# Hepatic gene expression

## Purpose:

To make a heatmap of the normalized counts for a list of liver-specific drug metabolism enzymes that have been used to assess HLC differentiation as well as liver health (PMID:21746904 and PMID: 23728495).

Load required libraries

```
library(gage)
library(gageData)
library(dplyr)
```

```
##
## Attaching package: 'dplyr'
```

```
## The following objects are masked from 'package:stats':
##
##     filter, lag
```

```
## The following objects are masked from 'package:base':
##
##     intersect, setdiff, setequal, union
```

```
library(stringr)
library(ggplot2)
library(reshape2)
library(openxlsx)
library(DESeq2)
```

```
## Loading required package: S4Vectors
```

```
## Loading required package: stats4
```

```
## Loading required package: BiocGenerics
```

```
## Loading required package: parallel
```

```
##
## Attaching package: 'BiocGenerics'
```

```
## The following objects are masked from 'package:parallel':
##
##     clusterApply, clusterApplyLB, clusterCall, clusterEvalQ,
##     clusterExport, clusterMap, parApply, parCapply, parLapply,
##     parLapplyLB, parRapply, parSapply, parSapplyLB
```

```
## The following objects are masked from 'package:dplyr':
##
##     combine, intersect, setdiff, union
```

```
## The following objects are masked from 'package:stats':
##
##     IQR, mad, xtabs
```

```
## The following objects are masked from 'package:base':
##
##     anyDuplicated, append, as.data.frame, cbind, colnames,
##     do.call, duplicated, eval, evalq, Filter, Find, get, grep,
```

```
##     grepl, intersect, is.unsorted, lapply, lengths, Map, mapply,
##     match, mget, order, paste, pmax, pmax.int, pmin, pmin.int,
##     Position, rank, rbind, Reduce, rownames, sapply, setdiff,
##     sort, table, tapply, union, unique, unsplit
```

```
##
## Attaching package: 'S4Vectors'
```

```
## The following objects are masked from 'package:dplyr':
##
##     first, rename
```

```
## The following objects are masked from 'package:base':
##
##     colMeans, colSums, expand.grid, rowMeans, rowSums
```

```
## Loading required package: IRanges
```

```
##
## Attaching package: 'IRanges'
```

```
## The following objects are masked from 'package:dplyr':
##
##     collapse, desc, slice
```

```
## Loading required package: GenomicRanges
```

```
## Loading required package: GenomeInfoDb
```

```
## Loading required package: SummarizedExperiment
```

```
## Loading required package: Biobase
```

```
## Welcome to Bioconductor
##
##     Vignettes contain introductory material; view with
##     'browseVignettes()'. To cite Bioconductor, see
##     'citation("Biobase")', and for packages 'citation("pkgname")'.
```

```
library(gplots)
```

```
##
## Attaching package: 'gplots'
```

```
## The following object is masked from 'package:IRanges':
##
##     space
```

```
## The following object is masked from 'package:S4Vectors':
##
##     space
```

```
## The following object is masked from 'package:stats':
##
##     lowess
```

```
library(dplyr)
library(tibble)
library(RColorBrewer)
library(stringr)
library(genefilter)
library(data.table)
```

```
##
## Attaching package: 'data.table'

## The following object is masked from 'package:SummarizedExperiment':
##
##     shift

## The following object is masked from 'package:GenomicRanges':
##
##     shift

## The following object is masked from 'package:IRanges':
##
##     shift

## The following objects are masked from 'package:S4Vectors':
##
##     first, second

## The following objects are masked from 'package:reshape2':
##
##     dcast, melt

## The following objects are masked from 'package:dplyr':
##
##     between, first, last
```

```
library(genefilter)
library(ggrepel)
library(viridis)
```

```
## Loading required package: viridisLite
```

```
library(tidyr)
```

```
##
## Attaching package: 'tidyr'

## The following object is masked from 'package:S4Vectors':
##
##     expand

## The following object is masked from 'package:reshape2':
##
##     smiths
```

```
library(gtools)
data("egSymb")
library(org.Hs.eg.db)
```

```
## Loading required package: AnnotationDbi

##
## Attaching package: 'AnnotationDbi'

## The following object is masked from 'package:dplyr':
##
##     select

##
```

```
library(AnnotationDbi)
```

Read in the appropriate count files

```
humanHBVcounts <- "All human HBV genes"
humanHBV_sampleCounts <- basename(Sys.glob(file.path(humanHBVcounts, "*.txt")))

##Function to read in the feature counts
exptcounts <- function(files) {
  d <- read.table(files)
  d
}

##Read in all of the count files
humanHBVcounts_readin <- lapply(file.path(humanHBVcounts, humanHBV_sampleCounts),
                                exptcounts)
names(humanHBVcounts_readin) <-  sub('humanHBVgenes.txt', '', humanHBV_sampleCounts)
names(humanHBVcounts_readin)
```

```
##  [1] "BD330_Ctrl_D28"      "BD330_Ctrl_D8"       "BD330_HBV_D28"
##  [4] "BD330_HBV_D8"        "BD330_HBV_HDV_D28_b" "BD330_HBV_HDV_D28"
##  [7] "BD330_HBV_HDV_D8_a"  "BD330_HBV_HDV_D8"    "BD405A_Ctrl_D28"
## [10] "BD405A_Ctrl_D8"      "BD405A_HBV_D28"      "BD405A_HBV_D8"
## [13] "BD405A_HBV_HDV_D28"  "BD405A_HBV_HDV_D8"   "Ctrl_D28_sample_1"
## [16] "Ctrl_D28_sample_2"   "Ctrl_D28_sample_3"   "Ctrl_D8_sample_1"
## [19] "Ctrl_D8_sample_2"    "Ctrl_D8_sample_3"    "HBV_D28_sample_1"
## [22] "HBV_D28_sample_2"    "HBV_D28_sample_3"    "HBV_D8_sample_1"
## [25] "HBV_D8_sample_2"     "HBV_D8_sample_3"     "HU1016_BD_co_D28"
## [28] "HU1016_BD_co_D8"     "HU1016_B_D28"        "HU1016_B_D8"
```

```
##Function to perform regularized log transformation on all counts for each sample.
rld_generation <- function(sampledirectory, sampleset) {
  a <- basename(Sys.glob(file.path(sampledirectory, "*.txt")))
  sampleTable <- data.frame(sampleName = names(sampleset), sampleFile = a, treatment =
  ifelse(grepl("Ctrl", a), "mock", ifelse(grepl("*co|*HDV", a), "coinf", "HBV")), donor =
  ifelse(grepl("BD330*", a), "HU1019", ifelse(grepl("BD405*", a), "HU1020",
      ifelse(grepl("HU1016*",  a), "HU1016", "HU1007"))), time = ifelse(grepl("*D8", a),
      "d8", "d28"), replicate = ifelse(grepl("*sample_1|*D8_ah|*D8_aa", a), "a",
ifelse(grepl("*sample_2|D28_bh|D28_ba", a),"b", ifelse(grepl("*sample_3", a), "c","")))))
sampleTable$sampleName <- with(sampleTable, paste(donor, treatment, time, replicate))
dds <- DESeqDataSetFromHTSeqCount(sampleTable = sampleTable, directory = sampledirectory,
  design = ~ donor + treatment)
  dds@colData
  rld <- rlog(dds, blind = TRUE)
}

##Execute function on the human and HBV gene counts.
rld_humanHBV <- rld_generation(humanHBVcounts, humanHBVcounts_readin)

##Pulling just the normalized gene counts out and making into a data frame.
mat_humanHBV <- assay(rld_humanHBV)
humanHBV_df <- as.data.frame(mat_humanHBV) %>%
  rownames_to_column(var = "ENSEMBL")
```

Now to limit our gene counts down to the ones of interest from the hepatic gene list first mentioned in PMID:

23728495.

```
##Read in the downloaded table of genes from PMID: 23728495.
hepatic_genes <- read.delim("Hepatic gene subset.csv", header = FALSE, sep = ",")
hepatic_genes <- hepatic_genes$V1 %>%
  droplevels() %>%
  as.character

##Since the genes in the table above are only given by gene SYMBOL, convert first to
##ENTREZ IDs
##and then ENSEMBL to compare with the normalized counts of our data set.
##Note that skipping the ENTREZ ID conversion first and going straight to ENSEMBL
##resulted in double mapping of some ALIASes to the same ENSEMBL ID.
hepatic_eg <- sym2eg(hepatic_genes)

hepatic_ENSEMBL <- as.data.frame(mapIds(org.Hs.eg.db, keys = hepatic_eg, column =
    "ENSEMBL", keytype = "ENTREZID", multiVals= "first"))
```

```
## 'select()' returned 1:many mapping between keys and columns
```

```
colnames(hepatic_ENSEMBL) <- c("ENSEMBL")
hepatic_ENSEMBL <- rownames_to_column(hepatic_ENSEMBL, var = "ENTREZID") %>%
  cbind(hepatic_genes) %>%
  dplyr::select(ENSEMBL, hepatic_genes)

##Now find the hepatic genes in our data set and generate a matrix.
all_IDed <- left_join(hepatic_ENSEMBL, humanHBV_df, by = "ENSEMBL") %>%
  na.omit()
```

```
## Warning: Column `ENSEMBL` joining factor and character vector, coercing
## into character vector
```

```
IDed_m <- as.matrix(all_IDed[,c(3:31)])
rownames(IDed_m) <- all_IDed[,2]

##In the above matrix, you only get 86 of the original 87 inputs because "Stable ##ID
##ENSG00000277656 not present in GRCh37" according to ENSEMBL which is GSTT1, ENTREZ ID
##2952.
##Also note that in the original file, SULT1A3/4 is listed - here I broke it up
##into SULT1A3 and SULT1A4; constiutive androstane receptor (CAR in the original
##document) goes by the gene symbol NR1I3 which was used here; LTB4DH goes by PTGR1;
##PXR now goes by NR1I2.
```

Now making a heat map of the normalized counts of these hepatic genes for each of our samples.

```
##Setting up color scheme.
##The rld function is log2-like, so log2 values of zero do not come up as -Inf but rather
##as zero. Counts that are less than 1 (i.e. a decimal number) come up as negative. Thus,
##my color scale is a light purple-grey for negative values, white for 0, and then shades
##of purple in increasing intensity.

my_breaks = c(seq(-2.5, -0.1, length=100), seq(-0.09, 0.1, length=10), seq(0.11, 18,
                                                                            length=100))
palette <- colorRampPalette(c('#d8daeb', "white", '#542788'))(n=209)

##Reorganizing the row order of samples to what we want for visualization.
sampleTable <- data.frame(sampleName = colnames(IDed_m), treatment = ifelse(grepl("mock",
```

```
    colnames(IDed_m)), "mock", ifelse(grepl("coinf", colnames(IDed_m)), "coinf", "HBV")),
    donor = ifelse(grepl("HU1019", colnames(IDed_m)), "HU1019", ifelse(grepl("HU1007",
    colnames(IDed_m)), "HU1007", ifelse(grepl("HU1016", colnames(IDed_m)), "HU1016",
    "HU1020"))), time = ifelse(grepl("d8", colnames(IDed_m)), "d8", "d28"))
sampleTable <- with(sampleTable, sampleTable[order(time, treatment),])
col.order <- as.character(rev(sampleTable$sampleName))
mat_hep_subset <- IDed_m[, col.order]

##Now plotting the heatmap
png(file = file.path(paste(Sys.Date(), "hepatic genes_heatmap.png")), units = 'in',
    height = 15, width = 30, res = 300)
distance_heatmap <- heatmap.2(t(mat_hep_subset), trace="none", keysize = 0.7,
      symm=F,symkey=F,symbreaks=F, col = palette, breaks = my_breaks, dendrogram =
        "column", sepwidth=c(0.05,0.05), sepcolor = "grey",
      colsep=1:nrow(mat_hep_subset),
##rowsep and colsep have to be set to ncol and nrow, respectively, since you have flipped
##your heatmap
    rowsep=1:ncol(mat_hep_subset), density.info = "none", margin = c(18, 18), Rowv =
  FALSE, srtCol = 90, cexRow = 1, cexCol = 2, scale = "none")
print(distance_heatmap)
```

```
## $rowInd
##  [1] 29 28 27 26 25 24 23 22 21 20 19 18 17 16 15 14 13 12 11 10  9  8  7
## [24]  6  5  4  3  2  1
##
## $colInd
##  [1] 73 71 78 40 31 28 79 24 36 10 75 27 52  9 19 42 26 55  8 53 63 84 39
## [24] 77 66  4 43 50 47 49 29 45 56 20 76 34 51 11 12  2 25 86 69  5 30 74
## [47] 57 64 68 67 14 62 82 16 17 13 37  7 61 81 58 80  6 21 35 65 85 32 33
## [70] 72 41 48 46 18 38 70 23 15 60 54  3 83 44 59 22  1
##
## $call
## heatmap.2(x = t(mat_hep_subset), Rowv = FALSE, dendrogram = "column",
##     symm = F, scale = "none", breaks = my_breaks, symbreaks = F,
##     col = palette, colsep = 1:nrow(mat_hep_subset), rowsep = 1:ncol(mat_hep_subset),
##     sepcolor = "grey", sepwidth = c(0.05, 0.05), trace = "none",
##     margins = c(18, 18), cexRow = 1, cexCol = 2, srtCol = 90,
##     keysize = 0.7, density.info = "none", symkey = F)
##
## $carpet
##         HU1019 coinf d28 b HU1019 coinf d28  HU1020 coinf d28
## SLCO1A2         -2.1416171        -2.1376428        -2.1369034
## SLC10A2         -2.0705960        -2.0692502        -2.0689998
## SULT1A3         -1.8289830        -1.8571421        -1.8564492
## CYP7A1          -0.7063911        -0.7440653        -0.7419287
## CYP2C19         -0.5809527        -0.5666477        -0.5639864
## CYP2A13         -0.2745909        -0.2585003        -0.1663803
## SULT1A4          0.0000000         0.0000000         0.0000000
## CYP11B2          0.0000000         0.0000000         0.0000000
## CYP2F1           0.0000000         0.0000000         0.0000000
## ABCG4            0.6600956         0.4264164         0.4275206
## SLCO1B3          2.3786457         2.4076779         2.9727324
## CYP1B1           4.1691869         4.2756941         5.1796907
## GSTM2            4.6265945         4.1033618         5.2326415
```

```
## ABCG2          4.4641406        4.0688760        4.5622805
## NR1I3          4.8840353        3.7331516        4.9129812
## DHRS2          4.8659772        4.0598161        4.6368187
## CYP1A2         5.7986188        4.8107129        5.5523219
## HNF4G          6.0313836        5.7322992        5.6802394
## ABCC4          5.4866785        5.9339244        5.7250674
## GSTP1          5.3744301        6.0459982        5.2550036
## NAT1           4.8526325        5.2210645        4.6585076
## UGT1A3         5.2468017        5.6198467        4.9124407
## CYP3A7         5.6489347        5.2297725        4.4211587
## SULT1A2        6.4850383        5.0409677        4.6724094
## NQO1           5.2020630        4.5864525        5.4188602
## ABCB11         4.9218806        5.0175894        6.2298153
## DHRS4          5.2707109        5.1150315        5.4035433
## GSTA4          5.6757860        5.7607675        5.5908841
## FMO4           5.4912636        5.8124505        5.8171202
## GSTA1          8.9600062        6.2848071        6.8312133
## CYP2A6         9.2881278        6.8827090        9.3309698
## EPHX2          8.3439093        8.8004140        9.1794003
## HNMT           7.8615217        8.3475104        7.2879555
## CBR1           8.3104148        7.4181865        7.4058125
## SULT1A1        8.7959311        7.8195390        7.6221737
## CYP2D6         8.2292451        7.8784236        8.7835674
## GSTM1          9.6140987        8.0399664        7.6198488
## ABCG5          7.5377196        6.7589799        8.3665492
## ABCG8          8.0945639        7.3235477        8.2630263
## ABCA6          7.4485383        7.5249609        7.7953024
## CYP1A1         7.2075704        9.5716079        6.8320305
## UGT1A9         7.3819461        5.9753722        6.5845263
## RARA           6.7172761        6.8195798        7.5342127
## ABCC1          7.6246930        8.0063464        7.7965967
## CYP2B6         7.2916744        5.2559349        6.8748459
## SLCO1B1        7.0569136        5.8327083        6.3972995
## HSD11B1        7.4509566        6.4146731        6.9508729
## NAT2           6.7722190        6.4769302        6.1662800
## NR1I2          7.1647288        5.4487024        7.2936458
## NQO2           7.1940208        6.9065765        7.4397816
## AHR            6.9109423        7.1245772        6.7655097
## MGST2          7.4196893        6.9075116        6.5932752
## TPMT           7.3485970        6.8335836        7.1472112
## ALB           17.0233792       17.7360164       16.7852345
## ALDH1A1       14.1087187       12.9702997       13.0061264
## ACTB          13.3121109       13.3947392       12.6930633
## CYP3A4        11.1824429        8.1789007        8.5554348
## ABCC3         11.8492936       11.8171548       12.1481938
## MGST1         12.4076080       12.1340090       12.1409279
## TFRC          10.7541763       10.8642504       11.1627399
## PTGR1         11.0359350       11.2788643       10.9695921
## SULT2A1       10.9208337       10.7872387       11.3172423
## ABCC2         10.5715924       10.0929043       10.8163744
## CES1          10.3090658       10.4903134       10.8283285
## CYP2E1         7.3391848       11.3316176        8.9052366
## NNMT           8.9892208       10.5900171       10.2919138
## UGT1A6        10.0809842        8.1784048        9.0919304
```

```
## CYP2C8          10.0051259         9.8274710         9.9348271
## CYP2C9           9.4706094         8.7175987         9.5165629
## SLC22A1          9.3834045         8.4014392         9.3711115
## DCXR             9.5361397         8.7981130         8.7847854
## NR1H4            9.0676948         9.2284075         8.5769564
## FMO3             8.9124229         9.3337755         9.5661180
## ALDH2            8.5588130         9.2460025         9.0160371
## CYP3A5          11.3056184        10.3091225        10.0117276
## RXRA             9.8030058        10.0834959        10.3481423
## COMT             9.5730811        10.1285973        10.2675140
## AKR1A1           9.6432912         9.2088634         9.5657407
## MAOB             9.2395299         9.1222475         9.4555978
## HNF4A            9.9849890         9.0562805        10.1322521
## ABCB1            9.0925514         9.1623760         9.1202559
## UGT1A1          11.0032838        10.6041127         9.9327377
## EPHX1            9.9036017        10.1216015        10.4190441
## MAOA            10.4484459        10.0705258        10.4625399
## CES2            10.2929690         9.4243358        10.0917199
## ABCA2            9.9807481         9.9103696        10.3402403
##         HU1016 coinf d28  HU1019 HBV d28  HU1020 HBV d28  HU1007 HBV d28 a
## SLCO1A2        -2.1413586      -2.1487159      -2.1356335       -2.1481222
## SLC10A2        -2.0705085      -2.0730000      -2.0685697       -2.0727990
## SULT1A3        -1.8606242      -1.8515771      -1.8552591       -1.8669625
## CYP7A1         -0.7548031      -0.7343407      -0.7382589       -0.7619806
## CYP2C19        -0.5800222      -0.5859459      -0.5594155       -0.5857843
## CYP2A13        -0.2743453      -0.2796243      -0.2480728       -0.2793160
## SULT1A4         0.0000000       0.0000000       0.0000000        0.0000000
## CYP11B2         0.0000000       0.0000000       0.0000000        0.0000000
## CYP2F1          0.0000000       0.0000000       0.0000000        0.0000000
## ABCG4           0.4216594       0.4156731       0.5425839        0.6021651
## SLCO1B3         2.7880129       2.3435306       2.4249048        2.3457288
## CYP1B1          3.5784994       4.8834271       4.1324335        3.8992531
## GSTM2           5.0759653       4.6682476       4.9297600        3.5121626
## ABCG2           4.5164787       4.0013558       4.5304126        4.8276327
## NR1I3           4.1530083       4.0567936       4.8422496        3.4276205
## DHRS2           4.6877372       4.1930278       4.6056911        4.0397651
## CYP1A2          6.2058941       4.2305483       6.8293455        6.5007379
## HNF4G           6.3074046       5.7037454       6.0863712        5.9096219
## ABCC4           6.6256230       6.4240342       6.0842080        7.0240835
## GSTP1           6.2424919       6.3168312       4.6369118        5.9732845
## NAT1            4.6285982       4.6200109       5.0176661        5.1428169
## UGT1A3          5.3197591       5.3030632       5.3691928        5.4415205
## CYP3A7          6.1426204       4.6281453       4.3810643        4.3766500
## SULT1A2         5.8738433       5.1669882       6.0996722        4.9772653
## NQO1            4.8723130       5.8442175       4.7806904        6.0121132
## ABCB11          4.8091898       4.7033776       5.3376247        5.1803792
## DHRS4           5.2002846       5.4638989       5.6699231        5.8302079
## GSTA4           5.8893662       5.6476722       5.8799174        5.1191258
## FMO4            5.7488823       6.0632872       5.2603469        5.0662235
## GSTA1           7.4709662       4.7266976       9.3495338        7.1642484
## CYP2A6          8.7555172       5.3371400       9.6763911        7.0135988
## EPHX2           8.0340908       8.6704879       8.7771785        7.2571690
## HNMT            8.1838361       8.1715312       7.9986974        8.0509218
## CBR1            7.9968942       7.6328638       8.2318949        7.6343189
```

```
## SULT1A1         8.8471526       7.9446100       8.7337655       8.1916203
## CYP2D6          6.9162134       7.8448726       8.1986444       6.2039596
## GSTM1           7.3254119       8.2624844       8.6423745       6.4779837
## ABCG5           7.2601540       7.5491068       7.7289383       6.1964464
## ABCG8           7.5437044       7.7637257       7.9683915       6.6538865
## ABCA6           7.3940056       7.4653229       7.4468022       7.5346318
## CYP1A1          5.6688570       5.4292112       7.3151832       8.1791448
## UGT1A9          7.8745870       5.0212260       6.8092597       8.8552444
## RARA            7.4564892       7.4218061       6.9614845       7.7207795
## ABCC1           8.1175334       7.8508755       7.9469646       8.3401074
## CYP2B6          6.1083113       5.8755811       7.5825271       6.9377545
## SLCO1B1         7.0528121       5.5860921       7.6783352       7.1694160
## HSD11B1         7.0632620       7.2567610       6.2411551       6.9202508
## NAT2            6.4585968       5.9181562       6.3804508       6.0930333
## NR1I2           6.7621548       5.8988938       7.4922752       5.8208634
## NQO2            7.0519285       7.1075909       7.4775435       5.8136835
## AHR             6.7494044       6.6035465       7.3806364       7.0245054
## MGST2           6.9017395       6.7410038       6.6392013       6.8054638
## TPMT            6.7679938       6.9762127       7.0895373       6.7444869
## ALB            16.9477573      16.6195920      17.0098763      16.0736697
## ALDH1A1        13.4352316      11.6682568      14.4383061      13.4335483
## ACTB           13.5056134      13.2750544      13.0283337      13.5506356
## CYP3A4         11.1665387       6.9979458      11.6433154      11.5365859
## ABCC3          11.9401060      11.6236553      11.7706235      11.1693497
## MGST1          11.8727804      11.8336577      12.3486742      11.4597259
## TFRC           10.9177311      10.9250803      10.7001015      10.9706702
## PTGR1          10.1469712      10.3352979      11.2402709       9.9567794
## SULT2A1         9.5831415       9.9756772      11.1946230       9.4551299
## ABCC2          10.4430821      10.0817432      10.8014358       9.9688401
## CES1           10.1758155      10.3565350      10.9678486      10.1995572
## CYP2E1          6.9176590      10.4649214       8.0440528       6.6108367
## NNMT            8.1321047      11.2715751       8.2615134       8.3805704
## UGT1A6         10.2646503       6.8325465      10.7958600       9.8509673
## CYP2C8          9.3465600       8.3012527       9.9677664       8.3828461
## CYP2C9          9.2290256       8.4310876       9.4972383       8.4352277
## SLC22A1         9.3957260       8.4618390       9.5746870       8.0504540
## DCXR            9.0182478       8.3866532       9.4228213       7.7446367
## NR1H4           8.2096468       8.6453774       8.7553622       7.9781462
## FMO3            8.8316501       8.9813088       8.9767880       8.3152439
## ALDH2           8.9602926       9.5271174       8.9100842       8.4980528
## CYP3A5         10.1038855       8.9900728      10.5371674       8.6154373
## RXRA            9.3570967      10.0570418       9.4400382       9.1428055
## COMT            9.6565353      10.2839280       9.5121320       9.2219763
## AKR1A1          9.4362101       9.2223136       9.6892205       9.0283758
## MAOB            9.6424284       9.5521944       9.6083824       9.6064036
## HNF4A           9.6526974       9.4641048       9.9435845       9.1684756
## ABCB1          10.2793703       8.6171462       9.8730157      10.1375176
## UGT1A1          9.1225012       8.8654808      10.6700643       9.8978445
## EPHX1          10.1499452       9.1759686      10.4843111       9.3011203
## MAOA            9.8800807      10.2170810      10.5806037       9.5486472
## CES2           10.1878677       9.4857780      10.2312593       9.8584088
## ABCA2          10.4799777       9.8451600      10.1328605      10.1272977
##         HU1007 HBV d28 b HU1007 HBV d28 c HU1016 HBV d28  HU1019 mock d28
## SLCO1A2       -2.1505157       -2.1487624      -2.1395331       -2.1436320
```

```
## SLC10A2      -2.0736095      -2.0730158      -2.0698903      -2.0712784
## SULT1A3      -1.8688560      -1.8675624      -1.8589135      -1.8627547
## CYP7A1       -0.7623952      -0.7621018      -0.7495280      -0.7608731
## CYP2C19      -0.5863801      -0.5859582      -0.5734517      -0.2325997
## CYP2A13      -0.2804564      -0.2796477       0.4029479      -0.2763442
## SULT1A4       0.0000000       0.0000000       0.0000000       0.0000000
## CYP11B2       0.0000000       0.0000000       0.0000000       0.0000000
## CYP2F1        0.0000000       0.0000000       0.0000000       0.0000000
## ABCG4         0.4147482       0.5904902       0.4238330       0.7022791
## SLCO1B3       3.0148787       2.3433633       2.4884466       2.3665885
## CYP1B1        4.9180240       5.0429754       3.8638139       4.6605867
## GSTM2         3.4032419       3.8872428       5.0602606       5.2918478
## ABCG2         4.0332347       3.9161521       3.8343177       4.8519090
## NR1I3         3.7543030       3.7579446       4.8055211       5.0597062
## DHRS2         4.6759003       4.0662853       5.1138039       4.9989201
## CYP1A2        6.4262871       6.0558773       5.0707642       5.2713278
## HNF4G         6.0221563       5.8577297       6.5662362       5.9207426
## ABCC4         6.9400734       6.8051754       6.1678556       6.1094649
## GSTP1         6.7810667       8.1105794       5.8722986       5.3530377
## NAT1          4.8973899       4.4655755       4.8271331       4.3814330
## UGT1A3        4.5785816       3.8837791       4.8429838       4.8024204
## CYP3A7        5.2329390       5.0080704       6.9405773       5.5577074
## SULT1A2       4.6028779       5.2893320       6.4356296       5.8500646
## NQO1          6.1786289       6.3499558       5.1274947       5.0710177
## ABCB11        5.0668139       5.4497095       5.1204083       5.5647885
## DHRS4         5.3591561       5.2986548       5.4398817       5.2648875
## GSTA4         5.6298378       5.4679706       5.8221911       5.6618024
## FMO4          5.8385773       5.0747056       6.0037584       6.1017718
## GSTA1         5.1513761       5.4707210       6.6261925       7.2655131
## CYP2A6        6.8697202       6.6253667       8.0774064       9.6016587
## EPHX2         7.7431041       7.4665996       8.0550207       8.9941049
## HNMT          8.2818574       7.6440697       8.0450419       7.7708634
## CBR1          7.6557870       7.9717712       7.9319688       7.4372222
## SULT1A1       7.5765301       7.9911789       8.6530443       7.9136863
## CYP2D6        6.5768526       6.3654746       7.7312721       8.8341497
## GSTM1         6.1687486       6.5048821       7.2046799       9.0568594
## ABCG5         6.9255947       6.1215609       8.3778947       8.1637079
## ABCG8         6.6697760       6.8172090       7.8257604       8.5207784
## ABCA6         7.4300936       7.4521155       7.5534572       7.9784485
## CYP1A1        8.0382653       7.8521297       5.6622517       7.1367542
## UGT1A9        8.4450230       7.9893492       7.2275612       6.9645643
## RARA          7.8619186       7.7615328       7.6273118       7.5137644
## ABCC1         7.9124936       8.0983703       8.3682272       7.8915343
## CYP2B6        6.5425040       6.2887488       5.7966648       8.3472956
## SLCO1B1       6.7335721       6.6576607       6.2555072       6.4606819
## HSD11B1       6.3613231       6.5014805       7.0532186       7.5467566
## NAT2          5.8616773       5.5180154       6.1300947       6.4814293
## NR1I2         6.3038183       5.7984209       5.9841621       7.1219257
## NQO2          6.2391394       6.8272986       6.7231692       7.6842611
## AHR           6.8512646       7.1529511       6.4295456       6.8107380
## MGST2         7.0980602       7.0354892       6.9439287       6.6225682
## TPMT          6.7781374       6.7968512       7.0469690       6.7775856
## ALB          16.1851149      15.9599022      16.8572861      17.0826659
## ALDH1A1      12.8705220      12.6058621      12.9076668      13.0276232
```

```
## ACTB          13.3954758       14.0054501      13.3955680       12.9494191
## CYP3A4        11.3048599       11.0292766      11.4627306        8.7063130
## ABCC3         11.4297865       11.2501251      12.2438267       12.2059595
## MGST1         11.6025969       11.6508450      11.6743573       11.9859712
## TFRC          11.1238826       10.8306451      10.7016762       11.0421470
## PTGR1          9.5635540        9.6867914       9.9228456       10.9627335
## SULT2A1        9.9172582        9.8340335      10.1563251       10.8415132
## ABCC2         10.1022389        9.8444437      10.6569688       10.6678373
## CES1          10.1556444        9.9949648      10.1561155       10.1242844
## CYP2E1         8.4985114        8.6954769       8.4000051        9.1227295
## NNMT           9.9033820        9.6590547       9.3837754        9.9989412
## UGT1A6         9.2217386        8.9151332       9.4790032        8.9771928
## CYP2C8         8.3984859        8.1752018       9.5839640       10.6895791
## CYP2C9         8.2732166        8.3602488      10.0524805        9.4481521
## SLC22A1        8.1317065        8.2668447       9.6558244        9.5418988
## DCXR           7.8570399        8.4937032       9.4524948        9.4725242
## NR1H4          8.4279910        8.2423932       8.6056407        8.2818123
## FMO3           8.5315340        8.4048684       8.6794310        9.6854324
## ALDH2          8.8289737        8.9697598       9.1454261        9.4050607
## CYP3A5         8.5698958        8.7237758      10.5944298       10.5987148
## RXRA           9.6956879        9.4976578       9.6831954       10.4871415
## COMT           9.5357330        9.6100104       9.3678501       10.4820072
## AKR1A1         9.2577276        9.2675993       9.3719038        9.6772325
## MAOB           9.5775501        9.3212707       9.6367182        9.4684570
## HNF4A          9.2794992        9.2260709      10.0227332       10.1122418
## ABCB1          9.6997364        9.2665798       9.8899201        8.8347120
## UGT1A1         9.7964592        9.6368672       8.9018093       10.1520597
## EPHX1          9.3477613        9.5304393      10.1127409       10.2153335
## MAOA           9.2980342        9.1818152       9.9294071       10.2062854
## CES2           9.7302659        9.8022239       9.8139923       10.0946363
## ABCA2         10.0703831        9.7264100      10.5185737       10.1467115
##         HU1020 mock d28  HU1007 mock d28 a HU1007 mock d28 b
## SLCO1A2       -2.1391339        -2.1516976        -2.1517088
## SLC10A2       -2.0697551        -2.0738580        -2.0527530
## SULT1A3       -1.8585394        -1.8689475        -1.8689579
## CYP7A1        -0.7483742        -0.7627750        -0.7628170
## CYP2C19       -0.5107842        -0.5869281        -0.5869889
## CYP2A13       -0.2662384        -0.2815146        -0.2816325
## SULT1A4        0.0000000         0.0000000         0.0000000
## CYP11B2        0.0000000         0.0000000         0.0000000
## CYP2F1         0.0000000         0.0000000         0.0000000
## ABCG4          0.4243501         0.5391677         0.4134492
## SLCO1B3        2.5839147         2.3298951         2.5241028
## CYP1B1         4.2825288         4.7031080         3.9316900
## GSTM2          4.7731295         3.2433429         3.4640960
## ABCG2          4.5951526         3.4824369         4.2796014
## NR1I3          4.4404280         3.4959352         3.7478477
## DHRS2          4.8544033         3.9317631         4.1512600
## CYP1A2         6.3635344         5.4377440         5.6142769
## HNF4G          6.4476583         6.1841779         5.5547940
## ABCC4          6.2072235         6.7925024         6.8134068
## GSTP1          4.0762612         8.4763069         7.5863435
## NAT1           5.1013533         5.0140955         4.6420101
## UGT1A3         5.7935887         4.5494349         4.8809680
```

```
## CYP3A7        4.8359010        3.8363053        4.5445588
## SULT1A2       5.3704888        4.7056467        4.6655345
## NQO1          4.9345928        6.2731819        5.8082453
## ABCB11        4.7986775        5.3064786        4.6902799
## DHRS4         4.6008884        5.5936256        5.8467193
## GSTA4         5.8121968        5.4310625        5.0435160
## FMO4          4.9035550        5.0568136        5.4277286
## GSTA1         9.1583323        4.8364451        5.1869752
## CYP2A6        8.9865751        4.7147053        5.2623463
## EPHX2         8.3796879        7.2563475        7.3127423
## HNMT          7.8325269        7.6311214        7.8372514
## CBR1          8.2737142        7.6144951        7.8080176
## SULT1A1       8.1290354        7.6873869        8.2570196
## CYP2D6        7.3798272        5.9668179        5.6336028
## GSTM1         8.1922112        5.8436657        5.6136944
## ABCG5         7.6875073        6.0886469        6.5658085
## ABCG8         7.8233965        6.6344302        7.0222744
## ABCA6         7.3682244        7.0123665        7.3684875
## CYP1A1        7.7696550        7.6662803        7.5393399
## UGT1A9        6.9579338        7.4952756        8.0022393
## RARA          6.7873717        7.8314994        7.8356307
## ABCC1         7.4800791        8.1982869        8.1366398
## CYP2B6        6.5667605        5.6276057        5.2669833
## SLCO1B1       6.8880373        6.1035401        6.6960482
## HSD11B1       5.6880235        6.7697150        6.4602548
## NAT2          6.2828931        5.4279148        5.6780732
## NR1I2         7.2662309        5.4416394        5.8722056
## NQO2          7.3147527        6.5505930        6.3978587
## AHR           7.0589904        7.1998128        6.7517593
## MGST2         6.8504426        6.6402422        7.0745357
## TPMT          7.2859326        6.4567067        6.7397561
## ALB          16.8622272       15.5043185       15.9032950
## ALDH1A1      14.5819516       12.1442381       12.4946517
## ACTB         12.7852918       13.9191744       13.7389887
## CYP3A4       11.6793247        8.6787008        9.4551330
## ABCC3        11.6610364       11.2697804       11.4870026
## MGST1        12.2867878       11.3468373       11.3362300
## TFRC         11.0120590       11.1165895       10.8416572
## PTGR1        11.1196168        9.1220883        9.5590361
## SULT2A1      11.3614100        9.2248059        9.4718859
## ABCC2        10.7742147        9.2157565        9.6154615
## CES1         10.6248875        9.7980759       10.0144097
## CYP2E1        7.3218519        8.3966915        7.9128392
## NNMT          8.5736095        9.8404564       10.0660871
## UGT1A6       10.8947779        8.4252408        8.8598736
## CYP2C8        9.4771126        7.2167727        7.3918684
## CYP2C9        9.5012295        7.4843751        8.0647841
## SLC22A1       8.9301721        7.4812837        7.6678987
## DCXR          8.6130471        8.1282358        7.9792815
## NR1H4         9.2172735        7.9362297        8.0062945
## FMO3          8.8195016        8.3295408        8.6078837
## ALDH2         8.6009031        8.4898231        8.7466578
## CYP3A5       10.5841210        8.1674729        8.1893366
## RXRA          9.3059454        9.2909874        9.5635217
```

```
## COMT           9.3812713         9.4502772         9.4604586
## AKR1A1         9.5027632         9.0542938         9.1584860
## MAOB           9.5724733         9.0469099         9.4042405
## HNF4A          9.7913325         8.9769161         9.3521350
## ABCB1          9.7871196         8.8404552         9.3846882
## UGT1A1        10.9713128         9.1381169         9.6540597
## EPHX1         10.0951260         8.6174938         8.7954179
## MAOA          10.4507399         9.5691957         9.4641464
## CES2          10.1143041         9.4305200         9.3850782
## ABCA2          9.8516904         9.6729387        10.0640035
##         HU1007 mock d28 c HU1019 coinf d8 a HU1019 coinf d8
## SLCO1A2        -2.1517330        -2.1472345       -2.1435651
## SLC10A2        -2.0738619        -2.0724984       -2.0712557
## SULT1A3        -1.8689787        -1.8661306       -1.8626920
## CYP7A1         -0.7629076        -0.7617988       -0.7608527
## CYP2C19        -0.5871200        -0.5855239       -0.5841765
## CYP2A13        -0.2818874        -0.2788209       -0.2762904
## SULT1A4         0.0000000         0.0000000        0.0000000
## CYP11B2         0.0000000         0.0000000        0.0000000
## CYP2F1          0.0000000         0.0000000        0.0000000
## ABCG4           0.5230719         0.4900378        0.6628533
## SLCO1B3         2.4315261         2.7349152        2.8823561
## CYP1B1          3.7893113         3.6907589        4.4929470
## GSTM2           3.5253995         4.0302315        4.1355705
## ABCG2           4.0129819         4.3877031        4.2365687
## NR1I3           3.3916872         3.4393227        3.7108714
## DHRS2           4.1182301         3.7907011        4.1491125
## CYP1A2          5.8541085         4.8162177        4.5463814
## HNF4G           5.9719708         5.2794306        5.4893223
## ABCC4           6.8151742         6.0516398        6.1600489
## GSTP1           6.4448527         5.9576960        5.5514396
## NAT1            4.4232470         4.5110574        4.7453216
## UGT1A3          4.9118553         5.8156059        5.4740087
## CYP3A7          4.8173233         5.5786936        4.5399014
## SULT1A2         5.1010540         5.0061681        4.5474472
## NQO1            5.4695462         5.4780459        4.9004455
## ABCB11          5.0799403         4.0648735        4.9901583
## DHRS4           5.6865600         5.4911122        5.2702392
## GSTA4           5.2688579         5.1127460        5.3794213
## FMO4            5.2957291         5.5630846        5.5906277
## GSTA1           4.8013894         5.1533827        5.6223333
## CYP2A6          5.5303365         5.7810923        5.8198448
## EPHX2           7.3640564         8.5777294        8.8394239
## HNMT            7.9950257         8.4670098        7.9283793
## CBR1            7.8761638         7.7239866        7.5853511
## SULT1A1         8.0960144         7.3761040        7.7158126
## CYP2D6          6.5124382         7.4405037        8.1738363
## GSTM1           5.6128133         8.0333785        7.5341922
## ABCG5           6.6201863         6.7833242        7.5157921
## ABCG8           7.0311430         7.3638717        7.6087835
## ABCA6           7.1995499         7.7338682        7.7657013
## CYP1A1          7.9889481         8.0528069        7.6645333
## UGT1A9          8.4783159         5.4773174        6.0200344
## RARA            7.9446957         7.0103289        7.5745022
```

```
## ABCC1           8.3072349         7.9554120        7.7561317
## CYP2B6          5.7334956         5.6967477        6.0791084
## SLCO1B1         6.7734030         6.4813467        6.7097736
## HSD11B1         6.9364236         6.6845179        7.1738050
## NAT2            5.8418926         6.0927078        6.3621648
## NR1I2           5.8048759         4.9264493        5.5582301
## NQO2            6.6521960         7.0537175        7.1660543
## AHR             6.8386462         6.9812172        6.7769210
## MGST2           6.8740332         6.6348986        6.6648698
## TPMT            6.8233688         6.9879302        6.7634465
## ALB            16.1932138        17.2186585       17.1229124
## ALDH1A1        12.4888503        12.2322946       12.2011918
## ACTB           13.7773395        13.3210748       13.2858989
## CYP3A4          9.6327639         8.0628559        7.5459305
## ABCC3          11.4508666        11.4899903       11.8420369
## MGST1          11.7472754        12.3854223       12.2962897
## TFRC           10.9692883        10.6087948       10.6238478
## PTGR1           9.7702470        10.9071776       11.1837715
## SULT2A1         9.7023081        10.5690234       10.4226944
## ABCC2           9.9339292        10.2948897       10.3509787
## CES1           10.1447590        10.5361575       10.5716616
## CYP2E1          9.1020098        11.9411458       10.7730742
## NNMT           10.3014242        10.9364715       10.8939260
## UGT1A6          8.9967255         7.4320590        7.9688086
## CYP2C8          7.4929772         9.1907100        9.4656793
## CYP2C9          8.1095034         8.4702701        9.1561793
## SLC22A1         7.8201025         8.8462207        9.1962478
## DCXR            8.2507355         9.1344907        9.2357521
## NR1H4           8.3103626         9.7029623        8.9907979
## FMO3            8.6446953         9.0985845        9.4567708
## ALDH2           8.6077204         9.4690847        9.3710686
## CYP3A5          8.1546223        10.9753996        9.2213121
## RXRA            9.7151449         9.8269709       10.4472455
## COMT            9.5483493        10.0316414       10.5907632
## AKR1A1          9.2867892         9.4018276        9.4503914
## MAOB            9.4490105         9.3392063        9.3314657
## HNF4A           9.3388060         8.7267161        9.8111745
## ABCB1           9.4858330         9.4464389        8.6980425
## UGT1A1          9.5704844         9.7171502        9.3122727
## EPHX1           9.0616637        10.0375667        9.6228432
## MAOA            9.0237360        10.1127974        9.7865482
## CES2            9.5287372         9.2715793        9.5145970
## ABCA2           9.9216256         9.5261486       10.0820977
##          HU1020 coinf d8  HU1016 coinf d8  HU1019 HBV d8  HU1020 HBV d8
## SLCO1A2       -2.1407747     -2.142080827     -2.1426955     -2.1396740
## SLC10A2       -2.0703108     -2.070753080     -2.0709612     -2.0699380
## SULT1A3       -1.8600771     -1.861301031     -1.8618771     -1.8590456
## CYP7A1        -0.7531158     -0.560253778     -0.6126690     -0.7499351
## CYP2C19       -0.5779206     -0.582621748     -0.5255936     -0.5739588
## CYP2A13       -0.2737728     -0.007868856     -0.2755643     -0.2690416
## SULT1A4        0.0000000      0.000000000      0.0000000      0.0000000
## CYP11B2        0.0000000      0.000000000      0.0000000      0.0000000
## CYP2F1         0.0000000      0.000000000      0.0000000      0.0000000
## ABCG4          0.4223212      0.420883315      0.5877911      0.5761270
```

```
## SLCO1B3       2.3842165     2.650212376     2.7397195     2.7906556
## CYP1B1        3.4207818     3.558328602     4.4015762     3.4396905
## GSTM2         3.9877650     4.589101966     4.5921973     4.4836159
## ABCG2         4.2720542     4.004193827     4.5784384     4.4306638
## NR1I3         4.3765689     4.957177914     4.6965842     4.9165921
## DHRS2         4.3439076     4.635876876     4.1929554     4.8130039
## CYP1A2        5.0721003     5.472656030     4.7192351     5.1126522
## HNF4G         5.5327710     6.117483706     5.7408484     6.6166081
## ABCC4         5.8024346     6.184885340     5.3665948     5.4953419
## GSTP1         4.3067439     5.633320760     4.6039842     4.3752611
## NAT1          5.1381066     5.288198524     5.0097776     5.2283818
## UGT1A3        5.2333755     5.756809932     4.9638921     5.6127106
## CYP3A7        5.2735560     5.739853243     5.7552362     4.7978300
## SULT1A2       6.1106498     6.061401372     6.2582216     6.1459858
## NQO1          4.5581212     5.193533008     4.9294771     5.1555220
## ABCB11        5.1033812     5.463519134     5.8054809     5.0662175
## DHRS4         5.6431039     5.837872973     5.4744422     4.6423136
## GSTA4         5.4323712     5.613698015     5.2779985     5.6633281
## FMO4          5.4792596     5.889486898     6.1964899     5.6022653
## GSTA1         8.3901047     8.380354681     8.5604107     9.3894463
## CYP2A6        9.8991166     9.634533944     9.0713357     9.3561124
## EPHX2         8.4669123     8.700186370     8.6961529     8.4942823
## HNMT          8.3874066     8.339858112     8.3467994     8.0864166
## CBR1          8.4367200     8.377041774     8.0048801     8.2773277
## SULT1A1       8.5939763     9.103709791     8.7068970     8.2068460
## CYP2D6        7.7776870     7.314167353     8.7117742     8.1228794
## GSTM1         8.2542641     7.485291271     8.9229305     8.2586171
## ABCG5         7.5993786     7.741160245     7.7792381     7.9656711
## ABCG8         8.0458105     8.037774547     8.1172010     8.1141879
## ABCA6         8.0912338     7.921540976     7.8420509     8.0346702
## CYP1A1        7.4364565     5.779269586     4.8361474     5.4424382
## UGT1A9        6.6504059     7.335965289     7.9514657     7.3348960
## RARA          6.7410392     7.459373918     7.4747211     7.1416516
## ABCC1         7.2593568     7.578216785     7.5727260     6.8232910
## CYP2B6        7.1627032     6.860015290     7.0700028     6.7481525
## SLCO1B1       7.5561108     7.849886019     7.2790651     7.4214366
## HSD11B1       6.6972423     7.808714139     7.9876294     6.6493754
## NAT2          6.6684425     6.425481064     6.9186006     6.9547199
## NR1I2         6.5383585     7.086360623     7.3285857     7.3506498
## NQO2          7.5942003     7.574046009     7.7068488     7.4173830
## AHR           7.3442185     6.764489735     7.0102785     7.3803825
## MGST2         7.3680101     7.476661476     7.6346980     7.2792774
## TPMT          7.2539867     7.196368277     7.2711665     7.3505201
## ALB          17.4652788    17.540231330    17.5455110    17.2909445
## ALDH1A1      13.6862915    13.610503102    13.4827245    14.3755721
## ACTB         12.9423847    13.584004751    13.3982167    12.8563653
## CYP3A4       12.8260631    12.093990095    11.9467105    12.7467342
## ABCC3        11.5966771    11.916495781    11.9686639    11.6842317
## MGST1        12.4414130    12.559043258    12.5561634    12.5880641
## TFRC         10.6183937    10.988153409    10.8095252    10.7312332
## PTGR1        10.5318326    10.374338519    10.8628154    10.6970446
## SULT2A1      11.0412635    10.361238698    10.5769903    11.1323623
## ABCC2        10.7418570    10.659492335    10.5467898    10.8517991
## CES1         11.1992968    10.974090456    10.9312907    11.2508882
```

```
## CYP2E1          8.2072035      6.893487250      7.2641064      7.1750808
## NNMT            7.3699846      8.471571560      9.9530029      9.0102086
## UGT1A6         10.3837370     10.378772310      9.6176460     10.8110482
## CYP2C8         10.1377075      9.871946224      9.6518495      9.2009560
## CYP2C9          9.8033871      9.779545135      9.7306820      9.4585549
## SLC22A1        10.1062889     10.229955138     10.1771984      9.4616334
## DCXR            9.4748002      9.353821239      9.3654398      8.5355205
## NR1H4           9.4869096      8.910851556      9.1728951      9.3028565
## FMO3            9.0214180      9.235975449      9.2046843      9.1840294
## ALDH2           9.3304073      9.682381813      9.3462722      8.8424244
## CYP3A5         10.0979581     10.155804532      9.9737152      9.6562577
## RXRA            9.4646131      9.509128931      9.6607782      9.0908711
## COMT            9.6630812      9.851920803      9.9676993      9.4137767
## AKR1A1          9.4603150      9.570194565      9.5252528      9.4367217
## MAOB            9.8327750      9.778751792      9.9151661      9.9336250
## HNF4A           9.7973698      9.841280610     10.0600011      9.9300536
## ABCB1           9.6397172      9.638909063      9.0395664      9.7577622
## UGT1A1          9.8774059      9.608900140      9.8178420     10.0477178
## EPHX1          10.8033486     10.801597268     10.3995760     10.4069884
## MAOA            9.6821881      9.930447267     10.0242611     10.0708105
## CES2            9.9518738     10.429906783     10.4076200     10.3137198
## ABCA2           9.9000402     10.066003372      9.9440028      9.7734065
##          HU1007 HBV d8 a HU1007 HBV d8 b HU1007 HBV d8 c HU1019 mock d8
## SLCO1A2      -2.1491626      -2.1462098      -2.1488774      -2.1437045
## SLC10A2      -2.0731513      -2.0721514      -2.0730547      -2.0713029
## SULT1A3      -1.8679375      -1.8651704      -1.8676702      -1.8628226
## CYP7A1       -0.5931410      -0.7615678      -0.7621227      -0.7608951
## CYP2C19      -0.5860613      -0.5851937      -0.5859882      -0.5842365
## CYP2A13      -0.2798448      -0.2282399      -0.2417724      -0.2764021
## SULT1A4       0.0000000       0.0000000       0.0000000       0.0000000
## CYP11B2       0.0000000       0.0000000       0.0000000       0.0000000
## CYP2F1        0.0000000       0.0000000       0.0000000       0.0000000
## ABCG4         0.4154275       0.4172727       0.4155831       0.4193025
## SLCO1B3       3.3509686       3.4136794       2.8753190       2.9143097
## CYP1B1        4.4098384       3.8766399       3.8862411       4.0814178
## GSTM2         3.7241601       3.8344058       3.7975757       4.4868468
## ABCG2         5.2136667       4.9371575       5.1891807       3.9359559
## NR1I3         4.7682271       5.3063570       4.3822746       5.3089169
## DHRS2         4.9927133       5.2844978       5.0456297       4.4644953
## CYP1A2        7.8404010       7.8930354       7.7390904       5.2045289
## HNF4G         5.8555566       5.9833202       6.3952999       5.2985845
## ABCC4         6.6081694       5.9418249       6.3300745       5.4107347
## GSTP1         4.7203532       5.1078716       5.2150388       5.6012784
## NAT1          4.7916835       4.9513283       4.7981863       4.6505031
## UGT1A3        5.7437131       5.0722491       5.4611114       5.5729365
## CYP3A7        5.1772263       5.6249635       5.4222744       4.8575695
## SULT1A2       5.7341680       4.8985470       5.1384833       5.5422283
## NQO1          5.2604862       5.4277055       5.6097279       5.2595172
## ABCB11        6.6641576       6.4691223       6.7198894       5.4051657
## DHRS4         5.2019648       5.9586000       5.8259547       5.5567799
## GSTA4         5.8554488       5.2667507       6.2962342       5.2258229
## FMO4          6.2402122       5.7445399       6.1793024       5.9445150
## GSTA1         8.7795778       8.4575070       8.7214828       6.1699925
## CYP2A6        9.1130610       8.8466409       9.1912703       7.9232413
```

```
## EPHX2       8.8137686     8.9870256     8.9944715     8.7346552
## HNMT        8.7451988     8.6795909     8.7775141     8.2653526
## CBR1        8.4895083     7.9664442     8.2551266     7.5887615
## SULT1A1     8.5607418     8.2643861     8.3756889     8.0239237
## CYP2D6      8.0911290     7.8640538     7.8593443     8.4612223
## GSTM1       7.8551866     8.0290072     8.2305085     8.3511059
## ABCG5       7.3478671     7.8911764     7.8825292     7.6416854
## ABCG8       8.0084831     8.0806891     8.1941489     8.2931802
## ABCA6       8.4041371     8.1063717     8.6592653     7.9007858
## CYP1A1      8.6194633     7.9715242     7.7007279     7.9092021
## UGT1A9      8.8039346     8.5544781     9.0355057     6.0064503
## RARA        7.2563566     7.4790992     7.0784928     7.6776214
## ABCC1       7.4971415     7.2432934     7.6136172     7.5942632
## CYP2B6      8.5458999     8.2670489     8.5369431     6.9436038
## SLCO1B1     8.5610689     8.6928330     8.6386438     6.8303267
## HSD11B1     8.1273025     8.6196473     8.5610202     7.5380262
## NAT2        6.5439419     6.7675116     6.5076459     6.4183564
## NR1I2       6.7325826     7.2337365     7.0151648     6.5401639
## NQO2        7.2573785     7.3362368     7.3443591     7.1035176
## AHR         7.0578490     7.1951835     7.0379212     7.0291196
## MGST2       7.0643745     7.1113906     6.9575607     6.9854872
## TPMT        7.3933474     7.4193576     7.3441815     7.0474618
## ALB        17.6109648    17.5791004    17.6041323    17.0560738
## ALDH1A1    13.9045521    14.0751086    14.0827093    12.7567193
## ACTB       13.3408616    13.3764868    13.3559455    12.9479615
## CYP3A4     13.2187211    13.0600841    13.1542489     8.2305067
## ABCC3      11.2252371    11.3282074    11.2711606    12.1231884
## MGST1      12.4101963    12.4392657    12.3695437    12.0128759
## TFRC       11.0818780    11.4574275    11.4248621    10.9876223
## PTGR1      10.7803877    10.7374836    10.8385073    10.9742780
## SULT2A1    11.6638226    11.3518796    11.3689413    10.8569013
## ABCC2      10.9462621    10.9756481    10.9069195    10.1869436
## CES1       11.4933249    11.3168785    11.5624151    10.1638450
## CYP2E1     10.2516749     9.2803845     9.9392711     8.9777753
## NNMT        7.8819469     8.0925481     8.0520765    10.5720184
## UGT1A6     10.1508201     9.9120120    10.1803564     8.3398868
## CYP2C8     10.2734672    10.1441934    10.5004853    10.2828630
## CYP2C9      9.9207342     9.5126656     9.9797877     9.2108240
## SLC22A1    10.2694123    10.2146786    10.1917876     9.0535429
## DCXR        9.1029070     9.1585989     9.2038165     8.9537668
## NR1H4       9.3069195     9.0177112     8.8313597     8.9612703
## FMO3        9.4722993     9.6466318     9.7402940     9.4487566
## ALDH2       9.3953805     9.5068215     9.4799701     9.2374270
## CYP3A5      9.5615997     9.1725216     9.0071656     9.9947787
## RXRA        9.7176754     9.6074845     9.7820669    10.3651960
## COMT        9.6124896     9.6384970     9.6463940    10.0883984
## AKR1A1      9.6240216     9.6357708     9.2688607     9.3981761
## MAOB        9.8182592     9.9838662    10.1176052     9.6502525
## HNF4A       9.8105870     9.9188149    10.0949137     9.7904066
## ABCB1       9.7493828     9.7859631     9.9169184     9.0341788
## UGT1A1     10.5145688    10.2162360    10.4015778     9.7600866
## EPHX1      10.6820857    10.5381801    10.7110522     9.6525288
## MAOA        9.9707668     9.9623909    10.0077208    10.2427650
## CES2       10.3633740    10.4302066    10.6120444     9.8447316
```

```
## ABCA2        10.0479999      10.0457316      10.1712879      10.3559154
##         HU1020 mock d8  HU1007 mock d8 a HU1007 mock d8 b HU1007 mock d8 c
## SLCO1A2      -2.1401042       -2.1506686       -2.1501901       -2.1513138
## SLC10A2      -2.0700837       -2.0736613       -2.0734992       -2.0738504
## SULT1A3      -1.8594487       -1.8688615       -1.8688442       -1.8281368
## CYP7A1       -0.7511783       -0.7624183       -0.7157898       -0.7625119
## CYP2C19      -0.5142770       -0.5864134       -0.3953356       -0.5180301
## CYP2A13      -0.2712742       -0.2805204       -0.2803167       -0.2515125
## SULT1A4       0.0000000        0.0000000        0.0000000        0.0000000
## CYP11B2       0.0000000        0.0000000        0.0000000        0.0000000
## CYP2F1        0.0000000        0.0000000        0.0000000        0.0000000
## ABCG4         0.4231197        0.4146772        0.5192196        0.4143898
## SLCO1B3       2.6390320        2.4031146        3.1790095        3.5741433
## CYP1B1        4.1254620        3.5993280        3.8215648        4.0601471
## GSTM2         3.9650537        3.2341866        3.5547378        3.5157724
## ABCG2         4.9659640        4.4358220        4.8250948        4.6975988
## NR1I3         4.4649574        4.4110776        4.7581889        4.2799672
## DHRS2         3.9650087        5.1011036        4.5654860        4.7496635
## CYP1A2        4.9696625        6.4134616        6.7181807        6.3934135
## HNF4G         6.0443962        5.5195542        6.4375246        5.8923203
## ABCC4         5.8909721        6.7289728        6.6210988        6.8371846
## GSTP1         4.3483188        4.7331342        4.8967064        5.1299241
## NAT1          4.5752890        5.1197084        5.0990452        4.7507145
## UGT1A3        5.6603074        4.6422384        4.5385459        5.4130928
## CYP3A7        5.1409968        5.2484002        5.2419766        5.6451284
## SULT1A2       5.9248960        4.9791808        5.1918592        5.3677326
## NQO1          4.7130647        4.6974217        5.6648095        5.5583095
## ABCB11        4.9432151        6.2500550        6.3904297        5.9252303
## DHRS4         5.2295455        5.9579896        5.8086642        5.2537712
## GSTA4         5.5993797        5.9520360        5.7430952        5.7139721
## FMO4          5.4426449        6.2504298        6.0685218        5.7005021
## GSTA1         8.7565239        7.3743517        8.3666306        7.7611443
## CYP2A6        8.6954340        8.0157142        8.6532200        8.0314821
## EPHX2         8.1787704        8.6906250        8.8533557        8.4207173
## HNMT          8.4801035        8.5202324        8.6701287        8.8155897
## CBR1          7.8326569        7.9527562        7.9961063        7.7618069
## SULT1A1       7.8494125        7.8536301        7.9818944        7.6026140
## CYP2D6        7.2056798        8.3235125        7.7392667        7.6415444
## GSTM1         7.9548127        7.2123940        7.9037099        7.2522032
## ABCG5         7.2441219        7.0052059        7.2812976        7.2647223
## ABCG8         7.8875980        8.2844346        7.8255565        7.8241249
## ABCA6         8.1151642        8.2129927        8.4770157        8.3647432
## CYP1A1        6.0029722        6.2266073        6.5403013        7.0653899
## UGT1A9        7.0524905        8.1806885        8.9345875        8.6384362
## RARA          7.2181948        7.3689697        7.3098201        6.9324728
## ABCC1         7.4472670        8.1068814        7.4826924        7.8265708
## CYP2B6        6.4821605        7.4052663        8.4211519        7.6158243
## SLCO1B1       6.7461262        8.6043004        8.7296189        8.3150160
## HSD11B1       6.4074158        8.1665615        8.9899781        8.1715249
## NAT2          6.9605555        6.6314345        6.4449938        6.0456636
## NR1I2         7.2738403        6.5799774        6.6473414        6.3824448
## NQO2          6.9174375        7.0440973        7.3129187        6.8375527
## AHR           7.5759323        6.6496290        7.4132556        7.1083711
## MGST2         7.2095313        6.9713518        6.8311972        6.8529313
```

```
## TPMT          7.1651540       7.4204636       6.9311410       7.0583192
## ALB          17.0587520      17.1517778      17.5496364      17.3000478
## ALDH1A1      14.1662760      13.1982822      13.7542894      13.4200302
## ACTB         12.9226230      13.2261522      13.3089865      13.2521454
## CYP3A4       12.2626384      11.7406159      12.9347121      12.2126915
## ABCC3        11.6699127      11.1884251      11.0859826      11.0382787
## MGST1        12.4118062      12.2990386      12.3284246      12.2920156
## TFRC         10.8482222      11.2666673      11.4456773      11.2863488
## PTGR1        10.5111963      10.4968211      10.3972824      10.4380910
## SULT2A1      10.8231664      11.0528572      10.5262122      10.6895821
## ABCC2        10.7078050      10.5746125      10.8552522      10.6588110
## CES1         10.9780030      11.0232429      11.1647728      10.9591152
## CYP2E1        6.1047538      10.8728436       8.9190721       9.9622475
## NNMT          8.4869080       9.9591368       7.6508624       9.3870203
## UGT1A6       10.9658372       9.5089124      10.1343769       9.8151667
## CYP2C8        9.0564489       9.5312781      10.1638387       9.5109320
## CYP2C9        9.4216254       9.0901592       9.7417278       9.3391131
## SLC22A1       9.3017110       9.7089322       9.9258006       9.4590080
## DCXR          7.8797615       9.0473148       8.4073663       8.3665747
## NR1H4         9.1218824       8.9974155       8.8797184       9.1066092
## FMO3          8.6199704       9.7608623       9.7505728       9.4115491
## ALDH2         8.7711940       9.4962352       9.4209672       9.2565203
## CYP3A5        9.7756368       8.7402171       8.9051053       9.3019991
## RXRA          9.1417759       9.8039279       9.3588797       9.5049327
## COMT          9.1693281       9.9471834       9.3905322       9.5219875
## AKR1A1        9.3820261       9.6748375       9.1941956       9.3513245
## MAOB          9.6887832       9.9670023      10.2793618       9.9908317
## HNF4A         9.9483701       9.8628740       9.7826968       9.6463650
## ABCB1         9.8492004       9.5707506      10.1250640       9.9461959
## UGT1A1       10.1599465       9.9516899       9.9317559       9.9803789
## EPHX1         9.9755222      10.2408140      10.3123617      10.0923519
## MAOA         10.1307095       9.6300439       9.7627858       9.5641816
## CES2         10.1182400      10.0457365      10.0720609       9.8396557
## ABCA2        10.1117270       9.9996334       9.7401063       9.7693365
##
## $rowDendrogram
## 'dendrogram' with 2 branches and 29 members total, at height 1.414214
##
## $colDendrogram
## 'dendrogram' with 2 branches and 86 members total, at height 102.9304
##
## $breaks
##   [1] -2.500000000 -2.475757576 -2.451515152 -2.427272727 -2.403030303
##   [6] -2.378787879 -2.354545455 -2.330303030 -2.306060606 -2.281818182
##  [11] -2.257575758 -2.233333333 -2.209090909 -2.184848485 -2.160606061
##  [16] -2.136363636 -2.112121212 -2.087878788 -2.063636364 -2.039393939
##  [21] -2.015151515 -1.990909091 -1.966666667 -1.942424242 -1.918181818
##  [26] -1.893939394 -1.869696970 -1.845454545 -1.821212121 -1.796969697
##  [31] -1.772727273 -1.748484848 -1.724242424 -1.700000000 -1.675757576
##  [36] -1.651515152 -1.627272727 -1.603030303 -1.578787879 -1.554545455
##  [41] -1.530303030 -1.506060606 -1.481818182 -1.457575758 -1.433333333
##  [46] -1.409090909 -1.384848485 -1.360606061 -1.336363636 -1.312121212
##  [51] -1.287878788 -1.263636364 -1.239393939 -1.215151515 -1.190909091
##  [56] -1.166666667 -1.142424242 -1.118181818 -1.093939394 -1.069696970
```

```
##  [61] -1.045454545 -1.021212121 -0.996969697 -0.972727273 -0.948484848
##  [66] -0.924242424 -0.900000000 -0.875757576 -0.851515152 -0.827272727
##  [71] -0.803030303 -0.778787879 -0.754545455 -0.730303030 -0.706060606
##  [76] -0.681818182 -0.657575758 -0.633333333 -0.609090909 -0.584848485
##  [81] -0.560606061 -0.536363636 -0.512121212 -0.487878788 -0.463636364
##  [86] -0.439393939 -0.415151515 -0.390909091 -0.366666667 -0.342424242
##  [91] -0.318181818 -0.293939394 -0.269696970 -0.245454545 -0.221212121
##  [96] -0.196969697 -0.172727273 -0.148484848 -0.124242424 -0.100000000
## [101] -0.090000000 -0.068888889 -0.047777778 -0.026666667 -0.005555556
## [106]  0.015555556  0.036666667  0.057777778  0.078888889  0.100000000
## [111]  0.110000000  0.290707071  0.471414141  0.652121212  0.832828283
## [116]  1.013535354  1.194242424  1.374949495  1.555656566  1.736363636
## [121]  1.917070707  2.097777778  2.278484848  2.459191919  2.639898990
## [126]  2.820606061  3.001313131  3.182020202  3.362727273  3.543434343
## [131]  3.724141414  3.904848485  4.085555556  4.266262626  4.446969697
## [136]  4.627676768  4.808383838  4.989090909  5.169797980  5.350505051
## [141]  5.531212121  5.711919192  5.892626263  6.073333333  6.254040404
## [146]  6.434747475  6.615454545  6.796161616  6.976868687  7.157575758
## [151]  7.338282828  7.518989899  7.699696970  7.880404040  8.061111111
## [156]  8.241818182  8.422525253  8.603232323  8.783939394  8.964646465
## [161]  9.145353535  9.326060606  9.506767677  9.687474747  9.868181818
## [166] 10.048888889 10.229595960 10.410303030 10.591010101 10.771717172
## [171] 10.952424242 11.133131313 11.313838384 11.494545455 11.675252525
## [176] 11.855959596 12.036666667 12.217373737 12.398080808 12.578787879
## [181] 12.759494949 12.940202020 13.120909091 13.301616162 13.482323232
## [186] 13.663030303 13.843737374 14.024444444 14.205151515 14.385858586
## [191] 14.566565657 14.747272727 14.927979798 15.108686869 15.289393939
## [196] 15.470101010 15.650808081 15.831515152 16.012222222 16.192929293
## [201] 16.373636364 16.554343434 16.735050505 16.915757576 17.096464646
## [206] 17.277171717 17.457878788 17.638585859 17.819292929 18.000000000
##
## $col
##   [1] "#D8DAEB" "#D8DAEB" "#D8DAEB" "#D9DBEB" "#D9DBEB" "#D9DBEB" "#DADCEC"
##   [8] "#DADCEC" "#DBDCEC" "#DBDDEC" "#DBDDEC" "#DCDDED" "#DCDEED" "#DCDEED"
##  [15] "#DDDEED" "#DDDFED" "#DEDFEE" "#DEE0EE" "#DEE0EE" "#DFE0EE" "#DFE1EE"
##  [22] "#DFE1EF" "#E0E1EF" "#E0E2EF" "#E1E2EF" "#E1E2EF" "#E1E3F0" "#E2E3F0"
##  [29] "#E2E3F0" "#E2E4F0" "#E3E4F0" "#E3E5F0" "#E4E5F1" "#E4E5F1" "#E4E6F1"
##  [36] "#E5E6F1" "#E5E6F1" "#E5E7F2" "#E6E7F2" "#E6E7F2" "#E7E8F2" "#E7E8F2"
##  [43] "#E7E8F3" "#E8E9F3" "#E8E9F3" "#E8EAF3" "#E9EAF3" "#E9EAF4" "#EAEBF4"
##  [50] "#EAEBF4" "#EAEBF4" "#EBECF4" "#EBECF4" "#EBECF5" "#ECEDF5" "#ECEDF5"
##  [57] "#EDEDF5" "#EDEEF5" "#EDEEF6" "#EEEEF6" "#EEEFF6" "#EEEFF6" "#EFF0F6"
##  [64] "#EFF0F7" "#F0F0F7" "#F0F1F7" "#F0F1F7" "#F1F1F7" "#F1F2F8" "#F1F2F8"
##  [71] "#F2F2F8" "#F2F3F8" "#F3F3F8" "#F3F3F9" "#F3F4F9" "#F4F4F9" "#F4F5F9"
##  [78] "#F4F5F9" "#F5F5FA" "#F5F6FA" "#F6F6FA" "#F6F6FA" "#F6F7FA" "#F7F7FA"
##  [85] "#F7F7FB" "#F7F8FB" "#F8F8FB" "#F8F8FB" "#F9F9FB" "#F9F9FC" "#F9FAFC"
##  [92] "#FAFAFC" "#FAFAFC" "#FAFBFC" "#FBFBFD" "#FBFBFD" "#FCFCFD" "#FCFCFD"
##  [99] "#FCFCFD" "#FDFDFE" "#FDFDFE" "#FDFDFE" "#FEFEFE" "#FEFEFE" "#FFFFFF"
## [106] "#FDFCFD" "#FBFAFC" "#FAF8FB" "#F8F6FA" "#F6F4F9" "#F5F2F8" "#F3F0F6"
## [113] "#F1EEF5" "#F0ECF4" "#EEEAF3" "#ECE8F2" "#EBE6F1" "#E9E4F0" "#E7E1EE"
## [120] "#E6DFED" "#E4DDEC" "#E3DBEB" "#E1D9EA" "#DFD7E9" "#DED5E8" "#DCD3E6"
## [127] "#DAD1E5" "#D9CFE4" "#D7CDE3" "#D5CBE2" "#D4C9E1" "#D2C6E0" "#D0C4DE"
## [134] "#CFC2DD" "#CDC0DC" "#CCBEDB" "#CABCDA" "#C8BAD9" "#C7B8D8" "#C5B6D6"
## [141] "#C3B4D5" "#C2B2D4" "#C0B0D3" "#BEAED2" "#BDABD1" "#BBA9D0" "#B9A7CE"
## [148] "#B8A5CD" "#B6A3CC" "#B5A1CB" "#B39FCA" "#B19DC9" "#B09BC8" "#AE99C6"
```

```
## [155] "#AC97C5" "#AB95C4" "#A993C3" "#A790C2" "#A68EC1" "#A48CC0" "#A28ABE"
## [162] "#A188BD" "#9F86BC" "#9D84BB" "#9C82BA" "#9A80B9" "#997EB8" "#977CB6"
## [169] "#957AB5" "#9478B4" "#9275B3" "#9073B2" "#8F71B1" "#8D6FB0" "#8B6DAE"
## [176] "#8A6BAD" "#8869AC" "#8667AB" "#8565AA" "#8363A9" "#8261A8" "#805FA6"
## [183] "#7E5DA5" "#7D5AA4" "#7B58A3" "#7956A2" "#7854A1" "#7652A0" "#74509E"
## [190] "#734E9D" "#714C9C" "#6F4A9B" "#6E489A" "#6C4699" "#6B4498" "#694196"
## [197] "#673F95" "#663D94" "#643B93" "#623992" "#613791" "#5F3590" "#5D338E"
## [204] "#5C318D" "#5A2F8C" "#582D8B" "#572B8A" "#552989" "#542788"
##
## $colorTable
##              low         high   color
## 1   -2.500000000 -2.475757576 #D8DAEB
## 2   -2.475757576 -2.451515152 #D8DAEB
## 3   -2.451515152 -2.427272727 #D8DAEB
## 4   -2.427272727 -2.403030303 #D9DBEB
## 5   -2.403030303 -2.378787879 #D9DBEB
## 6   -2.378787879 -2.354545455 #D9DBEB
## 7   -2.354545455 -2.330303030 #DADCEC
## 8   -2.330303030 -2.306060606 #DADCEC
## 9   -2.306060606 -2.281818182 #DBDCEC
## 10  -2.281818182 -2.257575758 #DBDDEC
## 11  -2.257575758 -2.233333333 #DBDDEC
## 12  -2.233333333 -2.209090909 #DCDDED
## 13  -2.209090909 -2.184848485 #DCDEED
## 14  -2.184848485 -2.160606061 #DCDEED
## 15  -2.160606061 -2.136363636 #DDDEED
## 16  -2.136363636 -2.112121212 #DDDFED
## 17  -2.112121212 -2.087878788 #DEDFEE
## 18  -2.087878788 -2.063636364 #DEE0EE
## 19  -2.063636364 -2.039393939 #DEE0EE
## 20  -2.039393939 -2.015151515 #DFE0EE
## 21  -2.015151515 -1.990909091 #DFE1EE
## 22  -1.990909091 -1.966666667 #DFE1EF
## 23  -1.966666667 -1.942424242 #E0E1EF
## 24  -1.942424242 -1.918181818 #E0E2EF
## 25  -1.918181818 -1.893939394 #E1E2EF
## 26  -1.893939394 -1.869696970 #E1E2EF
## 27  -1.869696970 -1.845454545 #E1E3F0
## 28  -1.845454545 -1.821212121 #E2E3F0
## 29  -1.821212121 -1.796969697 #E2E3F0
## 30  -1.796969697 -1.772727273 #E2E4F0
## 31  -1.772727273 -1.748484848 #E3E4F0
## 32  -1.748484848 -1.724242424 #E3E5F0
## 33  -1.724242424 -1.700000000 #E4E5F1
## 34  -1.700000000 -1.675757576 #E4E5F1
## 35  -1.675757576 -1.651515152 #E4E6F1
## 36  -1.651515152 -1.627272727 #E5E6F1
## 37  -1.627272727 -1.603030303 #E5E6F1
## 38  -1.603030303 -1.578787879 #E5E7F2
## 39  -1.578787879 -1.554545455 #E6E7F2
## 40  -1.554545455 -1.530303030 #E6E7F2
## 41  -1.530303030 -1.506060606 #E7E8F2
## 42  -1.506060606 -1.481818182 #E7E8F2
## 43  -1.481818182 -1.457575758 #E7E8F3
```

```
## 44  -1.457575758 -1.433333333 #E8E9F3
## 45  -1.433333333 -1.409090909 #E8E9F3
## 46  -1.409090909 -1.384848485 #E8EAF3
## 47  -1.384848485 -1.360606061 #E9EAF3
## 48  -1.360606061 -1.336363636 #E9EAF4
## 49  -1.336363636 -1.312121212 #EAEBF4
## 50  -1.312121212 -1.287878788 #EAEBF4
## 51  -1.287878788 -1.263636364 #EAEBF4
## 52  -1.263636364 -1.239393939 #EBECF4
## 53  -1.239393939 -1.215151515 #EBECF4
## 54  -1.215151515 -1.190909091 #EBECF5
## 55  -1.190909091 -1.166666667 #ECEDF5
## 56  -1.166666667 -1.142424242 #ECEDF5
## 57  -1.142424242 -1.118181818 #EDEDF5
## 58  -1.118181818 -1.093939394 #EDEEF5
## 59  -1.093939394 -1.069696970 #EDEEF6
## 60  -1.069696970 -1.045454545 #EEEEF6
## 61  -1.045454545 -1.021212121 #EEEFF6
## 62  -1.021212121 -0.996969697 #EEEFF6
## 63  -0.996969697 -0.972727273 #EFF0F6
## 64  -0.972727273 -0.948484848 #EFF0F7
## 65  -0.948484848 -0.924242424 #F0F0F7
## 66  -0.924242424 -0.900000000 #F0F1F7
## 67  -0.900000000 -0.875757576 #F0F1F7
## 68  -0.875757576 -0.851515152 #F1F1F7
## 69  -0.851515152 -0.827272727 #F1F2F8
## 70  -0.827272727 -0.803030303 #F1F2F8
## 71  -0.803030303 -0.778787879 #F2F2F8
## 72  -0.778787879 -0.754545455 #F2F3F8
## 73  -0.754545455 -0.730303030 #F3F3F8
## 74  -0.730303030 -0.706060606 #F3F3F9
## 75  -0.706060606 -0.681818182 #F3F4F9
## 76  -0.681818182 -0.657575758 #F4F4F9
## 77  -0.657575758 -0.633333333 #F4F5F9
## 78  -0.633333333 -0.609090909 #F4F5F9
## 79  -0.609090909 -0.584848485 #F5F5FA
## 80  -0.584848485 -0.560606061 #F5F6FA
## 81  -0.560606061 -0.536363636 #F6F6FA
## 82  -0.536363636 -0.512121212 #F6F6FA
## 83  -0.512121212 -0.487878788 #F6F7FA
## 84  -0.487878788 -0.463636364 #F7F7FA
## 85  -0.463636364 -0.439393939 #F7F7FB
## 86  -0.439393939 -0.415151515 #F7F8FB
## 87  -0.415151515 -0.390909091 #F8F8FB
## 88  -0.390909091 -0.366666667 #F8F8FB
## 89  -0.366666667 -0.342424242 #F9F9FB
## 90  -0.342424242 -0.318181818 #F9F9FC
## 91  -0.318181818 -0.293939394 #F9FAFC
## 92  -0.293939394 -0.269696970 #FAFAFC
## 93  -0.269696970 -0.245454545 #FAFAFC
## 94  -0.245454545 -0.221212121 #FAFBFC
## 95  -0.221212121 -0.196969697 #FBFBFD
## 96  -0.196969697 -0.172727273 #FBFBFD
## 97  -0.172727273 -0.148484848 #FCFCFD
```

```
## 98  -0.148484848 -0.124242424 #FCFCFD
## 99  -0.124242424 -0.100000000 #FCFCFD
## 100 -0.100000000 -0.090000000 #FDFDFE
## 101 -0.090000000 -0.068888889 #FDFDFE
## 102 -0.068888889 -0.047777778 #FDFDFE
## 103 -0.047777778 -0.026666667 #FEFEFE
## 104 -0.026666667 -0.005555556 #FEFEFE
## 105 -0.005555556  0.015555556 #FFFFFF
## 106  0.015555556  0.036666667 #FDFCFD
## 107  0.036666667  0.057777778 #FBFAFC
## 108  0.057777778  0.078888889 #FAF8FB
## 109  0.078888889  0.100000000 #F8F6FA
## 110  0.100000000  0.110000000 #F6F4F9
## 111  0.110000000  0.290707071 #F5F2F8
## 112  0.290707071  0.471414141 #F3F0F6
## 113  0.471414141  0.652121212 #F1EEF5
## 114  0.652121212  0.832828283 #F0ECF4
## 115  0.832828283  1.013535354 #EEEAF3
## 116  1.013535354  1.194242424 #ECE8F2
## 117  1.194242424  1.374949495 #EBE6F1
## 118  1.374949495  1.555656566 #E9E4F0
## 119  1.555656566  1.736363636 #E7E1EE
## 120  1.736363636  1.917070707 #E6DFED
## 121  1.917070707  2.097777778 #E4DDEC
## 122  2.097777778  2.278484848 #E3DBEB
## 123  2.278484848  2.459191919 #E1D9EA
## 124  2.459191919  2.639898990 #DFD7E9
## 125  2.639898990  2.820606061 #DED5E8
## 126  2.820606061  3.001313131 #DCD3E6
## 127  3.001313131  3.182020202 #DAD1E5
## 128  3.182020202  3.362727273 #D9CFE4
## 129  3.362727273  3.543434343 #D7CDE3
## 130  3.543434343  3.724141414 #D5CBE2
## 131  3.724141414  3.904848485 #D4C9E1
## 132  3.904848485  4.085555556 #D2C6E0
## 133  4.085555556  4.266262626 #D0C4DE
## 134  4.266262626  4.446969697 #CFC2DD
## 135  4.446969697  4.627676768 #CDC0DC
## 136  4.627676768  4.808383838 #CCBEDB
## 137  4.808383838  4.989090909 #CABCDA
## 138  4.989090909  5.169797980 #C8BAD9
## 139  5.169797980  5.350505051 #C7B8D8
## 140  5.350505051  5.531212121 #C5B6D6
## 141  5.531212121  5.711919192 #C3B4D5
## 142  5.711919192  5.892626263 #C2B2D4
## 143  5.892626263  6.073333333 #C0B0D3
## 144  6.073333333  6.254040404 #BEAED2
## 145  6.254040404  6.434747475 #BDABD1
## 146  6.434747475  6.615454545 #BBA9D0
## 147  6.615454545  6.796161616 #B9A7CE
## 148  6.796161616  6.976868687 #B8A5CD
## 149  6.976868687  7.157575758 #B6A3CC
## 150  7.157575758  7.338282828 #B5A1CB
## 151  7.338282828  7.518989899 #B39FCA
```

```
## 152  7.518989899  7.699696970 #B19DC9
## 153  7.699696970  7.880404040 #B09BC8
## 154  7.880404040  8.061111111 #AE99C6
## 155  8.061111111  8.241818182 #AC97C5
## 156  8.241818182  8.422525253 #AB95C4
## 157  8.422525253  8.603232323 #A993C3
## 158  8.603232323  8.783939394 #A790C2
## 159  8.783939394  8.964646465 #A68EC1
## 160  8.964646465  9.145353535 #A48CC0
## 161  9.145353535  9.326060606 #A28ABE
## 162  9.326060606  9.506767677 #A188BD
## 163  9.506767677  9.687474747 #9F86BC
## 164  9.687474747  9.868181818 #9D84BB
## 165  9.868181818 10.048888889 #9C82BA
## 166 10.048888889 10.229595960 #9A80B9
## 167 10.229595960 10.410303030 #997EB8
## 168 10.410303030 10.591010101 #977CB6
## 169 10.591010101 10.771717172 #957AB5
## 170 10.771717172 10.952424242 #9478B4
## 171 10.952424242 11.133131313 #9275B3
## 172 11.133131313 11.313838384 #9073B2
## 173 11.313838384 11.494545455 #8F71B1
## 174 11.494545455 11.675252525 #8D6FB0
## 175 11.675252525 11.855959596 #8B6DAE
## 176 11.855959596 12.036666667 #8A6BAD
## 177 12.036666667 12.217373737 #8869AC
## 178 12.217373737 12.398080808 #8667AB
## 179 12.398080808 12.578787879 #8565AA
## 180 12.578787879 12.759494949 #8363A9
## 181 12.759494949 12.940202020 #8261A8
## 182 12.940202020 13.120909091 #805FA6
## 183 13.120909091 13.301616162 #7E5DA5
## 184 13.301616162 13.482323232 #7D5AA4
## 185 13.482323232 13.663030303 #7B58A3
## 186 13.663030303 13.843737374 #7956A2
## 187 13.843737374 14.024444444 #7854A1
## 188 14.024444444 14.205151515 #7652A0
## 189 14.205151515 14.385858586 #74509E
## 190 14.385858586 14.566565657 #734E9D
## 191 14.566565657 14.747272727 #714C9C
## 192 14.747272727 14.927979798 #6F4A9B
## 193 14.927979798 15.108686869 #6E489A
## 194 15.108686869 15.289393939 #6C4699
## 195 15.289393939 15.470101010 #6B4498
## 196 15.470101010 15.650808081 #694196
## 197 15.650808081 15.831515152 #673F95
## 198 15.831515152 16.012222222 #663D94
## 199 16.012222222 16.192929293 #643B93
## 200 16.192929293 16.373636364 #623992
## 201 16.373636364 16.554343434 #613791
## 202 16.554343434 16.735050505 #5F3590
## 203 16.735050505 16.915757576 #5D338E
## 204 16.915757576 17.096464646 #5C318D
## 205 17.096464646 17.277171717 #5A2F8C
```

```
## 206 17.277171717 17.457878788 #582D8B
## 207 17.457878788 17.638585859 #572B8A
## 208 17.638585859 17.819292929 #552989
## 209 17.819292929 18.000000000 #542788
##
## $layout
## $layout$lmat
##      [,1] [,2]
## [1,]    4    3
## [2,]    2    1
##
## $layout$lhei
## [1] 0.7 4.0
##
## $layout$lwid
## [1] 0.7 4.0
```

```
dev.off()
```

```
## pdf
##   2
```

Session Info

```
sessionInfo()
```

```
## R version 3.3.3 (2017-03-06)
## Platform: x86_64-apple-darwin13.4.0 (64-bit)
## Running under: macOS Sierra 10.12.6
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
## [1] parallel  stats4    stats     graphics  grDevices utils     datasets
## [8] methods   base
##
## other attached packages:
##  [1] org.Hs.eg.db_3.3.0         AnnotationDbi_1.34.4
##  [3] gtools_3.5.0               tidyr_0.7.1
##  [5] viridis_0.4.0              viridisLite_0.2.0
##  [7] ggrepel_0.6.5              data.table_1.10.0
##  [9] genefilter_1.54.2          RColorBrewer_1.1-2
## [11] tibble_1.3.3               gplots_3.0.1
## [13] DESeq2_1.12.4              SummarizedExperiment_1.2.3
## [15] Biobase_2.32.0             GenomicRanges_1.24.3
## [17] GenomeInfoDb_1.8.7         IRanges_2.6.1
## [19] S4Vectors_0.10.3           BiocGenerics_0.18.0
## [21] openxlsx_4.0.17            reshape2_1.4.2
## [23] ggplot2_2.2.1              stringr_1.2.0
## [25] dplyr_0.7.3                gageData_2.10.0
## [27] gage_2.22.0
##
## loaded via a namespace (and not attached):
##  [1] httr_1.2.1          splines_3.3.3       Formula_1.2-1
##  [4] assertthat_0.2.0    latticeExtra_0.6-28 yaml_2.1.14
```

```
##  [7] RSQLite_1.1-2       backports_1.0.5     lattice_0.20-35
## [10] glue_1.1.1          digest_0.6.12       XVector_0.12.1
## [13] checkmate_1.8.2     colorspace_1.3-2    htmltools_0.3.5
## [16] Matrix_1.2-8        plyr_1.8.4          XML_3.98-1.9
## [19] pkgconfig_2.0.1     zlibbioc_1.18.0     purrr_0.2.2
## [22] xtable_1.8-2        scales_0.4.1        gdata_2.17.0
## [25] BiocParallel_1.6.6  htmlTable_1.9       annotate_1.50.1
## [28] KEGGREST_1.12.3     nnet_7.3-12         lazyeval_0.2.0
## [31] survival_2.41-3     magrittr_1.5        memoise_1.0.0
## [34] evaluate_0.10       foreign_0.8-67      graph_1.50.0
## [37] tools_3.3.3         locfit_1.5-9.1      munsell_0.4.3
## [40] cluster_2.0.6       bindrcpp_0.2        Biostrings_2.40.2
## [43] caTools_1.17.1      rlang_0.1.2         grid_3.3.3
## [46] RCurl_1.95-4.8      htmlwidgets_0.9     bitops_1.0-6
## [49] base64enc_0.1-3     rmarkdown_1.4       gtable_0.2.0
## [52] DBI_0.6-1           R6_2.2.0            gridExtra_2.2.1
## [55] knitr_1.16          bindr_0.1           Hmisc_4.0-2
## [58] rprojroot_1.2       KernSmooth_2.23-15  stringi_1.1.5
## [61] Rcpp_0.12.10        geneplotter_1.50.0  rpart_4.1-10
## [64] acepack_1.4.1       png_0.1-7
```