Class_15

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Load the contData and colData

it requires 2 things: 1. count data 2. colData (the metadata that tells us about the design of the experiment)

```
library(BiocManager)
```

read in the data

```
counts <- read.csv("airway_scaledcounts.csv", row.names=1)
metadata <-  read.csv("airway_metadata.csv")
```

look at the files

```
head(counts)
```

```
##                 SRR1039508 SRR1039509 SRR1039512 SRR1039513 SRR1039516
## ENSG00000000003        723        486        904        445       1170
## ENSG00000000005          0          0          0          0          0
## ENSG00000000419        467        523        616        371        582
## ENSG00000000457        347        258        364        237        318
## ENSG00000000460         96         81         73         66        118
## ENSG00000000938          0          0          1          0          2
##                 SRR1039517 SRR1039520 SRR1039521
## ENSG00000000003       1097        806        604
## ENSG00000000005          0          0          0
## ENSG00000000419        781        417        509
## ENSG00000000457        447        330        324
## ENSG00000000460         94        102         74
## ENSG00000000938          0          0          0
```

```
head(metadata)
```

```
##           id     dex celltype     geo_id
## 1 SRR1039508 control   N61311 GSM1275862
## 2 SRR1039509 treated   N61311 GSM1275863
## 3 SRR1039512 control  N052611 GSM1275866
## 4 SRR1039513 treated  N052611 GSM1275867
## 5 SRR1039516 control  N080611 GSM1275870
## 6 SRR1039517 treated  N080611 GSM1275871
```

Side-note: Lets check the correspondence of the metadata and count data setup.

```
metadata$id
```

```
## [1] "SRR1039508" "SRR1039509" "SRR1039512" "SRR1039513" "SRR1039516"
## [6] "SRR1039517" "SRR1039520" "SRR1039521"
```

or we can use:

```
colnames(counts)
```

```
## [1] "SRR1039508" "SRR1039509" "SRR1039512" "SRR1039513" "SRR1039516"
## [6] "SRR1039517" "SRR1039520" "SRR1039521"
```

We can use the `==` things to see if they are the same.

```
metadata$id==colnames(counts)
```

```
## [1] TRUE TRUE TRUE TRUE TRUE TRUE TRUE TRUE
```

This function will look at what you are telling it to and tell if you it is true or not

```
all( c(T,T,F))
```

```
## [1] FALSE
```

For example:

```
all(metadata$id==colnames(counts))
```

```
## [1] TRUE
```

> Q1.How many genes ?

```
nrow(counts)
```

```
## [1] 38694
```

> Q2.How many control groups are there?

```
head(metadata)
```

```
##           id     dex celltype     geo_id
## 1 SRR1039508 control   N61311 GSM1275862
## 2 SRR1039509 treated   N61311 GSM1275863
## 3 SRR1039512 control  N052611 GSM1275866
## 4 SRR1039513 treated  N052611 GSM1275867
## 5 SRR1039516 control  N080611 GSM1275870
## 6 SRR1039517 treated  N080611 GSM1275871
```

There are 38694 rows/genes in this dataset. There are 3 control gorups in this dataset.

Compare control to treated

First, extract the data from the control groups(columns) in our counts data

```
control.inds <- metadata$dex=="control"
metadata[control.inds, ]
```

```
##          id     dex celltype     geo_id
## 1 SRR1039508 control   N61311 GSM1275862
## 3 SRR1039512 control  N052611 GSM1275866
## 5 SRR1039516 control  N080611 GSM1275870
## 7 SRR1039520 control  N061011 GSM1275874
```

Just to get the ID use:

```
control.inds <- metadata[control.inds, ]$id
```

Now we use these ids to access just the control columns for our `counts` data

```
head(counts[, control.inds])
```

```
##                 SRR1039508 SRR1039512 SRR1039516 SRR1039520
## ENSG00000000003        723        904       1170        806
## ENSG00000000005          0          0          0          0
## ENSG00000000419        467        616        582        417
## ENSG00000000457        347        364        318        330
## ENSG00000000460         96         73        118        102
## ENSG00000000938          0          1          2          0
```

this is the count data just for the control groups.

now get the mean of the genes (rows):

```
control.mean <- rowMeans(counts[, control.inds])
head(control.mean)
```

```
## ENSG00000000003 ENSG00000000005 ENSG00000000419 ENSG00000000457 ENSG00000000460
##          900.75            0.00          520.50          339.75           97.25
## ENSG00000000938
##            0.75
```

Now do the same for the treated groups:

```
treated.id <- metadata[ metadata$dex=="treated",] $id
head(treated.id)
```

```
## [1] "SRR1039509" "SRR1039513" "SRR1039517" "SRR1039521"
```

```
treated.mean <- rowMeans(counts[, treated.id])
head(treated.mean)
```

```
## ENSG00000000003 ENSG00000000005 ENSG00000000419 ENSG00000000457 ENSG00000000460
##          658.00            0.00          546.00          316.50           78.75
## ENSG00000000938
##            0.00
```

Now combine these two means

```
meancounts <- data.frame(control.mean, treated.mean)
# meancounts
colSums(meancounts)
```

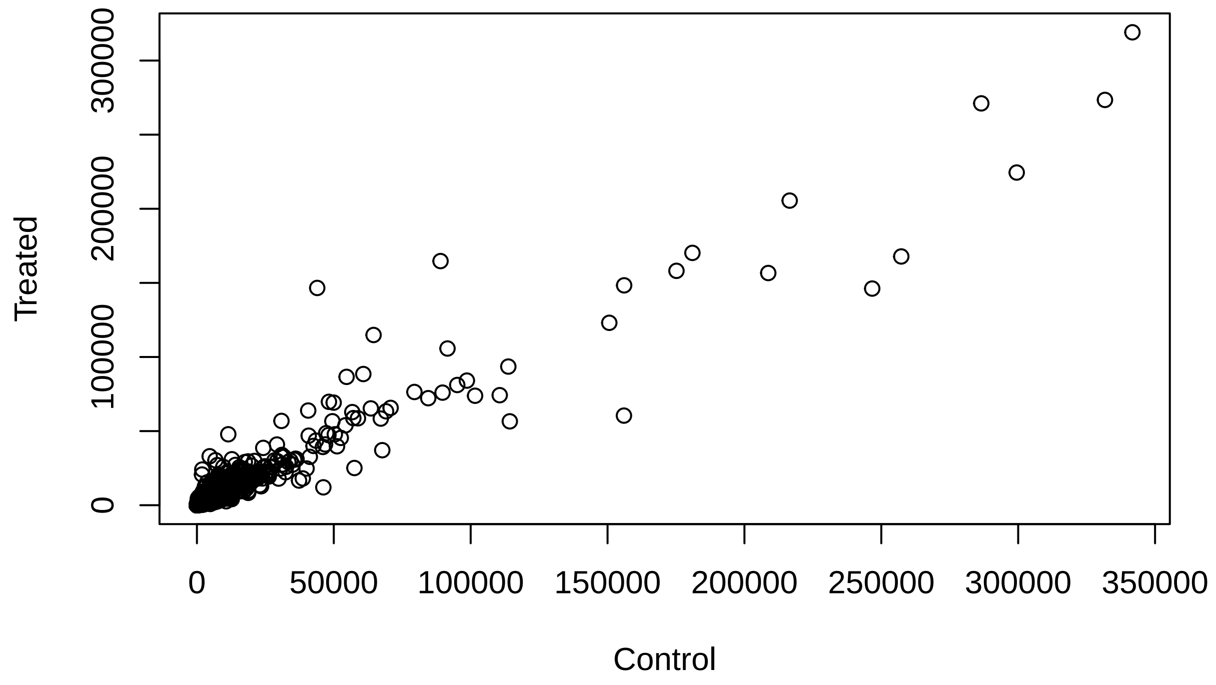
```
## control.mean treated.mean
##     23005324     22196524
```

The colSums shows you the summary for both columns

Now visualize by plotting

```
library(ggplot2)
```

```
plot(meancounts[,1],meancounts[,2], xlab="Control", ylab="Treated")
```

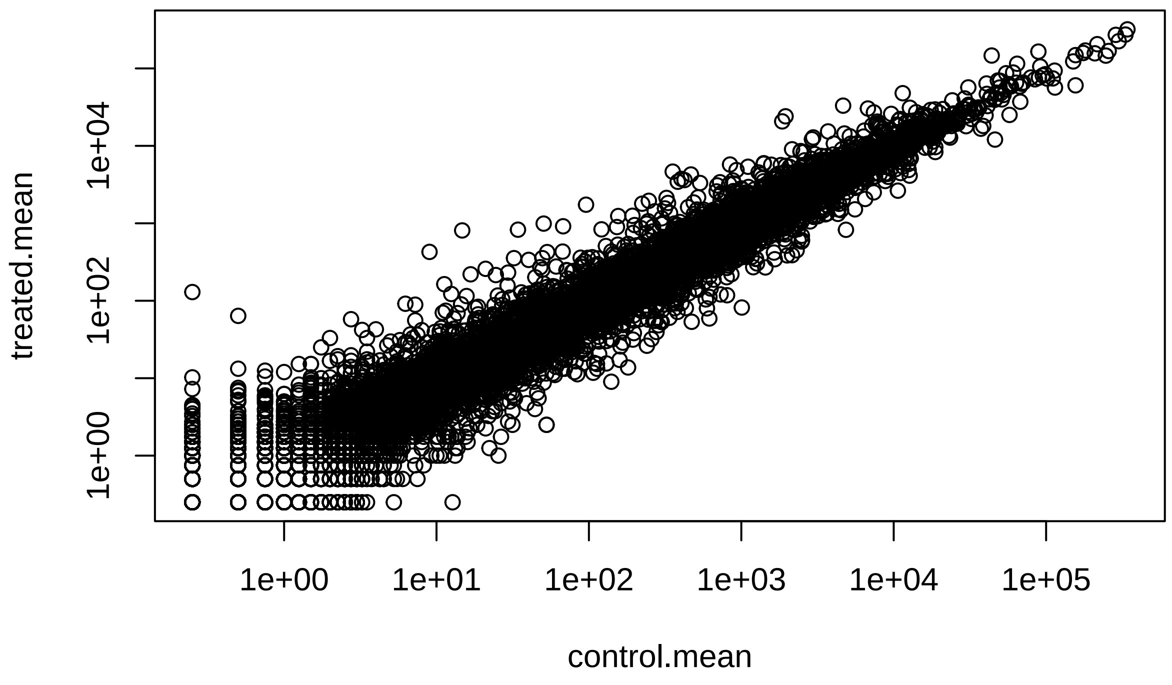


This would benefit from a log transformation.

```r
plot(meancounts, log="xy")
```

```
## Warning in xy.coords(x, y, xlabel, ylabel, log): 15032 x values <= 0 omitted
## from logarithmic plot

## Warning in xy.coords(x, y, xlabel, ylabel, log): 15281 y values <= 0 omitted
## from logarithmic plot
```



We often use log transformations as they make life much nicer in this world.

For example:

```r
log2(20/20)
```

```
## [1] 0
```

```r
# this indicates that there is no change
```

```r
log2(40/20)
```

```
## [1] 1
```

```
log2(10/20)
```

```
## [1] -1
```

```
log2(80/20)
```

```
## [1] 2
```

```
#this is doubling. Gene expression would be doubling
```

```
meancounts$log2fc <- log2(meancounts[,"treated.mean"]/meancounts[,"control.mean"])
head(meancounts)
```

```
##                 control.mean treated.mean      log2fc
## ENSG00000000003       900.75       658.00 -0.45303916
## ENSG00000000005         0.00         0.00         NaN
## ENSG00000000419       520.50       546.00  0.06900279
## ENSG00000000457       339.75       316.50 -0.10226805
## ENSG00000000460        97.25        78.75 -0.30441833
## ENSG00000000938         0.75         0.00        -Inf
```

Now remove the genes that have 0 values

```
head(meancounts[,1:2])
```

```
##                 control.mean treated.mean
## ENSG00000000003       900.75       658.00
## ENSG00000000005         0.00         0.00
## ENSG00000000419       520.50       546.00
## ENSG00000000457       339.75       316.50
## ENSG00000000460        97.25        78.75
## ENSG00000000938         0.75         0.00
```

Lets look at which ones have zero values

```
head(meancounts[,1:2] ==0)
```

```
##                 control.mean treated.mean
## ENSG00000000003        FALSE        FALSE
## ENSG00000000005         TRUE         TRUE
## ENSG00000000419        FALSE        FALSE
## ENSG00000000457        FALSE        FALSE
## ENSG00000000460        FALSE        FALSE
## ENSG00000000938        FALSE         TRUE
```

Now remove those that have zero values

The `which` function tells us teh indices of the TRUE entries in a logical vector.

```r
which(c(T,F,T))
```

```
## [1] 1 3
```

However, it isnt that useful in the default mode on our type of multi column input …

```r
ind <- which(meancounts[,1:2] == 0, arr.ind=T)[,"row"]
head(ind)
```

```
## ENSG00000000005 ENSG00000004848 ENSG00000004948 ENSG00000005001 ENSG00000006059
##               2              65              70              73             121
## ENSG00000006071
##             123
```

I only care about the rows here (if there is a zero in any column I will exclude this row eventually)

```r
to.rm <- unique(sort(ind))
mycounts <- meancounts[-to.rm,]
head(mycounts)
```

```
##                 control.mean treated.mean      log2fc
## ENSG00000000003       900.75       658.00 -0.45303916
## ENSG00000000419       520.50       546.00  0.06900279
## ENSG00000000457       339.75       316.50 -0.10226805
## ENSG00000000460        97.25        78.75 -0.30441833
## ENSG00000000971      5219.00      6687.50  0.35769358
## ENSG00000001036      2327.00      1785.75 -0.38194109
```

We now hae 21817 genes remaining

```r
nrow(mycounts)
```

```
## [1] 21817
```

How many of these genes are upregulated at the log2 fold-change threshold of +2 or greater?

```r
sum(mycounts$log2fc > +2)
```

```
## [1] 250
```

What percetnage is this?

```r
round(sum(mycounts$log2fc > +2) / nrow(mycounts) * 100, 2)
```

```
## [1] 1.15
```

How many of these genes are down regulated at the log2 fold-change threshold of -2 or greater?

```
sum(mycounts$log2fc < -2)
```

```
## [1] 367
```

```
round(sum(mycounts$log2fc < -2) / nrow(mycounts) * 100, 2)
```

```
## [1] 1.68
```

DESeq Analysis

First set it up

```
library(DESeq2)
```

```
## Loading required package: S4Vectors

## Loading required package: stats4

## Loading required package: BiocGenerics

##
## Attaching package: 'BiocGenerics'

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

## The following objects are masked from 'package:base':
##
##     anyDuplicated, append, as.data.frame, basename, cbind, colnames,
##     dirname, do.call, duplicated, eval, evalq, Filter, Find, get, grep,
##     grepl, intersect, is.unsorted, lapply, 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, which.max, which.min

##
## Attaching package: 'S4Vectors'

## The following objects are masked from 'package:base':
##
##     expand.grid, I, unname

## Loading required package: IRanges

## Loading required package: GenomicRanges

## Loading required package: GenomeInfoDb
## Loading required package: SummarizedExperiment

## Loading required package: MatrixGenerics

## Loading required package: matrixStats

##
## Attaching package: 'MatrixGenerics'

## The following objects are masked from 'package:matrixStats':
##
##     colAlls, colAnyNAs, colAnys, colAvgsPerRowSet, colCollapse,
##     colCounts, colCummaxs, colCummins, colCumprods, colCumsums,
##     colDiffs, colIQRDiffs, colIQRs, colLogSumExps, colMadDiffs,
##     colMads, colMaxs, colMeans2, colMedians, colMins, colOrderStats,
##     colProds, colQuantiles, colRanges, colRanks, colSdDiffs, colSds,
##     colSums2, colTabulates, colVarDiffs, colVars, colWeightedMads,
##     colWeightedMeans, colWeightedMedians, colWeightedSds,
##     colWeightedVars, rowAlls, rowAnyNAs, rowAnys, rowAvgsPerColSet,
##     rowCollapse, rowCounts, rowCummaxs, rowCummins, rowCumprods,
##     rowCumsums, rowDiffs, rowIQRDiffs, rowIQRs, rowLogSumExps,
##     rowMadDiffs, rowMads, rowMaxs, rowMeans2, rowMedians, rowMins,
##     rowOrderStats, rowProds, rowQuantiles, rowRanges, rowRanks,
##     rowSdDiffs, rowSds, rowSums2, rowTabulates, rowVarDiffs, rowVars,
##     rowWeightedMads, rowWeightedMeans, rowWeightedMedians,
##     rowWeightedSds, rowWeightedVars

## 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")'.

##
## Attaching package: 'Biobase'

## The following object is masked from 'package:MatrixGenerics':
##
##     rowMedians

## The following objects are masked from 'package:matrixStats':
##
##     anyMissing, rowMedians
```

```
dds <- DESeqDataSetFromMatrix(countData=counts,
                              colData=metadata,
                              design=~dex)
```

```
## converting counts to integer mode
## Warning in DESeqDataSet(se, design = design, ignoreRank): some variables in
## design formula are characters, converting to factors
```

```
dds
```

```
## class: DESeqDataSet
## dim: 38694 8
## metadata(1): version
## assays(1): counts
## rownames(38694): ENSG00000000003 ENSG00000000005 ... ENSG00000283120
##   ENSG00000283123
## rowData names(0):
## colnames(8): SRR1039508 SRR1039509 ... SRR1039520 SRR1039521
## colData names(4): id dex celltype geo_id
```

Run the DESeq analysis pipeline.

```
dds <- DESeq(dds)
```

```
## estimating size factors

## estimating dispersions

## gene-wise dispersion estimates

## mean-dispersion relationship

## final dispersion estimates

## fitting model and testing
```

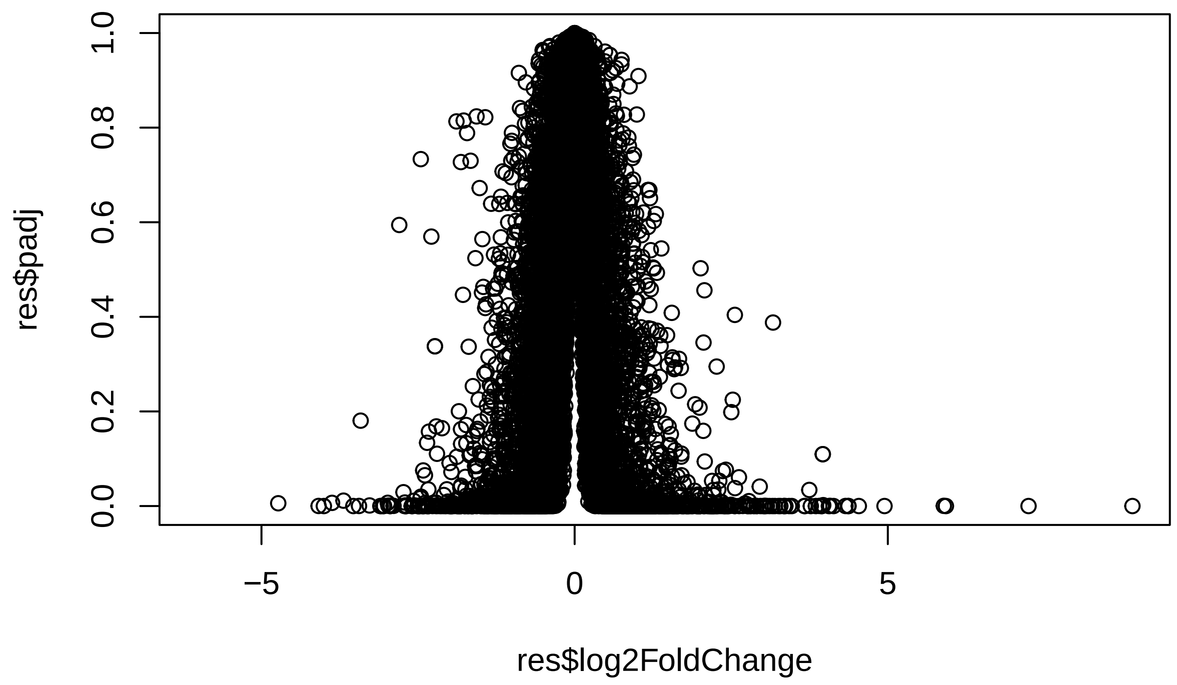
```
res <- results(dds)
res
```

```
## log2 fold change (MLE): dex treated vs control
## Wald test p-value: dex treated vs control
## DataFrame with 38694 rows and 6 columns
##                  baseMean log2FoldChange     lfcSE      stat    pvalue
##                 <numeric>      <numeric> <numeric> <numeric> <numeric>
## ENSG00000000003  747.1942     -0.3507030  0.168246 -2.084470 0.0371175
## ENSG00000000005    0.0000             NA        NA        NA        NA
## ENSG00000000419  520.1342      0.2061078  0.101059  2.039475 0.0414026
## ENSG00000000457  322.6648      0.0245269  0.145145  0.168982 0.8658106
## ENSG00000000460   87.6826     -0.1471420  0.257007 -0.572521 0.5669691
## ...                   ...            ...       ...       ...       ...
## ENSG00000283115  0.000000             NA        NA        NA        NA
## ENSG00000283116  0.000000             NA        NA        NA        NA
## ENSG00000283119  0.000000             NA        NA        NA        NA
## ENSG00000283120  0.974916      -0.668258   1.69456 -0.394354  0.693319
## ENSG00000283123  0.000000             NA        NA        NA        NA
##                      padj
##                    <numeric>
## ENSG00000000003     0.163035
## ENSG00000000005           NA
## ENSG00000000419     0.176032
## ENSG00000000457     0.961694
## ENSG00000000460     0.815849
## ...                      ...
## ENSG00000283115           NA
## ENSG00000283116           NA
## ENSG00000283119           NA
## ENSG00000283120           NA
## ENSG00000283123           NA
```

A Volcano Plot

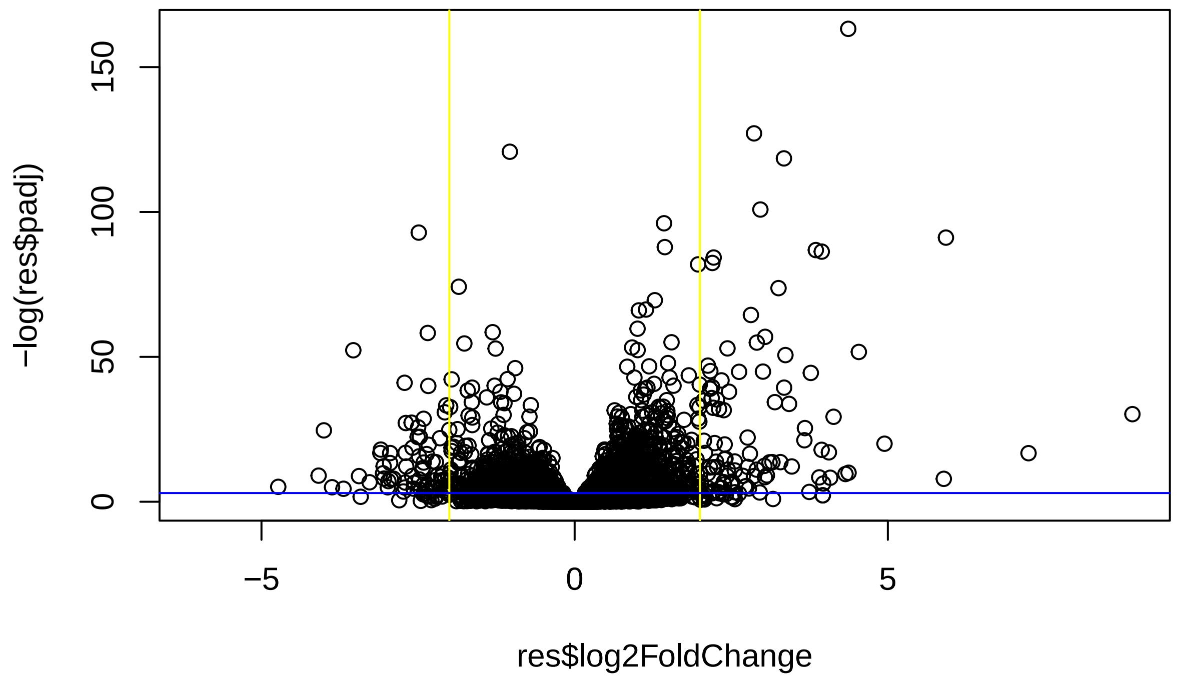
This is a very common

```
plot(res$log2FoldChange, res$padj)
```



Run it but take the log

```
plot(res$log2FoldChange, -log(res$padj))
# add a line
abline(v=c(-2,2), col="yellow")
abline(h=-log(0.05), col="blue")
```



Add extra information by annotating gene names and colors. Adding meaningful gene names to our dataset allows us to make sense of what is going on here.

```
library("AnnotationDbi")
```

```
## Warning: package 'AnnotationDbi' was built under R version 4.1.2
```

```
library("org.Hs.eg.db")
```

```
##
```

```
columns(org.Hs.eg.db)
```

```
##  [1] "ACCNUM"       "ALIAS"        "ENSEMBL"      "ENSEMBLPROT"  "ENSEMBLTRANS"
##  [6] "ENTREZID"     "ENZYME"       "EVIDENCE"     "EVIDENCEALL"  "GENENAME"
## [11] "GENETYPE"     "GO"           "GOALL"        "IPI"          "MAP"
## [16] "OMIM"         "ONTOLOGY"     "ONTOLOGYALL"  "PATH"         "PFAM"
## [21] "PMID"         "PROSITE"      "REFSEQ"       "SYMBOL"       "UCSCKG"
## [26] "UNIPROT"
```

Here we map to "SYMBOL" the common gene name that the world understands and wants.

```
res$symbol <- mapIds(org.Hs.eg.db,
                     keys=row.names(res),
                     keytype="ENSEMBL",
                     column="SYMBOL",
                     multiVals="first")
```

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

```
head(res$symbol)
```

```
## ENSG00000000003 ENSG00000000005 ENSG00000000419 ENSG00000000457 ENSG00000000460
##        "TSPAN6"          "TNMD"          "DPM1"         "SCYL3"      "C1orf112"
## ENSG00000000938
##           "FGR"
```

```
head(res)
```

```
## log2 fold change (MLE): dex treated vs control
## Wald test p-value: dex treated vs control
## DataFrame with 6 rows and 7 columns
##                   baseMean log2FoldChange     lfcSE      stat    pvalue
##                  <numeric>      <numeric> <numeric> <numeric> <numeric>
## ENSG00000000003 747.194195     -0.3507030  0.168246 -2.084470 0.0371175
## ENSG00000000005   0.000000             NA        NA        NA        NA
## ENSG00000000419 520.134160      0.2061078  0.101059  2.039475 0.0414026
## ENSG00000000457 322.664844      0.0245269  0.145145  0.168982 0.8658106
## ENSG00000000460  87.682625     -0.1471420  0.257007 -0.572521 0.5669691
## ENSG00000000938   0.319167     -1.7322890  3.493601 -0.495846 0.6200029
##                      padj      symbol
##                 <numeric> <character>
## ENSG00000000003  0.163035      TSPAN6
## ENSG00000000005        NA        TNMD
## ENSG00000000419  0.176032        DPM1
## ENSG00000000457  0.961694       SCYL3
## ENSG00000000460  0.815849    C1orf112
## ENSG00000000938        NA         FGR
```

Lets save our results to date

```
write.csv(res,file="allmyresults.csv")
```

We will be merging some files using the `merge() function`

PATHWAY ANALYSIS

Let's try to bring some biology insight back into our first analysis

```
library(pathview)
```

```
## ##############################################################################
## Pathview is an open source software package distributed under GNU General
## Public License version 3 (GPLv3). Details of GPLv3 is available at
## http://www.gnu.org/licenses/gpl-3.0.html. Particullary, users are required to
## formally cite the original Pathview paper (not just mention it) in publications
## or products. For details, do citation("pathview") within R.
##
## The pathview downloads and uses KEGG data. Non-academic uses may require a KEGG
## license agreement (details at http://www.kegg.jp/kegg/legal.html).
## ##############################################################################
```

```
library(gage)
```

```
##
```

```
library(gageData)
```

Visualize the first rows of data

```
data(kegg.sets.hs)
head(kegg.sets.hs, 2)
```

```
## $`hsa00232 Caffeine metabolism`
## [1] "10"   "1544" "1548" "1549" "1553" "7498" "9"
##
## $`hsa00983 Drug metabolism - other enzymes`
##  [1] "10"     "1066"   "10720"  "10941"  "151531" "1548"   "1549"   "1551"
##  [9] "1553"   "1576"   "1577"   "1806"   "1807"   "1890"   "221223" "2990"
## [17] "3251"   "3614"   "3615"   "3704"   "51733"  "54490"  "54575"  "54576"
## [25] "54577"  "54578"  "54579"  "54600"  "54657"  "54658"  "54659"  "54963"
## [33] "574537" "64816"  "7083"   "7084"   "7172"   "7363"   "7364"   "7365"
## [41] "7366"   "7367"   "7371"   "7372"   "7378"   "7498"   "79799"  "83549"
## [49] "8824"   "8833"   "9"      "978"
```

Before we can use KEGG we need to get our gene identifiers in the correct format for KEGG, which is ENTREZ format in this case.

```
head(res)
```

```
## log2 fold change (MLE): dex treated vs control
## Wald test p-value: dex treated vs control
## DataFrame with 6 rows and 7 columns
##                   baseMean log2FoldChange     lfcSE      stat    pvalue
##                  <numeric>      <numeric> <numeric> <numeric> <numeric>
## ENSG00000000003 747.194195     -0.3507030  0.168246 -2.084470 0.0371175
## ENSG00000000005   0.000000             NA        NA        NA        NA
## ENSG00000000419 520.134160      0.2061078  0.101059  2.039475 0.0414026
## ENSG00000000457 322.664844      0.0245269  0.145145  0.168982 0.8658106
## ENSG00000000460  87.682625     -0.1471420  0.257007 -0.572521 0.5669691
## ENSG00000000938   0.319167     -1.7322890  3.493601 -0.495846 0.6200029
##                      padj      symbol
##                 <numeric> <character>
## ENSG00000000003  0.163035      TSPAN6
## ENSG00000000005        NA        TNMD
## ENSG00000000419  0.176032        DPM1
## ENSG00000000457  0.961694       SCYL3
## ENSG00000000460  0.815849    C1orf112
## ENSG00000000938        NA         FGR
```

```
head(rownames(res))
```

```
## [1] "ENSG00000000003" "ENSG00000000005" "ENSG00000000419" "ENSG00000000457"
## [5] "ENSG00000000460" "ENSG00000000938"
```

```
res$entrez <- mapIds(org.Hs.eg.db,
                     keys=row.names(res),
                     keytype="ENSEMBL",
                     column="ENTREZID",
                     multiVals="first")
```

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

```
res$genename <- mapIds(org.Hs.eg.db,
                     keys=row.names(res),
                     keytype="ENSEMBL",
                     column="GENENAME",
                     multiVals="first")
```

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

The main **gage()** function requires a named vector of fold changes, where the names of the values are the Entrez gene IDs.

Note that we used the mapIDs() function above to obtain Entrez gene IDs (stored in res$entrez)andwehavethefoldchangeresul$

```
foldchanges <- res$log2FoldChange
head(foldchanges)
```

```
## [1] -0.35070302          NA  0.20610777  0.02452695 -0.14714205 -1.73228897
```

Assign names to this vector that are the gene IDs that KEGG wants

```
names(foldchanges) = res$entrez
head(foldchanges)
```

```
##        7105       64102        8813       57147       55732        2268
## -0.35070302          NA  0.20610777  0.02452695 -0.14714205 -1.73228897
```

```
#not meaningful so you could change to symbol, but not necessary at this time because...
```

Now we are ready for the **gage()** function. Get the results

```
keggres = gage(foldchanges, gsets=kegg.sets.hs)
View(keggres)
```

We can look at the attributes() of this or any R object.

```
attributes(keggres)
```

```
## $names
## [1] "greater" "less"    "stats"
```

```
head(keggres$less)
```

```
##                                                       p.geomean stat.mean
## hsa05332 Graft-versus-host disease                 0.0004250461 -3.473346
## hsa04940 Type I diabetes mellitus                  0.0017820293 -3.002352
## hsa05310 Asthma                                    0.0020045888 -3.009050
## hsa04672 Intestinal immune network for IgA production 0.0060434515 -2.560547
## hsa05330 Allograft rejection                       0.0073678825 -2.501419
## hsa04340 Hedgehog signaling pathway                0.0133239547 -2.248547
##                                                           p.val      q.val
## hsa05332 Graft-versus-host disease                 0.0004250461 0.09053483
## hsa04940 Type I diabetes mellitus                  0.0017820293 0.14232581
## hsa05310 Asthma                                    0.0020045888 0.14232581
## hsa04672 Intestinal immune network for IgA production 0.0060434515 0.31387180
## hsa05330 Allograft rejection                       0.0073678825 0.31387180
## hsa04340 Hedgehog signaling pathway                0.0133239547 0.47300039
##                                                    set.size         exp1
## hsa05332 Graft-versus-host disease                       40 0.0004250461
## hsa04940 Type I diabetes mellitus                        42 0.0017820293
## hsa05310 Asthma                                          29 0.0020045888
## hsa04672 Intestinal immune network for IgA production       47 0.0060434515
## hsa05330 Allograft rejection                             36 0.0073678825
## hsa04340 Hedgehog signaling pathway                      56 0.0133239547
```

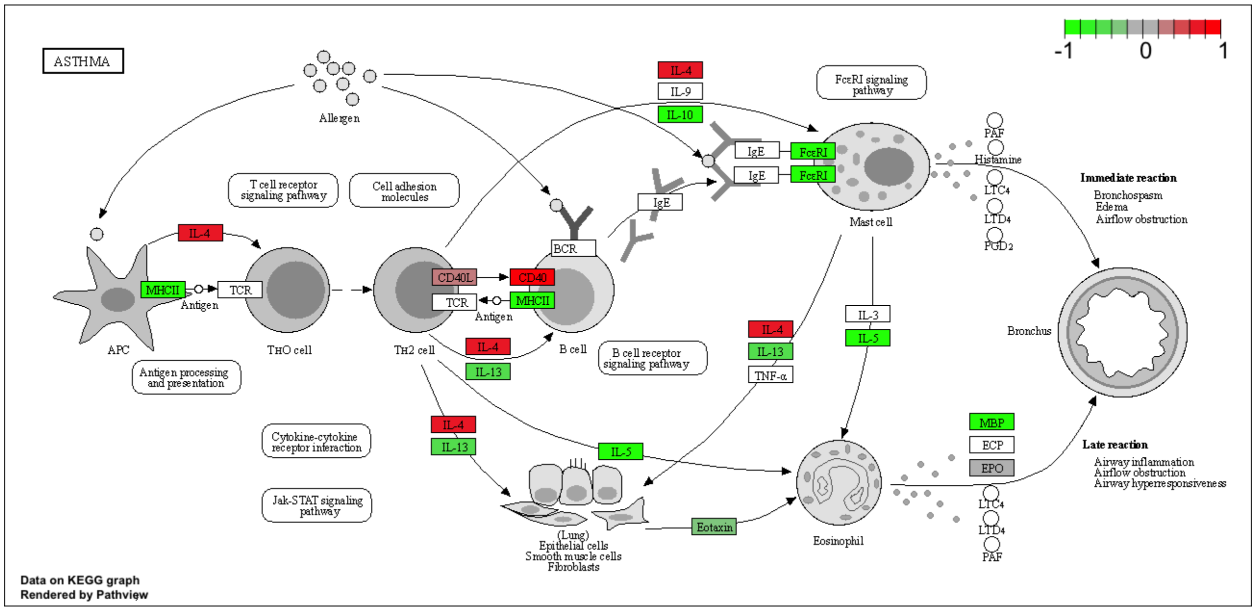
The pathview() function will add our genes to a KEGG pathway

```
pathview(gene.data=foldchanges, pathway.id="hsa05310")
```

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

```
## Info: Working in directory /Users/zaidarodriguez/Desktop/UCSD/Fall2021/BGGN213/bggn213_github/Class15
```

```
## Info: Writing image file hsa05310.pathview.png
```


ASTHMA
-1 0 1
Allergen
IL-4
IL-9
IL-10
FcεRI signaling pathway
IgE
FcεRI
IgE
FcεRI
Mast cell
PAF
Histamine
LTC4
LTD4
PGD2
Immediate reaction
Bronchospasm
Edema
Airflow obstruction
T cell receptor signaling pathway
Cell adhesion molecules
IgE
BCR
IL-4
MHCII
TCR
Antigen
APC
TH0 cell
CD40L
CD40
TCR
MHCII
Antigen
TH2 cell
B cell
IL-4
IL-13
B cell receptor signaling pathway
IL-4
IL-13
TNF-α
IL-3
IL-5
Bronchus
Antigen processing and presentation
Cytokine-cytokine receptor interaction
Jak-STAT signaling pathway
IL-4
IL-13
IL-5
MBP
ECP
EPO
Late reaction
Airway inflammation
Airflow obstruction
Airway hyperresponsiveness
(Lung)
Epithelial cells
Smooth muscle cells
Fibroblasts
Eotaxin
Eosinophil
LTC4
LTD4
PAF
Data on KEGG graph
Rendered by Pathview