Figure 4A-D & Sup. Fig. 4 A & D

RAC

05/01/2021

Script below was used to uniting bed file of mapped reads (cross-links) with bed file of all TUs exons

```
#!/bin/bash
#script for ubiting bg values with annotation file 200113
#all dir paths should contain / at the end.
#InputVariables

bedAnnotation=$1
inBedDir=$2
outDir=$3


echo "Merging bedgraph counts with $bedAnnotation"
echo "Using bedgraphs in $inBedDir"
echo "Saving outputs in $outDir"

#constructing output suffix for filename.
outFileName=$(basename $bedAnnotation | sed 's/.bed//g')

#mk output dir
mkdir -p $outDir

#perform on each bed file (mapped tiCLIP cross-link sites)
for inBed in ${inBedDir}*.bed;
    do
    #make variables
    ID=$(basename $inBed | sed 's/.bed//g;s/-/_/g' )

    echo "starting analysis for $ID"

    bedtools intersect -loj -s \
    -a <( sort -k1,1 -k2,2n $inBed | sed 's/^chr//g' ) \
    -b <( sort -k1,1 -k2,2n $bedAnnotation | sed 's/^chr//g' ) \
    | awk '{OFS="\t"} $8 > -1' \
    | awk -v ID=$ID '{OFS="\t"}{print ID,$7,$8,$9,$10,$11,$12,$1,$2,$3,$4,$5,$6}' > ${outDir}${ID}"_"${

    echo "completed for $ID"

done
```

```
library(scales)
library(ggformula)
```

```
## Loading required package: ggplot2
```

```
## Loading required package: ggstance
```

```
##
## Attaching package: 'ggstance'
```

```
## The following objects are masked from 'package:ggplot2':
##
##     geom_errorbarh, GeomErrorbarh
```

```
## Loading required package: ggridges
```

```
##
## New to ggformula?  Try the tutorials:
##  learnr::run_tutorial("introduction", package = "ggformula")
##  learnr::run_tutorial("refining", package = "ggformula")
```

```
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(tibble)
library(tidyr)
library(ggplot2)
library(ggsignif)
library(ggpubr)
knitr::opts_chunk$set(tidy.opts=list(width.cutoff=60), tidy=TRUE)
```

load input files generated from script above annotation bed file, and expression vector

```
dfFilePath = "../../data/ALYREF_5primepos_hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.exonNu

annoFilePath = "../../data/hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.exonNumber.sizeRange.

EXPRESSION_VECTOR_FILEPATH = "../../data/log2_mean_cov_RNAseq_TTseq.RData"

load(EXPRESSION_VECTOR_FILEPATH)

# wrangle expression vector
expression_vector <- left_join((as.data.frame(ctrl_RNAseq_expr) %>%
    add_rownames(var = "geneName")), (as.data.frame(ctrl_TTseq_expr) %>%
    add_rownames(var = "geneName"))) %>%
    mutate(ctrl_RNAseq_expr = case_when(ctrl_RNAseq_expr == 0 ~
        min(ctrl_RNAseq_expr[ctrl_RNAseq_expr > 0]), TRUE ~ ctrl_RNAseq_expr))
```

```
## Warning: `add_rownames()` was deprecated in dplyr 1.0.0.
## i Please use `tibble::rownames_to_column()` instead.
```

```
## Joining, by = "geneName"
```

#Functions used for processing input

```r
#refined Function finds relative distance of xlinksite across feature. RNA split into 100 bins in total
#Also genes are annotated with mature and gene size.

process_distToTSS_1 <- function(dfFilePath, annotationFilePath){

#input file is a bed intersection between annotation file containing exons of genes
df<-read.csv(dfFilePath, sep = "\t", header =F)
col.names<-c("Sample",
             #annotationfile
             "chrAnno","startAnno", "stopAnno", "IDAnno", "scoreAnno",
             "strandAnno",
             #bed file of cross-link mapped bam file
             "chrRead","startRead","stopRead","IDRead","scoreRead","strandRead")




head(df)

print("wrangling data")

df1<-df %>%
    setNames(col.names) %>%
      select(-chrRead, -IDRead, -scoreRead, -scoreAnno) %>%
      separate(IDAnno, c("geneName","biotype","exonID", "totalExons", "exonSize","cumSumExons", "distTo
      select(-exonDesc)

#cumSumExons = distance
#distToTSS = the distance
col.numeric<- c("chrAnno","startAnno","stopAnno","totalExons","exonSize","cumSumExons","distToTSS","sta
df1[col.numeric] <- sapply(df1[col.numeric],as.numeric)

print("processing rel distance from TSS")
#calculate postion of cross-link within the mature RNA. i.e. distance of cross-link to 5' end of RNA ex
df2<-df1 %>%
    mutate(rel.pos = ifelse(strandAnno == "+", ( (startRead-startAnno) + (cumSumExons-exonSize) ),
                     ifelse(strandAnno == "-", ( (stopAnno-stopRead) + (cumSumExons-exonSize) ),
                     "no"))) %>%
    select(Sample, geneName, biotype, geneDesc, rel.pos)


print("loading annotation file")

annoDF<-read.csv(annoFilePath , sep = "\t", header =F)

print("making table with total sizes of RNAs")

totalSizes<-annoDF %>%
    setNames(c("chr","start","stop","ID","score","strand")) %>%
    separate(ID, c("geneName","biotype","exonID", "totalExons", "exonSize","cumSumExons", "distToTSS",
    filter(exonID == totalExons) %>%
    mutate(matureRNA = as.numeric(cumSumExons),
           geneSize = as.numeric(ifelse(totalExons > 1, distToTSS, exonSize))) %>%
```

```
    select(geneName, biotype, matureRNA, geneSize)

df3<-df2 %>%
  left_join(totalSizes)

return(df3)

}
```

```
ScaledNormalise_2_3_RPM_Normalisation <- function(DF, MINSIZE,
    MAXSIZE, annoFilePath, RPMFactorsFilePath) {

    annoDF <- read.csv(annoFilePath, sep = "\t", header = F)

    totalSizes <- annoDF %>%
        setNames(c("chr", "start", "stop", "ID", "score", "strand")) %>%
        separate(ID, c("geneName", "biotype", "exonID", "totalExons",
            "exonSize", "cumSumExons", "distToTSS", "exonDesc",
            "geneDesc"), sep = ":::") %>%
        filter(exonID == totalExons) %>%
        mutate(matureRNA = as.numeric(cumSumExons), geneSize = as.numeric(ifelse(totalExons >
            1, distToTSS, exonSize))) %>%
        select(geneName, biotype, matureRNA, geneSize)

    calculated_test <- relDist_ALYREF %>%
        left_join(totalSizes) %>%
        mutate(rel.pos = as.numeric(rel.pos), matureRNA = as.numeric(matureRNA)) %>%
        filter(matureRNA %in% c(MINSIZE:MAXSIZE)) %>%
        mutate(rel.pos.2 = rel.pos/matureRNA)

    # assigning bin numbers to the rel.pos.2

    ALL <- calculated_test %>%
        mutate(rel.pos.2 = ifelse(rel.pos.2 == 0, rel.pos.2 +
            1e-07, rel.pos.2))
    max(ALL$rel.pos.2)
    min(ALL$rel.pos.2)
    ALL$new_distBin <- cut(ALL$rel.pos.2, seq(0, 1, by = 0.01),
        labels = seq("1", "100", by = 1))

    combined <- ALL %>%
        separate(Sample, into = c("Protein", "Rep", "Timepoint",
            "readType"), sep = "_") %>%
        # filter(Timepoint == 'DMSO' &
        # grepl('coding|histone',biotype) &
        # !grepl('\\*|non', biotype)) %>%
    group_by(geneName, biotype, Protein, Timepoint, Rep, matureRNA,
        geneSize, new_distBin) %>%
        summarise(tally = n()) %>%
        # new steo to normalise to gene expression level
    left_join(expression_vector) %>%
        mutate(tally_n = (tally/ctrl_RNAseq_expr)/(matureRNA/100))  #step to normalise count to bin siz

    # mutate(tally_n = tally/(matureRNA/100)) #step to
```

```
    # normalise count to bin size.

    totalLibrarySizes <- read.table(RPMFactorsFilePath) %>%
        setNames(c("Sample", "RPMFactor")) %>%
        separate(Sample, into = c("Protein", "Rep", "Timepoint",
            "readType"), sep = "_") %>%
        mutate(Rep = as.character(Rep)) %>%
        mutate(RPMFactor = 1e+06/RPMFactor)

    # this step taken from norm profile 3
    combined_2 <- combined %>%
        left_join(totalLibrarySizes) %>%
        mutate(tally_n = tally_n * RPMFactor) %>%
        select(-RPMFactor) %>%
        group_by(geneName, biotype, Protein, Timepoint, Rep,
            matureRNA) %>%
        mutate(totals_unNorm = sum(tally), pct = tally_n/sum(tally_n) *
            100) %>%
        ungroup() %>%
        select(Protein, Timepoint, Rep, matureRNA, geneName,
            biotype, new_distBin, totals_unNorm, pct) %>%
        spread(new_distBin, pct, fill = 0) %>%
        gather("distBin", "value", c("1":"100")) %>%
        mutate(distBin = factor(distBin, levels = c(1:100)))

    return(combined_2)
}
```

```
# calculate profiles
kMeansClustering_4 <- function(inputDF, CENTRES, REP, MINCOUNTS) {

    # filter for DMSO and protein Codingg
    DF <- inputDF %>%
        filter(Timepoint == "DMSO") %>%
        spread(distBin, value)

    # filter by rep and only use genes with a minumum of 40
    # counts per gene.
    DF1 <- DF %>%
        filter(Rep == REP & totals_unNorm >= MINCOUNTS) %>%
        column_to_rownames(var = "geneName") %>%
        select("1":"100")

    # kmeans clustering analysis (set seed for
    # reproducibility)
    set.seed(42)
    kClusters <- kmeans(DF1, centers = CENTRES)

    clusters <- as.data.frame(kClusters$cluster) %>%
        rownames_to_column(var = "geneName") %>%
        rename(clusterID = `kClusters$cluster`)

    DF_merge <- DF %>%
        right_join(clusters) %>%
```

```
        group_by(clusterID, Rep) %>%
        mutate(n = n()) %>%
        ungroup() %>%
        gather("distBin", "value", c("1":"100")) %>%
        mutate(distBin = factor(distBin, levels = c(1:100)))

    return(DF_merge)

}
```

```
dfFilePath = "../../data/ALYREF_5primepos_hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.exonNu
annoFilePath = "../../data/hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.exonNumber.sizeRange.

rRNAFactorsFilePath = "../../data/rRNAFactor.tab"
RPMFactorsFilePath = "../../data/RPM_factors.tab"

annoDF <- read.csv(annoFilePath, sep = "\t", header = F)

geneStructures <- annoDF %>%
    setNames(c("chr", "start", "stop", "ID", "score", "strand")) %>%
    separate(ID, c("geneName", "biotype", "exonID", "totalExons",
        "exonSize", "cumSumExons", "distToTSS", "exonDesc", "geneDesc"),
        sep = ":::") %>%
    separate(geneDesc, into = c("geneStructure"), sep = "-") %>%
    select(geneName, geneStructure) %>%
    unique()
```

```
## Warning: Expected 1 pieces. Additional pieces discarded in 117503 rows [1, 2, 3,
## 4, 5, 6, 7, 8, 9, 12, 13, 14, 15, 21, 22, 23, 24, 25, 26, 29, ...].
```

```
head(geneStructures)
```

```
##         geneName    geneStructure
## 1           PRKX  multiExonicGene
## 10      NA.v8937 singleExonicGene
## 11      NA.v8938 singleExonicGene
## 12 RP11-706O15.1  multiExonicGene
## 16      NA.v9224 singleExonicGene
## 17      NA.v9223 singleExonicGene
```

```
totalSizes <- annoDF %>%
    setNames(c("chr", "start", "stop", "ID", "score", "strand")) %>%
    separate(ID, c("geneName", "biotype", "exonID", "totalExons",
        "exonSize", "cumSumExons", "distToTSS", "exonDesc", "geneDesc"),
        sep = ":::") %>%
    filter(exonID == totalExons) %>%
    mutate(matureRNA = as.numeric(cumSumExons), geneSize = as.numeric(ifelse(totalExons >
        1, distToTSS, exonSize))) %>%
    select(geneName, biotype, matureRNA, geneSize)

head(totalSizes)
```

```
##        geneName        biotype matureRNA geneSize
## 1          PRKX protein_coding      1817   104704
## 2      NA.v8937           nHtH       454      454
## 3      NA.v8938           nTtT      1628     1628
```

```
## 4 RP11-706O15.1        lincRNA     11264    25788
## 5      NA.v9224     intergenic       349      349
## 6      NA.v9223     intergenic       736      736
```

```
relDist_ALYREF <- process_distToTSS_1(dfFilePath, annoFilePath)
```

```
## [1] "wrangling data"
## [1] "processing rel distance from TSS"
## [1] "loading annotation file"
## [1] "making table with total sizes of RNAs"
```

```
## Joining, by = c("geneName", "biotype")
```

```
head(relDist_ALYREF)
```

```
##                     Sample geneName        biotype                 geneDesc
## 1 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
## 2 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
## 3 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
## 4 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
## 5 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
## 6 ALYREF_1_DMSO_5primepos NA.v1000 protein_coding multiExonicGene-lastExon
##   rel.pos matureRNA geneSize
## 1    1936      1990     2289
## 2    1936      1990     2289
## 3    1916      1990     2289
## 4    1911      1990     2289
## 5    1893      1990     2289
## 6    1889      1990     2289
```

```
ALYREF_100bins_scaled <- ScaledNormalise_2_3_RPM_Normalisation(relDist_ALYREF,
    200, 1e+05, annoFilePath, RPMFactorsFilePath)
```

```
## Joining, by = c("geneName", "biotype", "matureRNA", "geneSize")
## `summarise()` has grouped output by 'geneName', 'biotype', 'Protein',
## 'Timepoint', 'Rep', 'matureRNA', 'geneSize'. You can override using the
## `.groups` argument.
## Joining, by = "geneName"
## Joining, by = c("Protein", "Timepoint", "Rep")
```

```
head(ALYREF_100bins_scaled)
```

```
## # A tibble: 6 x 9
##   Protein Timepoint Rep   matureRNA geneName       biotype total~1 distBin value
##   <chr>   <chr>     <chr>     <dbl> <chr>          <chr>     <int> <fct>   <dbl>
## 1 ALYREF  DMSO      1          1406 5S_rRNA,DTNBP1 rRNA          6 1           0
## 2 ALYREF  DMSO      2          1406 5S_rRNA,DTNBP1 rRNA          4 1           0
## 3 ALYREF  PBSDRB    1          1406 5S_rRNA,DTNBP1 rRNA          2 1           0
## 4 ALYREF  PBSDRB    2          1406 5S_rRNA,DTNBP1 rRNA          2 1           0
## 5 ALYREF  t00       1          1406 5S_rRNA,DTNBP1 rRNA          2 1           0
## 6 ALYREF  t05       2          1406 5S_rRNA,DTNBP1 rRNA          3 1           0
## # ... with abbreviated variable name 1: totals_unNorm
```

```
ALYREF_100bins_scaled_clusters_1 <- kMeansClustering_4(ALYREF_100bins_scaled,
    2, 1, 20)
```

```
## Joining, by = "geneName"
```

```
head(ALYREF_100bins_scaled_clusters_1)
```

```
## # A tibble: 6 x 11
##   Protein Timepoint Rep   mature~1 geneN~2 biotype total~3 clust~4     n distBin
##   <chr>   <chr>     <chr>    <dbl> <chr>   <chr>     <int>   <int> <int> <fct>
## 1 ALYREF  DMSO      1         3254 AACS    protei~      20       2  2794 1
## 2 ALYREF  DMSO      2         3254 AACS    protei~       9       2  2794 1
## 3 ALYREF  DMSO      1        50238 AAK1    protei~      38       1  1361 1
## 4 ALYREF  DMSO      2        50238 AAK1    protei~       9       1  1359 1
## 5 ALYREF  DMSO      1         3382 AARS    protei~      62       2  2794 1
## 6 ALYREF  DMSO      2         3382 AARS    protei~      27       2  2794 1
## # ... with 1 more variable: value <dbl>, and abbreviated variable names
## #   1: matureRNA, 2: geneName, 3: totals_unNorm, 4: clusterID
```

```
ALYREF_100bins_scaled_clusters_2 <- kMeansClustering_4(ALYREF_100bins_scaled,
    2, 2, 20)
```

```
## Joining, by = "geneName"
```

```
head(ALYREF_100bins_scaled_clusters_2)
```

```
## # A tibble: 6 x 11
##   Protein Timepoint Rep   mature~1 geneN~2 biotype total~3 clust~4     n distBin
##   <chr>   <chr>     <chr>    <dbl> <chr>   <chr>     <int>   <int> <int> <fct>
## 1 ALYREF  DMSO      1         3382 AARS    protei~      62       2   865 1
## 2 ALYREF  DMSO      2         3382 AARS    protei~      27       2   865 1
## 3 ALYREF  DMSO      1         8122 ABCA2   protei~     115       2   865 1
## 4 ALYREF  DMSO      2         8122 ABCA2   protei~      48       2   865 1
## 5 ALYREF  DMSO      1        20558 ABCA5   protei~      77       2   865 1
## 6 ALYREF  DMSO      2        20558 ABCA5   protei~      25       2   865 1
## # ... with 1 more variable: value <dbl>, and abbreviated variable names
## #   1: matureRNA, 2: geneName, 3: totals_unNorm, 4: clusterID
```

Join clusters

```
clusters <- full_join((ALYREF_100bins_scaled_clusters_1 %>%
    select(Rep, geneName, clusterID) %>%
    unique() %>%
    mutate(Rep1_clusterID = paste0(clusterID)) %>%
    select(-clusterID)), (ALYREF_100bins_scaled_clusters_2 %>%
    select(Rep, geneName, clusterID) %>%
    unique() %>%
    mutate(Rep2_clusterID = paste0(clusterID)) %>%
    select(-clusterID)))
```

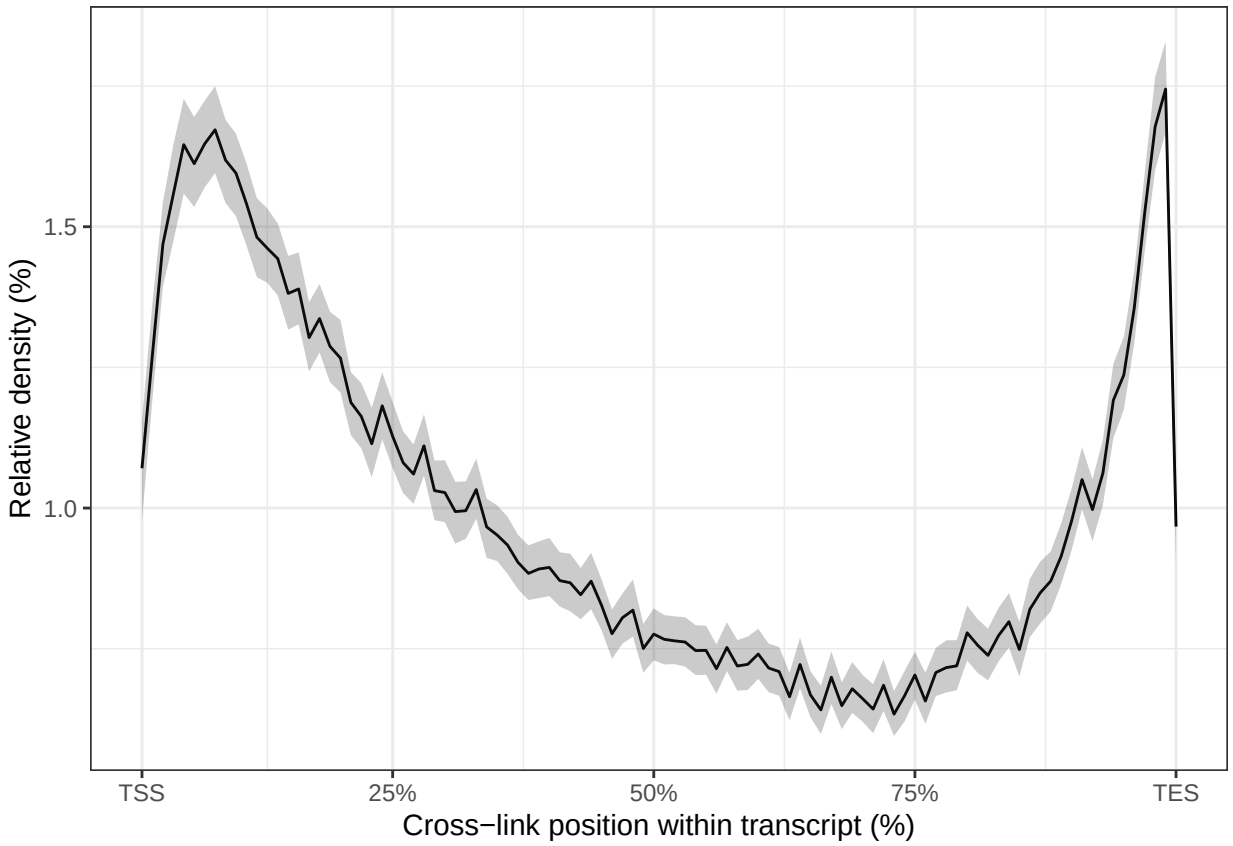
```
## Joining, by = c("Rep", "geneName")
```

```
clusters[is.na(clusters)] <- "0"
```

#Figure 4 A Plot profile of ALYREF-DMSO cross-links across exonic portions of TUs

```
ALYREF_100bins_scaled %>%
    filter(Timepoint == "DMSO" & grepl("coding", biotype) & !grepl("\\*|non",
        biotype) & totals_unNorm >= 20) %>%
    spread(distBin, value) %>%
    gather("distBin", "value", 8:107) %>%
    ggplot(aes(x = as.numeric(distBin), y = value)) + stat_summary(fun = mean,
    geom = "line", size = 0.5) + stat_summary(fun.data = "mean_cl_boot",
```

```
    geom = "ribbon", alpha = 0.25, col = NA) + theme_bw() + xlab("Cross-link position within transcript
    scale_x_continuous(breaks = c(1, 25, 50, 75, 100), labels = c("TSS",
        "25%", "50%", "75%", "TES")) + theme(legend.position = "none") +
    ylab("Relative density (%)")
```



#Venn diagram for Supplementary Figure 4 a. Intersect genes identified in kmeans clustering from ALYREF-1-DMSO and ALYREF-2-DMSO

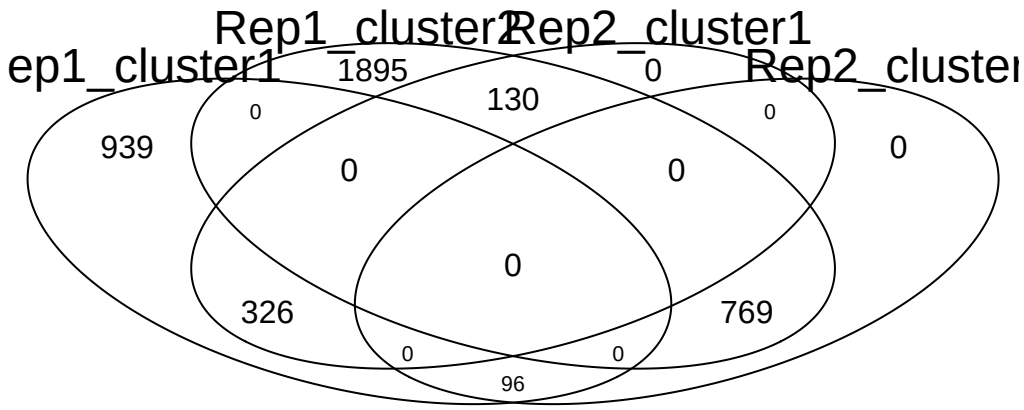
```
Rep1_cluster1 <- ALYREF_100bins_scaled_clusters_1 %>%
    filter(clusterID == 1 & Rep == "1") %>%
    select(geneName, clusterID, Rep) %>%
    unique()

Rep1_cluster2 <- ALYREF_100bins_scaled_clusters_1 %>%
    filter(clusterID == 2 & Rep == "1") %>%
    select(geneName, clusterID, Rep) %>%
    unique()

Rep2_cluster1 <- ALYREF_100bins_scaled_clusters_2 %>%
    filter(clusterID == 1 & Rep == "2") %>%
    select(geneName, clusterID, Rep) %>%
    unique()

Rep2_cluster2 <- ALYREF_100bins_scaled_clusters_2 %>%
    filter(clusterID == 2 & Rep == "2") %>%
    select(geneName, clusterID, Rep) %>%
    unique()
```

```
# make venn diagram of cluster id overlaps
library(gplots)
```

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

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

```
# df('resultsFigs/210119/ven.pdf')
venn(list(Rep1_cluster1 = (Rep1_cluster1 %>%
    select(geneName) %>%
    as.list() %>%
    unlist()), Rep1_cluster2 = (Rep1_cluster2 %>%
    select(geneName) %>%
    as.list() %>%
    unlist()), Rep2_cluster1 = (Rep2_cluster1 %>%
    select(geneName) %>%
    as.list() %>%
    unlist()), Rep2_cluster2 = (Rep2_cluster2 %>%
    select(geneName) %>%
    as.list() %>%
    unlist())))
```




```
# dev.off()

# Rep1_cluster1 %>% select(geneName) %>% as.list() %>%
# unlist()

# intersect the 2 different genes groups identified
clus_1 <- intersect(Rep1_cluster1$geneName, Rep2_cluster1$geneName) %>%
    as.data.frame() %>%
    mutate(cluster = "1")
clus_2 <- intersect(Rep1_cluster2$geneName, Rep2_cluster2$geneName) %>%
    as.data.frame() %>%
    mutate(cluster = "2")

# combine to one dataframe
clust_all <- rbind(clus_1, clus_2) %>%
    setNames(c("geneName", "clusterID")) %>%
```

```
    mutate(geneName = as.character(geneName))

clust_all
```

```
##                                                geneName clusterID
## 1                                                 ABCC1         1
## 2                                                 ABCC4         1
## 3                                             AC093838.4         1
## 4                                                 ACACA         1
## 5                                      ACEA_U3,SNORD3B-2         1
## 6                                  ADARB2,RP11-398B16.2         1
## 7                              AGAP10,BMS1P2,RP11-144G6.12         1
## 8                                                 AMD1         1
## 9                                               ANAPC1         1
## 10                                            ANKRD10.v2         1
## 11                                              ANKRD27         1
## 12                                              ANKRD32         1
## 13                                              ANKRD36         1
## 14                                              ANTXR1         1
## 15                                                AP1G1         1
## 16                                             ARHGAP11B         1
## 17                                                ARID2         1
## 18                                               ARID5B         1
## 19                                                ASAP1         1
## 20                                                ASCC3         1
## 21                                                ATAD1         1
## 22                                               ATP2B1         1
## 23                                               ATP2C1         1
## 24                                                 ATRX         1
## 25                                                ATXN2         1
## 26                                                AZIN1         1
## 27                                                 BDP1         1
## 28                                                BNIP2         1
## 29                                                 BRD4         1
## 30                                                BRIP1         1
## 31                                                BRWD1         1
## 32                                              C5orf42         1
## 33                                                CCAT1         1
## 34                                              CCDC88A         1
## 35                                                CCNL1         1
## 36                                                CCNT1         1
## 37                                      CD44,RP1-68D18.2         1
## 38                                              CDC42BPA         1
## 39                                                CDK12         1
## 40                                                CEP72         1
## 41                                               CHCHD3         1
## 42                                     CHD9,RP1-295M3.2         1
## 43                                                  CIT         1
## 44                                                CKAP5         1
## 45                                               CLASP1         1
## 46                                              CLEC16A         1
## 47                                                CLIP1         1
## 48                                               CLTCL1         1
## 49                                                  COG5         1
```

## 50	CPS1	1
## 51	CTC-338M12.2	1
## 52	CTD-2340D6.1,VPS13B	1
## 53	CTNNA1	1
## 54	CTPS1	1
## 55	CUX1	1
## 56	DDX5	1
## 57	DENND4A,RP11-16E23.3	1
## 58	DEPDC1	1
## 59	DIAPH3	1
## 60	DMXL1	1
## 61	DNM1L	1
## 62	DOCK1	1
## 63	DOCK7	1
## 64	DOT1L	1
## 65	DPP8	1
## 66	DPY19L4	1
## 67	DYNC2H1	1
## 68	EEF1A1	1
## 69	EIF3A	1
## 70	EIF3E	1
## 71	EIF4EBP3,ANKHD1	1
## 72	ELK4	1
## 73	EP400	1
## 74	EPT1	1
## 75	ERC1,RP5-951N9.2	1
## 76	ERCC6-PGBD3	1
## 77	EXOSC2	1
## 78	EYA4	1
## 79	FAM13B	1
## 80	FASTKD2	1
## 81	FBXW2	1
## 82	FNDC3B	1
## 83	FOXJ3	1
## 84	FTX	1
## 85	FUBP1	1
## 86	FXR1	1
## 87	G3BP1	1
## 88	GAPVD1	1
## 89	GART	1
## 90	GBF1	1
## 91	GDA	1
## 92	GFM1	1
## 93	GMPS	1
## 94	GNL3L	1
## 95	GPC5	1
## 96	GPR126	1
## 97	GSK3B	1
## 98	GTF2I	1
## 99	GTF3C1	1
## 100	HELLS	1
## 101	HELZ	1
## 102	HERC2	1
## 103	HIATL2	1

```
## 104                                                HIST1H3G         1
## 105                                                    HLTF         1
## 106                                hsa-mir-7706,RP11-815J21.1,AKAP13         1
## 107                                                   HSPA4         1
## 108                                                     IDE         1
## 109                                                  IGF2BP3         1
## 110                                                    ILF3         1
## 111                                                   INADL         1
## 112                                                   INTS7         1
## 113                                                    IPO5         1
## 114                                                    IPO7         1
## 115                                                   IREB2         1
## 116                                                   ITPR2         1
## 117                                                   KDM5A         1
## 118                                                 KIAA0825         1
## 119                                                 KIAA1033         1
## 120                                                 KIAA1109         1
## 121                                                 KIAA1549         1
## 122                                                 KIAA1841         1
## 123                                                 KIAA1958         1
## 124                                                  KIF20B         1
## 125                                                   KIF2C         1
## 126                                                   KMT2C         1
## 127                                                    KYNU         1
## 128                                                   LARP4         1
## 129                                 LIMA1,RP3-405J10.2,RP3-405J10.3         1
## 130                                                  LIMCH1         1
## 131                                                   LIMD1         1
## 132                                                  LPGAT1         1
## 133                                                     LPP         1
## 134                                                    LRBA         1
## 135                                                    LRP6         1
## 136                                                  LUC7L3         1
## 137                                                  MAMDC2         1
## 138                                                    MAP4         1
## 139                                                  MARCH6         1
## 140                                                   MAT2A         1
## 141                                                   MBNL2         1
## 142                                                    MDN1         1
## 143                                                 METTL16         1
## 144                                                     MGA         1
## 145  MICAL3,XXbac-B476C20.14,XXbac-B476C20.13,XXbac-B461K10.4         1
## 146                                                    MID1         1
## 147                                               MIR4444-2         1
## 148                                             MIR5006,VWA8         1
## 149                                            MIR6125,USP15         1
## 150                                           MIR6861,HECTD4         1
## 151                                            MIR8072,SBNO1         1
## 152                                                    MKLN1         1
## 153                                                  MMS22L         1
## 154                                                 MPHOSPH9         1
## 155                                       MRE11A,RP11-685N10.1         1
## 156                                                    MSI2         1
## 157                                                    MTAP         1
```

```
## 158                    MTF2         1
## 159                   MTPAP         1
## 160                 MYBBP1A         1
## 161                    MYOF         1
## 162                NA.v3445         1
## 163                NA.v3852         1
## 164                NA.v7958         1
## 165                NA.v8004         1
## 166                NAT10.v1         1
## 167                    NBAS         1
## 168                   NCBP1         1
## 169                   NCOA3         1
## 170                    NFIA         1
## 171                    NFIB         1
## 172                    NFX1         1
## 173                  NHLRC2         1
## 174                   NLRC5         1
## 175                    NPM1         1
## 176                   NR3C1         1
## 177                    NSD1         1
## 178                  NUFIP2         1
## 179                   NUMA1         1
## 180                  NUP188         1
## 181                  NUP214         1
## 182                   NUP98         1
## 183                    OGDH         1
## 184                    OPN3         1
## 185                    OSMR         1
## 186                   OXCT1         1
## 187                   PALLD         1
## 188 PANK3,SLC2A3P1         1
## 189                  PAPOLA         1
## 190                   PBRM1         1
## 191                   PDE3A         1
## 192                    PDPR         1
## 193                    PDXK         1
## 194                    PHC3         1
## 195                    PHIP         1
## 196                   PI4KA         1
## 197                  POLR1A         1
## 198                   PPIL2         1
## 199                  PPP6R2         1
## 200                  PPP6R3         1
## 201                   PRKD3         1
## 202                   PRKDC         1
## 203                   PRMT3         1
## 204                  PRRC2B         1
## 205                   PSMD1         1
## 206                   PSPC1         1
## 207                   PTBP2         1
## 208                   PTPLB         1
## 209                 RACGAP1         1
## 210                 RALGAPB         1
## 211                 RAPGEF6         1
```

```
## 212                                  RASAL2,Metazoa_SRP         1
## 213                                                RBL1         1
## 214                                               RBM25         1
## 215                                               RBM27         1
## 216                                                RBMX         1
## 217                                               RC3H1         1
## 218                                              RIMKLB         1
## 219                                                RLIM         1
## 220                                              RNF169         1
## 221                                              RNF216         1
## 222                                              RNU1-1         1
## 223                                             RNU5E-1         1
## 224                                             RNU5F-1         1
## 225                                RNU6-29P,AC115617.2         1
## 226                                              RNU6-8         1
## 227                              RP1-102G20.2,RABGAP1L         1
## 228                             RP11-11N7.5,HNRNPU-AS1         1
## 229                                   RP11-142O6.1,NF1         1
## 230                                      RP11-274B21.1         1
## 231                                       RP11-354B3.1         1
## 232                 RP11-611O2.3,MDM2,RP11-611O2.1         1
## 233                                               RPTOR         1
## 234                                              RSL1D1         1
## 235                                               RUNX1         1
## 236                                             S100PBP         1
## 237                                                SACS         1
## 238                                                SBF2         1
## 239                                              SCAF11         1
## 240                                                 SCD         1
## 241                                                SDHA         1
## 242                                              SEC24B         1
## 243                                              SEC31A         1
## 244                                             SEC61A1         1
## 245                                              SEMA3C         1
## 246                                SENP5,AC127904.2         1
## 247                                              SERBP1         1
## 248                                              SETDB1         1
## 249                                                SETX         1
## 250                                                SFI1         1
## 251                                                SFPQ         1
## 252                                              SLC1A3         1
## 253                                             SLC38A1         1
## 254                                             SLC7A5P2         1
## 255                                                SMAD5         1
## 256                             SMARCC1,RP11-717D12.1         1
## 257                                              SMEK2         1
## 258                                              SMPD4         1
## 259                                            SNORD118         1
## 260                                             SNORD13         1
## 261                                                 SP1         1
## 262                                              SPATA5         1
## 263                                              SPECC1         1
## 264                                               SPIDR         1
## 265                                SRGAP1,RP11-274J7.2         1
```

```
## 266                                          SRP72         1
## 267                                          SRSF1         1
## 268                                          SRSF3         1
## 269                                          SRSF6         1
## 270                                           SSR3         1
## 271                                          STAG1         1
## 272                                          SUGP2         1
## 273                                SYNCRIP,RP11-321N4.5         1
## 274                                           TAF1D         1
## 275                                           TANC2         1
## 276                                TANGO6,RP11-521L9.2         1
## 277                                          TARDBP         1
## 278                TAS2R43,RP11-785H5.2,PRR4,TAS2R30         1
## 279                                          THADA         1
## 280                                         TIMM10B         1
## 281                              TIMM23B,LINC00843         1
## 282                                         TMEM131         1
## 283                                        TMEM194A         1
## 284                                           TMOD3         1
## 285                                           TNPO1         1
## 286                                           TNPO2         1
## 287                                         TRAPPC9         1
## 288                                           TRMT1         1
## 289                                           TRPM7         1
## 290                                           TRPS1         1
## 291                                            TSC1         1
## 292                                         TUBGCP4         1
## 293                                         TUBGCP5         1
## 294                                              U1         1
## 295                                         U12,RNU12         1
## 296                                            UBN2         1
## 297                                            UBR1         1
## 298                                            UBR2         1
## 299                                           UGGT2         1
## 300                                           UHMK1         1
## 301                                            ULK4         1
## 302                                            URB1         1
## 303                                           USP25         1
## 304                                           USP33         1
## 305                                           UTP20         1
## 306                              UVRAG,RP11-263C24.1         1
## 307                                          VPS13C         1
## 308                                          VPS13D         1
## 309                                            WDR4         1
## 310                                           WHSC1         1
## 311                                         WHSC1L1         1
## 312                                             WRN         1
## 313                                            XRN1         1
## 314                                       Y_RNA.v174         1
## 315                                            YOD1         1
## 316                                             ZFX         1
## 317                                          ZMYND8         1
## 318                                          ZNF121         1
## 319                                          ZNF148         1
```

```
## 320                                ZNF207         1
## 321                                ZNF562         1
## 322                                ZNF587         1
## 323                                ZNF638         1
## 324                                ZNF644         1
## 325                                ZNF800         1
## 326                                ZYG11A         1
## 327                                  AARS         2
## 328                                 ABCA2         2
## 329                                 ABCA5         2
## 330                                 ABCC2         2
## 331                                  ABL2         2
## 332                           AC006014.7         2
## 333                           AC006042.8         2
## 334                    AC006483.1,ACTB         2
## 335                  AC139149.1,ACTG1          2
## 336                                 ACAD9         2
## 337                   ACEA_U3,SNORD3A          2
## 338                   ACEA_U3,SNORD3C          2
## 339                                 ACIN1         2
## 340                                  ACLY         2
## 341                                 ACOT9         2
## 342                                 ACTN4         2
## 343                                ADARB1         2
## 344                                  ADNP         2
## 345                                  AFF4         2
## 346                                AFG3L1P         2
## 347                                   AGL         2
## 348                  AGRN,RP11-54O7.14         2
## 349                                AHCTF1         2
## 350                                 AHNAK         2
## 351                                 AKAP9         2
## 352                           AL161626.1         2
## 353                           AL442127.2         2
## 354                                ANAPC5         2
## 355                                ANKFY1         2
## 356                                ANKLE2         2
## 357                               ANKRD17         2
## 358                               ANKRD28         2
## 359                                   ANLN         2
## 360                  AP001469.9,MCM3AP         2
## 361                                   APC         2
## 362                        APOPT1,KLC1         2
## 363                                   AQR         2
## 364                                ARFGEF2         2
## 365                              ARHGAP11A         2
## 366                               ARHGAP21         2
## 367                               ARHGAP29         2
## 368                                ARHGAP5         2
## 369                                 ARID4B         2
## 370                                   ASPH         2
## 371                                   ASPM         2
## 372                                  ASXL1         2
## 373                                  ATAD2         2
```

## 374	ATAD5	2
## 375	ATL2	2
## 376	ATM	2
## 377	ATN1	2
## 378	ATP11A	2
## 379	ATP11C	2
## 380	ATP13A3	2
## 381	ATP1B3	2
## 382	ATP2A2	2
## 383	ATP5B	2
## 384	ATR,RP11-383G6.3	2
## 385	ATXN10	2
## 386	ATXN2L	2
## 387	B2M	2
## 388	B4GALT1	2
## 389	BASP1	2
## 390	BAZ1B	2
## 391	BIRC6	2
## 392	BMI1	2
## 393	BPTF	2
## 394	BRCA2	2
## 395	BRD2	2
## 396	BRD8	2
## 397	BRD9	2
## 398	BTBD3	2
## 399	BUB1	2
## 400	BUB3	2
## 401	C16orf72	2
## 402	C20orf24	2
## 403	C4BPA	2
## 404	C4BPB	2
## 405	C5orf24	2
## 406	C6orf100	2
## 407	C6orf48	2
## 408	C6orf62	2
## 409	C7orf55-LUC7L2	2
## 410	CACNB2	2
## 411	CAD	2
## 412	CALM2	2
## 413	CALR	2
## 414	CAMSAP2	2
## 415	CAND1	2
## 416	CANX	2
## 417	CAPN2	2
## 418	CAPN7	2
## 419	CAPRIN1	2
## 420	CAPZA1	2
## 421	CARS2	2
## 422	CASP2	2
## 423	CBX3	2
## 424	CCAR1	2
## 425	CCDC14	2
## 426	CCDC57	2
## 427	CCT2	2

```
## 428                                          CCT3         2
## 429                                          CCT4         2
## 430                                          CCT5         2
## 431                                         CCT6A         2
## 432                                  CCT8,AF129075.5         2
## 433                                          CD46         2
## 434                                          CD97         2
## 435                                         CDC16         2
## 436                                       CDC42BPB         2
## 437                                          CDCA7         2
## 438                                           CDK1         2
## 439                                        CDK5RAP2         2
## 440                                 CELF1,RP11-750H9.7         2
## 441                               CEP152,RP11-227D13.4         2
## 442                                         CEP192         2
## 443                                           CHD1         2
## 444                                           CHD2         2
## 445                                           CHD3         2
## 446                                           CHD4         2
## 447                                         CLINT1         2
## 448                                           CLK1         2
## 449                                        CLPTM1L         2
## 450                                         CLSTN3         2
## 451                                           CLUH         2
## 452                                           CNBP         2
## 453                                         CNOT10         2
## 454                                         COL12A1         2
## 455                                          COL1A1         2
## 456                                          COL4A5         2
## 457                                            COPA         2
## 458                                           COPB1         2
## 459                                           COPB2         2
## 460                                     CPSF1,MIR939         2
## 461                                          CREBBP         2
## 462                                          CREBZF         2
## 463                                           CRIM1         2
## 464                                  CS,RP11-977G19.10         2
## 465                                            CSAD         2
## 466                                           CSDE1         2
## 467                                          CSNK1D         2
## 468                                           CSPP1         2
## 469                                CTB-89H12.4,CSNK1A1         2
## 470                               CTD-2006C1.12,ZNF700         2
## 471 CTD-2047H16.3,CTD-2047H16.2,RNF213         2
## 472                                         CTNNAL1         2
## 473                                          CTNNB1         2
## 474                                            CUL1         2
## 475                                           CUL4A         2
## 476                                           CUL4B         2
## 477                                           CYR61         2
## 478                                            DAB2         2
## 479                                          DAZAP1         2
## 480                                           DCAF6         2
## 481                                           DDX10         2
```

```
## 482                                  DDX12P         2
## 483                                   DDX17         2
## 484                                   DDX21         2
## 485                      DDX39B,AL662801.1         2
## 486                                   DDX3X         2
## 487                                   DDX42         2
## 488                                   DDX46         2
## 489                                   DDX47         2
## 490                                   DDX56         2
## 491                                  DDX60L         2
## 492                                  DENND4C        2
## 493                                    DGKD         2
## 494                                    DGKH         2
## 495                                   DHX15         2
## 496                         DHX30,uc_338            2
## 497                                   DHX36         2
## 498                                  DICER1         2
## 499                                    DIO2         2
## 500                                   DIP2B         2
## 501                                   DIS3L         2
## 502                                    DKC1         2
## 503                                    DLG1         2
## 504                                   DMXL2         2
## 505                                  DNAJC13        2
## 506                                   DNAJC2         2
## 507                                   DNMT1         2
## 508                                  DROSHA         2
## 509                                     DSP         2
## 510                                   DUS1L         2
## 511                                   DUSP1         2
## 512                                  DYNC1H1        2
## 513                                 DYNC1LI2        2
## 514                                   DYRK1A         2
## 515                                     E2F3         2
## 516                                     E2F4         2
## 517                                     ECT2         2
## 518                                    EDRF1         2
## 519                                     EEF2         2
## 520                                   EIF2S3         2
## 521                                    EIF3B         2
## 522                                   EIF4A1         2
## 523                                   EIF4A2         2
## 524                                   EIF4G1         2
## 525                                   EIF4G2         2
## 526                                    ELAC2         2
## 527                                     ENO1         2
## 528                                   ENOSF1         2
## 529                         EP300,MIR1281            2
## 530                                    EPPK1         2
## 531                                  ERBB2IP         2
## 532                                   ESPL1         2
## 533                                    ETF1         2
## 534                                   EWSR1         2
## 535                                     FAF1         2
```

```
## 536      FAM120A     2
## 537      FAM122B     2
## 538     FAM160B1     2
## 539      FAM208B     2
## 540       FAM46A     2
## 541        FANCI     2
## 542         FASN     2
## 543         FAT1     2
## 544       FBRSL1     2
## 545       FBXO38     2
## 546        FBXO9     2
## 547         FLNA     2
## 548         FMR1     2
## 549       FNBP1L     2
## 550        FNBP4     2
## 551       FNDC3A     2
## 552        FUBP3     2
## 553          FUS     2
## 554        GABRE     2
## 555       GALNT2     2
## 556        GANAB     2
## 557        GAPDH     2
## 558         GAS5     2
## 559         GBA2     2
## 560         GDI2     2
## 561         GEN1     2
## 562       GIGYF1     2
## 563          GK5     2
## 564      GLG1.v2     2
## 565        GLYR1     2
## 566         GNAS     2
## 567       GOLGA3     2
## 568      GOLGA8A     2
## 569      GOLGA8B     2
## 570        GPBP1     2
## 571      GPBP1L1     2
## 572          GPI     2
## 573       GPR125     2
## 574        GSPT1     2
## 575       GTPBP4     2
## 576        H2AFY     2
## 577        HCFC1     2
## 578        HDLBP     2
## 579         HEG1     2
## 580      HERC2P2     2
## 581        HERC4     2
## 582       HEXIM1     2
## 583          HGS     2
## 584        HIAT1     2
## 585        HIF1A     2
## 586        HIPK1     2
## 587        HIPK3     2
## 588         HIRA     2
## 589        HMGCR     2
```

```
## 590                                        HMGXB3         2
## 591                                        HNRNPA0        2
## 592                                       HNRNPA2B1       2
## 593                                        HNRNPAB        2
## 594                                         HNRNPD        2
## 595                                        HNRNPDL        2
## 596                                        HNRNPH1        2
## 597                                        HNRNPH3        2
## 598                                         HNRNPK        2
## 599                                         HNRNPL        2
## 600                                         HNRNPM        2
## 601                                         HNRNPR        2
## 602                              HNRNPU,RP11-11N7.5       2
## 603                                         HP1BP3        2
## 604                  hsa-mir-3180-4,PKD1P6,MIR6511B1      2
## 605                              hsa-mir-6724-1           2
## 606                                       HSP90AA1       2
## 607                                       HSP90AB1       2
## 608                                       HSP90AB3P      2
## 609                                        HSP90B1       2
## 610                                          HSPA8       2
## 611                                          HSPD1       2
## 612                                          HUWE1       2
## 613                                           IARS       2
## 614                                           IBTK       2
## 615                                           ICE1       2
## 616                                         IKBKAP       2
## 617                                         INCENP       2
## 618                                          INO80       2
## 619                                         INPPL1       2
## 620                                         INTS10       2
## 621                                           IPO9       2
## 622                                          ITGB1       2
## 623                                          ITPR1       2
## 624                                          ITPR3       2
## 625                                           JAK1       2
## 626                                         JMJD1C       2
## 627                                         KANSL1       2
## 628                                         KANSL2       2
## 629                                          KAT2A       2
## 630                                 KHSRP,MIR3940        2
## 631                                       KIAA0020       2
## 632                                       KIAA0100       2
## 633                                       KIAA0368       2
## 634                                       KIAA1468       2
## 635                                       KIAA1524       2
## 636                                       KIAA1731       2
## 637                                          KIF14       2
## 638                                         KIF18B       2
## 639                                          KIF1B       2
## 640                                          KIF23       2
## 641                                          KIF5B       2
## 642                                          KLHL5       2
## 643                                          KMT2A       2
```

```
## 644                                  KMT2B         2
## 645                                  KMT2D         2
## 646                                  KNTC1         2
## 647                      KRIT1,AC000120.7         2
## 648                                   KRT7         2
## 649                                   KTN1         2
## 650                                  LAMA1         2
## 651                                  LAMA5         2
## 652                                  LAMC1         2
## 653                                  LARP1         2
## 654                                   LARS         2
## 655                                    LBR         2
## 656                                   LDHA         2
## 657                                   LDHB         2
## 658                                   LGR4         2
## 659                                   LIFR         2
## 660                              LINC00324         2
## 661                              LINC00472         2
## 662                              LINC00657         2
## 663                              LINC00969         2
## 664                                  LMAN1         2
## 665                                   LMO4         2
## 666                                   LMO7         2
## 667                                 LPCAT1         2
## 668                                  LRIG2         2
## 669                      LRP8,RP4-784A16.3         2
## 670                                 LRPPRC         2
## 671                          LSMEM1,IFRD1         2
## 672                                  MACF1         2
## 673                                   MADD         2
## 674                                   MAFK         2
## 675                                 MALAT1         2
## 676                                 MAN2A1         2
## 677                                 MAP3K2         2
## 678                                 MAP4K5         2
## 679                                 MAPK14         2
## 680                                  MARC1         2
## 681                                  MARK3         2
## 682                                  MATR3         2
## 683                                  MBNL3         2
## 684                                  MBTD1         2
## 685                                 MBTPS1         2
## 686                                   MCM4         2
## 687                                   MCM7         2
## 688                                  MCMBP         2
## 689                                  MED14         2
## 690                                  MED15         2
## 691                                  MED17         2
## 692                                    MET         2
## 693                                  MGEA5         2
## 694                                MIR3916         2
## 695                           MIR4442,TOP2B         2
## 696                  MIR612,mascRNA-menRNA         2
## 697                              MIRLET7BHG         2
```

```
## 698                                    MKI67         2
## 699                                    MLLT1         2
## 700                                    MLXIP         2
## 701                                    MMS19         2
## 702                                     MON2         2
## 703                                  MORF4L2         2
## 704                                     MPP6         2
## 705                          MSH2,HCG2040054         2
## 706                                     MSL1         2
## 707                                     MST4         2
## 708                                    MTCH1         2
## 709                                    MTCL1         2
## 710                                  MTHFD1L         2
## 711                                     MTRR         2
## 712                                    MUC16         2
## 713                                      MYC         2
## 714                                   MYCBP2         2
## 715                                    MYO19         2
## 716                                    MYO1E         2
## 717                                     MYPN         2
## 718                                  NA.v1539         2
## 719                                  NA.v1540         2
## 720                                   NA.v326         2
## 721                                  NA.v5750         2
## 722                                  NA.v7259         2
## 723                                  NA.v7454         2
## 724                                  NA.v8191         2
## 725                                  NA.v8558         2
## 726                                  NAA16.v1         2
## 727                                  NAA25.v1         2
## 728                                 NAP1L1.v1         2
## 729                                 NAP1L4.v1         2
## 730                                    NBEAL2         2
## 731                                    NBPF12         2
## 732                                    NBPF8P         2
## 733                                    NCAPD3         2
## 734                                    NCAPG2         2
## 735                                       NCL         2
## 736                                     NEAT1         2
## 737                  NEAT1_2,NEAT1_1,NEAT1           2
## 738                          NEAT1_3,NEAT1           2
## 739                                      NEK7         2
## 740                                     NFAT5         2
## 741                                    NFE2L2         2
## 742                                     NFXL1         2
## 743                                      NKTR         2
## 744                                     NLGN2         2
## 745                                     NOL11         2
## 746                                      NOL8         2
## 747                                     NOLC1         2
## 748                                      NOM1         2
## 749                                      NONO         2
## 750                                      NOP2         2
## 751                                     NOP56         2
```

```
## 752                                  NOP58 2
## 753                                 NOTCH2 2
## 754                                 NPEPPS 2
## 755                        NPIPB3,SMG1P3 2
## 756                                 NPLOC4 2
## 757                                  NPTX1 2
## 758                                  NR2C1 2
## 759                                   NRD1 2
## 760                                  NSUN2 2
## 761                                 NUP107 2
## 762                                 NUP133 2
## 763                                 NUP153 2
## 764                                 NUP155 2
## 765                                 NUP160 2
## 766                                 NUP205 2
## 767                                 NUP210 2
## 768                                    NVL 2
## 769                                  OBSCN 2
## 770                                   OCRL 2
## 771                                    OGT 2
## 772                                   OLR1 2
## 773                                  OSER1 2
## 774                                    P4HB 2
## 775                                 PABPC1 2
## 776                                 PABPC4 2
## 777                                   PAN3 2
## 778                                  PAPD7 2
## 779                                 PAXBP1 2
## 780                                  PCBP1 2
## 781                                  PCBP2 2
## 782                  PCF11,RP11-727A23.4 2
## 783                                  PCID2 2
## 784                                   PCM1 2
## 785                                   PCNA 2
## 786                                   PCNT 2
## 787                                   PCNX 2
## 788                                 PCNXL3 2
## 789                                 PDCD11 2
## 790                                  PDCD6 2
## 791                                  PDE7A 2
## 792                                  PDS5A 2
## 793                                  PDS5B 2
## 794                                   PFAS 2
## 795                       PGAM1P11,UBE4B 2
## 796                                   PHB2 2
## 797                                  PHF12 2
## 798                                  PHKA2 2
## 799                                  PHTF2 2
## 800                                 PICALM 2
## 801                                 PIEZO1 2
## 802                                 PIEZO2 2
## 803                                PIK3C2B 2
## 804                                 PIK3R4 2
## 805                                PIP5K1A 2
```

```
## 806                  PKD1,MIR3180-5,RP11-304L19.3,MIR6511B1         2
## 807                                                   PKD2         2
## 808                                                    PKM         2
## 809                                                   PKN2         2
## 810                                                 PLAGL1         2
## 811                                                   PLEC         2
## 812                                                PLEKHA1         2
## 813                                                   PLK2         2
## 814                                                  PLOD2         2
## 815                                                 PLXNB2         2
## 816                                                  PMPCB         2
## 817                                                   POGZ         2
## 818                                                   POLG         2
## 819                                                 POLR1B         2
## 820                                                 POLR2A         2
## 821                                                 POLR2B         2
## 822                                                POLR2J2         2
## 823                                                   PON2         2
## 824                                               PPP1R15B         2
## 825                                                PPP1R3C         2
## 826                                                PPP2R1B         2
## 827                                                   PRC1         2
## 828                                                  PRDX1         2
## 829                                                 PRKAA1         2
## 830                                                pRNA.v3         2
## 831                                                  PRPF3         2
## 832                                                PRPF38B         2
## 833                                                 PRPF39         2
## 834                                                 PRPF4B         2
## 835                                                  PRPF8         2
## 836                                                  PRR12         2
## 837                                                 PRRC2A         2
## 838                                               PSMA1.v2         2
## 839                                                  PSMA5         2
## 840                                                  PSME4         2
## 841                                                  PTBP1         2
## 842                                                  PTCD3         2
## 843                                                 PTP4A1         2
## 844                                                 PTPN14         2
## 845                                                  PTPN4         2
## 846                                                  PTPRF         2
## 847                                                  PTPRM         2
## 848                                                  PTPRS         2
## 849                                                   PUM1         2
## 850                                                    PXN         2
## 851                                                   QARS         2
## 852                                                 QRICH1         2
## 853                                                  QSER1         2
## 854                                                  QSOX2         2
## 855                                        RABGGTB,ACADM         2
## 856                                                  RAD21         2
## 857                                                 RAD23A         2
## 858                                                 RAD54L         2
## 859                                                    RAF1         2
```

```
## 860                                        RAN         2
## 861                                     RANBP2         2
## 862                                    RANGAP1         2
## 863                                   RAP1GAP2         2
## 864                                    RAPGEF2         2
## 865                                     RB1CC1         2
## 866                                      RBBP7         2
## 867                                      RBM14         2
## 868                                      RBM17         2
## 869                                      RBM26         2
## 870                                       RBM3         2
## 871                                      RBM33         2
## 872                                      RBM39         2
## 873                                       RBM5         2
## 874                                       REV1         2
## 875                                      REV3L         2
## 876                                      RFWD3         2
## 877                                    RHOBTB3         2
## 878                                       RIF1         2
## 879                             RMRP,RNase_MRP         2
## 880                                      RN7SK         2
## 881                                     RNF145         2
## 882                                    RNU1-27P         2
## 883                                    RNU1-28P         2
## 884                                      ROCK2         2
## 885                  RP11-231L11.3,SLC25A36         2
## 886 RP11-298E9.7,PITRM1-AS1,PFKP         2
## 887                        RP11-396K3.1         2
## 888                  RP11-872D17.8,SLC43A3         2
## 889                         RP13-735L24.1         2
## 890                     RP4-620E11.4,CHD6         2
## 891                    RP5-1172N10.4,USP9X         2
## 892                                  RPL13A         2
## 893                       RPL21P5,HECTD1         2
## 894                                   RPL5         2
## 895                                 RPRD1B         2
## 896                                  RRP1B         2
## 897                                 SACM1L         2
## 898                                 SCARB1         2
## 899                                SCARNA2         2
## 900                                  SCML1         2
## 901                                 SEC16A         2
## 902                                  SENP6         2
## 903                                 SETD1A         2
## 904                    SETD1B,RP11-347I19.7         2
## 905                                  SETD2         2
## 906                                  SETD5         2
## 907                                    SF1         2
## 908                                  SF3B1         2
## 909                                 SFMBT2         2
## 910                                   SGK1         2
## 911                                SH3PXD2A         2
## 912                              SHC1,PYGO2         2
## 913                                   SHPRH         2
```

## 914	SKIL	2
## 915	SKIV2L2	2
## 916	SLC12A6	2
## 917	SLC16A1	2
## 918	SLC20A1	2
## 919	SLC25A3	2
## 920	SLC30A1	2
## 921	SLC38A2	2
## 922	SLC3A2	2
## 923	SLC4A7	2
## 924	SLC7A5	2
## 925	SLC7A6	2
## 926	SLMAP	2
## 927	SLMO2	2
## 928	SLTM	2
## 929	SMC1A	2
## 930	SMC3	2
## 931	SMC4	2
## 932	SMC5	2
## 933	SMCHD1	2
## 934	SMG1	2
## 935	SMG1P2,RP11-368N21.5	2
## 936	SMG1P4	2
## 937	SMG7	2
## 938	SMS	2
## 939	SNHG1	2
## 940	SNHG12	2
## 941	SNHG17	2
## 942	SNORA76C	2
## 943	SNORD3D	2
## 944	SNRNP200	2
## 945	SNX5	2
## 946	SON	2
## 947	SPAG5	2
## 948	SPDL1	2
## 949	SPIN1	2
## 950	SPTAN1	2
## 951	SPTBN1	2
## 952	SPTLC1	2
## 953	SQSTM1	2
## 954	SRBD1	2
## 955	SRCAP	2
## 956	SREK1	2
## 957	SRRM2	2
## 958	SRRT	2
## 959	SRSF11	2
## 960	SRSF2	2
## 961	SRSF5	2
## 962	SSFA2	2
## 963	SSR1	2
## 964	STT3B	2
## 965	SUN1	2
## 966	SUPT6H	2
## 967	SUZ12	2

```
## 968                                    SVEP1         2
## 969                                    SYNE2         2
## 970                                     SZT2         2
## 971                                     TAF1         2
## 972                                    TAF15         2
## 973                                     TAF2         2
## 974                                   TARBP1         2
## 975                                   TBC1D8         2
## 976                                     TBK1         2
## 977                                     TBX3         2
## 978                                   TCERG1         2
## 979                                    TCF25         2
## 980                                     TCP1         2
## 981                                    TDRD9         2
## 982                      TEAD1,RP11-47J17.1         2
## 983                                    TELO2         2
## 984                                    TEX10         2
## 985                                   TFAP2A         2
## 986                                      TFG         2
## 987                                     TFRC         2
## 988                                   TGFBR1         2
## 989                                   TGFBR3         2
## 990                                THAP9-AS1         2
## 991                                    THOC2         2
## 992                                    TIAL1         2
## 993                                TIAM2,SCAF8         2
## 994                                     TICRR         2
## 995                                  TIMELESS         2
## 996                                     TJP1         2
## 997                                   TM4SF1         2
## 998                                   TM9SF3         2
## 999                                   TMEM259         2
## 1000                                  TMEM87A         2
## 1001                                     TMPO         2
## 1002          TNFRSF10B,RP11-875O11.3         2
## 1003                                   TNKS2         2
## 1004                                   TNPO3         2
## 1005                                  TNRC6A         2
## 1006                                    TOB1         2
## 1007                                   TOP2A         2
## 1008                                   TPCN1         2
## 1009                                    TPP2         2
## 1010                                     TPR         2
## 1011                                   TRA2A         2
## 1012                                    TRAP1         2
## 1013                                   TRIM28         2
## 1014                                   TRIM33         2
## 1015                                   TRIM37         2
## 1016                                   TRIM44         2
## 1017                                   TRIM66         2
## 1018                                     TRIO         2
## 1019                                   TRIP12         2
## 1020                                   TRIP13         2
## 1021                                    TROAP         2
```

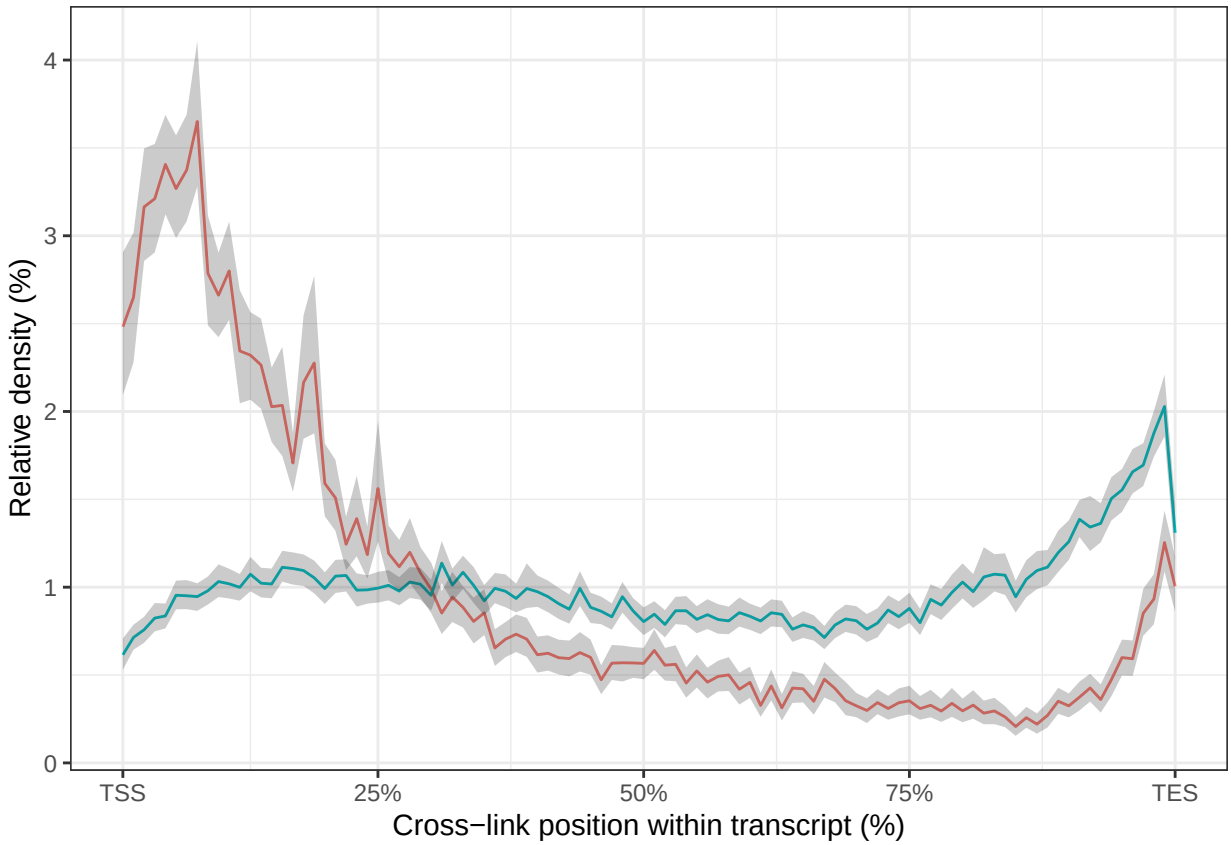
## 1022	TSC22D1	2
## 1023	TSPYL1	2
## 1024	TSR1	2
## 1025	TTC37	2
## 1026	TTI1	2
## 1027	TXLNG	2
## 1028	U2SURP	2
## 1029	UBA2	2
## 1030	UBAP2	2
## 1031	UBAP2L	2
## 1032	UBE2I	2
## 1033	UBE3C	2
## 1034	UBP1	2
## 1035	UBR4	2
## 1036	UBR5	2
## 1037	UBXN4	2
## 1038	ULK1	2
## 1039	ULK3	2
## 1040	UPF1	2
## 1041	UPF2	2
## 1042	UQCRC2	2
## 1043	URI1	2
## 1044	USP1	2
## 1045	USP10	2
## 1046	USP22	2
## 1047	USP24	2
## 1048	USP3	2
## 1049	USP34	2
## 1050	USP47	2
## 1051	USP7	2
## 1052	VCP	2
## 1053	VIM	2
## 1054	VMP1,MIR21	2
## 1055	VPRBP	2
## 1056	VPS13A	2
## 1057	WDR11	2
## 1058	WDR26	2
## 1059	WDR44	2
## 1060	WDR6	2
## 1061	WDR90	2
## 1062	WEE1	2
## 1063	WLS	2
## 1064	WNK1	2
## 1065	WSB1	2
## 1066	XPO1	2
## 1067	XPO6	2
## 1068	XPOT	2
## 1069	XRN2	2
## 1070	YARS	2
## 1071	YBX3	2
## 1072	YLPM1	2
## 1073	YTHDC2	2
## 1074	YTHDF3	2
## 1075	YWHAG	2

```
## 1076                                                ZBED5         2
## 1077                                              ZC3H11A         2
## 1078                                               ZC3H7A         2
## 1079                                              ZCCHC11         2
## 1080                                              ZDHHC11         2
## 1081                                              ZDHHC17         2
## 1082                                               ZDHHC5         2
## 1083                                               ZDHHC6         2
## 1084                                               ZFAND5         2
## 1085                                  ZFAS1,ZNFX1-AS1_2         2
## 1086                                               ZFC3H1         2
## 1087                                              ZFP36L1         2
## 1088                                                  ZFR         2
## 1089                                               ZMYM2         2
## 1090                                              ZNF106         2
## 1091                                              ZNF131         2
## 1092                                              ZNF146         2
## 1093                                              ZNF195         2
## 1094                                               ZZEF1         2
## 1095                                                ZZZ3         2
```

#Figure 4B Plot profile of ALYREF-DMSO cross-links across group 1 and 2 genes

```
ALYREF_100bins_scaled %>%
    filter(geneName %in% clust_all$geneName) %>%
    left_join(clust_all) %>%
    filter(Timepoint == "DMSO" & totals_unNorm >= 20) %>%
    spread(distBin, value) %>%
    gather("distBin", "value", "1":"100") %>%
    ggplot(aes(x = as.numeric(distBin), y = value, col = as.factor(clusterID),
        group = as.factor(clusterID))) + stat_summary(fun = mean,
    geom = "line", size = 0.5) + stat_summary(fun.data = "mean_cl_boot",
    geom = "ribbon", alpha = 0.25, col = NA) + theme_bw() + xlab("Cross-link position within transcript
    scale_x_continuous(breaks = c(1, 25, 50, 75, 100), labels = c("TSS",
        "25%", "50%", "75%", "TES")) + theme(legend.position = "none") +
    ylab("Relative density (%)")
```

```
## Joining, by = "geneName"
```



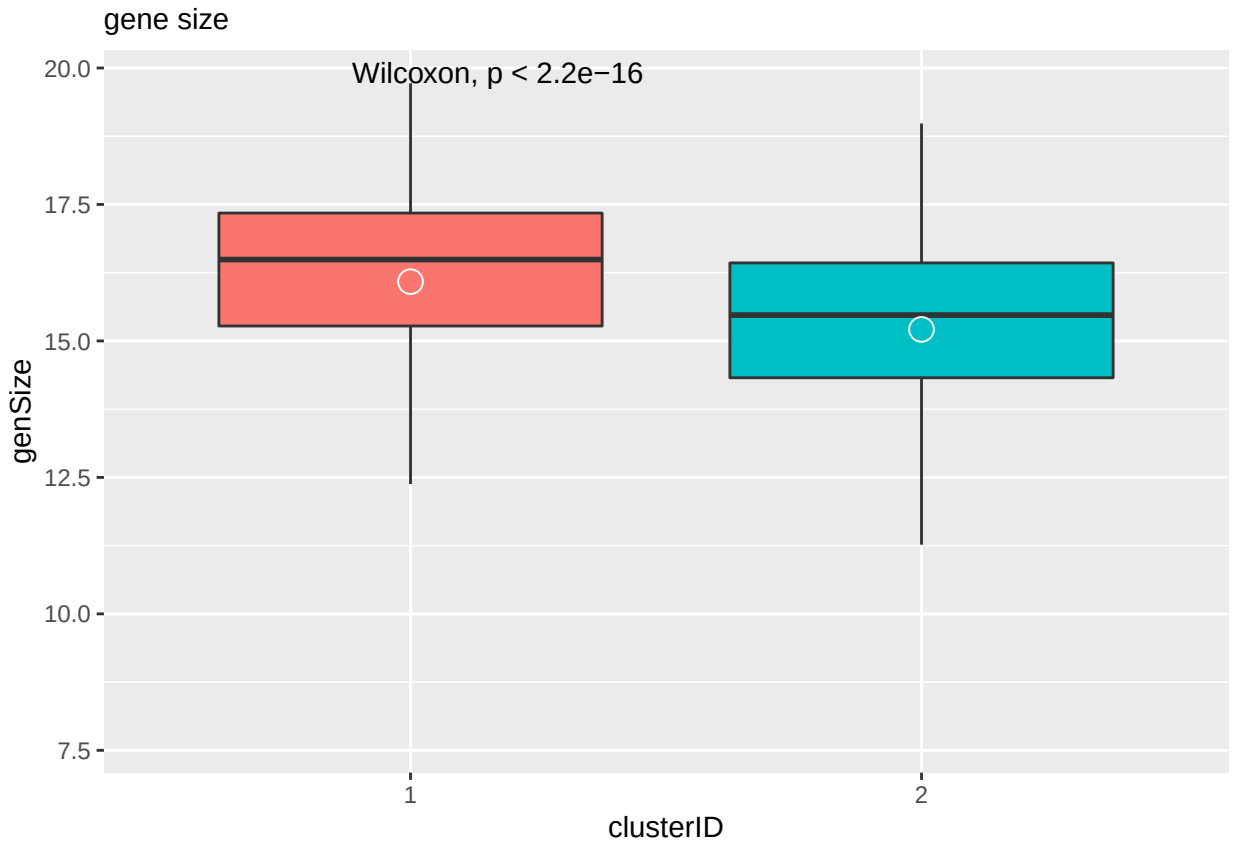
#Figure 4 C analyse expression, gene size, exonic size (cDNA size) and number of exons associated with group 1 and 2 genes

```
annotation_metaData <- read.table("../../data/hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.ex
    sep = "\t", header = T)



data_for_boxplots <- merge(annotation_metaData, clust_all) %>%
    filter(exonID == totalExons) %>%
    mutate(genSize = exonSize + genDistToTSS) %>%
    select(-exonID, -exonSize, -stop, -start, -chr, -strand,
        -score, -genDistToTSS) %>%
    select(c("geneName", "clusterID", "totalExons", "relSize",
        "genSize")) %>%
    mutate_at(vars("totalExons", "relSize", "genSize"), log2) %>%
    left_join(expression_vector)
```

```
## Joining, by = "geneName"
```

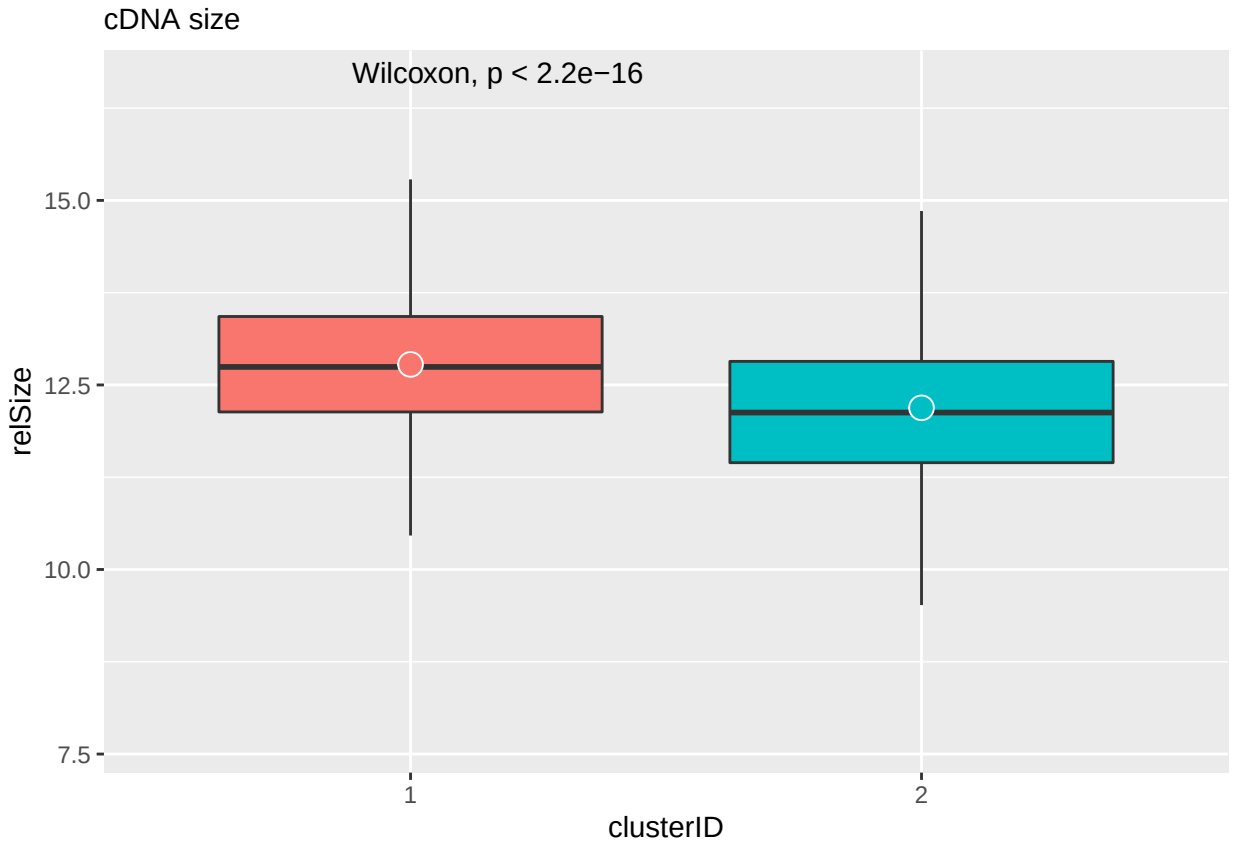
```
data_for_boxplots %>%
    ggplot(aes(x = clusterID, y = genSize, fill = as.factor(clusterID),
        group = clusterID)) + geom_boxplot(outlier.shape = NA) +
    geom_point(stat = "summary", shape = 21, col = "white", size = 4) +
    labs(subtitle = "gene size") + stat_compare_means(method = "wilcox.test") +
    theme(legend.position = "none")
```

```
## No summary function supplied, defaulting to `mean_se()`
```



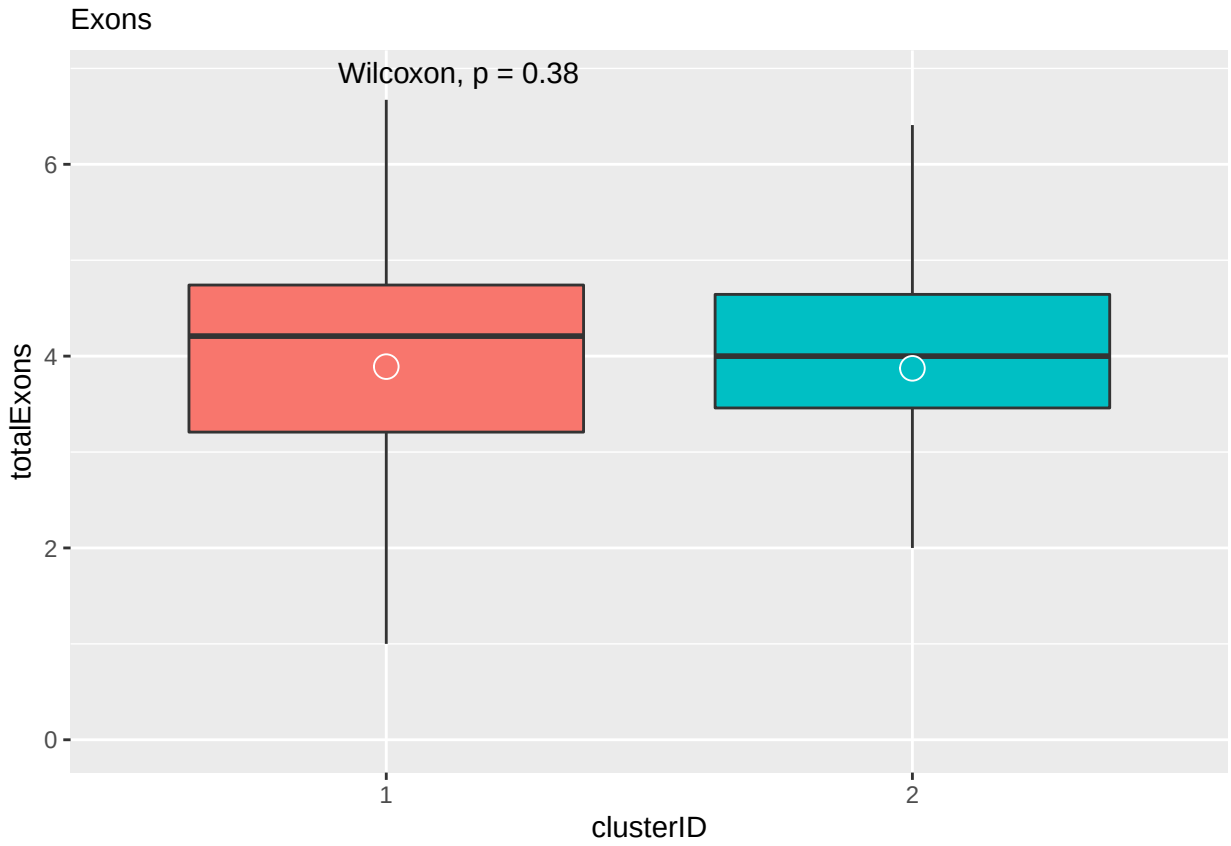

```
data_for_boxplots %>%
    ggplot(aes(x = clusterID, y = relSize, fill = as.factor(clusterID),
        group = clusterID)) + geom_boxplot(outlier.shape = NA) +
    geom_point(stat = "summary", shape = 21, col = "white", size = 4) +
    labs(subtitle = "cDNA size") + stat_compare_means(method = "wilcox.test") +
    theme(legend.position = "none")
```

```
## No summary function supplied, defaulting to `mean_se()`
```



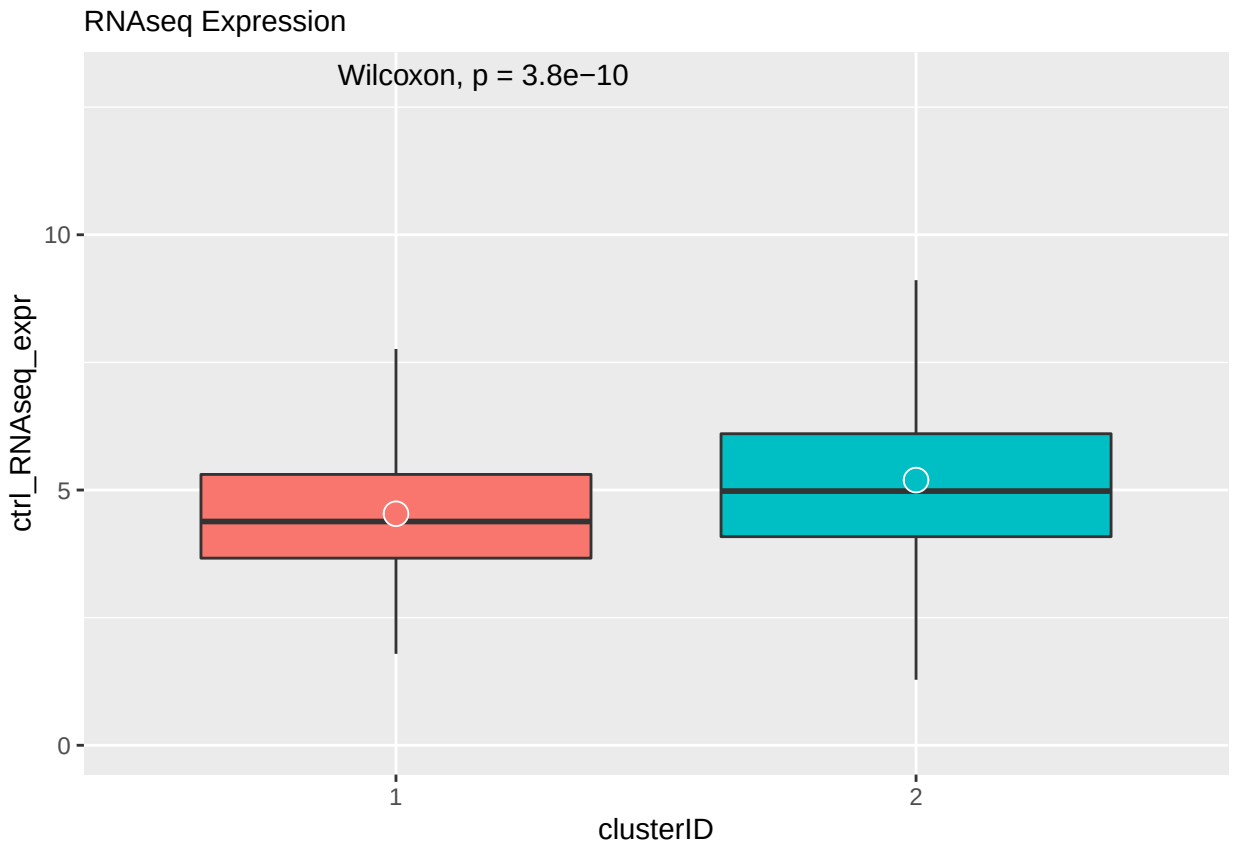

```
data_for_boxplots %>%
    ggplot(aes(x = clusterID, y = totalExons, fill = as.factor(clusterID),
        group = clusterID)) + geom_boxplot(outlier.shape = NA) +
    geom_point(stat = "summary", shape = 21, col = "white", size = 4) +
    labs(subtitle = "Exons") + stat_compare_means(method = "wilcox.test") +
    theme(legend.position = "none")
```

```
## No summary function supplied, defaulting to `mean_se()`
```




```
data_for_boxplots %>%
    ggplot(aes(x = clusterID, y = ctrl_RNAseq_expr, fill = as.factor(clusterID),
        group = clusterID)) + geom_boxplot(outlier.shape = NA) +
    geom_point(stat = "summary", shape = 21, col = "white", size = 4) +
    labs(subtitle = "RNAseq Expression") + stat_compare_means(method = "wilcox.test") +
    theme(legend.position = "none")
```

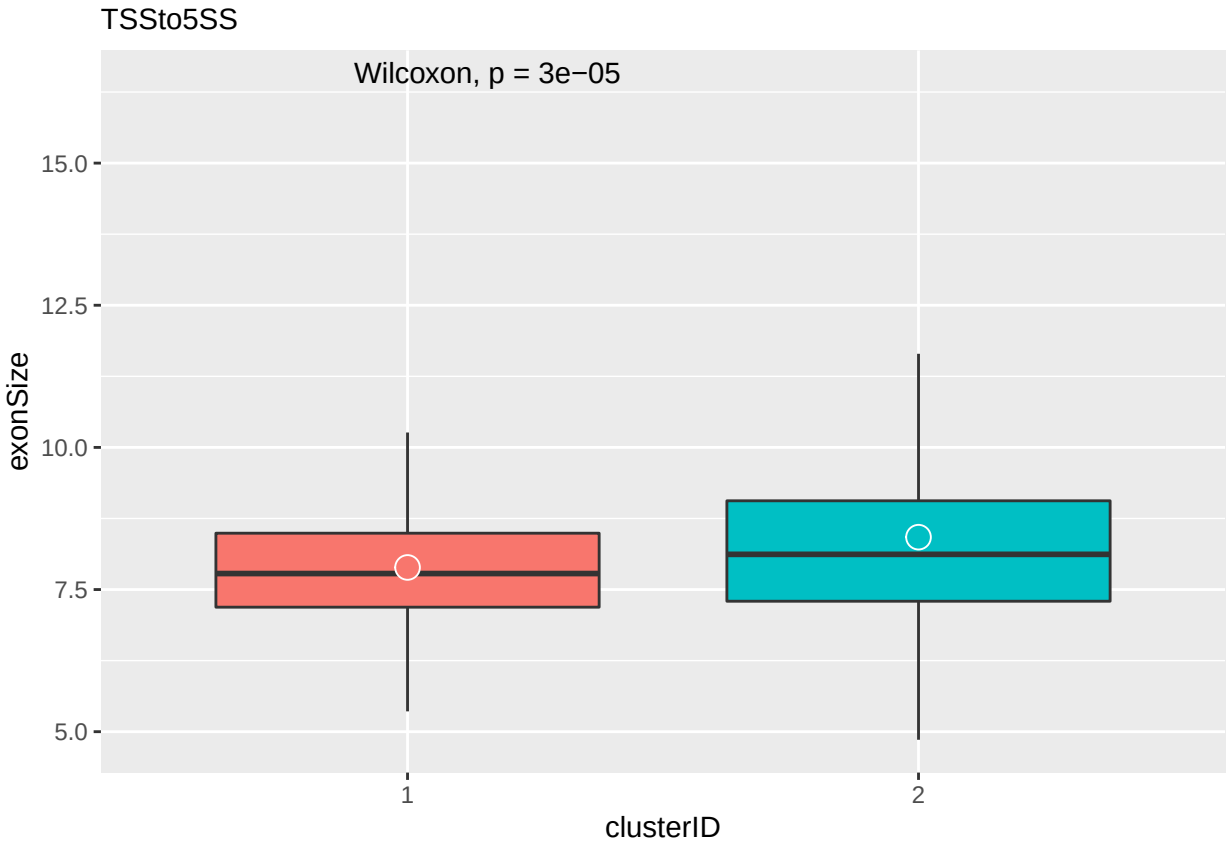
```
## Warning: Removed 2 rows containing non-finite values (stat_boxplot).
## Warning: Removed 2 rows containing non-finite values (stat_summary).
## No summary function supplied, defaulting to `mean_se()`
## Warning: Removed 2 rows containing non-finite values (stat_compare_means).
```



#Supplementary Figure 4 D boxplot of 1st exons size in group 1 and 2 genes

```
annotation_metaData <- read.table("../../data/hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.ex
    sep = "\t", header = T)



data_for_boxplots <- merge(annotation_metaData, clust_all) %>%
    filter(exonID == 1) %>%
    select(c("geneName", "clusterID", "exonSize")) %>%
    mutate_at(vars("exonSize"), log2)

data_for_boxplots %>%
    ggplot(aes(x = clusterID, y = exonSize, fill = as.factor(clusterID),
        group = clusterID)) + geom_boxplot(outlier.shape = NA) +
    geom_point(stat = "summary", shape = 21, col = "white", size = 4) +
    labs(subtitle = "TSSto5SS") + stat_compare_means(method = "wilcox.test") +
    theme(legend.position = "none")
```

```
## No summary function supplied, defaulting to `mean_se()`
```



#Figure 4 D plot profile of exon junction density across group 1 and 2 genes

```
# make profile of positions of exon junctions first prepair
# all genes
annoDF.WholeGene <- read.csv("../../data/hg38_HeLa_trimmed_loci_major_primary_isoform_annotated.exonNumb
    sep = "\t", header = F) %>%
    setNames(c("chr", "start", "stop", "IDAnno", "score", "strand")) %>%
    separate(IDAnno, c("geneName", "biotype", "WholeGene.exonID",
        "WholeGene.totalExons", "WholeGene.exonSize", "WholeGene.relSize",
        "WholeGene.distToTSS", "WholeGene.geneDesc", "WholeGene.distToDist5SS",
        "WholeGene.distToDist3SS", "WholeGene.relSizeof5UTR",
        "WholeGene.genSizeof5UTR", "WholeGene.relSize3UTR", "WholeGene.genSizeof3UTR",
        "WholeGene.relSizeofCDS", "WholeGene.genSizeofCDS", "WholeGene.pAtoUp3ss",
        "WholeGene.pAtoUp5ss", "WholeGene.exonDesc"), sep = ":::")

all_genes <- annoDF.WholeGene


totalSizes_WholeGene.mRNASize <- annoDF.WholeGene %>%
    filter(WholeGene.exonID == WholeGene.totalExons) %>%
    mutate(WholeGene.matureRNAsize = as.numeric(WholeGene.relSize),
        WholeGene.geneSize = as.numeric(ifelse(WholeGene.totalExons >
            1, (as.numeric(WholeGene.distToTSS) + as.numeric(WholeGene.exonSize)),
            WholeGene.exonSize))) %>%
    select(geneName, WholeGene.matureRNAsize)

totalSizes_relSize <- annoDF.WholeGene %>%
    select(geneName, WholeGene.relSize, WholeGene.exonID, WholeGene.totalExons)
```

```
# annotation for multiexonic genes for profiles
exonic_geneName <- all_genes %>%
    mutate(exonic = case_when(WholeGene.totalExons > 1 ~ "multiexonic",
        TRUE ~ "monoexonic")) %>%
    select(geneName, exonic) %>%
    unique()

# generate profiles for group 1 and 2

EJ_profiles_cluster <- clust_all %>%
    # add total mRNA sizes, exon ids and relative size of
    # mRNA up to exon displayed
mutate(geneName = as.character(geneName)) %>%
    left_join(totalSizes_WholeGene.mRNASize) %>%
    left_join(totalSizes_relSize) %>%
    mutate(WholeGene.relSize = as.integer(WholeGene.relSize),
        WholeGene.exonID = as.integer(WholeGene.exonID), WholeGene.matureRNAsize = as.integer(WholeGene
    # calculate relative positions of junction
mutate(rel_position_of_EJ = WholeGene.relSize/WholeGene.matureRNAsize) %>%
    # remove last exon as this is does not end with an
    # exonjunction
filter(WholeGene.exonID != WholeGene.totalExons)
```

```
## Joining, by = "geneName"
## Joining, by = "geneName"
```

```
EJ_profiles_1 <- EJ_profiles_cluster

# add bins
EJ_profiles_1$new_distBin <- cut(EJ_profiles_1$rel_position_of_EJ,
    seq(0, 1, by = 0.01), labels = seq("1", "100", by = 1))


EJ_profiles_2 <- EJ_profiles_1 %>%
    group_by(clusterID, geneName, WholeGene.matureRNAsize, new_distBin) %>%
    summarise(tally = n()) %>%
    # normalise to gene expression level
left_join(expression_vector) %>%
    mutate(tally_n = (tally/ctrl_RNAseq_expr)/(WholeGene.matureRNAsize/100),
        tally_nr = tally/(WholeGene.matureRNAsize/100))  #step to normalise count to bin size.
```

```
## `summarise()` has grouped output by 'clusterID', 'geneName',
## 'WholeGene.matureRNAsize'. You can override using the `.groups` argument.
## Joining, by = "geneName"
```

```
fig <- EJ_profiles_2 %>%
    mutate(totals_unNorm = sum(tally), pct = tally_nr/sum(tally_nr) *
        100) %>%
    spread(new_distBin, pct, fill = 0) %>%
    gather("distBin", "value", c("1":"100")) %>%
    mutate(distBin = factor(distBin, levels = c(1:100))) %>%
    ggplot(aes(x = as.numeric(distBin), y = value)) + stat_summary(fun = mean,
    geom = "line", size = 0.5, aes(col = clusterID)) + stat_summary(fun.data = "mean_cl_boot",
    geom = "ribbon", alpha = 0.2, col = NA, aes(group = clusterID)) +
    theme_bw()
```

```
fig
```