main_junctions

September 5, 2021

1 eQTL boxplot

This is script ported from python to fix unknown plotting error.

[1]:
```
suppressPackageStartupMessages({
    library(tidyverse)
    library(ggpubr)
})
```

1.1 Functions

[2]:
```
feature = "junctions"
```

1.1.1 Cached functions

[3]:
```
get_eqtl_df <- function(){
    eGenes_file = paste0('/ceph/projects/v4_phase3_paper/analysis/eqtl_analysis/
 ↪all/',
                         feature, '/expression_gct/prepare_expression/
 ↪fastqtl_permutation/',
                         '_m/Brainseq_LIBD.genes.txt.gz')
    eGenes = data.table::fread(eGenes_file) %>%
        select(gene_id, variant_id, maf, slope, slope_se, pval_nominal, qval)␣
 ↪%>%
        arrange(qval)
    return(eGenes)
}
memEQTL <- memoise::memoise(get_eqtl_df)

get_residualized_df <- function(){
    expr_file = paste0("/ceph/projects/v4_phase3_paper/analysis/eqtl_analysis/
 ↪all/",
                       feature,"/expression_gct/covariates/
 ↪residualized_expression/_m/",
                       feature, "_residualized_expression.csv")
    return(data.table::fread(expr_file) %>% column_to_rownames("gene_id"))
}
memRES <- memoise::memoise(get_residualized_df)
```

```
get_genotypes <- function(){
    traw_file = paste0("/ceph/projects/brainseq/genotype/download/topmed/
 ↪convert2plink/",
                       "filter_maf_01/a_transpose/_m/LIBD_Brain_TopMed.traw")
    traw = data.table::fread(traw_file) %>% rename_with(~ gsub('\\_.*', '', .x))
    return(traw)
}
memSNPs <- memoise::memoise(get_genotypes)
```

1.1.2 Simple functions

[4]:
```
feature_map <- function(feature){
    return(list("genes"="Gene", "transcripts"= "Transcript",
                "exons"= "Exon", "junctions"= "Junction")[[feature]])
}

get_geno_annot <- function(){
    return(memSNPs() %>% select(CHR, SNP, POS, COUNTED, ALT))
}

get_snps_df <- function(){
    return(memSNPs() %>% select("SNP", starts_with("Br")))
}

letter_snp <- function(number, a0, a1){
    if(is.na(number)){ return(NA) }
    if( length(a0) == 1 & length(a1) == 1){
        seps = ""; collapse=""
    } else {
        seps = " "; collapse=NULL
    }
    return(paste(paste0(rep(a0, number), collapse = collapse),
                 paste0(rep(a1, (2-number)), collapse = collapse), sep=seps))
}

get_snp_df <- function(variant_id, gene_id){
    zz = get_geno_annot() %>% filter(SNP == variant_id)
    xx = get_snps_df() %>% filter(SNP == variant_id) %>%
        column_to_rownames("SNP") %>% t %>% as.data.frame %>%
        rownames_to_column("BrNum") %>% mutate(COUNTED=zz$COUNTED, ALT=zz$ALT)␣
 ↪%>%
        rename("SNP"=all_of(variant_id))
    yy = memRES()[gene_id, ] %>% t %>% as.data.frame %>%
        rownames_to_column("BrNum")
    ## Annotated SNPs
    letters = c()
```

```
    for(ii in seq_along(xx$COUNTED)){
        a0 = xx$COUNTED[ii]; a1 = xx$ALT[ii]; number = xx$SNP[ii]
        letters <- append(letters, letter_snp(number, a0, a1))
    }
    xx = xx %>% mutate(LETTER=letters, ID=paste(SNP, LETTER, sep="\n"))
    df = inner_join(xx, yy, by="BrNum") %>% mutate_if(is.character, as.factor)
    return(df)
}
memDF <- memoise::memoise(get_snp_df)

save_ggplots <- function(fn, p, w, h){
    for(ext in c('.pdf', '.png', '.svg')){
        ggsave(paste0(fn, ext), plot=p, width=w, height=h)
    }
}

get_biomart_df <- function(){
    biomart = data.table::fread("../_h/biomart.csv")
}
memMART <- memoise::memoise(get_biomart_df)

get_gene_symbol <- function(gene_id){
    ensemblID = gsub("\\..*", "", gene_id)
    geneid = memMART() %>% filter(ensembl_gene_id == gsub("\\..*", "", gene_id))
    if(dim(geneid)[1] == 0){
        return("")
    } else {
        return(geneid$external_gene_name)
    }
}

plot_simple_eqtl <- function(fn, gene_id, variant_id, eqtl_annot, prefix){
    bxp = memDF(variant_id, gene_id) %>%
        ggboxplot(x="ID", y=gene_id, fill="red", add="jitter", xlab="",
                  ylab="Residualized Expression", outlier.shape=NA,
                  add.params=list(alpha=0.5), alpha=0.4,
                  ggtheme=theme_pubr(base_size=20, border=TRUE)) +
        font("xy.title", face="bold") +
        ggtitle(paste(prefix, gene_id, eqtl_annot, sep='\n')) +
        theme(plot.title = element_text(hjust = 0.5, face="bold"))
    print(bxp)
    save_ggplots(fn, bxp, 7, 7)
}
```

1.1.3 GWAS plots

[5]:
```
get_gwas_snps <- function(){
    gwas_snp_file = paste0('../../summary_table/_m/Brainseq_LIBD_caudate',
                           '_4features_PGC2.signifpairs.txt.gz')
    gwas_df = data.table::fread(gwas_snp_file) %>% filter(Type ==␣
 ↪feature_map(feature)) %>%
        select(c("variant_id", "gene_id", "rsid", "hg38chrc", "OR", "SE", "P",␣
 ↪"A1",
                 "A2", "pval_nominal", "pgc2_a1_same_as_our_counted",␣
 ↪"is_index_snp")) %>%
        distinct() %>% arrange(P)
    return(gwas_df)
}
memGWAS <- memoise::memoise(get_gwas_snps)

get_gwas_snp <- function(variant){
    return(memGWAS() %>% filter(variant_id == variant))
}

get_risk_allele <- function(variant){
    gwas_snp = get_gwas_snp(variant)
    if(gwas_snp$OR > 1){
        ra = gwas_snp$A1
    }else{
        ra = gwas_snp$A2
    }
    return(ra)
}

get_eqtl_gwas_df <- function(){
    return(memEQTL() %>% inner_join(memGWAS(), by="variant_id"))
}

get_gwas_ordered_snp_df <- function(variant_id, gene_id,␣
 ↪pgc2_a1_same_as_our_counted, OR){
    df = memDF(variant_id, gene_id)
    if(!pgc2_a1_same_as_our_counted){
        if(OR < 1){ df = df %>% mutate(SNP = 2-SNP, ID=paste(SNP, LETTER,␣
 ↪sep="\n")) }
    } else {
        if(OR > 1){ df = df %>% mutate(SNP = 2-SNP, ID=paste(SNP, LETTER,␣
 ↪sep="\n")) }
    }
    return(df)
}
```

```
plot_gwas_eqtl <- function(fn, gene_id, variant_id, eqtl_annot,
                           pgc2_a1_same_as_our_counted, OR, title){
    bxp = get_gwas_ordered_snp_df(variant_id, gene_id,
                                  pgc2_a1_same_as_our_counted, OR) %>%
        mutate_if(is.character, as.factor) %>%
        ggboxplot(x="ID", y=gene_id, fill="red", add="jitter", xlab="",
                  ylab="Residualized Expression", outlier.shape=NA,
                  add.params=list(alpha=0.5), alpha=0.4,
                  ggtheme=theme_pubr(base_size=20, border=TRUE)) +
        font("xy.title", face="bold") + ggtitle(title) +
        theme(plot.title = element_text(hjust = 0.5, face="bold"))
    print(bxp)
    save_ggplots(fn, bxp, 7, 7)
}
```

1.2 Plot eQTL

[6]:
```
get_drd2_junction_annotation <- function(junction_id){
    return(list(
        'chr11:113424683-113474229(-)'= "DRD2 junction 1L-2",
        "chr11:113424683-113475075(-)"= "DRD2 junction 1-2",
        "chr11:113418137-113424366(-)"= "DRD2 junction 2-3",
        "chr11:113417000-113418026(-)"= "DRD2 junction 3-4",
        "chr11:113415612-113416862(-)"= "DRD2 junction 4-5",
        "chr11:113414462-113415420(-)"= "DRD2 junction 5-6",
        "chr11:113412884-113415420(-)"= "DRD2 junction 5-7",
        "chr11:113412884-113414374(-)"= "DRD2 junction 6-7",
        "chr11:113410921-113412555(-)"= "DRD2 junction 7-8")[[junction_id]])
}

get_drd2_junctions <- function(){
    cmd = paste0("cat <(head -1 /ceph/projects/v4_phase3_paper/analysis/
 ↪differential_expression/_m/junctions/diffExpr_szVctl_full.txt)",
                 " <(grep -i drd2 /ceph/projects/v4_phase3_paper/analysis/
 ↪differential_expression/_m/junctions/diffExpr_szVctl_full.txt)")
    return(data.table::fread(cmd=cmd) %>% rename("Feature"="V1"))
}

get_drd2 <- function(){
    drdj = get_drd2_junctions() %>% filter(str_detect(gencodeTx,␣
 ↪"ENST00000362072.7|ENST00000346454.7"))
    return(memEQTL() %>% filter(gene_id %in% drdj$Feature))
}
```

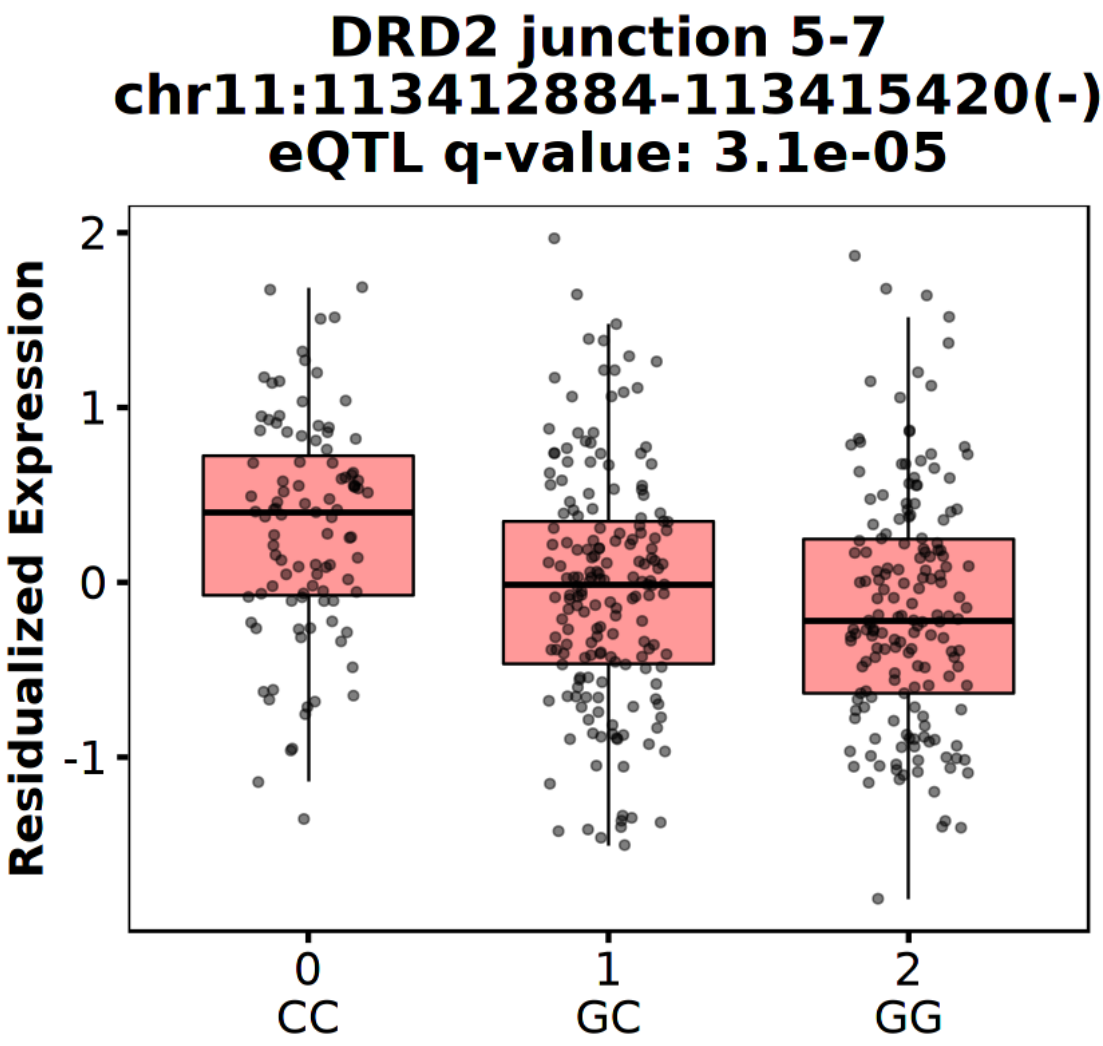
1.2.1 DRD2 plot

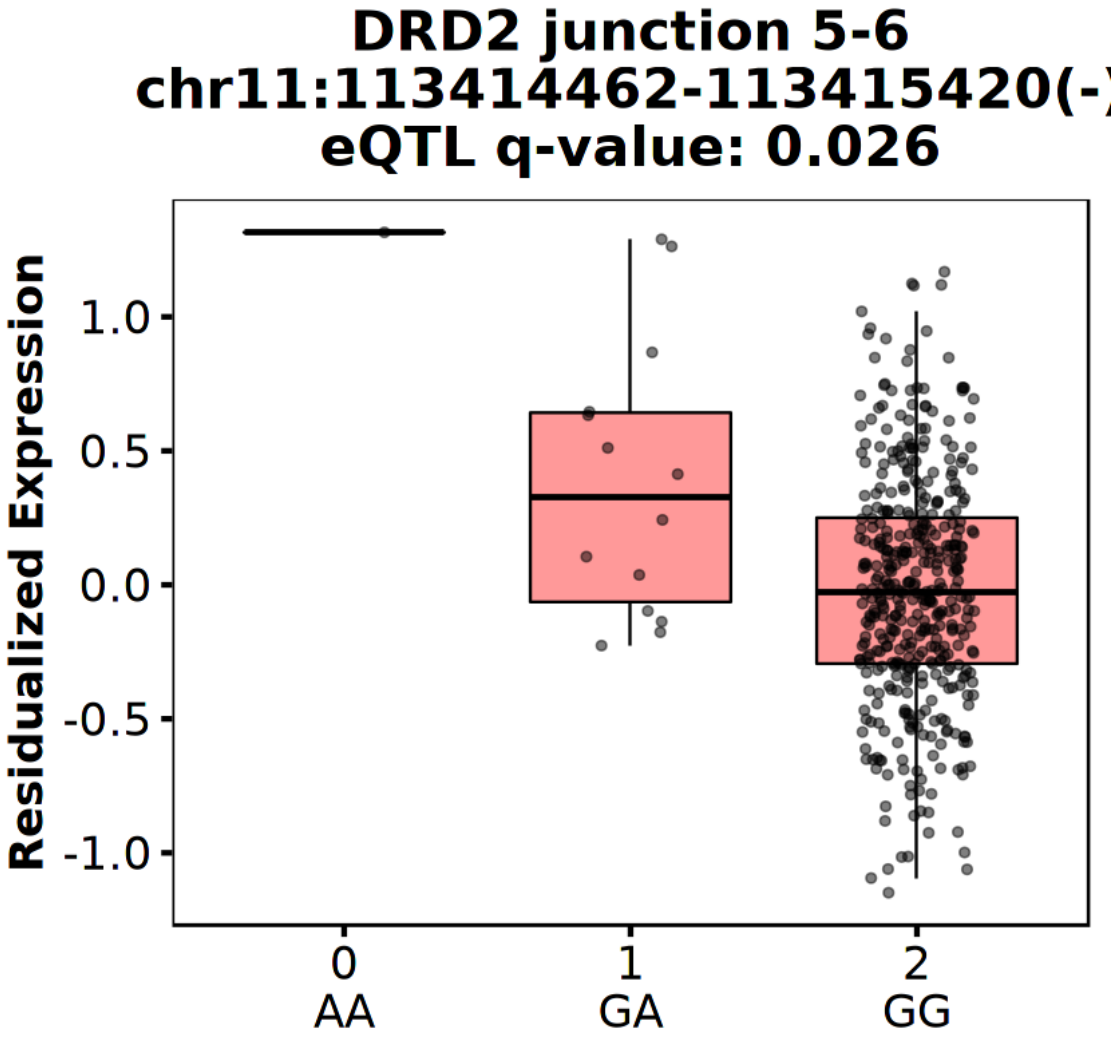
[7]:
```
drd2_df = get_drd2()
drd2_df
```

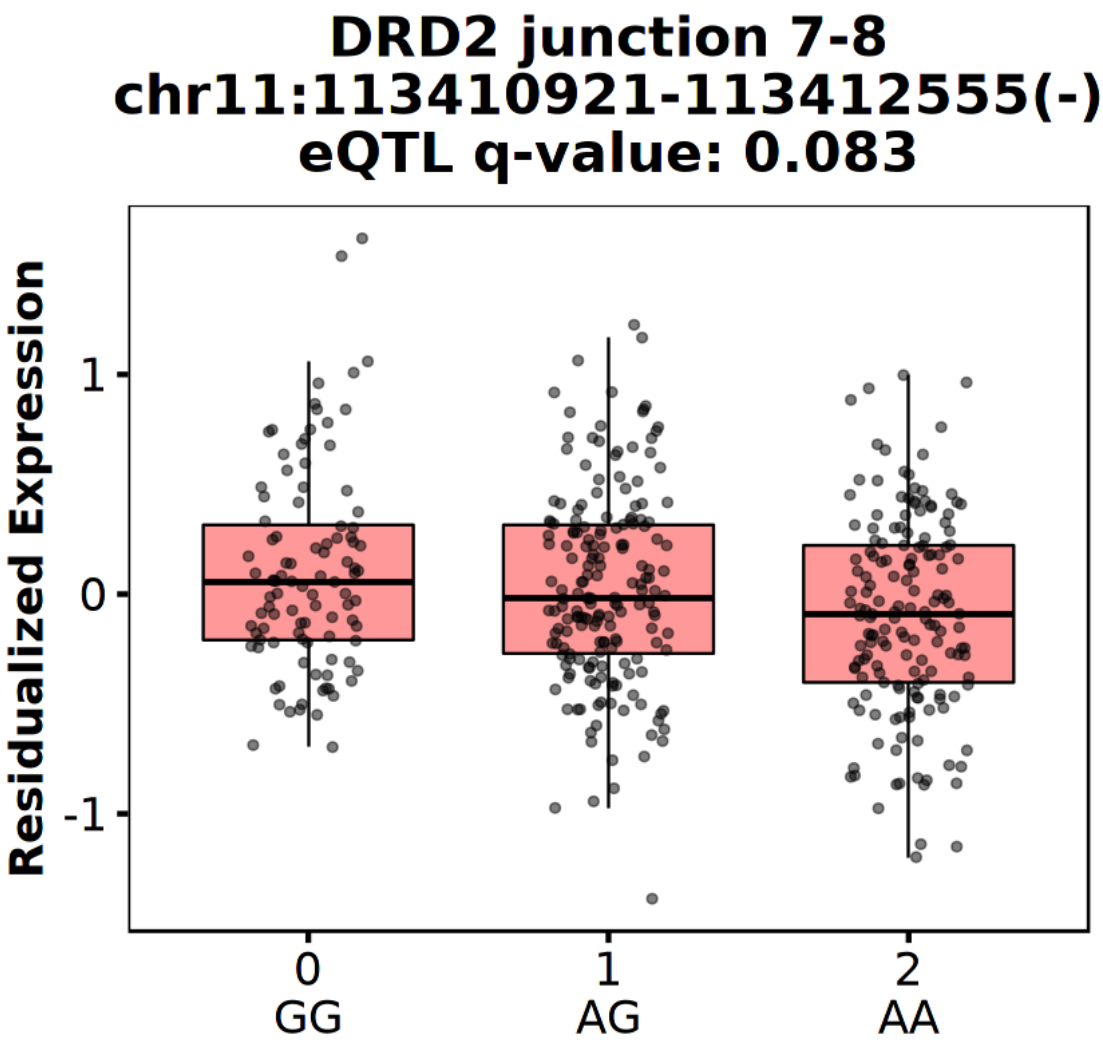
A data.table: 8 × 7

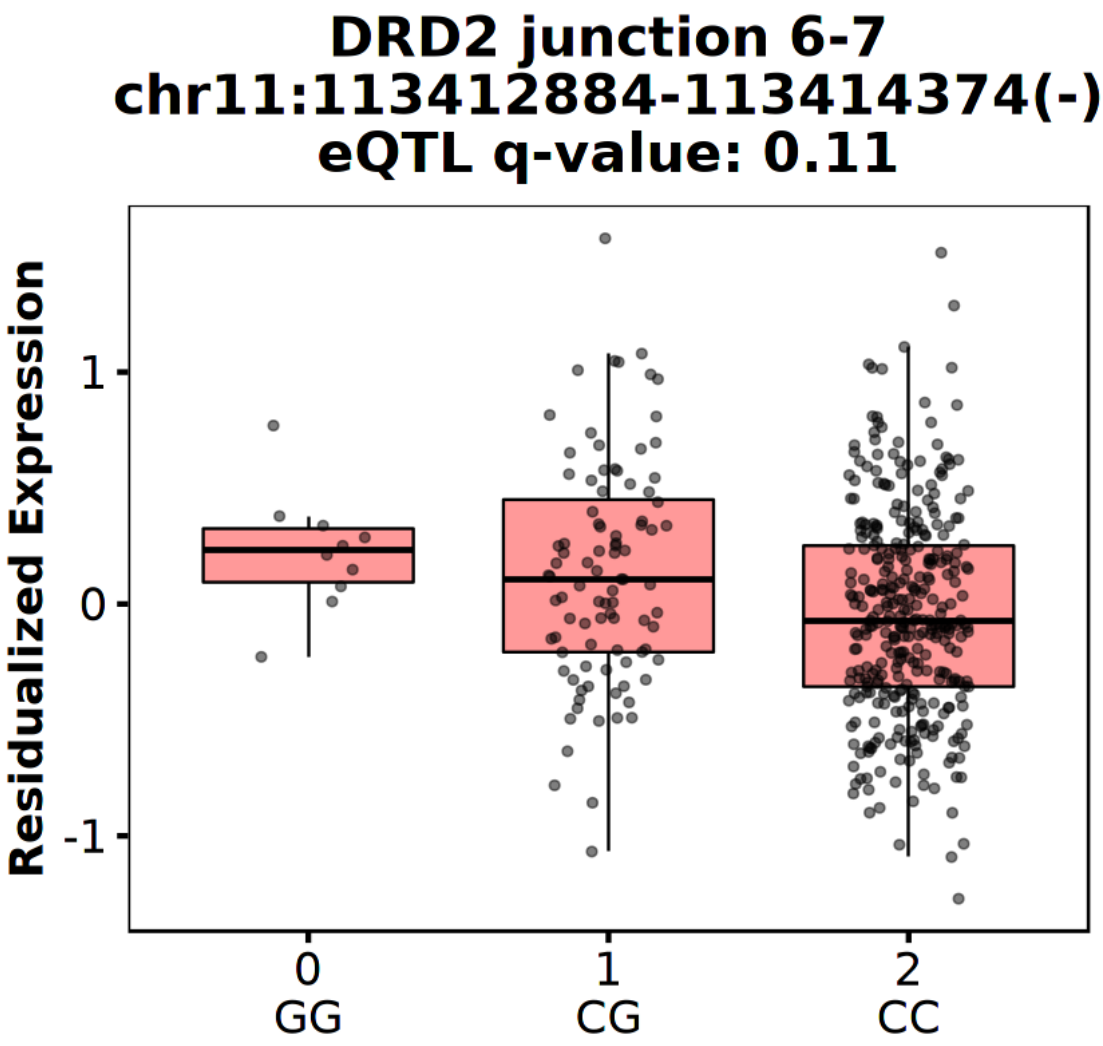
gene_id <chr>	variant_id <chr>	maf <dbl>	slope <dbl>	slope_se <dbl>
chr11:113412884-113415420(-)	chr11:113445380:G:C	0.4243790	0.310981	0.0510032
chr11:113414462-113415420(-)	chr11:113406477:G:A	0.0180587	0.506606	0.1132590
chr11:113410921-113412555(-)	chr11:113434592:A:G	0.4311510	0.141965	0.0346677
chr11:113412884-113414374(-)	chr11:113283958:C:G	0.1252820	0.205979	0.0518752
chr11:113417000-113418026(-)	chr11:113518643:A:G	0.0778781	-0.281897	0.0740031
chr11:113415612-113416862(-)	chr11:113540433:T:C	0.0293454	-0.389309	0.1023110
chr11:113418137-113424366(-)	chr11:113630933:G:A	0.4796840	-0.136264	0.0389540
chr11:113424683-113475075(-)	chr11:113399652:C:T	0.2945820	0.135346	0.0414205

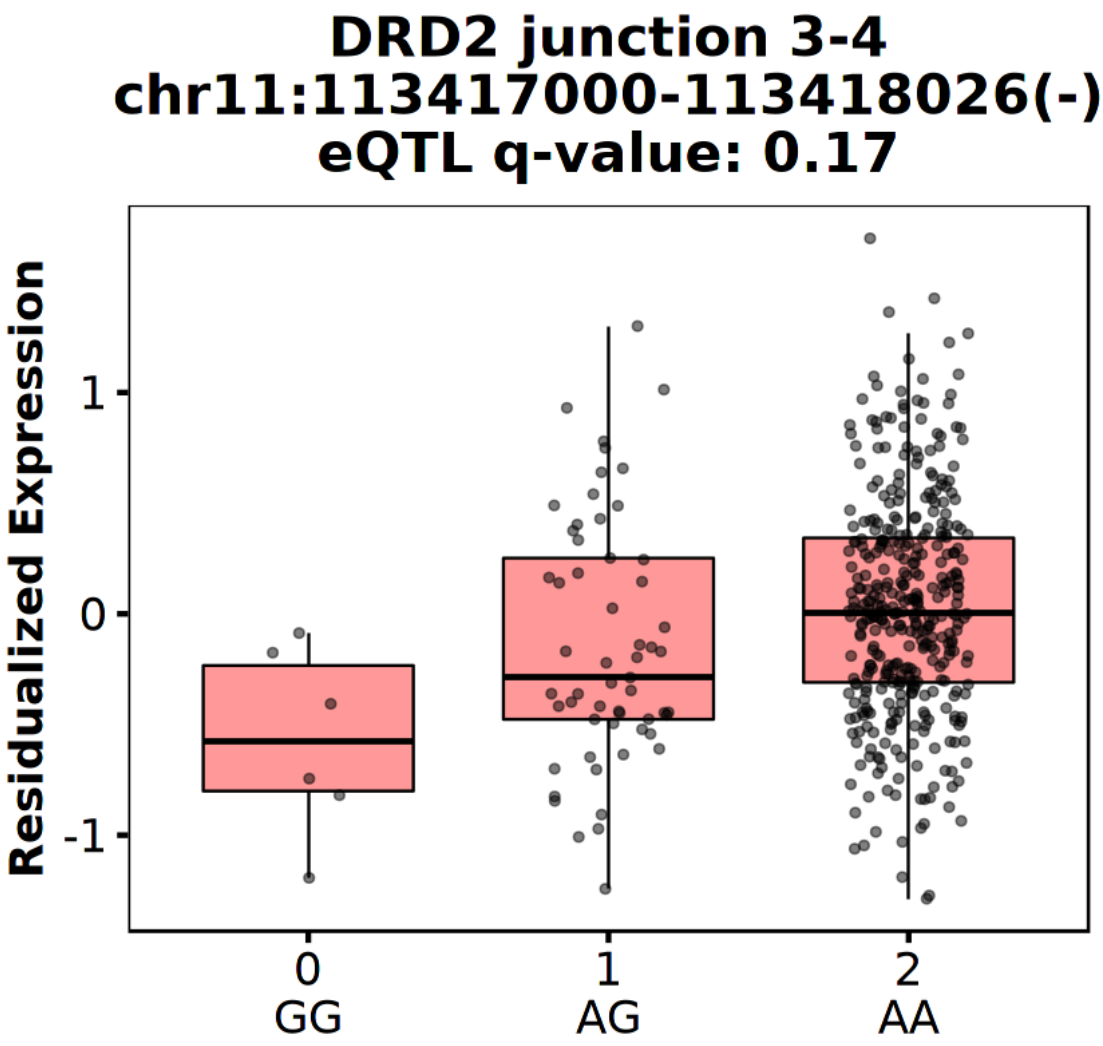
[8]:
```
for(x in seq_along(drd2_df$gene_id)){
    anno = get_drd2_junction_annotation(drd2_df$gene_id[x])
    en = gsub("-", "_", gsub(" ", "_", anno))
    fn = paste("drd2_eqtl", en, sep="_")
    eqtl_annot = paste("eQTL q-value:", signif(drd2_df$qval[x], 2))
    prefix = anno
    plot_simple_eqtl(fn, drd2_df$gene_id[x], drd2_df$variant_id[x], eqtl_annot,␣
 ↪prefix)
    #print(prefix)
}
```

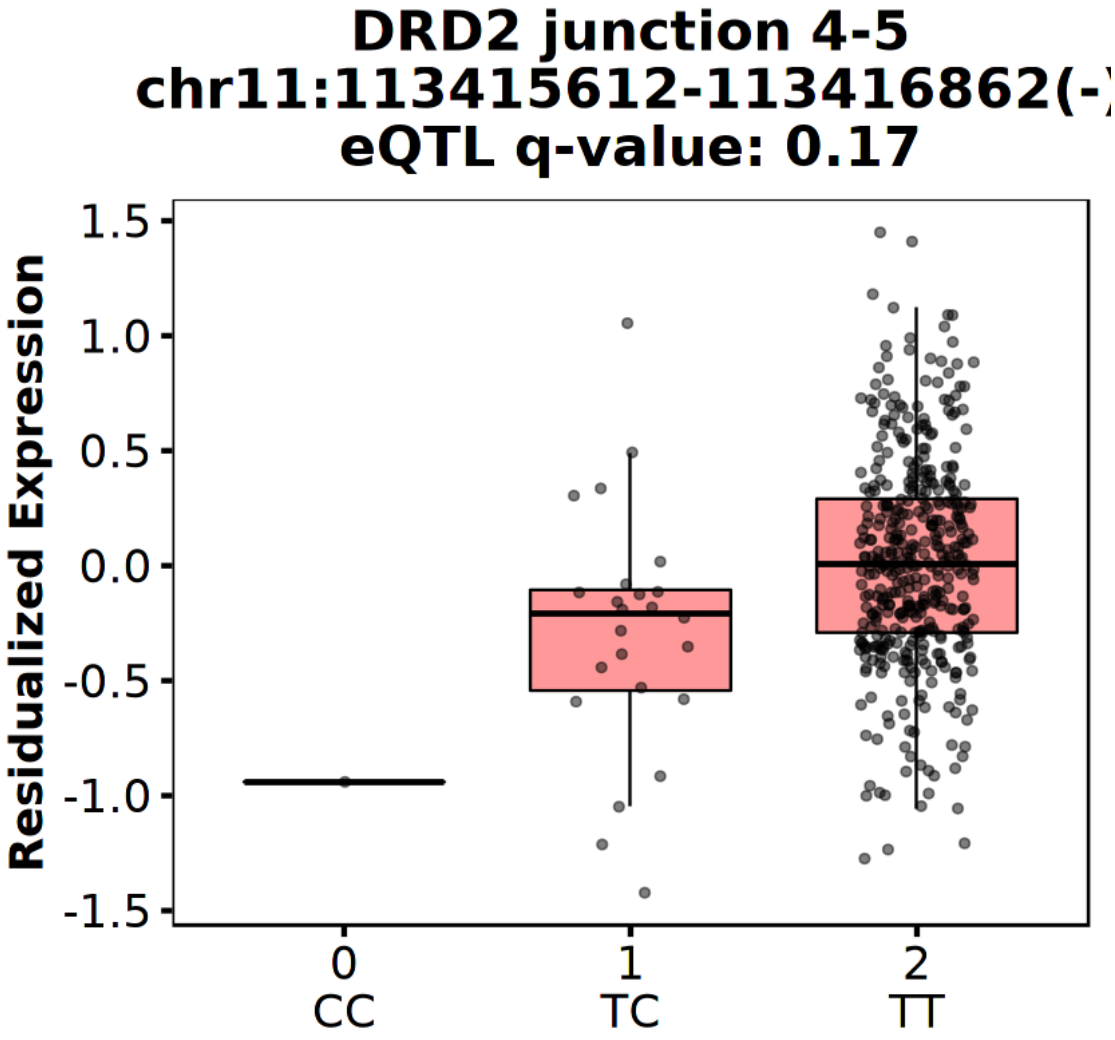

DRD2 junction 5-7
chr11:113412884-113415420(-)
eQTL q-value: 3.1e-05
Residualized Expression
2
1
0
-1
0
CC
1
GC
2
GG

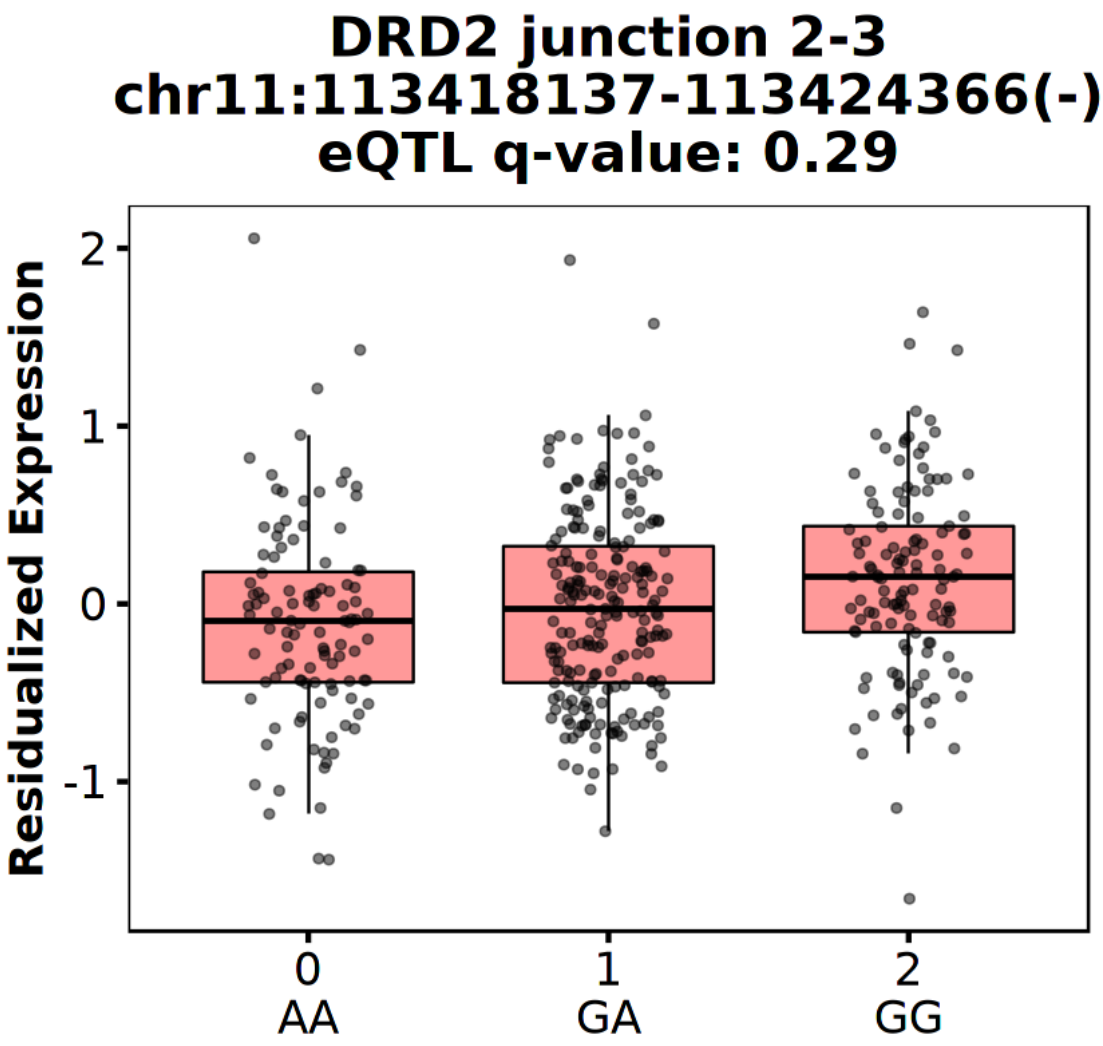

DRD2 junction 5-6
chr11:113414462-113415420(-)
eQTL q-value: 0.026
Residualized Expression
1.0
0.5
0.0
-0.5
-1.0
0
AA
1
GA
2
GG

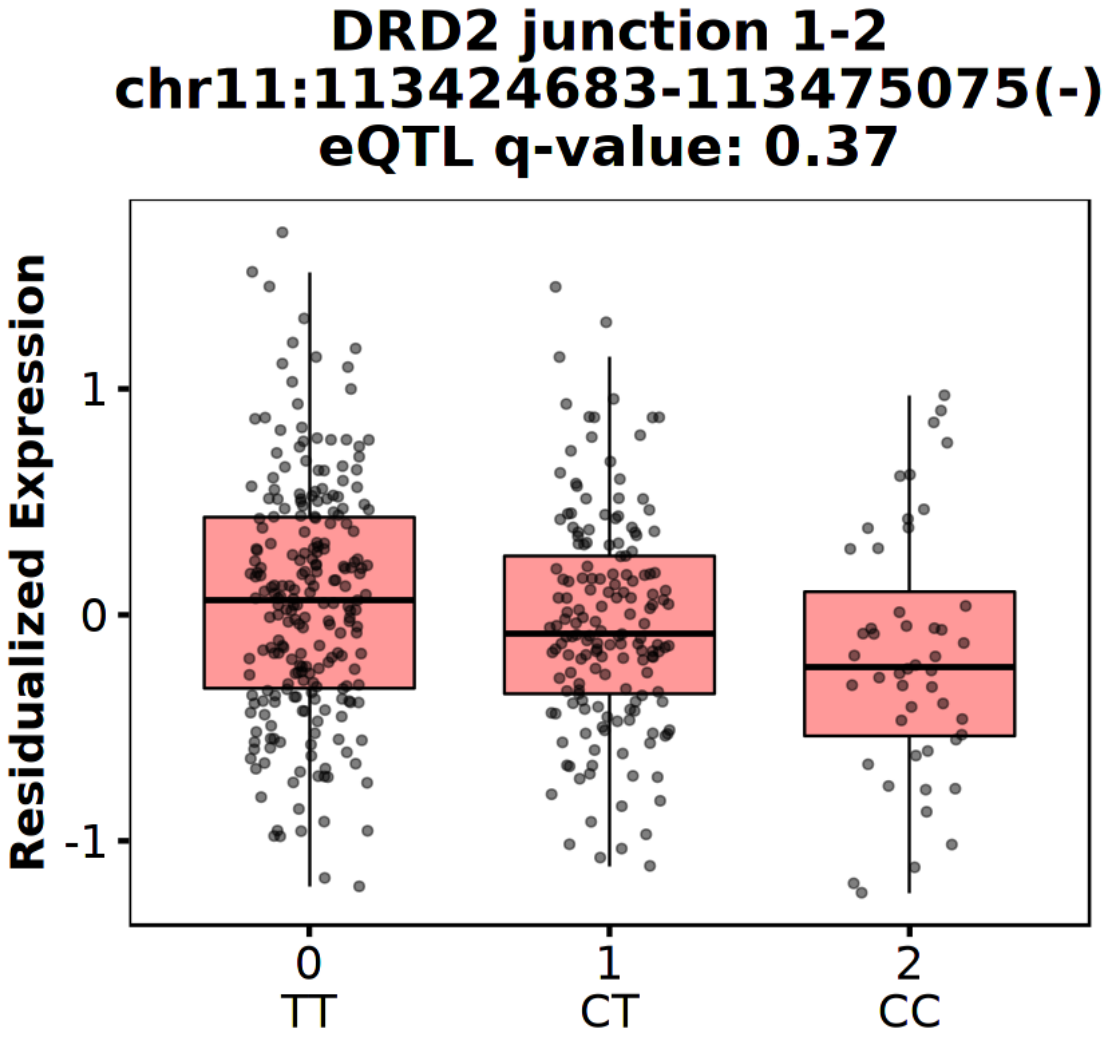

DRD2 junction 7-8
chr11:113410921-113412555(-)
eQTL q-value: 0.083
Residualized Expression
1
0
-1
0
GG
1
AG
2
AA


DRD2 junction 6-7
chr11:113412884-113414374(-)
eQTL q-value: 0.11
Residualized Expression
1
0
-1
0
GG
1
CG
2
CC


DRD2 junction 3-4
chr11:113417000-113418026(-)
eQTL q-value: 0.17
Residualized Expression
1
0
-1
0
GG
1
AG
2
AA


DRD2 junction 4-5
chr11:113415612-113416862(-)
eQTL q-value: 0.17
Residualized Expression
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
0
CC
1
TC
2
TT


DRD2 junction 2-3
chr11:113418137-113424366(-)
eQTL q-value: 0.29
Residualized Expression
2
1
0
-1
0
AA
1
GA
2
GG



1.2.2 GWAS association

[9]:
```
eqtl_gwas_df = memGWAS() %>% filter(gene_id %in% drd2_df$gene_id) %>%
    group_by(gene_id, is_index_snp) %>% slice(1)
eqtl_gwas_df
```

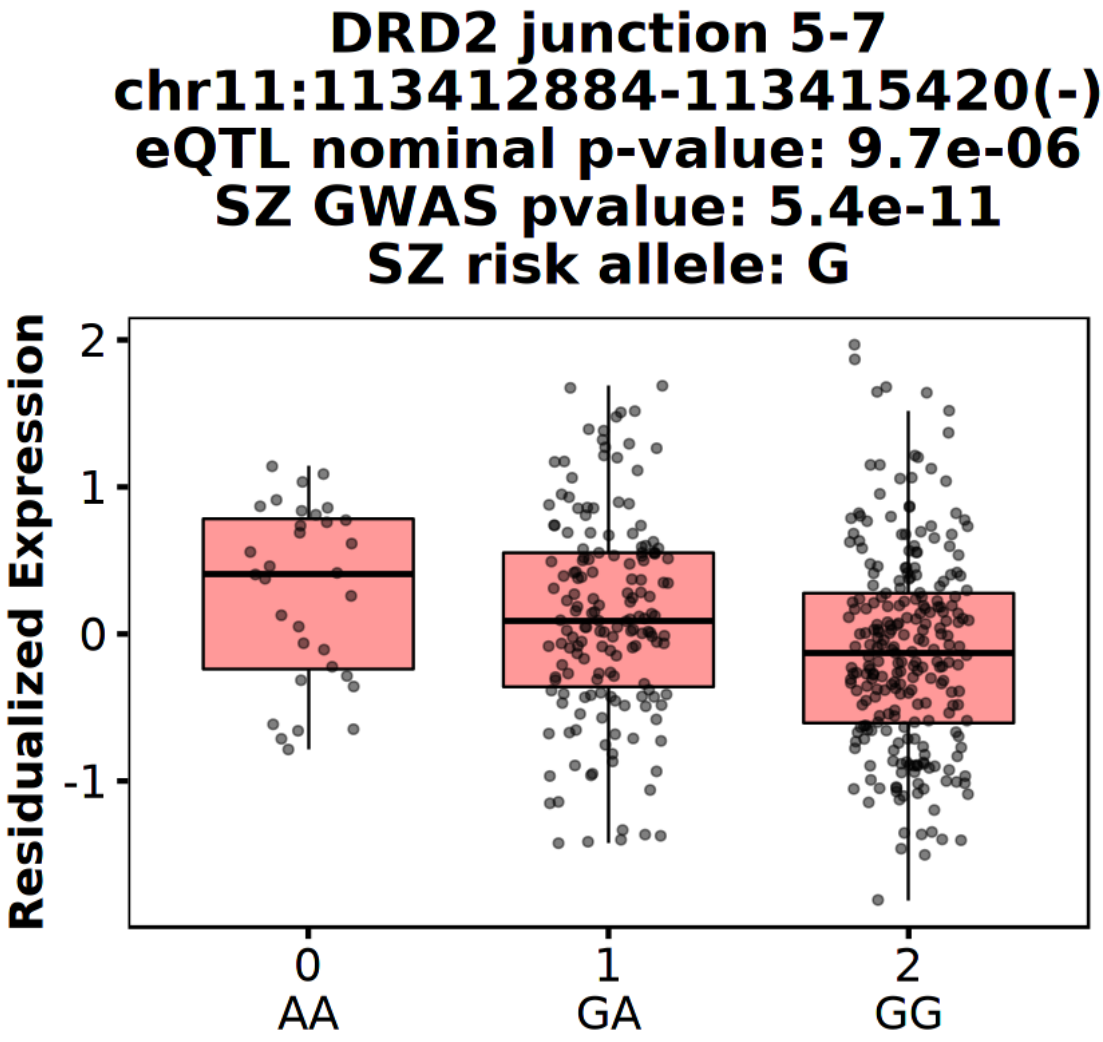
A grouped_df: 2 × 12

variant_id	gene_id	rsid	hg38chrc	OR
<chr>	<chr>	<chr>	<chr>	<dbl>
chr11:113500036:G:A	chr11:113412884-113415420(-)	rs61902811	chr11	1.0691
chr11:113522272:C:T	chr11:113412884-113415420(-)	rs2514218	chr11	1.0752

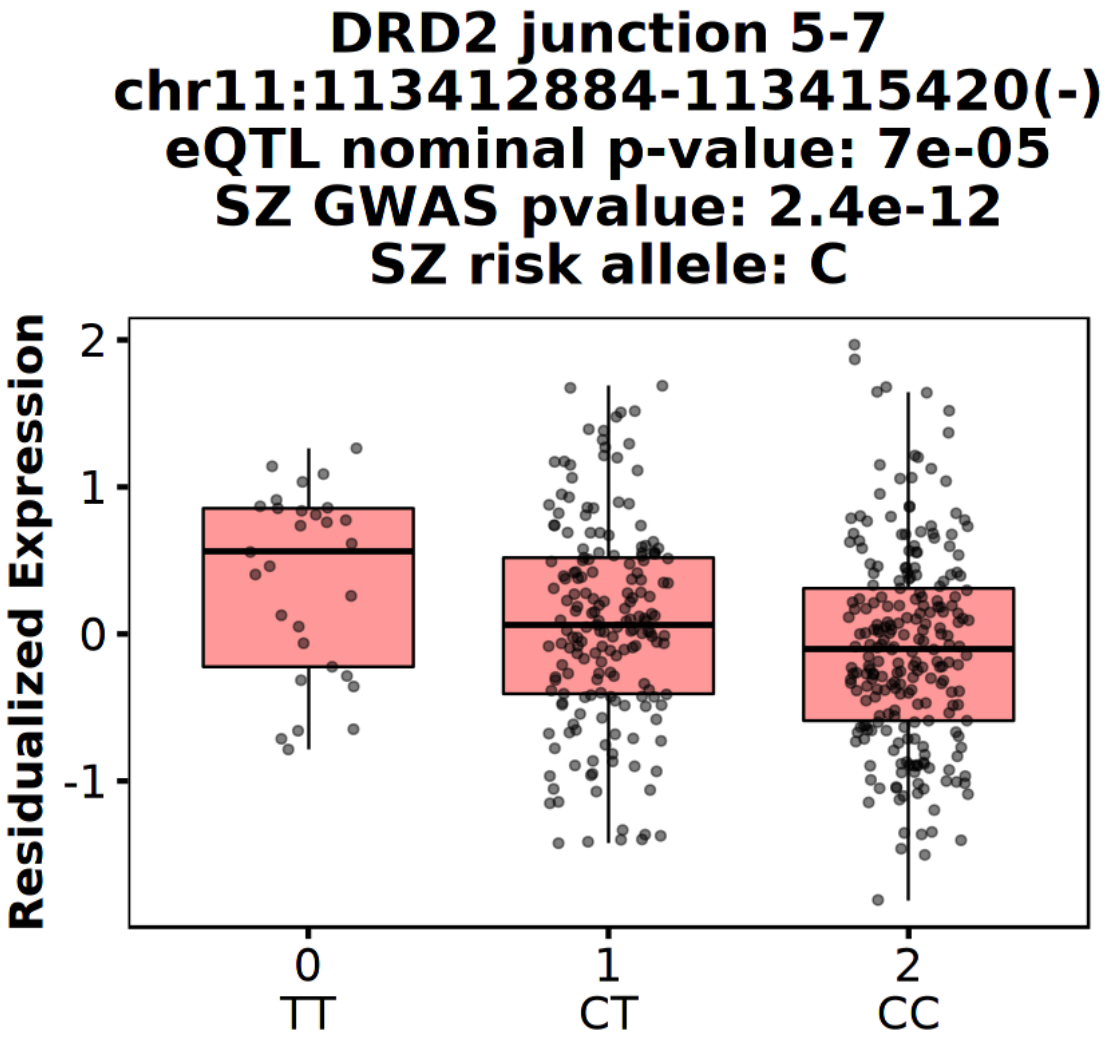
[10]:
```
for(num in seq_along(eqtl_gwas_df$variant_id)){
    anno = get_drd2_junction_annotation(eqtl_gwas_df$gene_id[num])
```

```
    en = gsub("-", "_", gsub(" ", "_", anno))
    variant_id = eqtl_gwas_df$variant_id[num]
    gene_id = eqtl_gwas_df$gene_id[num]
    pgc2_a1_same_as_our_counted = eqtl_gwas_df$pgc2_a1_same_as_our_counted[num]
    OR = eqtl_gwas_df$OR[num]
    eqtl_annot = paste("eQTL nominal p-value:",␣
↪signif(eqtl_gwas_df$pval_nominal[num], 2))
    gwas_annot = paste("SZ GWAS pvalue:", signif(eqtl_gwas_df$P[num], 2))
    risk_annot = paste("SZ risk allele:",␣
↪get_risk_allele(eqtl_gwas_df$variant_id[num]))
    title = paste(anno, gene_id, eqtl_annot, gwas_annot, risk_annot, sep='\n')
    if(eqtl_gwas_df$is_index_snp[num]){
        fn = paste("drd2_eqtl_in_gwas_significant_index_snp", en, sep="_")
    } else {
        fn = paste("drd2_eqtl_in_gwas_significant_snp", en, sep="_")
    }
    plot_gwas_eqtl(fn, gene_id, variant_id, eqtl_annot,
                   pgc2_a1_same_as_our_counted, OR, title)
    print(title)
}
```

```
[1] "DRD2 junction 5-7\nchr11:113412884-113415420(-)\neQTL nominal p-value:
9.7e-06\nSZ GWAS pvalue: 5.4e-11\nSZ risk allele: G"
```




```
[1] "DRD2 junction 5-7\nchr11:113412884-113415420(-)\neQTL nominal p-value:
7e-05\nSZ GWAS pvalue: 2.4e-12\nSZ risk allele: C"
```



1.3 Session Info

[11]:
```
Sys.time()
proc.time()
options(width = 120)
sessioninfo::session_info()
```

```
[1] "2021-09-05 16:06:01 EDT"
```

```
    user   system  elapsed
4243.495 1047.325  688.497
```

```
 Session info
 setting  value
```

```
version  R version 4.0.3 (2020-10-10)
os       Arch Linux
system   x86_64, linux-gnu
ui       X11
language (EN)
collate  en_US.UTF-8
ctype    en_US.UTF-8
tz       America/New_York
date     2021-09-05

 Packages
package     * version  date       lib source
abind         1.4-5    2016-07-21 [1] CRAN (R 4.0.2)
assertthat    0.2.1    2019-03-21 [1] CRAN (R 4.0.2)
backports     1.2.1    2020-12-09 [1] CRAN (R 4.0.2)
base64enc     0.1-3    2015-07-28 [1] CRAN (R 4.0.2)
broom         0.7.9    2021-07-27 [1] CRAN (R 4.0.3)
cachem        1.0.6    2021-08-19 [1] CRAN (R 4.0.3)
Cairo         1.5-12.2 2020-07-07 [1] CRAN (R 4.0.2)
car           3.0-11   2021-06-27 [1] CRAN (R 4.0.3)
carData       3.0-4    2020-05-22 [1] CRAN (R 4.0.2)
cellranger    1.1.0    2016-07-27 [1] CRAN (R 4.0.2)
cli           3.0.1    2021-07-17 [1] CRAN (R 4.0.3)
colorspace    2.0-2    2021-06-24 [1] CRAN (R 4.0.3)
crayon        1.4.1    2021-02-08 [1] CRAN (R 4.0.3)
curl          4.3.2    2021-06-23 [1] CRAN (R 4.0.3)
data.table    1.14.0   2021-02-21 [1] CRAN (R 4.0.3)
DBI           1.1.1    2021-01-15 [1] CRAN (R 4.0.2)
dbplyr        2.1.1    2021-04-06 [1] CRAN (R 4.0.3)
digest        0.6.27   2020-10-24 [1] CRAN (R 4.0.2)
dplyr       * 1.0.7    2021-06-18 [1] CRAN (R 4.0.3)
ellipsis      0.3.2    2021-04-29 [1] CRAN (R 4.0.3)
evaluate      0.14     2019-05-28 [1] CRAN (R 4.0.2)
fansi         0.5.0    2021-05-25 [1] CRAN (R 4.0.3)
farver        2.1.0    2021-02-28 [1] CRAN (R 4.0.3)
fastmap       1.1.0    2021-01-25 [1] CRAN (R 4.0.2)
forcats     * 0.5.1    2021-01-27 [1] CRAN (R 4.0.2)
foreign       0.8-80   2020-05-24 [2] CRAN (R 4.0.3)
fs            1.5.0    2020-07-31 [1] CRAN (R 4.0.2)
generics      0.1.0    2020-10-31 [1] CRAN (R 4.0.2)
ggplot2     * 3.3.5    2021-06-25 [1] CRAN (R 4.0.3)
ggpubr      * 0.4.0    2020-06-27 [1] CRAN (R 4.0.2)
ggsignif      0.6.2    2021-06-14 [1] CRAN (R 4.0.3)
glue          1.4.2    2020-08-27 [1] CRAN (R 4.0.2)
gtable        0.3.0    2019-03-25 [1] CRAN (R 4.0.2)
haven         2.4.3    2021-08-04 [1] CRAN (R 4.0.3)
hms           1.1.0    2021-05-17 [1] CRAN (R 4.0.3)
htmltools     0.5.2    2021-08-25 [1] CRAN (R 4.0.3)
```

```
httr          1.4.2    2020-07-20 [1] CRAN (R 4.0.2)
IRdisplay     1.0      2021-01-20 [1] CRAN (R 4.0.2)
IRkernel      1.2      2021-05-11 [1] CRAN (R 4.0.3)
jsonlite      1.7.2    2020-12-09 [1] CRAN (R 4.0.2)
labeling      0.4.2    2020-10-20 [1] CRAN (R 4.0.2)
lifecycle     1.0.0    2021-02-15 [1] CRAN (R 4.0.3)
lubridate     1.7.10   2021-02-26 [1] CRAN (R 4.0.3)
magrittr      2.0.1    2020-11-17 [1] CRAN (R 4.0.2)
memoise       2.0.0    2021-01-26 [1] CRAN (R 4.0.2)
modelr        0.1.8    2020-05-19 [1] CRAN (R 4.0.2)
munsell       0.5.0    2018-06-12 [1] CRAN (R 4.0.2)
openxlsx      4.2.4    2021-06-16 [1] CRAN (R 4.0.3)
pbdZMQ        0.3-5    2021-02-10 [1] CRAN (R 4.0.3)
pillar        1.6.2    2021-07-29 [1] CRAN (R 4.0.3)
pkgconfig     2.0.3    2019-09-22 [1] CRAN (R 4.0.2)
purrr       * 0.3.4    2020-04-17 [1] CRAN (R 4.0.2)
R.methodsS3   1.8.1    2020-08-26 [1] CRAN (R 4.0.3)
R.oo          1.24.0   2020-08-26 [1] CRAN (R 4.0.3)
R.utils       2.10.1   2020-08-26 [1] CRAN (R 4.0.3)
R6            2.5.1    2021-08-19 [1] CRAN (R 4.0.3)
Rcpp          1.0.7    2021-07-07 [1] CRAN (R 4.0.3)
readr       * 2.0.1    2021-08-10 [1] CRAN (R 4.0.3)
readxl        1.3.1    2019-03-13 [1] CRAN (R 4.0.2)
repr          1.1.3    2021-01-21 [1] CRAN (R 4.0.2)
reprex        2.0.1    2021-08-05 [1] CRAN (R 4.0.3)
rio           0.5.27   2021-06-21 [1] CRAN (R 4.0.3)
rlang         0.4.11   2021-04-30 [1] CRAN (R 4.0.3)
rstatix       0.7.0    2021-02-13 [1] CRAN (R 4.0.3)
rstudioapi    0.13     2020-11-12 [1] CRAN (R 4.0.2)
rvest         1.0.1    2021-07-26 [1] CRAN (R 4.0.3)
scales        1.1.1    2020-05-11 [1] CRAN (R 4.0.2)
sessioninfo   1.1.1    2018-11-05 [1] CRAN (R 4.0.2)
stringi       1.7.4    2021-08-25 [1] CRAN (R 4.0.3)
stringr     * 1.4.0    2019-02-10 [1] CRAN (R 4.0.2)
svglite       2.0.0    2021-02-20 [1] CRAN (R 4.0.3)
systemfonts   1.0.2    2021-05-11 [1] CRAN (R 4.0.3)
tibble      * 3.1.4    2021-08-25 [1] CRAN (R 4.0.3)
tidyr       * 1.1.3    2021-03-03 [1] CRAN (R 4.0.3)
tidyselect    1.1.1    2021-04-30 [1] CRAN (R 4.0.3)
tidyverse   * 1.3.1    2021-04-15 [1] CRAN (R 4.0.3)
tzdb          0.1.2    2021-07-20 [1] CRAN (R 4.0.3)
utf8          1.2.2    2021-07-24 [1] CRAN (R 4.0.3)
uuid          0.1-4    2020-02-26 [1] CRAN (R 4.0.2)
vctrs         0.3.8    2021-04-29 [1] CRAN (R 4.0.3)
withr         2.4.2    2021-04-18 [1] CRAN (R 4.0.3)
xml2          1.3.2    2020-04-23 [1] CRAN (R 4.0.2)
zip           2.2.0    2021-05-31 [1] CRAN (R 4.0.3)
```

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[1] /home/jbenja13/R/x86_64-pc-linux-gnu-library/4.0
[2] /usr/lib/R/library
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