may be infinite.
## qbm
## hnsc
## kich
## kirc
## kirp
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## lgg
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## lihc
## luad
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## meso
## oυ
## paad
## prad
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, : Ran out of
iterations and did not converge
## Warning in fitter(X, Y, strats, offset, init, control, weights = weights, : Ran out of
iterations and did not converge
## read
## sarc
## skcm
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
## thca
## ucec
## Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced
by coercion
```

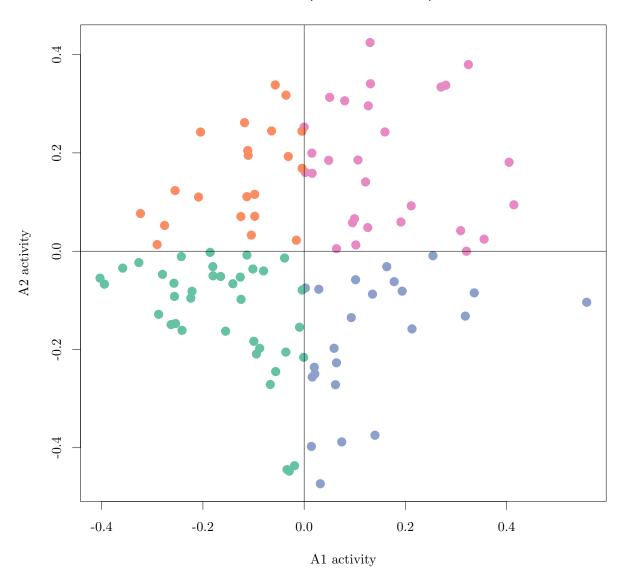
```
## ucs
rownames(val_pvals) = c("nevents", "ntotal", "p.score", "p.anova.pcna", "p.anova.pcna_score", "p.anova.s
val_pvals = as.data.frame(t(val_pvals))
val_pvals[val_pvals$nevents >= 50 | rownames(val_pvals) == "paad",]
       nevents ntotal p.score p.anova.pcna p.anova.pcna_score
           54
                143 2.287e-01
                                  8.185e-01
## gbm
                                                    0.1587102
## hnsc
           124
                 367 8.075e-03 4.719e-01
                                                    0.0107907
          153 497 2.034e-12 9.569e-11
                                                    0.0028892
## kirc
           53 272 1.493e-05 6.316e-04
## lgg
                                                    0.0078542
                431 8.336e-06
## luad
          106
                                  7.205e-03
                                                    0.0001042
          117 395 9.624e-01 7.035e-02
## lusc
                                                    0.4109578
          115 251 2.380e-02 5.903e-01
## ov
                                                    0.0178108
                 58 4.952e-03 8.549e-02
           17
                                                    0.0239990
## paad
##
       p.anova.axis1 p.anova.axis1_axis2
## gbm
          9.252e-01
                             6.877e-02
## hnsc
          4.367e-02
                             8.341e-02
## kirc
          2.673e-08
                              1.639e-05
          1.593e-04
                              3.350e-02
## lgg
## luad
          1.238e-03
                              1.543e-03
## lusc
          1.597e-01
                              2.559e-01
## ov
           3.655e-01
                              3.298e-02
         1.562e-02
## paad
                              1.249e-01
plot_km_axes = function(axis1, axis2, y, mc = FALSE, ...)
       t1 = t2 = 0
       if (mc == TRUE)
               t1 = median(axis1, na.rm = TRUE)
               t2 = median(axis2, na.rm = TRUE)
       class = paste(c("L", "H")[I(axis1 >= t1)+1], c("L", "H")[I(axis2 >= t2)+1], sep = "")
       class = ordered(class, levels = c("LL", "LH", "HL", "HH"))
       fit = survfit(y ~ class)
       print(fit)
       print(survdiff(y ~ class))
       pval = pchisq(survdiff(y ~ class)$chisq, 3, lower.tail = FALSE)
       pal = brewer.pal(4, "Set2")
       names(pal) = c("LL", "LH", "HL", "HH")
       plot(axis2 ~ axis1, xlab = "A1 activity", ylab = "A2 activity", col = pal[class], pch = 16, cex
       abline(h = t2)
       abline(v = t1)
       plot(fit, col = pal, lwd = 2, xlab = "Time from diagnosis (days)", ylab = "Fraction surviving",
plot_km_axes_tcga = function(code, mc)
```

Warning in FUN(c("acc", "blca", "brca", "cesc", "coad", "dlbc", "gbm", "hnsc", : NAs introduced

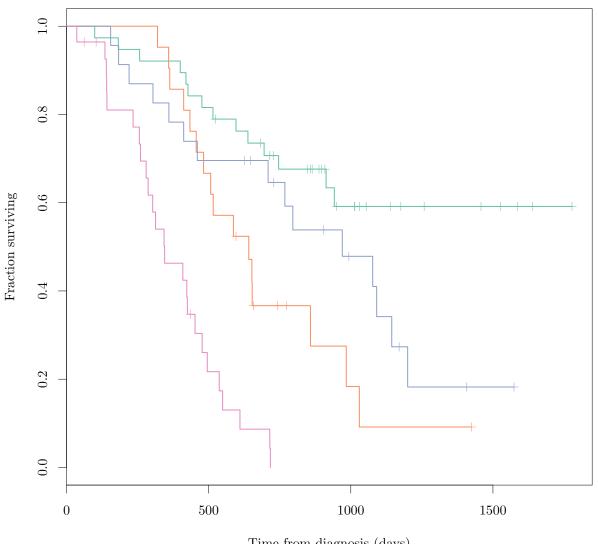
by coercion

```
if ("illuminahiseq_rnaseqv2" %in% names(data.merged[[code]]$gex))
                temp.gex = data.merged[[code]]$gex$illuminahiseq_rnaseqv2
                temp.gex = temp.gex[!grepl("^\\?\\|", rownames(temp.gex)),]
                rownames(temp.gex) = gsub("\\|.*", "", rownames(temp.gex))
                temp.gex.axes = temp.gex[match(rownames(val.basis), rownames(temp.gex)),]
                temp.gex.axes[apply(is.na(temp.gex.axes), 1, all),] = 0
                temp.gex.axes = temp.gex.axes - apply(temp.gex.axes, 1, min, na.rm = TRUE)
                temp.gex.axes = temp.gex.axes / apply(temp.gex.axes, 1, max, na.rm = TRUE)
                temp.gex.axes[is.na(temp.gex.axes)] = 0
                temp.coefs = apply(temp.gex.axes, 2, function(xcol) nnls(val.basis, xcol)$x)
                temp.axis1 = temp.coefs[1,] - temp.coefs[5,]
                temp.axis2 = temp.coefs[6,] - temp.coefs[2,]
                temp.clin = data.merged[[code]]$clin
                temp.days_to_death = temp.clin$days_to_death
                temp.days_to_death[temp.days_to_death == "[Not Applicable]"] = NA
                temp.days_to_death = as.numeric(as.character(temp.days_to_death))
                temp.days_to_initial_pathologic_diagnosis = temp.clin$days_to_initial_pathologic_diagnosis
                temp.days_to_initial_pathologic_diagnosis[temp.days_to_initial_pathologic_diagnosis == |
                temp.days_to_initial_pathologic_diagnosis = as.numeric(as.character(temp.days_to_initial
                temp.days_to_last_followup = temp.clin$days_to_last_followup
                temp.days_to_last_followup[temp.days_to_last_followup == "[Not Applicable]"] = NA
                temp.days_to_last_followup = as.numeric(as.character(temp.days_to_last_followup))
                temp.time_event = temp.days_to_death - temp.days_to_initial_pathologic_diagnosis
                temp.time_lfu = temp.days_to_last_followup - temp.days_to_initial_pathologic_diagnosis
                temp.time_obs = temp.time_event
                temp.time_obs[is.na(temp.time_obs)] = temp.time_lfu[is.na(temp.time_obs)]
                temp.time_obs[!is.na(temp.time_obs) & !is.na(temp.time_lfu)] = pmin(temp.time_obs[!is.na
                temp.event = (temp.time_event <= temp.time_lfu & !is.na(temp.time_event) & !is.na(temp.time_event)
                temp.y = Surv(temp.time_obs, temp.event)
                plot_km_axes(temp.axis1, temp.axis2, temp.y, mc = FALSE, main = code)
plot_km_axes(axis_coefs.diag_dsd[,1], axis_coefs.diag_dsd[,2], y.diag_dsd, mc = FALSE, main = "APGI (Res
## Call: survfit(formula = y ~ class)
##
           records n.max n.start events median 0.95LCL 0.95UCL
## class=LL
                 38
                       38
                               38
                                      14
                                             NA
                                                    913
                                                              NA
## class=LH
                 21
                       21
                               21
                                      16
                                            641
                                                     482
                                                              NA
## class=HL
                 23
                       23
                               23
                                      15
                                            970
                                                     709
                                                             NA
## class=HH
                 28
                                      25
                                            345
                                                     280
                                                             495
## Call:
## survdiff(formula = y ~ class)
##
             N Observed Expected (O-E)^2/E (O-E)^2/V
## class=LL 38
                     14
                           31.77
                                    9.942
                                              18.645
## class=LH 21
                     16
                           13.02
                                     0.683
                                               0.852
## class=HL 23
                     15
                           17.66
                                     0.401
                                               0.543
## class=HH 28
                     25
                           7.55
                                    40.376
                                              48.292
```

APGI (Resubstituted)

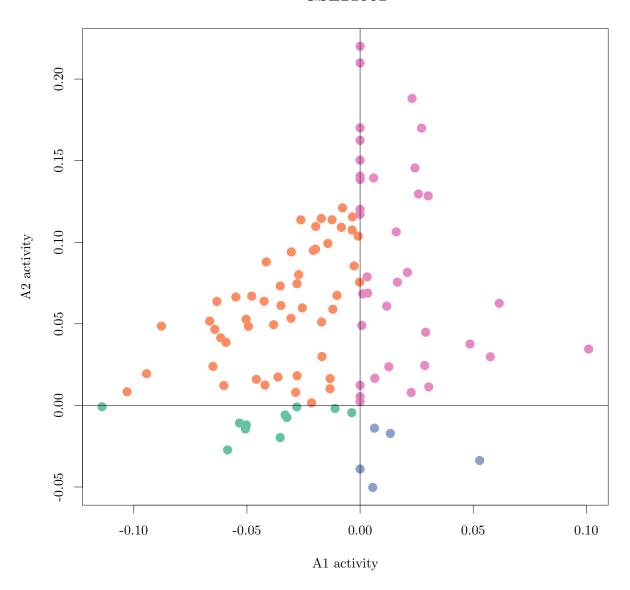


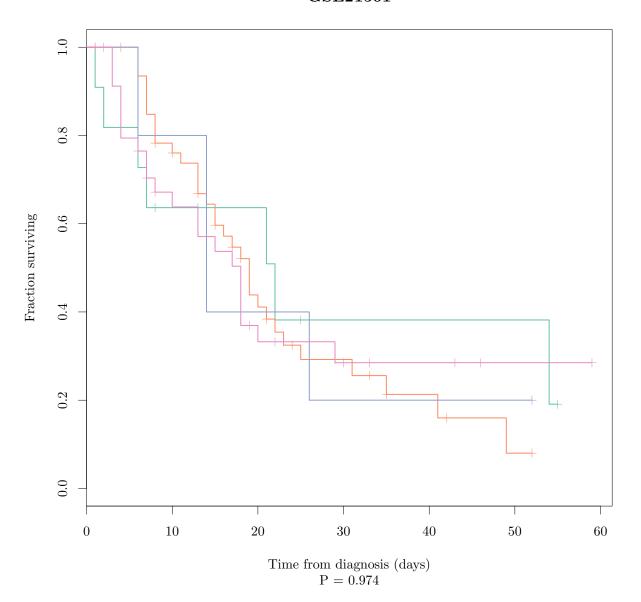
APGI (Resubstituted)



 $\begin{array}{c} {\rm Time\ from\ diagnosis\ (days)} \\ {\rm P} = 4.98 \text{e-} 12 \end{array}$

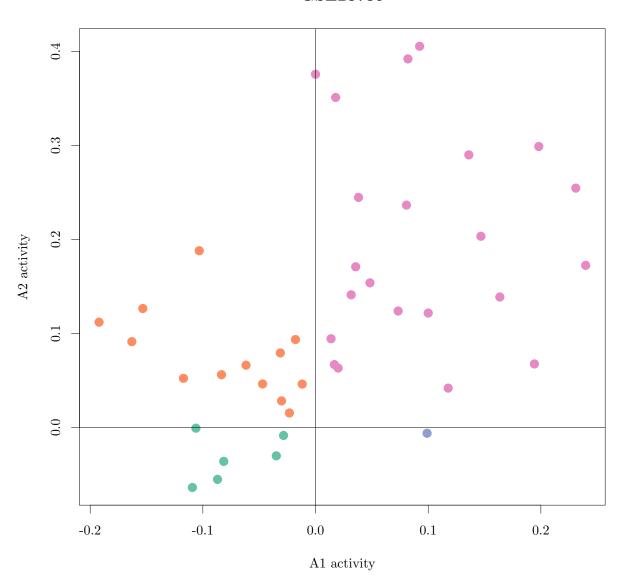
```
plot_km_axes(GSE21501.axis1, GSE21501.axis2, Surv(GSE21501.samp$time, GSE21501.samp$event), mc = FALSE,
## Call: survfit(formula = y ~ class)
##
##
            records n.max n.start events median 0.95LCL 0.95UCL
                                             22
                 11
                       11
                               11
                                      7
                                                      7
                                                             NA
## class=LL
## class=LH
                 50
                       50
                               50
                                      33
                                             19
                                                     15
                                                             25
                                       4
                  5
                        5
                               5
## class=HL
                                             14
                                                     14
                                                             NA
## class=HH
                 36
                       36
                               36
                                      22
                                             18
                                                     10
                                                             NA
## Call:
## survdiff(formula = y ~ class)
##
##
             N Observed Expected (0-E)^2/E (0-E)^2/V
## class=LL 11 7 8.12 1.56e-01 1.95e-01
```

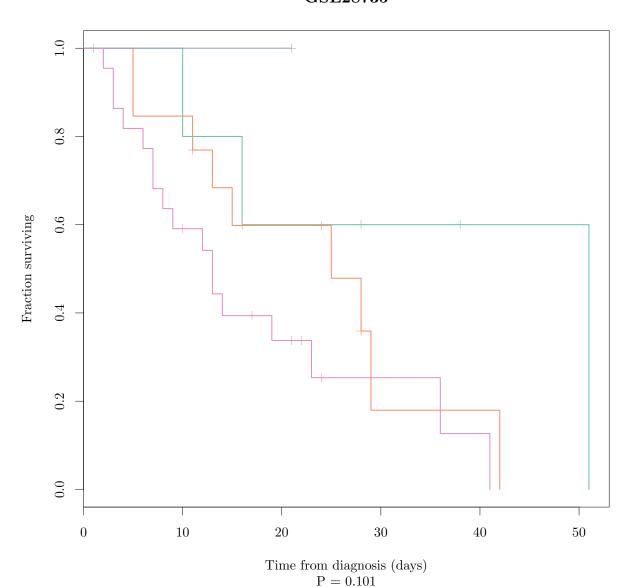




plot_km_axes(GSE28735.axis1, GSE28735.axis2, Surv(GSE28735.samp\$time, GSE28735.samp\$event), mc = FALSE, ## Call: survfit(formula = y ~ class) ## ## records n.max n.start events median 0.95LCL 0.95UCL ## class=LL 6 3 51 6 6 16 NA ## class=LH 13 13 13 9 25 13 NA 1 1 0 NANA ## class=HL 1 NA ## class=HH 22 22 22 17 13 NA 8 ## Call: ## survdiff(formula = y ~ class) ## ## N Observed Expected (0-E)^2/E (0-E)^2/V ## class=LL 6 3 6.651 2.004 3.168

```
## class=LH 13
                                               0.186
                          10.078
                                     0.115
## class=HL 1
                      0
                           0.735
                                     0.735
                                               0.779
## class=HH 22
                          11.536
                     17
                                     2.588
                                               4.733
##
   Chisq= 6.2 on 3 degrees of freedom, p= 0.101
```

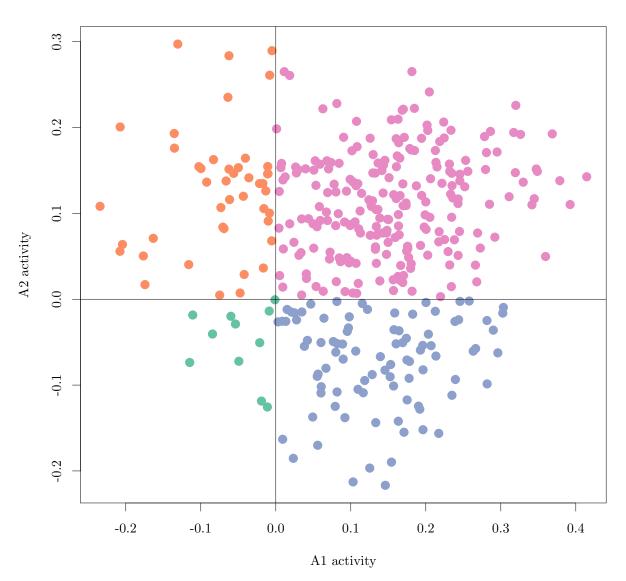




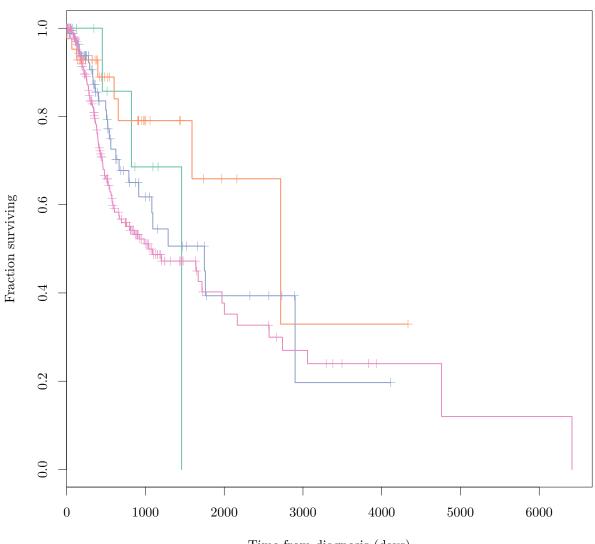
```
plot_km_axes_tcga("hnsc", mc = FALSE)
## Call: survfit(formula = y ~ class)
##
##
      1 observation deleted due to missingness
##
            records n.max n.start events median 0.95LCL 0.95UCL
                                11
                                        3
                                            1459
                                                      822
## class=LL
                 11
                       11
                                                               NA
## class=LH
                 43
                       43
                                43
                                        8
                                            2717
                                                     1591
                                                               NA
                 90
                                90
## class=HL
                       90
                                       26
                                            1748
                                                      914
                                                               NA
                223
                       223
                               223
                                       87
                                            1037
                                                      669
## class=HH
                                                             2002
## Call:
## survdiff(formula = y ~ class)
##
## n=367, 1 observation deleted due to missingness.
```

```
##
##
              N Observed Expected (O-E)^2/E (O-E)^2/V
                       3
                             3.77
                                       0.156
## class=LL
                                                 0.162
                       8
##
   class=LH
            43
                            15.60
                                       3.700
                                                 4.249
   class=HL 90
                      26
                            29.68
                                       0.457
                                                 0.606
                            74.95
##
   class=HH 223
                      87
                                       1.936
                                                 4.969
##
##
   Chisq= 6.3 on 3 degrees of freedom, p= 0.0969
```

\mathbf{hnsc}



hnsc

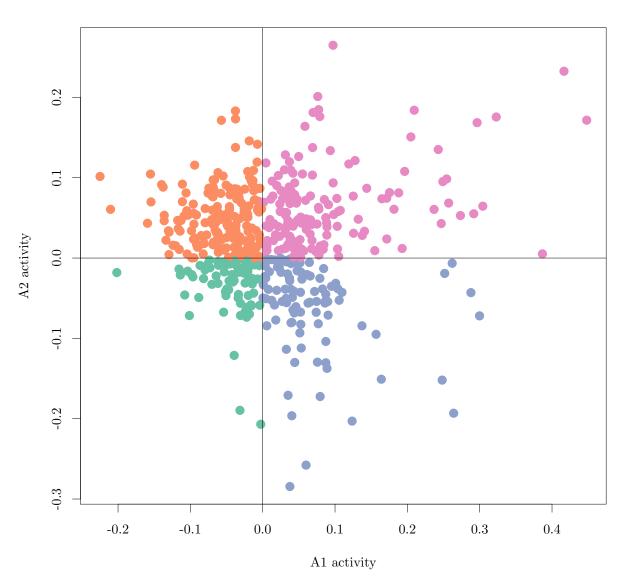


Time from diagnosis (days) P = 0.0969

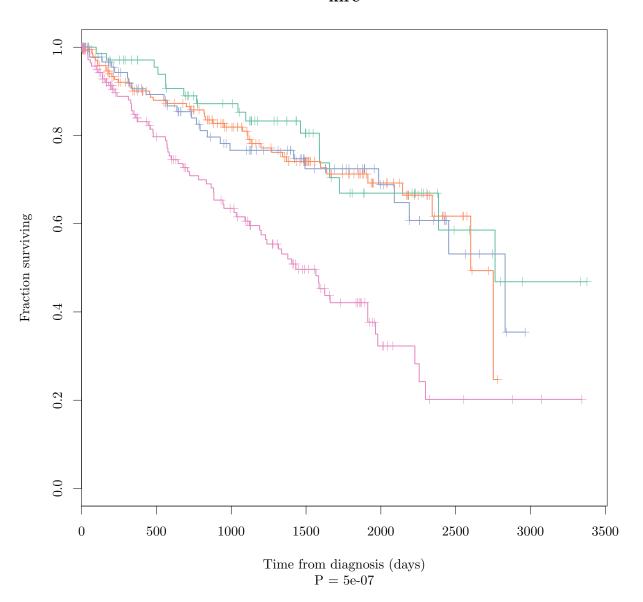
```
plot_km_axes_tcga("kirc", mc = FALSE)
## Call: survfit(formula = y ~ class)
##
##
           records n.max n.start events median 0.95LCL 0.95UCL
                                          2763
                                                  2385
                                                            NA
## class=LL
                77
                      77
                              77
                                     17
## class=LH
                179
                      179
                             179
                                     42
                                          2600
                                                  2343
                                                            NA
                      96
                              96
                                     25
## class=HL
                96
                                          2830
                                                  2190
                                                            NA
## class=HH
                146
                     146
                             146
                                     69
                                          1432
                                                  1200
                                                          1964
## Call:
## survdiff(formula = y ~ class)
##
##
             N Observed Expected (O-E)^2/E (O-E)^2/V
## class=LL 77 17 26.8 3.59 4.39
```

```
5.08
## class=LH 179
                      42
                             55.3
                                       3.21
## class=HL 96
                      25
                             32.0
                                       1.54
                                                 1.96
## class=HH 146
                      69
                             38.8
                                      23.44
                                                 31.71
##
   Chisq= 32.1 on 3 degrees of freedom, p= 5e-07
```

kirc



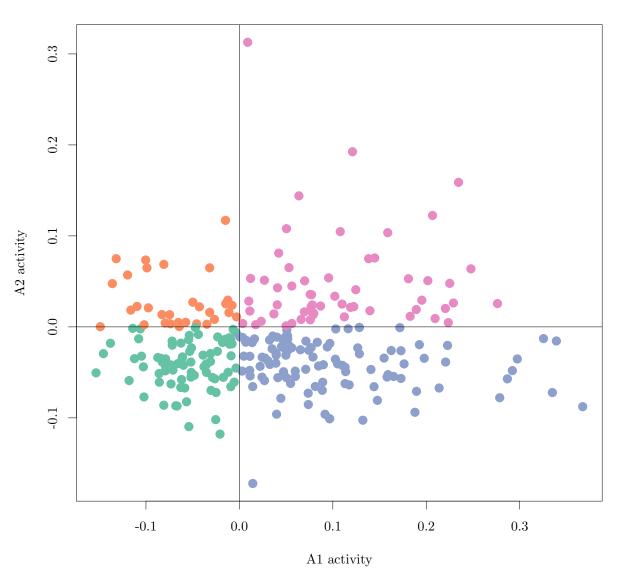
kirc



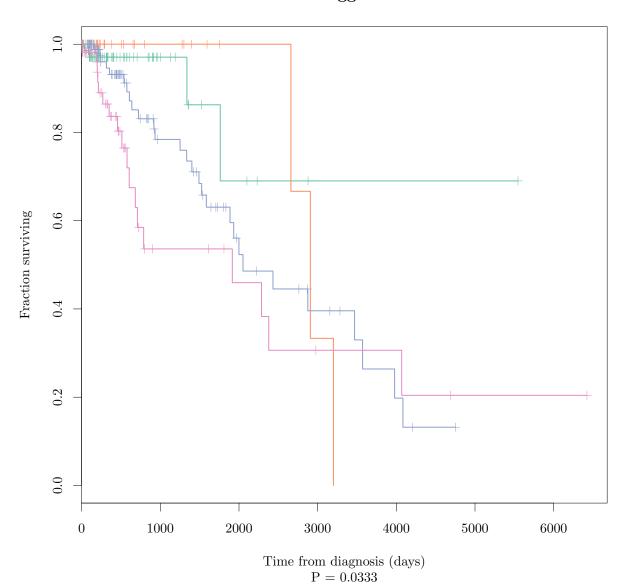
```
plot_km_axes_tcga("lgg", mc = FALSE)
## Warning in plot_km_axes_tcga("lgg", mc = FALSE): NAs introduced by coercion
## Call: survfit(formula = y ~ class)
##
            records n.max n.start events median 0.95LCL 0.95UCL
##
                 77
                        77
                                77
                                        4
                                               NA
                                                     1762
                                                               NA
## class=LL
## class=LH
                 32
                        32
                                32
                                        3
                                             2907
                                                     2660
                                                               NA
## class=HL
                106
                       106
                               106
                                       28
                                             2051
                                                     1886
                                                             3978
## class=HH
                 57
                        57
                                57
                                       18
                                             1915
                                                      682
                                                               NA
## Call:
## survdiff(formula = y ~ class)
##
```

```
N Observed Expected (O-E)^2/E (O-E)^2/V
                      4
                            9.86
                                      3.479
## class=LL 77
                                                4.389
                      3
## class=LH 32
                             5.38
                                      1.055
                                                1.191
## class=HL 106
                            26.36
                                      0.102
                                                0.207
                      28
## class=HH 57
                      18
                            11.40
                                      3.815
                                                4.950
##
## Chisq= 8.7 on 3 degrees of freedom, p= 0.0333
```

\lg



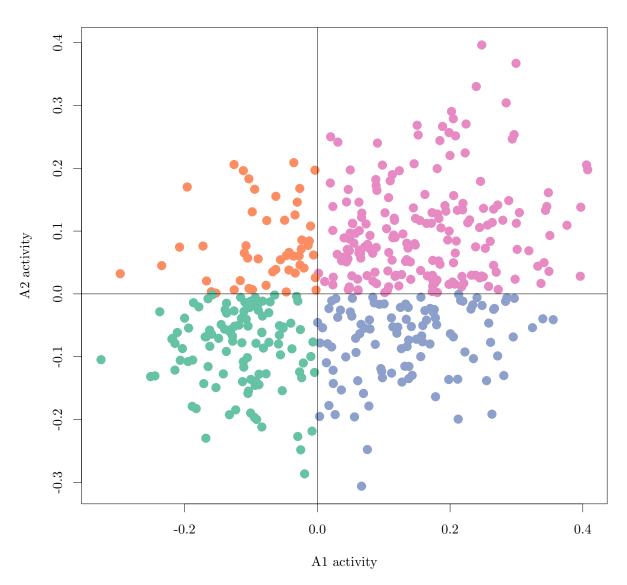
\lg



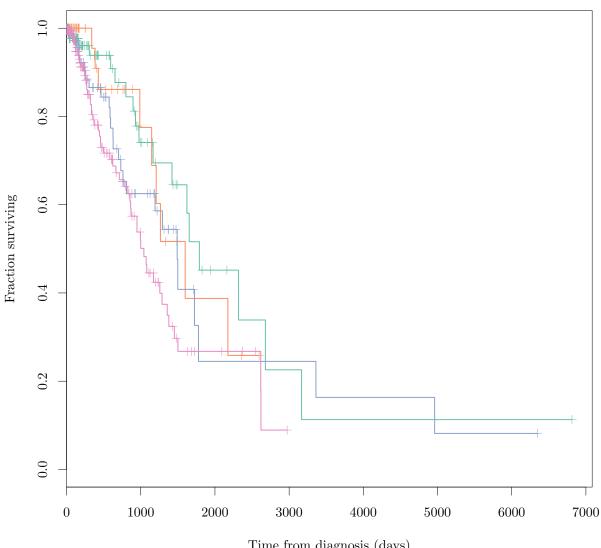
```
plot_km_axes_tcga("luad", mc = FALSE)
## Warning in plot_km_axes_tcga("luad", mc = FALSE): NAs introduced by coercion
## Call: survfit(formula = y ~ class)
##
##
      19 observations deleted due to missingness
##
            records n.max n.start events median 0.95LCL 0.95UCL
## class=LL
                102
                       102
                               102
                                       18
                                            1790
                                                     1421
## class=LH
                 49
                       49
                                49
                                        9
                                             1599
                                                     1147
                                                               NA
## class=HL
                 98
                        98
                                98
                                       26
                                             1491
                                                      807
                                                               NA
## class=HH
                182
                       182
                                       53
                                            1042
                                                      863
                               182
                                                             1379
## Call:
## survdiff(formula = y ~ class)
```

```
##
\mbox{\tt \#\#} n=431, 19 observations deleted due to missingness.
##
              N Observed Expected (O-E)^2/E (O-E)^2/V
                   18
                              28.0
                                      3.5523
## class=LL 102
                                                 4.875
## class=LH 49
                       9
                              11.9
                                      0.6911
                                                  0.786
## class=HL 98
                      26
                              27.5
                                      0.0801
                                                  0.112
## class=HH 182
                      53
                              38.7
                                      5.2967
                                                 8.567
##
   Chisq= 9.8 on 3 degrees of freedom, p= 0.0203
##
```

luad



luad

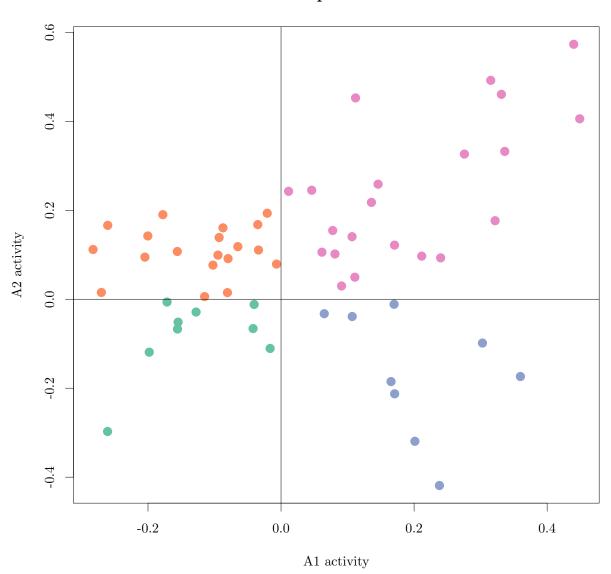


Time from diagnosis (days) P = 0.0203

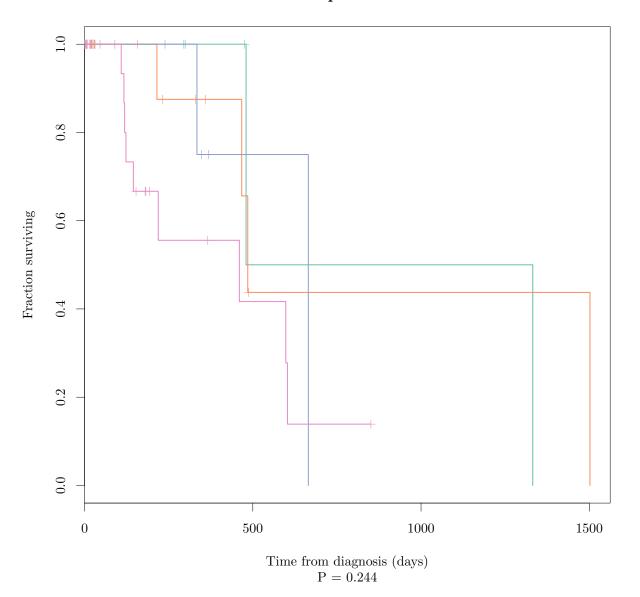
```
plot_km_axes_tcga("paad", mc = FALSE)
## Call: survfit(formula = y ~ class)
##
##
           records n.max n.start events median 0.95LCL 0.95UCL
## class=LL
                 9
                       9
                               9
                                      2
                                           906
                                                   480
                                                            NA
## class=LH
                19
                      19
                              19
                                           485
                                                   467
                                                            NA
                               9
                                      2
                 9
                       9
                                           665
## class=HL
                                                   334
                                                            NA
## class=HH
                21
                      21
                              21
                                           460
                                                   145
                                                           NA
## Call:
## survdiff(formula = y ~ class)
##
##
            N Observed Expected (O-E)^2/E (O-E)^2/V
## class=LL 9 2 3.13 0.408 0.536
```

```
## class=LH 19
                                                1.052
                            5.86
                                     0.592
## class=HL 9
                      2
                            2.71
                                     0.187
                                                0.233
## class=HH 21
                                     2.593
                      9
                            5.29
                                                4.105
##
   Chisq= 4.2 on 3 degrees of freedom, p= 0.244
```

paad



paad



```
sig.emt_groger_pos = c("ADAM12", "COL1A1", "COL3A1", "COL5A1", "COL6A1", "COL6A3", "CTGF",
sig.emt_groger_neg = c("CD24","CXCL16","DSG3","ELF3","EPCAM","EPHA1","JUP","MPZL2","OVOL2","PLXNB1","S10
x.medcent = x - apply(x, 1, median)
emt.scores.pos = apply(x.medcent[rownames(x.medcent) %in% sig.emt_groger_pos,], 2, median)
emt.scores.neg = apply(x.medcent[rownames(x.medcent) %in% sig.emt_groger_neg,], 2, median)
emt.scores = emt.scores.pos - emt.scores.neg
```

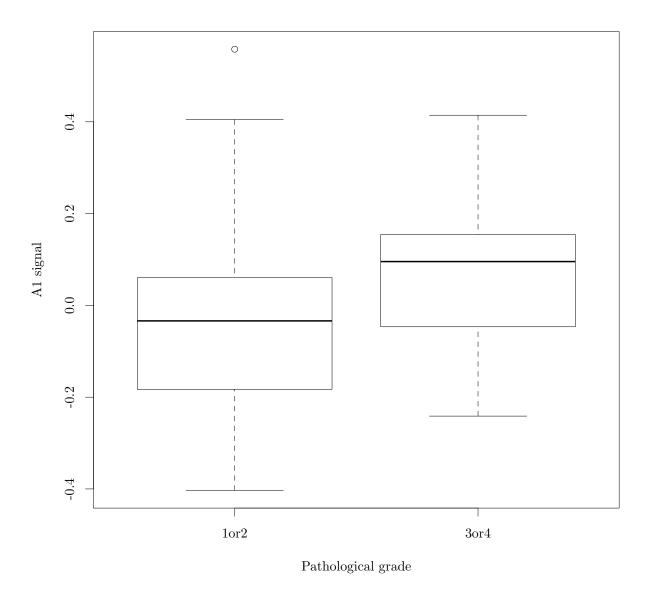
4.4 MSigDB score correlation thresholding

```
axis_coefs.msigdb.corr = cor(axis_coefs.diag_dsd, t(sigs), method = "kendall")
temp.sel_cols = apply(abs(axis_coefs.msigdb.corr) >= sig.corr.threshold, 2, any)
```

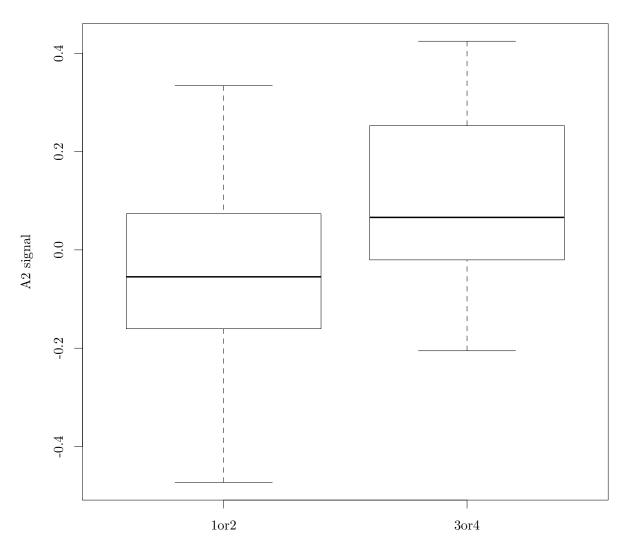
```
\#heatmap.2(axis\_coefs.msigdb.corr[, temp.sel\_cols], trace = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", useRaster = "none", useRaste
\#heatmap.2(axis\_coefs.msigdb.corr[, temp.sel\_cols], trace = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", scale = "none", useRaster = TRUE, colored = "none", useRaster = "none", useRaste
cpv.pvals = apply(axis_coefs.diag_dsd, 2, function(mg) sapply(cbind(cpvs.diag_dsd, purity = samps.diag_
                     s = !is.na(mg) & !is.na(x)
                     x = x[s]
                     mg = mg[s]
                     if (any(c("numeric", "integer") %in% class(x)))
                                           return(cor.test(x, mg, method = "pearson")$p.value)
                     else if (any(c("factor", "ordered", "logical") %in% class(x)) && length(unique(x)) > 1)
                                           return(anova(lm(mg ~ x))[,"Pr(>F)"][1])
                     NA
}))
cpv.pvals = cpv.pvals[!apply(is.na(cpv.pvals), 1, all),]
cpv.pvals = cpv.pvals[!grepl("^Surv\\.", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^Treat\\.", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^Path\\.Nodes", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^Staging\\.Version", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^History\\.Recurrence$", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^History\\.Status$", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^History\\.Death\\.Cause$", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^Path\\.Grade$", rownames(cpv.pvals)),]
cpv.pvals = cpv.pvals[!grepl("^Path\\.TumourLocation$", rownames(cpv.pvals)),]
temp = as.vector(cpv.pvals)
temp = p.adjust(temp, "holm")
cpv.qvals = matrix(temp, nrow = nrow(cpv.pvals))
rownames(cpv.qvals) = rownames(cpv.pvals)
colnames(cpv.qvals) = colnames(cpv.pvals)
cpv.pvals
##
                                                                                                                     axis1
                                                                                                                                               axis2
                                                                                                         0.1581541 0.0098535
## Patient.Gender
## Patient.Ethnicity
                                                                                                         0.7711156 0.1130046
## History.Smoking.PackYears
                                                                                                        0.3562152 0.2753851
## History.Diagnosis.AgeAtYears
                                                                                                        0.9250804 0.6658699
## Path.HistoType.Subtype
                                                                                                         0.6966533 0.1569139
## Path.TumourSizeMm
                                                                                                         0.8438715 0.1709600
## Path.Invasion.PN
                                                                                                         0.0951996 0.2251091
## Path.Invasion.VS
                                                                                                         0.6500594 0.0707968
                                                                                                         0.4414498 0.4245233
## Staging.pM
## Staging.pN
                                                                                                         0.2524195 0.2629997
## Staging.pT
                                                                                                         0.2640385 0.4273685
## Staging.Stage
                                                                                                        0.0605854 0.2355348
## History.Recurrence.Site.Peritoneum 0.9162045 0.0149891
## History.Recurrence.Site.PancRemnant 0.5341395 0.1839586
## History.Recurrence.Site.PancBed 0.8869735 0.5303110
## History.Recurrence.Site.Other
                                                                                                         0.1930828 0.1614602
## History.Recurrence.Site.Omentum 0.1388378 0.0820434
```

```
## History.Recurrence.Site.Mesentery 0.9326763 0.1206991
## History.Recurrence.Site.LymphNodes 0.9332622 0.8703023
## History.Recurrence.Site.Lung 0.3900712 0.7130517
## History.Recurrence.Site.Liver 0.1596616 0.1046158
## History.Recurrence.Site.Brain 0.4296978 0.0621650
## History.Recurrence.Site.Bone 0.7889803 0.4128670
## History.Recurrence.Site.Bone
## Path.Grade.Coarse
                                           0.0023854 0.0001297
                                        0.1767526 0.1392750
## Path.TumourLocation.Coarse
## purity
                                           0.0002129 0.0004113
cpv.qvals
##
                                             axis1
                                                       axis2
## Patient.Gender
                                           1.00000 0.472968
## Patient.Ethnicity
                                         1.00000 1.000000
## History.Smoking.PackYears
                                         1.00000 1.000000
## History.Diagnosis.AgeAtYears
                                         1.00000 1.000000
## Path.HistoType.Subtype
                                           1.00000 1.000000
## Path.TumourSizeMm
                                          1.00000 1.000000
## Path.Invasion.PN
                                         1.00000 1.000000
## Path.Invasion.VS
                                         1.00000 1.000000
## Staging.pM
                                         1.00000 1.000000
## Staging.pN
                                         1.00000 1.000000
## Staging.pT
                                          1.00000 1.000000
                                   1.00000 1.000000
## Staging.Stage
## History.Recurrence.Site.Peritoneum 1.00000 0.704486
## History.Recurrence.Site.PancRemnant 1.00000 1.000000
## History.Recurrence.Site.PancBed 1.00000 1.000000
## History.Recurrence.Site.Other 1.00000 1.000000 ## History.Recurrence.Site.Omentum 1.00000 1.000000
## History.Recurrence.Site.Mesentery 1.00000 1.000000
## History.Recurrence.Site.LymphNodes 1.00000 1.000000
## History.Recurrence.Site.Lung 1.00000 1.000000 ## History.Recurrence.Site.Liver 1.00000 1.000000
## History.Recurrence.Site.Brain
                                        1.00000 1.000000
1.00000 1.000000
0.11688 0.006743
## History.Recurrence.Site.Bone
## Path.Grade.Coarse
                                        1.00000 1.000000
## Path.TumourLocation.Coarse
                                          0.01086 0.020564
## purity
```

boxplot(axis_coefs.diag_dsd[,1] ~ cpvs.diag_dsd\$Path.Grade.Coarse, xlab = "Pathological grade", ylab = '



boxplot(axis_coefs.diag_dsd[,2] ~ cpvs.diag_dsd\$Path.Grade.Coarse, xlab = "Pathological grade", ylab = "



Pathological grade

```
lm(axis_coefs.diag_dsd[,2] ~ cpvs.diag_dsd$Path.Grade.Coarse)

##

## Call:
## lm(formula = axis_coefs.diag_dsd[, 2] ~ cpvs.diag_dsd$Path.Grade.Coarse)

##

## Coefficients:
## (Intercept) cpvs.diag_dsd$Path.Grade.Coarse.L

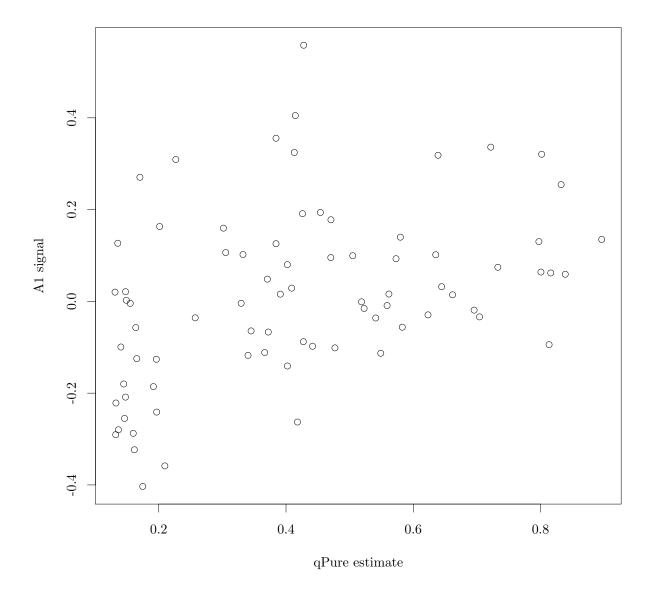
## 0.0261 0.1103

summary(lm(axis_coefs.diag_dsd[,2] ~ cpvs.diag_dsd$Path.Grade.Coarse))

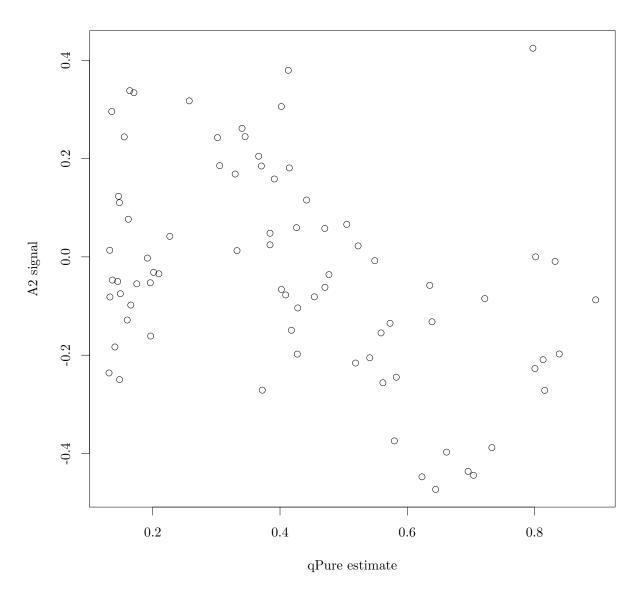
##

## Call:
```

```
## lm(formula = axis_coefs.diag_dsd[, 2] ~ cpvs.diag_dsd$Path.Grade.Coarse)
##
## Residuals:
             1Q Median 3Q
##
     Min
## -0.4212 -0.1130 -0.0137 0.1372 0.3860
##
## Coefficients:
##
                                   Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                                     0.0261 0.0197 1.33 0.18771
                                                       3.97 0.00013
                                                0.0278
## cpvs.diag_dsd$Path.Grade.Coarse.L
                                     0.1103
## Residual standard error: 0.185 on 108 degrees of freedom
## Multiple R-squared: 0.127, Adjusted R-squared: 0.119
## F-statistic: 15.8 on 1 and 108 DF, p-value: 0.00013
anova(lm(axis_coefs.diag_dsd[,2] ~ cpvs.diag_dsd$Path.Grade.Coarse))
## Analysis of Variance Table
## Response: axis_coefs.diag_dsd[, 2]
                                  Df Sum Sq Mean Sq F value Pr(>F)
## cpvs.diag_dsd$Path.Grade.Coarse 1 0.54 0.542 15.8 0.00013
## Residuals
                                 108
                                      3.71 0.034
plot(axis_coefs.diag_dsd[,1] ~ samps$purity_qpure, xlab = "qPure estimate", ylab = "A1 signal")
```



plot(axis_coefs.diag_dsd[,2] ~ samps\$purity_qpure, xlab = "qPure estimate", ylab = "A2 signal")



```
cor.test(axis_coefs.diag_dsd[,1], samps$purity_qpure, method = "kendall")

##

## Kendall's rank correlation tau

##

## data: axis_coefs.diag_dsd[, 1] and samps$purity_qpure

## z = 3.676, p-value = 0.0002369

## alternative hypothesis: true tau is not equal to 0

## sample estimates:

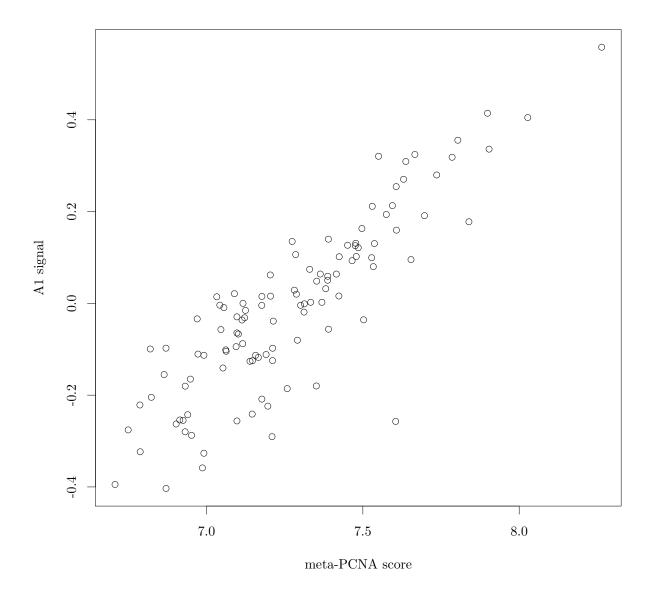
## tau

## 0.2838

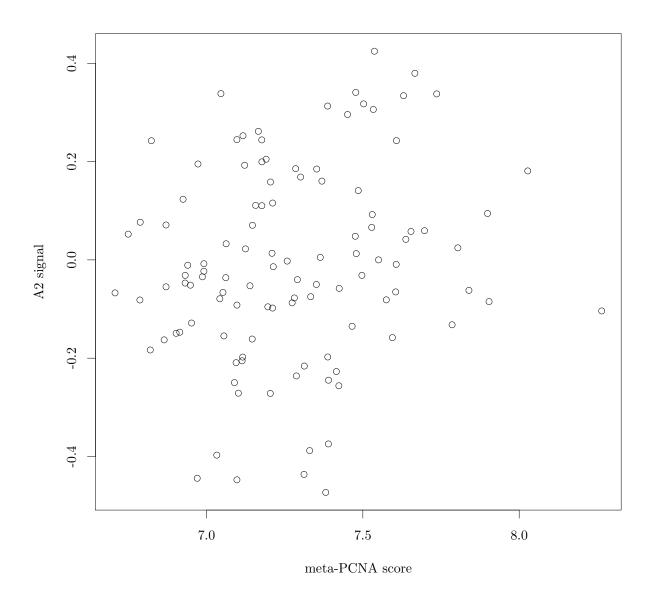
cor.test(axis_coefs.diag_dsd[,2], samps$purity_qpure, method = "kendall")

##
```

```
## Kendall's rank correlation tau
##
## data: axis_coefs.diag_dsd[, 2] and samps$purity_qpure
## z = -3.598, p-value = 0.0003203
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
##
      tau
## -0.2778
summary(lm(axis_coefs.diag_dsd[,1] ~ samps$purity_qpure))
## Call:
## lm(formula = axis_coefs.diag_dsd[, 1] ~ samps$purity_qpure)
## Residuals:
##
      Min
              1Q Median
                               3Q
## -0.3318 -0.1172 -0.0469 0.1011 0.5422
##
## Coefficients:
                     Estimate Std. Error t value Pr(>|t|)
##
                       -0.132 0.042 -3.14 0.00240
## (Intercept)
                      0.346
                                   0.089 3.89 0.00021
## samps$purity_qpure
##
## Residual standard error: 0.173 on 76 degrees of freedom
## (32 observations deleted due to missingness)
## Multiple R-squared: 0.166, Adjusted R-squared: 0.155
## F-statistic: 15.1 on 1 and 76 DF, p-value: 0.000213
summary(lm(axis_coefs.diag_dsd[,2] ~ samps$purity_qpure))
##
## Call:
## lm(formula = axis_coefs.diag_dsd[, 2] ~ samps$purity_qpure)
##
## Residuals:
     Min
               1Q Median
                               30
## -0.3541 -0.1356 -0.0213 0.1531 0.6002
##
## Coefficients:
##
                     Estimate Std. Error t value Pr(>|t|)
                       0.1195
                                 0.0473 2.53 0.01363
## (Intercept)
                                  0.1001 -3.70 0.00041
## samps$purity_qpure -0.3701
##
## Residual standard error: 0.195 on 76 degrees of freedom
## (32 observations deleted due to missingness)
## Multiple R-squared: 0.152, Adjusted R-squared:
## F-statistic: 13.7 on 1 and 76 DF, p-value: 0.000411
plot(axis_coefs.diag_dsd[,1] ~ metapcna.scores, xlab = "meta-PCNA score", ylab = "A1 signal")
```



plot(axis_coefs.diag_dsd[,2] ~ metapcna.scores, xlab = "meta-PCNA score", ylab = "A2 signal")



```
cor.test(axis_coefs.diag_dsd[,1], metapcna.scores, method = "kendall")

##

## Kendall's rank correlation tau

##

## data: axis_coefs.diag_dsd[, 1] and metapcna.scores

## z = 10.27, p-value < 2.2e-16

## alternative hypothesis: true tau is not equal to 0

## sample estimates:

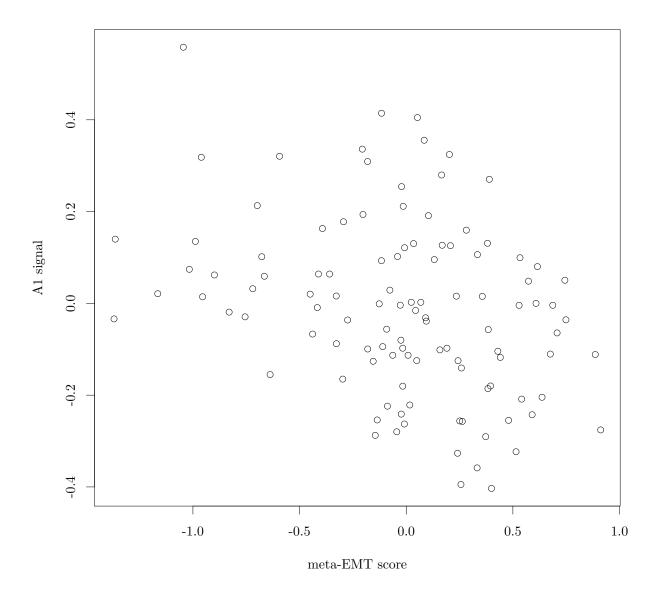
## tau

## 0.6634

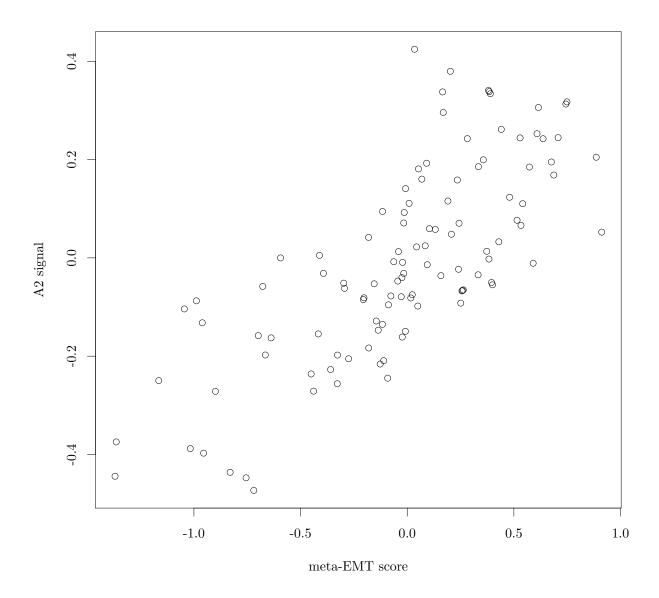
cor.test(axis_coefs.diag_dsd[,2], metapcna.scores, method = "kendall")

##</pre>
```

```
## Kendall's rank correlation tau
##
## data: axis_coefs.diag_dsd[, 2] and metapcna.scores
## z = 1.899, p-value = 0.05762
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
## tau
## 0.1226
summary(lm(axis_coefs.diag_dsd[,1] ~ metapcna.scores))
## Call:
## lm(formula = axis_coefs.diag_dsd[, 1] ~ metapcna.scores)
## Residuals:
##
      Min
             1Q Median
                            3Q
## -0.4295 -0.0477 0.0151 0.0622 0.1785
## Coefficients:
                  Estimate Std. Error t value Pr(>|t|)
## (Intercept)
                  -4.0135 0.2274 -17.6 <2e-16
## metapcna.scores 0.5504
                              0.0312 17.6 <2e-16
## Residual standard error: 0.0971 on 108 degrees of freedom
## Multiple R-squared: 0.742, Adjusted R-squared: 0.74
## F-statistic: 311 on 1 and 108 DF, p-value: <2e-16
summary(lm(axis_coefs.diag_dsd[,2] ~ metapcna.scores))
##
## lm(formula = axis_coefs.diag_dsd[, 2] ~ metapcna.scores)
##
## Residuals:
## Min 1Q Median 3Q
## -0.478 -0.117 0.000 0.132 0.402
## Coefficients:
##
                 Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.8487 0.4577 -1.85 0.066
## metapcna.scores 0.1156
                             0.0629 1.84
                                               0.069
##
## Residual standard error: 0.195 on 108 degrees of freedom
## Multiple R-squared: 0.0303, Adjusted R-squared: 0.0214
## F-statistic: 3.38 on 1 and 108 DF, p-value: 0.0688
plot(axis_coefs.diag_dsd[,1] ~ emt.scores, xlab = "meta-EMT score", ylab = "A1 signal")
```



plot(axis_coefs.diag_dsd[,2] ~ emt.scores, xlab = "meta-EMT score", ylab = "A2 signal")



```
cor.test(axis_coefs.diag_dsd[,1], emt.scores, method = "kendall")

##

## Kendall's rank correlation tau

##

## data: axis_coefs.diag_dsd[, 1] and emt.scores

## z = -3.371, p-value = 0.0007492

## alternative hypothesis: true tau is not equal to 0

## sample estimates:

## tau

## -0.2177

cor.test(axis_coefs.diag_dsd[,2], emt.scores, method = "kendall")

##
```

```
## Kendall's rank correlation tau
##
## data: axis_coefs.diag_dsd[, 2] and emt.scores
## z = 8.795, p-value < 2.2e-16
## alternative hypothesis: true tau is not equal to 0
## sample estimates:
## tau
## 0.568
summary(lm(axis_coefs.diag_dsd[,1] ~ emt.scores))
##
## Call:
## lm(formula = axis_coefs.diag_dsd[, 1] ~ emt.scores)
## Residuals:
              1Q Median 3Q
     Min
## -0.3487 -0.1156 -0.0137 0.1312 0.4365
##
## Coefficients:
##
              Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.0129 0.0172 -0.75 0.45511
                         0.0351 -3.68 0.00037
## emt.scores -0.1289
## Residual standard error: 0.18 on 108 degrees of freedom
## Multiple R-squared: 0.111, Adjusted R-squared: 0.103
## F-statistic: 13.5 on 1 and 108 DF, p-value: 0.000372
summary(lm(axis_coefs.diag_dsd[,2] ~ emt.scores))
##
## Call:
## lm(formula = axis_coefs.diag_dsd[, 2] ~ emt.scores)
## Residuals:
## Min
              1Q Median
                             30
## -0.2545 -0.0977 -0.0088 0.0914 0.4166
##
## Coefficients:
##
             Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.00235 0.01255 -0.19
## emt.scores 0.30063
                         0.02560 11.74
                                           <2e-16
## Residual standard error: 0.132 on 108 degrees of freedom
## Multiple R-squared: 0.561, Adjusted R-squared: 0.557
## F-statistic: 138 on 1 and 108 DF, p-value: <2e-16
anova(lm(axis_coefs.diag_dsd[,1] ~ samps$purity_qpure + emt.scores))
## Analysis of Variance Table
##
## Response: axis_coefs.diag_dsd[, 1]
                   Df Sum Sq Mean Sq F value Pr(>F)
## samps$purity_qpure 1 0.453 0.453 15.20 0.00021
## emt.scores 1 0.039 0.039
## Residuals 75 2.236 0.030
                                       1.32 0.25381
```

```
temp.sig_id = colnames(axis_coefs.msigdb.corr)
temp.sig_class = gsub("\\..*", "", temp.sig_id)
temp.nsigs = length(temp.sig_id)
temp.nmeta = nrow(axis_coefs.msigdb.corr)
tables = lapply(1:temp.nmeta, function(metagene_i) {
        tapply(1:temp.nsigs, temp.sig_class, function(sig_class_is) {
                all_cors = axis_coefs.msigdb.corr[, sig_class_is]
                this_cors = all_cors[metagene_i, ]
                this_ids = temp.sig_id[sig_class_is]
                all_sig_cors = abs(all_cors) >= sig.corr.threshold
                this_sig_cors = all_sig_cors[metagene_i, ]
                sigs_to_report = which(this_sig_cors)
                if (length(sigs_to_report) == 0)
                        table = data.frame(GeneSet = c(), Correlation = c(), Metagenes = c())
                else
                        table = data.frame(
                                GeneSet = this_ids[sigs_to_report],
                                Correlation = this_cors[sigs_to_report],
                                Metagenes = apply(all_cors[,sigs_to_report,drop=FALSE], 2, function(cors
                                         sel = abs(cors) >= sig.corr.threshold
                                         # A positive number implies that positive GSVA signal is associ
                                         paste(which(sel) * sign(cors[which(sel)]), collapse = ",")
                                }))
                        table = table[order(-(table$Correlation)),]
                        rownames(table) <- NULL</pre>
                table
        }, simplify = FALSE)
})
tables
## [[1]]
## [[1]]$c1
## data frame with 0 columns and 0 rows
## [[1]]$c2
##
```

```
## 1
## 2
## 3
## 4
## 5
## 6
## 7
## 8
## 9
## 10
                                                         c2.AMUNDSON_GAMMA_RADIATION_RESPONSE/c4.GNF2_CDC2
## 11
## 12
## 13
## 14
## 15
## 16
## 17
## 18
## 19
                                                          c2.EGUCHI_CELL_CYCLE_RB1_TARGETS/c2.ROSTY_CERVIO
## 20
## 21
## 22
## 23
## 24
## 25
## 26
## 27
## 28
## 29
## 30
## 31
## 32
## 33
## 34
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## 41
## 42
## 43
## 44
## 45
## 46
## 47
## 48
## 49
## 50
## 51
## 52
## 53
## 54
```

```
## 55
## 56
                                                                       c2.REACTOME_ACTIVATION_OF_THE_PRE_I
## 57
## 58
## 59
## 60
## 61
## 62
## 63
## 64
## 65
## 66
## 67
## 68
## 69 c2.REACTOME_CELL_CYCLE_CHECKPOINTS/c2.REACTOME_G1_S_TRANSITION/c2.REACTOME_SYNTHESIS_OF_DNA/c2.RI
## 70
## 71
## 72
## 73
## 74
## 75
## 76
## 77
## 78
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## 81
## 82
## 83
## 84
## 85
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## 90
## 91
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## 94
## 95
## 96
## 97
## 98
## 99
## 100
## 101
## 102
## 103
## 104
## 105
## 106
## 107
## 108
```

```
## 109
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## 158
## 159
## 160
## 161
## 162
```

```
## 163
## 164
## 165
## 166
## 167
## 168
## 169
## 170
## 171
## 172
## 173
## 174
## 175
##
       Correlation Metagenes
## 1
             0.7141
                             1
## 2
             0.6991
## 3
             0.6981
                             1
## 4
             0.6981
                             1
## 5
             0.6964
                             1
## 6
                             1
             0.6911
## 7
             0.6894
                             1
## 8
                             1
             0.6767
## 9
             0.6767
                             1
## 10
             0.6737
                             1
## 11
             0.6711
                             1
## 12
             0.6694
                             1
## 13
             0.6617
                             1
## 14
             0.6601
                             1
## 15
             0.6584
                             1
## 16
             0.6474
## 17
             0.6470
                             1
                             1
## 18
             0.6464
             0.6460
## 19
                             1
## 20
             0.6444
                             1
## 21
             0.6440
                             1
## 22
             0.6434
                             1
## 23
             0.6404
                             1
## 24
             0.6400
                             1
## 25
             0.6344
                             1
## 26
             0.6317
                             1
## 27
             0.6294
                             1
## 28
             0.6290
                             1
## 29
             0.6287
## 30
             0.6264
                             1
## 31
             0.6257
                             1
## 32
             0.6254
                             1
## 33
             0.6230
## 34
             0.6224
                             1
## 35
             0.6180
                             1
## 36
             0.6153
                             1
## 37
             0.6143
                             1
## 38
             0.6140
                             1
## 39
             0.6123
                             1
## 40
             0.6117
```

## 41	##	11	0 6072	1
## 43				
## 44				
## 45				
## 46				
## 47				
## 48				1
## 49	##	47	0.5993	1
## 49	##	48	0.5990	1
## 50	##	49		1
## 51				
## 52				
## 53				
## 54				
## 55				
## 56				
## 57				
## 58				
## 59				1
## 60	##	58	0.5807	1
## 60	##	59	0.5807	1
## 61				1
## 62				
## 63				
## 64				
## 65				
## 66				
## 67				
## 68				
## 69				1
## 70	##	68	0.5680	1
## 70	##	69	0.5660	1
## 71	##	70		1
## 72				
## 73				
## 74				
## 75				
## 76				
## 77				
## 78				
## 79	##	77	0.5536	1
## 80	##	78	0.5513	1
## 81	##	79	0.5500	1
## 81	##	80		
## 82				
## 83				
## 84				
## 85				
## 86				
## 87 0.5336 1 ## 88 0.5319 1 ## 89 0.5313 1 ## 90 0.5309 1 ## 91 0.5306 1 ## 92 0.5296 1 ## 93 0.5279 1				
## 88 0.5319 1 ## 89 0.5313 1 ## 90 0.5309 1 ## 91 0.5306 1 ## 92 0.5296 1 ## 93 0.5279 1				
## 89				1
## 90 0.5309 1 ## 91 0.5306 1 ## 92 0.5296 1 ## 93 0.5279 1	##	88	0.5319	1
## 90 0.5309 1 ## 91 0.5306 1 ## 92 0.5296 1 ## 93 0.5279 1	##	89	0.5313	1
## 91 0.5306 1 ## 92 0.5296 1 ## 93 0.5279 1				1
## 92 0.5296 1 ## 93 0.5279 1				
## 93 0.5279 1				
## 94 0.5276 1				
	##	94	0.5276	1

##	95	0.5273	1
##		0.5273	1
##		0.5246	1
	98	0.5243	1
	99	0.5239	1
##	100	0.5233	1
##	101	0.5226	1
##	102	0.5223	1
##	103	0.5199	1
	104	0.5199	1
	105	0.5196	1
	106	0.5179	1
	107	0.5179	1
	108	0.5173	1
	109	0.5173	1
##	110	0.5159	1
##	111	0.5146	1
##	112	0.5129	1
##	113	0.5103	1
	114	0.5103	1
	115	0.5099	1
	116	0.5086	1
	117		
		0.5073	1
	118	0.5063	1
	119	0.5059	1
	120	0.5056	1
##	121	0.5056	1
##	122	0.5043	1
##	123	0.5029	1
##	124	0.5019	1
	125	0.5019	1
	126	0.5016	1
	127	0.5013	1
	128	0.5009	1
	129	0.5003	1
	130	0.5003	1
##	131	-0.5009	-1
##	132	-0.5033	-1
##	133	-0.5043	-1
##	134	-0.5056	-1
	135	-0.5083	-1
	136	-0.5089	-1
	137	-0.5096	-1
	138	-0.5243	-1
	139	-0.5289	-1
	140	-0.5316	-1
	141	-0.5319	-1
	142	-0.5393	-1
##	143	-0.5399	-1
	144	-0.5416	-1
	145	-0.5433	-1
	146	-0.5516	-1
	147	-0.5520	-1
##	148	-0.5570	-1

```
## 149 -0.5580
                          -1
          -0.5583
## 150
                          -1
## 151
           -0.5640
                          -1
## 152
           -0.5646
                          -1
## 153
          -0.5730
                          -1
## 154
           -0.5733
                          -1
## 155
           -0.5750
                          -1
## 156
           -0.5893
                          -1
## 157
           -0.5900
                          -1
## 158
           -0.5913
                          -1
## 159
           -0.5940
                          -1
## 160
          -0.6047
                          -1
## 161
          -0.6063
                          -1
## 162
           -0.6147
                          -1
## 163
           -0.6153
                          -1
## 164
          -0.6217
                          -1
## 165
           -0.6247
                          -1
                          -1
## 166
           -0.6260
## 167
           -0.6310
                          -1
## 168
          -0.6347
                          -1
## 169
          -0.6357
                          -1
                          -1
## 170
           -0.6370
## 171
           -0.6387
                          -1
## 172
          -0.6454
                          -1
## 173
          -0.6791
                          -1
## 174
           -0.6894
                          -1
          -0.6951
                          -1
## 175
## [[1]]$c3
##
                   GeneSet Correlation Metagenes
              c3.V$ELK1_02 0.5740
## 1
                                          1
## 2 c3.SCGGAAGY_V$ELK1_02
                               0.5580
## 3 c3.CTGCAGY_UNKNOWN
                               -0.5046
                                              -1
## 4
             c3.V$OCT1 01
                               -0.5089
                                              -1
## 5
             c3.V$GATA_Q6
                            -0.5153
                                              -1
## 6
              c3.V$OCT1_04
                             -0.5313
                                              -1
## 7
                               -0.5436
               c3.V$OCT_C
                                              -1
##
## [[1]]$c4
                                                                               GeneSet
## 1 c4.GNF2_RFC3/c4.GNF2_RFC4/c4.GNF2_SMC2L1/c4.GNF2_CKS1B/c4.GNF2_CKS2/c4.GNF2_TTK
## 2
                                                                          c4.MODULE_17
## 3
                                                                         c4.MODULE_315
## 4
                                                                         c4.MORF_BUB1B
## 5
                                                                         c4.MODULE_244
## 6
                                                                         c4.MODULE_337
## 7
                                                                         c4.MORF_FEN1
## 8
                                                                         c4.MODULE_126
## 9
                                                                         c4.MODULE_124
## 10
                                                                         c4.MORF_ESPL1
## 11
                                                                         c4.MORF BUB1
## 12
                                                                         c4.MODULE_403
## 13
                                                           c4.MORF_BUB3/c4.MORF_RAD23A
                                                            c4.MORF_RFC4/c4.MORF_RRM1
## 14
```

```
## 15
                                               c4.MODULE_98/c4.MODULE_198/c4.MODULE_252
## 16
                                                             c4.MODULE_125/c4.MODULE_158
## 17
                                                                             c4.MORF_UNG
                                                                           c4.MODULE_278
## 18
## 19
                                                                           c4.MORF GSPT1
## 20
                                                                           c4.MODULE_320
## 21
                                                                             c4.MODULE_8
## 22
                                                                            c4.MORF_CCNF
## 23
                                                                            c4.MORF_EI24
## 24
                                                               c4.GNF2_PA2G4/c4.GNF2_RAN
                                                                           c4.MORF_PRKDC
## 25
## 26
                                                                            c4.MORF_GMPS
## 27
                                                                           c4.MODULE_219
## 28
                                                                            c4.GNF2_MCM5
                                                                           c4.MORF_DNMT1
## 29
## 30
                                                                            c4.GNF2_MSH2
## 31
                                                                          c4.MORF_CSNK2B
## 32
                                                                          c4.MORF_PTPN11
## 33
                                                                          c4.MORF_PPP1CC
## 34
                                                              c4.MORF_XRCC5/c4.MORF_GNB1
## 35
                                                                           c4.MODULE_451
## 36
                                                                            c4.MORF_SOD1
## 37
                                                                           c4.MORF_HDAC1
## 38
                                                                            c4.MODULE_51
## 39
                                                                            c4.GNF2_MAPT
                                                                            c4.MODULE_19
## 40
## 41
                                 c4.MODULE_11/c4.MODULE_66/c4.MODULE_100/c4.MODULE_137
##
      Correlation Metagenes
## 1
           0.6637
                           1
                           1
## 2
           0.6510
## 3
                           1
           0.6324
## 4
           0.6307
                           1
## 5
           0.6294
                           1
## 6
           0.6244
                           1
## 7
           0.5860
                           1
## 8
           0.5817
                           1
## 9
           0.5813
                           1
## 10
           0.5656
## 11
           0.5650
## 12
           0.5640
                           1
## 13
           0.5633
                           1
## 14
           0.5606
                           1
## 15
           0.5586
                           1
## 16
           0.5586
                           1
                           1
## 17
           0.5536
## 18
           0.5536
                           1
## 19
           0.5503
                           1
## 20
                           1
           0.5490
## 21
           0.5480
                           1
## 22
                           1
           0.5436
## 23
           0.5379
                           1
## 24
           0.5313
                           1
## 25
                           1
           0.5279
```

```
## 26
         0.5279
## 27
           0.5266
                           1
                           1
## 28
           0.5249
## 29
           0.5243
                           1
## 30
           0.5206
                           1
## 31
           0.5203
                           1
## 32
           0.5163
## 33
           0.5089
                           1
## 34
           0.5039
                           1
## 35
           0.5026
                           1
## 36
           0.5019
                           1
## 37
           0.5009
                           1
## 38
          -0.5066
                          -1
## 39
          -0.5259
                          -1
          -0.5656
## 40
                          -1
          -0.5967
## 41
                         -1
## [[1]]$c5
##
                                                                                       GeneSet
                                      c5.M_PHASE/c5.MITOSIS/c5.M_PHASE_OF_MITOTIC_CELL_CYCLE
## 1
## 2
                                                                     c5.REGULATION_OF_MITOSIS
## 3
                            c5.CELL_CYCLE_PROCESS/c5.MITOTIC_CELL_CYCLE/c5.CELL_CYCLE_PHASE
## 4
                                                                                    c5.SPINDLE
## 5
                                                                               c5.SPINDLE_POLE
## 6
                                           c5.ORGANELLE_PART/c5.INTRACELLULAR_ORGANELLE_PART
## 7
                                                                    c5.CHROMOSOME_SEGREGATION
## 8
                                                                     c5.CELL_CYCLE_G0_0007049
## 9
                                                                       c5.SPINDLE_MICROTUBULE
## 10
                                                             c5.MITOTIC_CELL_CYCLE_CHECKPOINT
## 11
                                                                       c5.CONDENSED_CHROMOSOME
                    c5.MITOTIC_SISTER_CHROMATID_SEGREGATION/c5.SISTER_CHROMATID_SEGREGATION
## 19
                                                          c5.CELL_CYCLE_CHECKPOINT_GO_0000075
## 13
      c5.MITOTIC_SPINDLE_ORGANIZATION_AND_BIOGENESIS/c5.SPINDLE_ORGANIZATION_AND_BIOGENESIS
## 14
## 15
                                                                c5.DOUBLE STRAND BREAK REPAIR
                                                                     c5.DNA_METABOLIC_PROCESS
## 16
## 17
                                                          c5.REGULATION_OF_MITOTIC_CELL_CYCLE
                      c5.RESPONSE_TO_ENDOGENOUS_STIMULUS/c5.RESPONSE_TO_DNA_DAMAGE_STIMULUS
## 18
## 19
                                              c5.CHROMOSOMEPERICENTRIC_REGION/c5.KINETOCHORE
## 20
                                                              c5.PORE_COMPLEX/c5.NUCLEAR_PORE
## 21
                                                                                 c5.DNA_REPAIR
## 22
                                                 c5.MACROMOLECULAR_COMPLEX/c5.PROTEIN_COMPLEX
## 23
                                           c5.INTERPHASE/c5.INTERPHASE_OF_MITOTIC_CELL_CYCLE
## 24
              c5.NON_MEMBRANE_BOUND_ORGANELLE/c5.INTRACELLULAR_NON_MEMBRANE_BOUND_ORGANELLE
                                                 c5.NUCLEAR_MEMBRANE/c5.NUCLEAR_MEMBRANE_PART
## 25
## 26
                                                            c5.CHROMOSOMAL_PART/c5.CHROMOSOME
## 27
                                                     c5.PHOSPHORIC_DIESTER_HYDROLASE_ACTIVITY
## 28
                              c5.CELL_SURFACE_RECEPTOR_LINKED_SIGNAL_TRANSDUCTION_GO_0007166
##
      Correlation Metagenes
## 1
           0.6894
                           1
## 2
           0.6821
## 3
           0.6527
                           1
## 4
           0.6437
                           1
## 5
           0.6280
                           1
## 6
           0.6244
```

```
## 7 0.5883
## 8
       0.5760
                    1
## 9
       0.5726
                    1
## 10
        0.5690
                    1
## 11
       0.5620
                    1
## 12
       0.5546
                    1
       0.5426
## 13
## 14
       0.5420
                    1
## 15
       0.5369
## 16
       0.5166
                    1
     0.5156
0.5146
## 17
                     1
## 18
                    1
## 19
       0.5136
## 20
       0.5083
                    1
      0.5063
## 21
## 22
       0.5059
                    1
## 23
       0.5033
                    1
## 24
       0.5029
                    1
## 25
       0.5013
                    1
## 26
       0.5003
                    1
## 27
       -0.5023
                    -1
                   -1
     -0.5176
## 28
##
## [[1]]$c6
##
                     GeneSet Correlation Metagenes
##
## [[1]]$c7
##
## 1
                                                                   c7.GSE15750_DAY6_VS_I
## 2
## 3
## 4
## 5
## 6
## 7
## 8
                                                               c7.GSE24634_TEFF_VS_TCONV
## 9
## 10
## 11
## 12
## 13
## 14
## 15
## 16
## 17
## 18
## 19
## 20
## 21
## 22
## 23
```

```
## 24
## 25
## 26
## 27
## 28
## 29
## 30
## 31
## 32
## 33
## 34
## 35
## 36
## 37
## 38
## 39
## 40
## 41
## 42
## 43
## 44
## 45
## 46
## 47
## 48
## 49
## 50
## 51
## 52
## 54 c7.GSE15930_NAIVE_VS_24H_IN_VITRO_STIM_CD8_TCELL_SIGNED/c7.GSE15930_NAIVE_VS_24H_IN_VITRO_STIM_IL
## 56
## 57
## 58
## 59
## 60
## 61
## 62
## 63
## 64
## 65
## 66
## 67
                                                             c7.GSE36476_CTRL_VS_TSST_ACT_40H_MEMORY_0
## 68
## 69
## 70
## 71
                                                          c7.GSE36476_CTRL_VS_TSST_ACT_40H_MEMORY_CD4_
## Correlation Metagenes
## 1
       0.6187
                  1
## 2
         0.6160
                        1
## 3
         0.6143
                        1
## 4
          0.5880
                         1
## 5 0.5857
```

##	6	0.5756	1
##	7	0.5696	1
##	8	0.5653	1
##		0.5630	1
	10	0.5623	1
	11	0.5580	1
	12	0.5553	1
	13	0.5546	1
	14	0.5476	1
##	15	0.5466	1
##	16	0.5423	1
##	17	0.5349	1
	18	0.5336	1
	19	0.5276	1
	20	0.5186	1
	21	0.5186	1
	22	0.5036	1
##	23	-0.5039	-1
##	24	-0.5086	-1
	25	-0.5109	-1
	26	-0.5119	-1
	27	-0.5119	-1
	28		
		-0.5149	-1
	29	-0.5179	-1
	30	-0.5183	-1
##	31	-0.5223	-1
##	32	-0.5239	-1
##	33	-0.5269	-1
	34	-0.5303	-1
	35	-0.5316	-1
	36	-0.5336	-1
	37	-0.5343	-1
	38	-0.5343	-1
##	39	-0.5426	-1
##	40	-0.5516	-1
##	41	-0.5520	-1
	42	-0.5543	-1
	43	-0.5560	-1
	44	-0.5603	-1
	45	-0.5603	-1
	46	-0.5613	-1
##	47	-0.5630	-1
##	48	-0.5636	-1
##	49	-0.5650	-1
	50	-0.5716	-1
	51	-0.5743	-1
	52	-0.5786	-1
	53	-0.5830	-1
	54	-0.5853	-1
##	55	-0.5860	-1
##	56	-0.5867	-1
##	57	-0.5920	-1
	58	-0.5950	-1
	59	-0.5953	-1
		0.0000	_

```
## 60
          -0.6007
                          -1
## 61
          -0.6010
                          -1
## 62
          -0.6090
                          -1
## 63
          -0.6190
                          -1
## 64
          -0.6193
                          -1
## 65
          -0.6254
                          -1
## 66
          -0.6417
                          -1
## 67
          -0.6500
                          -1
## 68
          -0.6530
                          -1
## 69
          -0.6637
                          -1
## 70
          -0.6654
                          -1
## 71
          -0.6667
                          -1
##
##
## [[2]]
## [[2]]$c1
## data frame with 0 columns and 0 rows
## [[2]]$c2
##
                                                                                                         Gei
## 1
                                                                                       c2.PID_INTEGRIN1_PAT
## 2
                                                             c2.VECCHI_GASTRIC_CANCER_ADVANCED_VS_EARLY_S
## 3
                                                         c2.LIEN_BREAST_CARCINOMA_METAPLASTIC_VS_DUCTAL_S
## 4
                                                                                       c2.PID_INTEGRIN3_PAT
## 5
                                                                    c2.SUZUKI_RESPONSE_TO_TSA_AND_DECITABIN
                                                                           c2.HUANG_DASATINIB_RESISTANCE_S
## 6
                                                                      c2.WIEDERSCHAIN_TARGETS_OF_BMI1_AND_I
## 7
## 8
                                                                                       c2.BURTON_ADIPOGENES
## 9
                                                                                 c2.POTTI_TOPOTECAN_SENSIT
## 10
                                                                                     c2.KARAKAS_TGFB1_SIGNA
## 11
                                                                                         c2.PID_UPA_UPAR_PAT
                                                                                 c2.CROMER_TUMORIGENESIS_S
## 12
                                                                                c2.ROZANOV_MMP14_TARGETS_SU
## 13
                                                                          c2.WOO_LIVER_CANCER_RECURRENCE_S
## 14
                                                                               c2.KEGG_ECM_RECEPTOR_INTERAC
## 15
## 16 c2.FARMER_BREAST_CANCER_CLUSTER_5/c2.ANASTASSIOU_CANCER_MESENCHYMAL_TRANSITION_SIGNATURE/c4.GNF2_
                                                                                       c2.PID_INTEGRIN5_PAT
## 17
                                 c2.REACTOME_EXTRACELLULAR_MATRIX_ORGANIZATION/c2.REACTOME_COLLAGEN_FORM
## 18
## 19
                                                                               c2.ROY_WOUND_BLOOD_VESSEL_S
## 20
                                                                                         c2.KEGG_FOCAL_ADHI
## 21
                                                                                c2.CHICAS_RB1_TARGETS_CONFI
## 22
                                                                                 c2.YIH_RESPONSE_TO_ARSENIT
## 23
                                                                          c2.PHONG_TNF_RESPONSE_VIA_P38_PAR
                                                                         c2.SERVITJA_ISLET_HNF1A_TARGETS_S
## 24
## 25
                                                                               c2.LI_PROSTATE_CANCER_EPIGE
                                                                                      c2.PID_SYNDECAN_1_PAT
## 26
## 27
                                                                                 c2.AGARWAL_AKT_PATHWAY_TAN
                                                            c2.REACTOME_CELL_EXTRACELLULAR_MATRIX_INTERAC
## 28
## 29
                                                                                     c2.PID_INTEGRIN_CS_PAT
## 30
                                                            c2.HELLEBREKERS_SILENCED_DURING_TUMOR_ANGIOGE
                                                                                        c2.MATTHEWS AP1 TAN
## 31
## 32
                                                                        c2.RODWELL_AGING_KIDNEY_NO_BLOOD_S
## 33
                                                           c2.YAO_TEMPORAL_RESPONSE_TO_PROGESTERONE_CLUSTI
```

34

c2.WESTON_VEGFA_TAR

```
## 35
                                                                                           c2.WU_CELL_MIGRA
                                                               c2.SCHUETZ_BREAST_CANCER_DUCTAL_INVASIVE_S
## 36
## 37
                                                                           c2.KAN_RESPONSE_TO_ARSENIC_TRIC
                                                                                 c2.VERHAAK_GLIOBLASTOMA_NI
## 38
## 39
                                                                c2.REACTOME_INTEGRIN_CELL_SURFACE_INTERACT
## 40
                                                                                           c2.GILDEA_METAS
## 41
                                                c2.TURASHVILI_BREAST_LOBULAR_CARCINOMA_VS_DUCTAL_NORMAL_S
## 42
                                                                  c2.HARRIS_HYPOXIA/c2.WINTER_HYPOXIA_META
## 43
                                                                                c2.BIOCARTA_PLATELETAPP_PAT
                                                                           c2.WANG_METHYLATED_IN_BREAST_CA
## 44
                                                         c2.RICKMAN_TUMOR_DIFFERENTIATED_WELL_VS_POORLY_S
## 45
## 46
                                                              c2.CHARAFE_BREAST_CANCER_LUMINAL_VS_BASAL_S
## 47
                                                                              c2.WALLACE_PROSTATE_CANCER_S
## 48
                                                        c2.WANG_BARRETTS_ESOPHAGUS_AND_ESOPHAGUS_CANCER_S
## 49
                                                                  c2.SMID_BREAST_CANCER_RELAPSE_IN_BONE_S
                                                               c2.MIYAGAWA_TARGETS_OF_EWSR1_ETS_FUSIONS_S
## 50
                                                                                  c2.LIU_PROSTATE_CANCER_S
## 51
                                                                                 c2.PASINI_SUZ12_TARGETS_S
## 52
## 53
                                                                          c2.NAKAMURA_ADIPOGENESIS_LATE_S
## 54
                                                                         c2.DOANE_BREAST_CANCER_CLASSES_S
                                                        c2.CHARAFE_BREAST_CANCER_LUMINAL_VS_MESENCHYMAL_S
## 55
      Correlation Metagenes
##
## 1
           0.6544
                           2
## 2
           0.6514
                           2
## 3
           0.6454
                           2
                           2
## 4
           0.6374
                           2
## 5
           0.6370
## 6
           0.6350
                           2
## 7
           0.6250
                           2
## 8
           0.6103
                           2
                           2
## 9
           0.6017
## 10
           0.5997
                           2
                           2
## 11
           0.5970
## 12
           0.5910
                           2
                           2
## 13
           0.5907
## 14
           0.5883
                           2
                           2
## 15
           0.5817
                           2
## 16
           0.5783
                           2
## 17
           0.5766
## 18
           0.5723
                           2
                           2
## 19
           0.5676
## 20
           0.5666
                           2
                           2
## 21
           0.5643
## 22
                           2
           0.5623
## 23
           0.5590
                           2
                           2
## 24
           0.5586
                           2
## 25
           0.5543
                           2
## 26
           0.5516
## 27
           0.5486
                           2
## 28
           0.5379
                           2
                           2
## 29
           0.5363
                           2
## 30
           0.5289
## 31
           0.5279
                           2
## 32 0.5256
```

```
## 33
      0.5239
                         2
                         2
## 34
          0.5229
## 35
                         2
          0.5209
## 36
                         2
          0.5206
                         2
## 37
          0.5206
## 38
          0.5203
                         2
## 39
          0.5179
                         2
## 40
          0.5179
                         2
                         2
## 41
         0.5146
## 42
                         2
         0.5119
## 43
          0.5056
                         2
## 44
                         2
         0.5009
## 45
        -0.5043
                        -2
## 46
        -0.5209
                        -2
## 47
         -0.5209
                        -2
## 48
                        -2
        -0.5443
## 49
        -0.5536
                        -2
## 50
         -0.5563
                        -2
## 51
         -0.5643
                        -2
## 52
        -0.5663
                        -2
## 53
                        -2
        -0.5680
                        -2
## 54
         -0.6010
         -0.6097
## 55
                        -2
##
## [[2]]$c3
## data frame with 0 columns and 0 rows
##
## [[2]]$c4
##
          GeneSet Correlation Metagenes
## 1 c4.GNF2_PTX3
                    0.5933
                                      2
## 2 c4.GNF2_MMP1
                       0.5750
## 3 c4.MODULE_412
                       0.5670
                                      2
                                      2
## 4 c4.MODULE_122
                       0.5600
## 5 c4.MODULE 47
                       0.5463
                                      2
                                      2
## 6 c4.MODULE_153
                      0.5426
## 7 c4.MODULE_321
                      0.5309
                                      2
                                      2
## 8 c4.MODULE_275
                      0.5253
## 9 c4.MODULE_562
                       0.5066
##
## [[2]]$c5
##
                                                            GeneSet
## 1
                                                   c5.AXON_GUIDANCE
## 2
                                               c5.TISSUE_DEVELOPMENT
## 3
                                                         c5.COLLAGEN
## 4 c5.AXONOGENESIS/c5.CELLULAR_MORPHOGENESIS_DURING_DIFFERENTIATION
## Correlation Metagenes
## 1
        0.5710
        0.5363
                        2
## 2
                        2
## 3
         0.5313
## 4
         0.5146
##
## [[2]]$c6
##
                                  GeneSet Correlation Metagenes
## 1 c6.CORDENONSI_YAP_CONSERVED_SIGNATURE 0.5256 2
```

```
## 2
                       c6.LEF1_UP.V1_SIGNED
                                                 0.5193
## 3
                       c6.STK33_NOMO_SIGNED
                                                  0.5073
                                                                 2
##
## [[2]]$c7
##
                                                                 GeneSet
## 1
                                c7.GSE17721_CTRL_VS_CPG_12H_BMDM_SIGNED
## 2 c7.GSE1460_INTRATHYMIC_T_PROGENITOR_VS_THYMIC_STROMAL_CELL_SIGNED
     Correlation Metagenes
## 1
         -0.5076
         -0.5079
                        -2
## 2
for (subtable_index in 1:length(tables))
        write.csv(do.call(rbind, tables[[subtable_index]]), file = sprintf("A%d_corrs.csv", subtable_index]
```

5 Session information

```
session_info
## R version 3.1.1 (2014-07-10)
## Platform: x86_64-unknown-linux-gnu (64-bit)
##
## locale:
## [1] LC_CTYPE=en_AU.UTF-8
                                      LC_NUMERIC=C
## [3] LC_TIME=en_AU.UTF-8
                                      LC_COLLATE=en_AU.UTF-8
## [5] LC_MONETARY=en_AU.UTF-8
                                      LC_MESSAGES=en_AU.UTF-8
## [7] LC_PAPER=en_AU.UTF-8
                                     LC_NAME=en_AU.UTF-8
## [9] LC_ADDRESS=en_AU.UTF-8
                                     LC_TELEPHONE=en_AU.UTF-8
## [11] LC_MEASUREMENT=en_AU.UTF-8
                                    LC_IDENTIFICATION=en_AU.UTF-8
##
## attached base packages:
## [1] splines
                 parallel methods
                                               graphics grDevices utils
                                     stats
## [8] datasets base
## other attached packages:
## [1] doParallel_1.0.8
                                                foreach_1.4.2
                            iterators_1.0.7
## [4] ahaz_1.14
                            survival_2.37-7
                                                NMF_0.20.5
## [7] Biobase_2.26.0
                           BiocGenerics_0.12.1 cluster_1.15.3
                            pkgmaker_0.22
## [10] rngtools_1.2.4
                                                registry_0.2
## [13] energy_1.6.2
                            glmnet_1.9-8
                                                Matrix_1.1-4
## [16] glmulti_1.0.7
                            rJava_0.9-6
##
## loaded via a namespace (and not attached):
## [1] boot_1.3-13
                           codetools_0.2-9
                                              colorspace_1.2-4
## [4] compiler_3.1.1
                           digest_0.6.4
                                              ggplot2_1.0.0
## [7] grid_3.1.1
                           gridBase_0.4-7
                                              gtable_0.1.2
## [10] lattice_0.20-29
                           MASS_7.3-35
                                              munsell_0.4.2
## [13] plyr_1.8.1
                           proto_0.3-10
                                              RColorBrewer_1.0-5
## [16] Rcpp_0.11.3
                          reshape2_1.4
                                              scales_0.2.4
## [19] stringr_0.6.2
                                              xtable_1.7-4
                           tools_3.1.1
```

```
sessionInfo()
## R version 3.1.1 (2014-07-10)
## Platform: x86_64-unknown-linux-gnu (64-bit)
##
## locale:
## [1] LC_CTYPE=en_AU.UTF-8
                                      LC_NUMERIC=C
## [3] LC_TIME=en_AU.UTF-8
                                      LC_COLLATE=en_AU.UTF-8
## [5] LC_MONETARY=en_AU.UTF-8
                                      LC_MESSAGES=en_AU.UTF-8
## [7] LC_PAPER=en_AU.UTF-8
                                     LC_NAME=en_AU.UTF-8
## [9] LC_ADDRESS=en_AU.UTF-8
                                     LC_TELEPHONE=en_AU.UTF-8
## [11] LC_MEASUREMENT=en_AU.UTF-8
                                     LC_IDENTIFICATION=en_AU.UTF-8
##
## attached base packages:
## [1] parallel methods
                                               graphics grDevices utils
                           splines
                                     stats
## [8] datasets base
##
## other attached packages:
## [1] MASS_7.3-35
                            stargazer_5.1
                                                xtable_1.7-4
## [4] gplots_2.14.2
                            RColorBrewer_1.0-5 glmnet_1.9-8
## [7] Matrix_1.1-4
                            glmulti_1.0.7
                                                rJava_0.9-6
## [10] bnlearn_3.7.1
                            nnls_1.4
                                                NMF_0.20.5
## [13] synchronicity_1.1.4 bigmemory_4.4.6
                                                BH_1.55.0-3
## [16] bigmemory.sri_0.1.3 Biobase_2.26.0
                                                BiocGenerics_0.12.1
## [19] cluster_1.15.3
                            rngtools_1.2.4
                                                pkgmaker_0.22
## [22] registry_0.2
                            energy_1.6.2
                                                survival_2.37-7
## [25] tikzDevice_0.8.1
                            knitr_1.8
##
## loaded via a namespace (and not attached):
## [1] bitops_1.0-6
                           boot_1.3-13
                                              caTools_1.17.1
## [4] codetools_0.2-9
                           colorspace_1.2-4
                                              digest_0.6.4
## [7] doParallel_1.0.8
                           evaluate_0.5.5
                                              filehash_2.2-2
## [10] foreach_1.4.2
                           formatR_1.0
                                              gdata_2.13.3
                                              gridBase_0.4-7
## [13] ggplot2_1.0.0
                           grid_3.1.1
## [16] gtable_0.1.2
                           gtools_3.4.1
                                              highr_0.4
## [19] iterators_1.0.7
                           KernSmooth_2.23-13 labeling_0.3
## [22] lattice_0.20-29
                           munsell_0.4.2
                                              plyr_1.8.1
## [25] proto_0.3-10
                           Rcpp_0.11.3
                                              reshape2_1.4
## [28] scales_0.2.4
                           stringr_0.6.2
                                              tools_3.1.1
```