RNF213 variation, a broader role in neurovascular disease in Caucasian and Japanese populations - File S1 - R code

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Supplementary File S1 for paper: *RNF213* variation, a broader role in neurovascular disease in Caucasian and Japanese populations - R code

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This file contains all the analyses that were performed in order to generate the results and plots from the current paper.

Load required libraries and set working directory

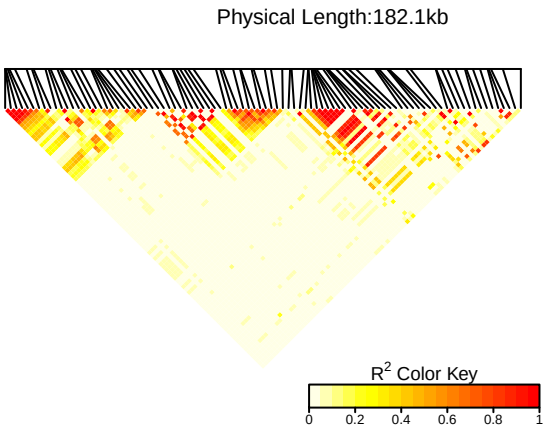
```
# Load required libraries
library(ggplot2)
require(extrafont)
library(ggbio)
library(grid)
library(gridExtra)
library(png)
library(gtable)
library(cowplot)
library(ensembldb)
library(genetics)
library(GenomicRanges)
library(grDevices)
library(Homo.sapiens)
library(BSgenome.Hsapiens.UCSC.hg19)
library(LDheatmap)
library(plyr)
library(raster)
library(reshape)
library(Rsamtools)
library(rtracklayer)
library(scales)
library(VariantAnnotation)

# Set working directory
dirname <- getwd()
setwd(dirname)
```

LD heatmaps for CEU population (Figure 1A and 1B)

```
# CEU population all common SNPs (n=91)
CEU_chr17 <- as.data.frame(read.table("input_files/CEU_files/CEU_SLC26A11_RN213_genotypes.txt",
                                      header = TRUE))
CEU_data <- as.data.frame(read.table("input_files/CEU_files/CEU_common_SNPs.bed",
                                     header = TRUE))
num_CEU <- ncol(CEU_chr17)
colnames_CEU <- as.vector(CEU_data[,4])

for(i in 1:num_CEU){
        CEU_chr17[,i]<-as.genotype(CEU_chr17[,i])
}

plot_title_CEU_r <- as.expression(bquote(atop('Pairwise LD (r'^{~2}~') for common SNPs located in the'~i

plot_title_CEU_D <- as.expression(bquote(atop('Pairwise LD (D\') for common SNPs located in the'~italic(

# Raw LD heatmap r2 CEU
CEU_SNPs_ALL_r <- LDheatmap(CEU_chr17, CEU_data[,2], LDmeasure = "r",
                            title = plot_title_CEU_r, add.map = TRUE,
                            flip = TRUE, color = heat.colors(20), name = "CEULDgrob",
                            add.key = TRUE, newpage = TRUE)
```

Pairwise LD (r^2) for common SNPs located in the *SLC26A11*

RNF213 genes region in CEU population




```
# Raw LD heatmap D' CEU
CEU_SNPs_ALL_D <- LDheatmap(CEU_chr17, CEU_data[,2], LDmeasure = "D'",
                            title = plot_title_CEU_D, add.map = TRUE,
                            flip = TRUE, color = heat.colors(20), name = "CEULDgrob",
                            add.key = TRUE, newpage = TRUE)
```

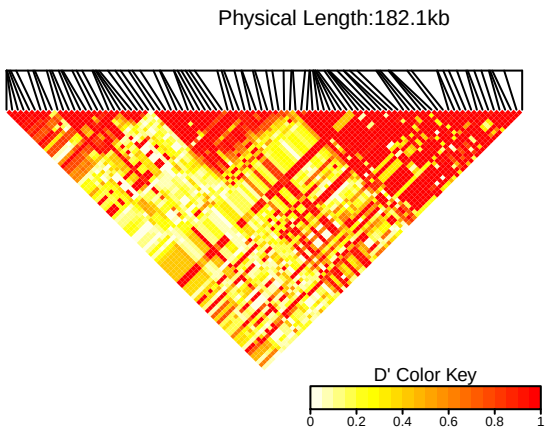
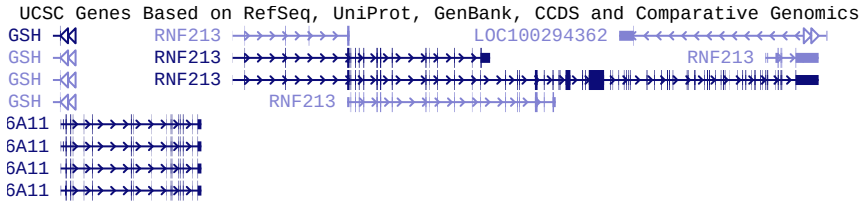
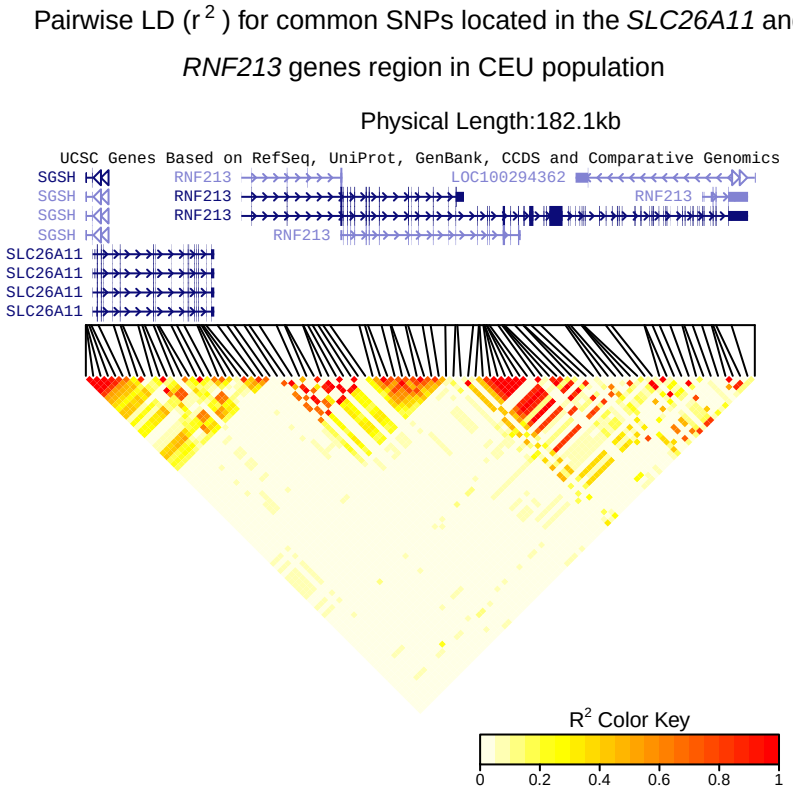


Figure 1A

```
CEU_SNPs_ALL_genes_r <- LDheatmap.addGenes(CEU_SNPs_ALL_r, chr="chr17", genome="hg19")
```



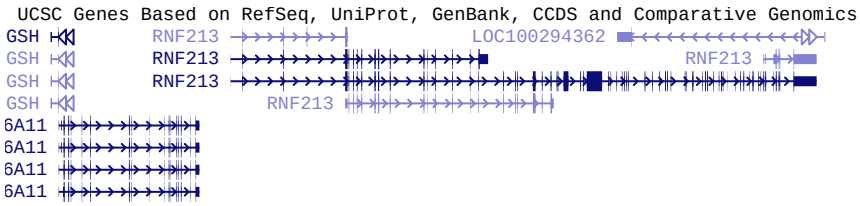


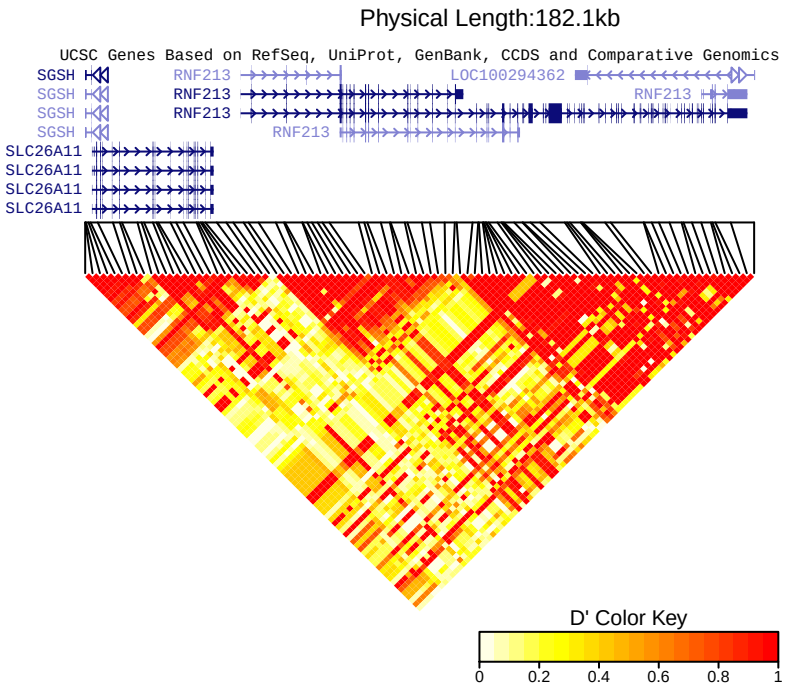

```
dev.off()
```

```
## null device
##           1
```

Figure 1B

```
CEU_SNPs_ALL_genes_D <- LDheatmap.addGenes(CEU_SNPs_ALL_D, chr="chr17", genome="hg19")
```






```
dev.off()
```

```
## null device
##           1
```

LD heatmaps for JPT population (Figure 1C and 1D)

```
# JPT population all common SNPs
JPT_chr17 <- as.data.frame(read.table("input_files/JPT_files/JPT_SLC26A11_RN213_genotypes.txt",
                                      header = TRUE))
JPT_data <- as.data.frame(read.table("input_files/JPT_files/JPT_common_SNPs.bed", header = TRUE))
num_JPT<-ncol(JPT_chr17)
colnames_JPT <- as.vector(JPT_data[,4])
class(colnames_JPT)
```

```
## [1] "character"
```

```
class(JPT_data[,4])
```

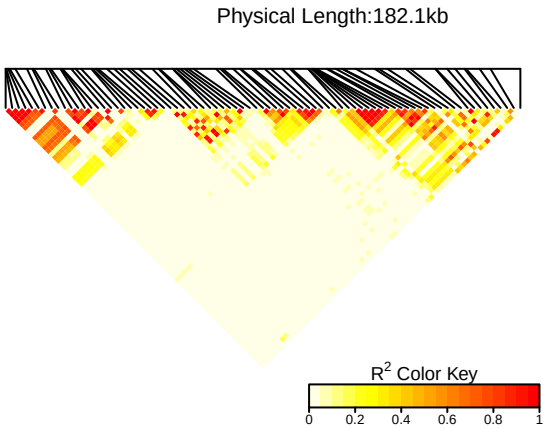
```
## [1] "factor"
```

```
for(j in 1:num_JPT){
        JPT_chr17[,j]<-as.genotype(JPT_chr17[,j])
}

plot_title_JPT_r <- as.expression(bquote(atop('Pairwise LD (r'^{~2}~') for common SNPs located in the'~i
```

```
plot_title_JPT_D <- as.expression(bquote(atop('Pairwise LD (D\') for common SNPs located in the'~italic(

# Raw LD heatmap r2 JPT
JPT_SNPs_ALL_r <- LDheatmap(JPT_chr17, JPT_data[,2], LDmeasure = "r",
                            title = plot_title_JPT_r, add.map = TRUE,
                            flip = TRUE, color = heat.colors(20), name = "JPTLDgrob",
                            add.key = TRUE, newpage = TRUE)
```

Pairwise LD (r^2) for common SNPs located in the *SLC26A11*

RNF213 genes region in JPT population




```
# Raw LD heatmap D' JPT
JPT_SNPs_ALL_D <- LDheatmap(JPT_chr17, JPT_data[,2], LDmeasure = "D'",
                            title = plot_title_JPT_D, add.map = TRUE,
                            flip = TRUE, color = heat.colors(20), name = "JPTLDgrob",
                            add.key = TRUE, newpage = TRUE)
```

Pairwise LD (D') for common SNPs located in the *SLC26A11*

RNF213 genes region in JPT population

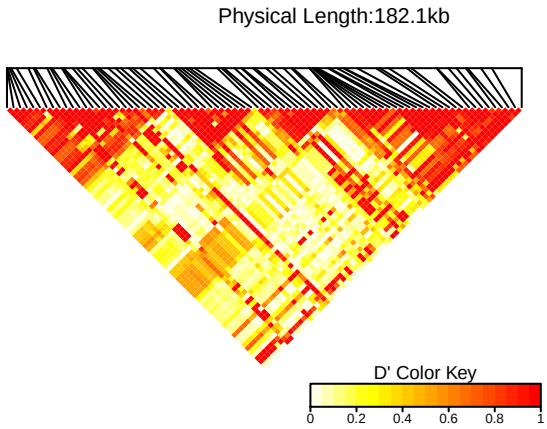
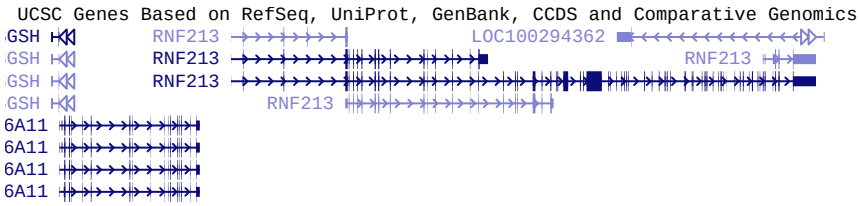
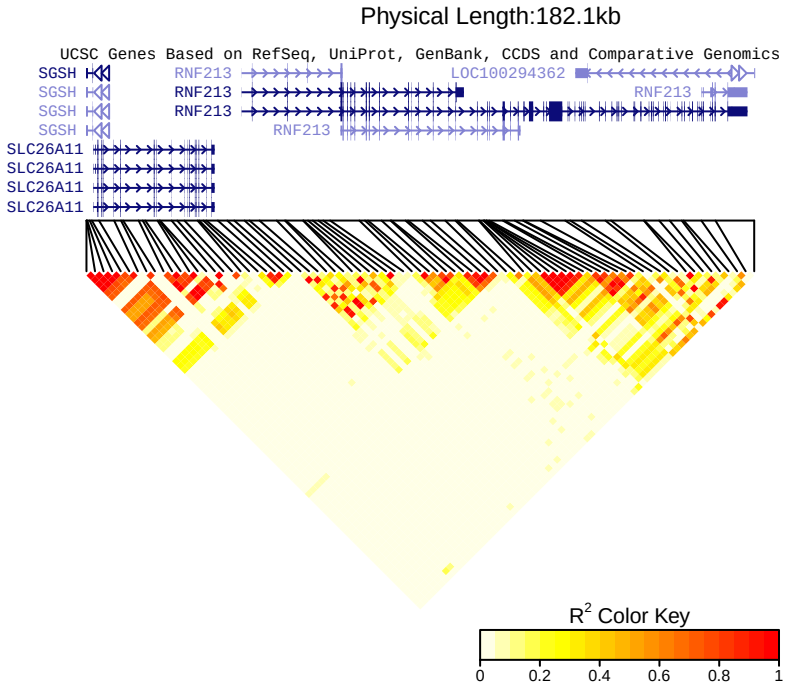


Figure 1C

```
JPT_SNPs_ALL_genes_r <- LDheatmap.addGenes(JPT_SNPs_ALL_r, chr="chr17", genome="hg19")
```



Pairwise LD (r^2) for common SNPs located in the *SLC26A11* and *RNF213* genes region in JPT population

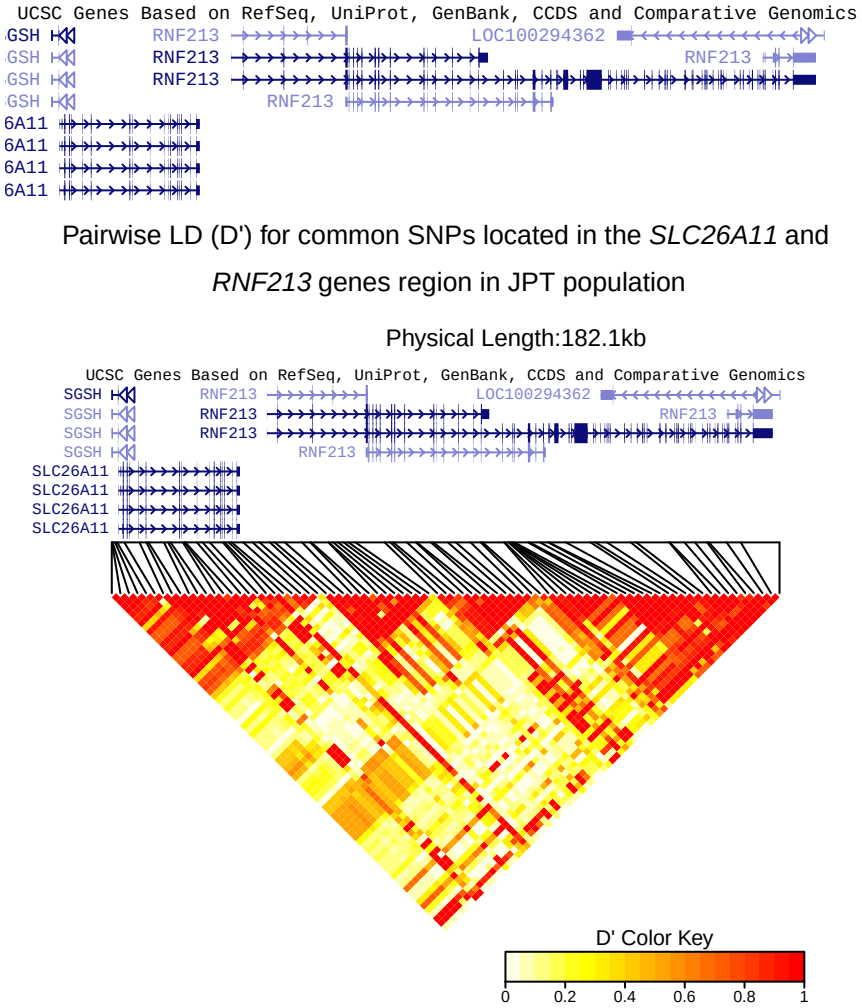



```
dev.off()
```

```
## null device
##           1
```

Figure 1D

```
JPT_SNPs_ALL_genes_D <- LDheatmap.addGenes(JPT_SNPs_ALL_D, chr="chr17", genome="hg19")
```



Pairwise LD (D') for common SNPs located in the *SLC26A11* and *RNF213* genes region in JPT population

```
dev.off()
```

```
## null device
##           1
```

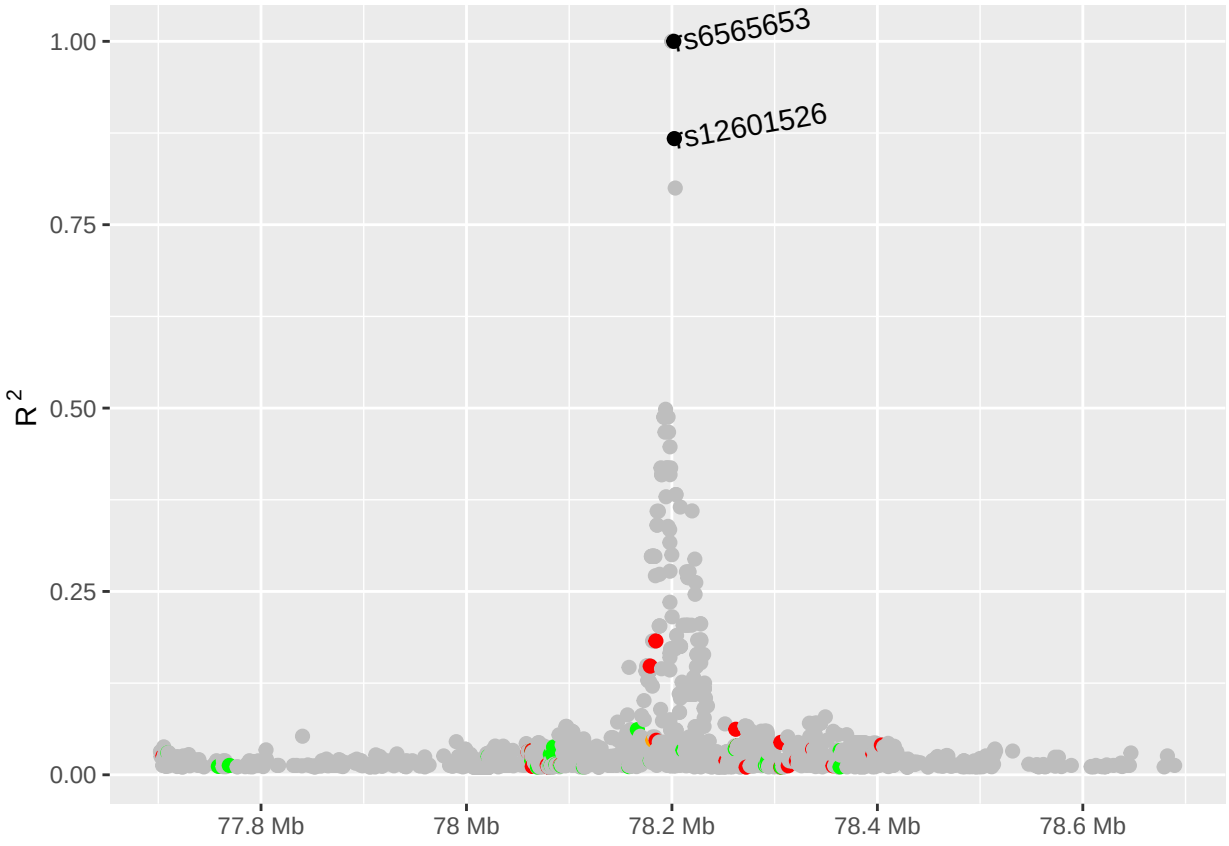
The four plots of Figure 1 were merged together using Illustrator software and the names of the SNPs of interest were added manually. The chromosome 17 ideogram for each of these plots was added manually also.

Proxy SNPs for CEU population

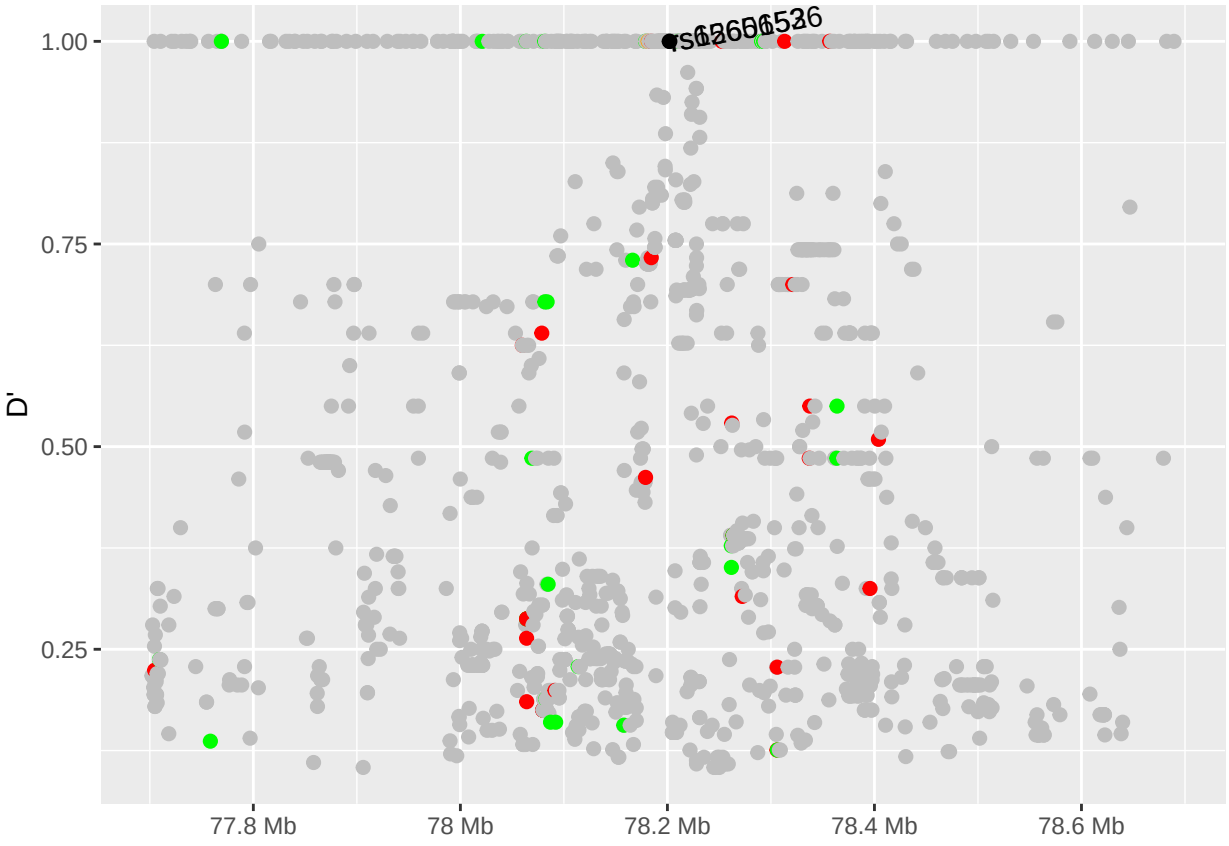
Get proxy SNPs for CEU population for for rs6565653 and rs12601526

```
data(hg19IdeogramCyto, package = "biovizBase")
data(hg19Ideogram, package = "biovizBase")
data(genesymbol, package = "biovizBase")

hg19 <- keepSeqlevels(hg19IdeogramCyto, paste0("chr", c(1:22, "X", "Y")))

# Set working directory
```

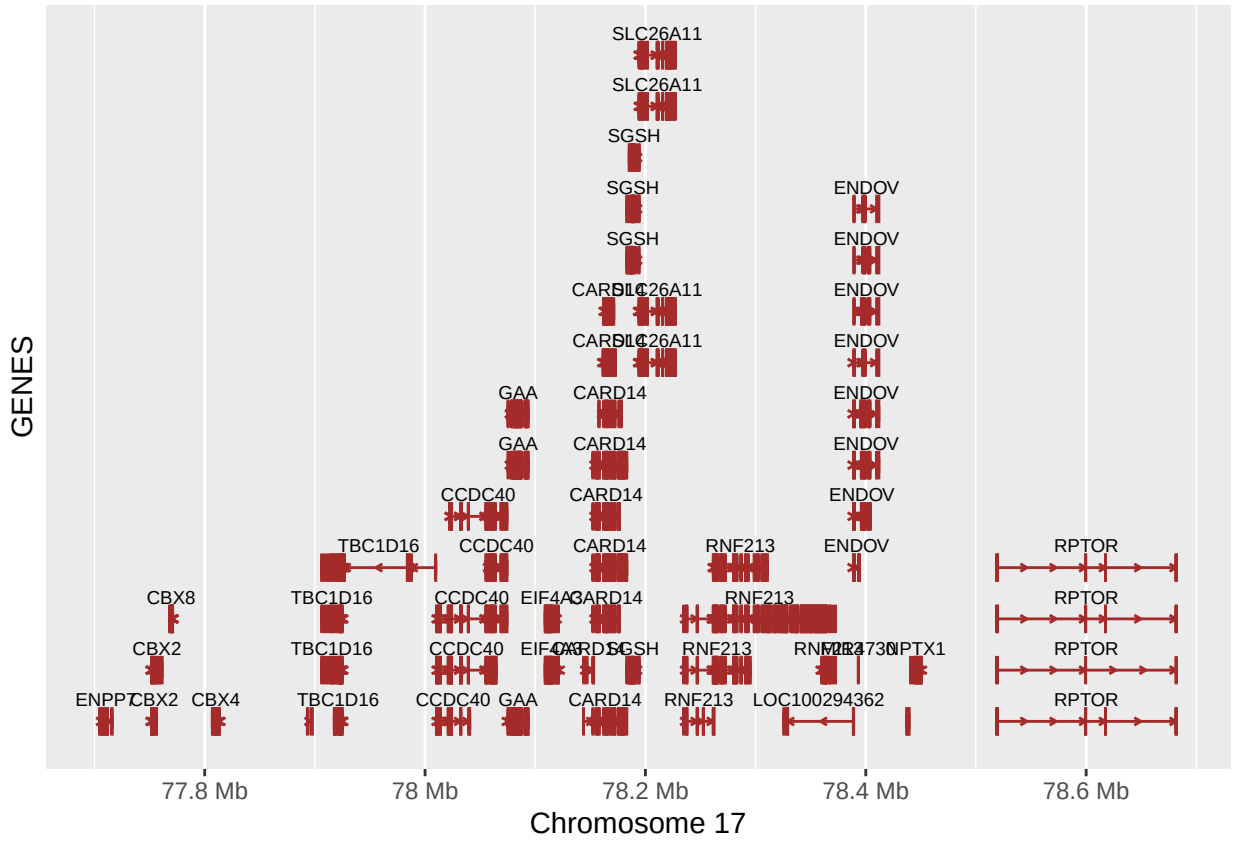
```
dirname <- getwd()
setwd(dirname)


# Plots for rs6565653 in CEU population
CEU_6565653_df <- as.data.frame(read.table("input_files/CEU_files/Proxy SNPs rs6565653 CEU population.tx
                                           sep = "\t", header = TRUE,
                                           na.strings = c(".", "NA"),
                                           stringsAsFactors = FALSE))

CEU_6565653_df$Function[is.na(CEU_6565653_df$Function)] <- "N/A"

range_start<-head(CEU_6565653_df$Start,n=1)
range_end<-tail(CEU_6565653_df$Start,n=1)
scale_combined <- GRanges('chr17', IRanges(start = range_start, end = range_end))

legend_title <- "SNP function"

y_lab_r <- as.expression(bquote('R'^{~2}~''))

rs6565653_r <- ggplot(CEU_6565653_df, aes(Start,R2)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(CEU_6565653_df, DisplayName == "Y"),
                   aes(Start, R2), color = "black") +
        geom_text(data=subset(CEU_6565653_df, DisplayName == "Y"),
                  aes(Start, R2,label=ID, hjust = 0, angle = 10)) +
        labs(y = y_lab_r, color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "nonsense", "synonymous"),
                           values = c("red", "grey", "orange", "green")) +
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs6565653_r) <- TRUE
rs6565653_r
```



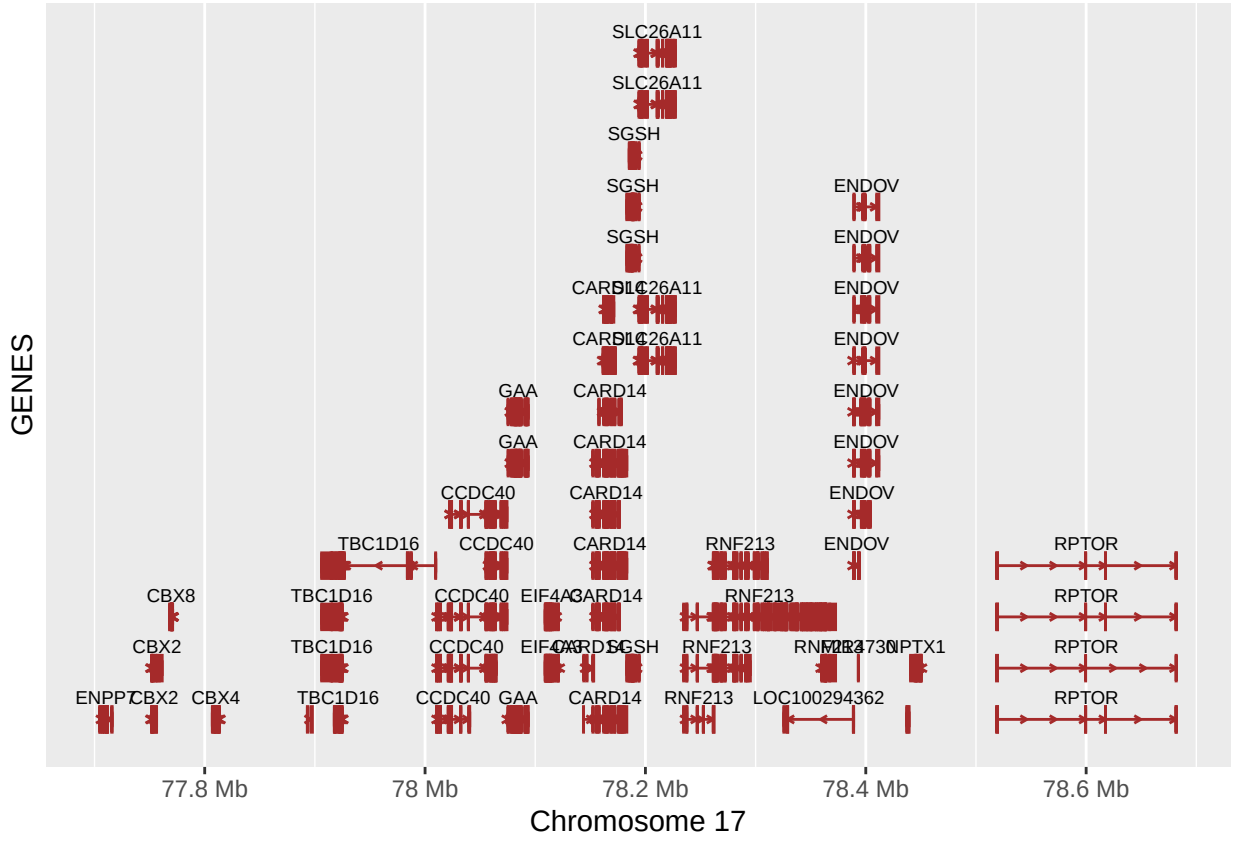

```
rs6565653_D <- ggplot(CEU_6565653_df, aes(Start,Dprime)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(CEU_6565653_df, DisplayName == "Y"),
                   aes(Start, Dprime), color = "black") +
        geom_text(data=subset(CEU_6565653_df, DisplayName == "Y"),
                  aes(Start, Dprime,label=ID, hjust = 0, angle = 10)) +
        labs(y = "D\'", color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "nonsense", "synonymous"),
                           values = c("red", "grey", "orange", "green")) +
        scale_x_sequnit("Mb")+
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs6565653_D) <- TRUE
rs6565653_D
```




```
# Missing genes: "LOC101928766", "LOC101928738", "MIR4730"
data(genesymbol, package = "biovizBase")
wh <- genesymbol[c("ENPP7", "RPTOR")]
wh <- range(wh, ignore.strand = TRUE)


rs6565653_GENES <- autoplot(Homo.sapiens, which = wh, xlab = "Chromosome 17", ylab = "GENES",
                            label.color = "black", color = "brown", fill = "brown", columns =
                              c("ALIAS", "GO"), scale = "Mb") +
        xlim (scale_combined) +
        scale_x_sequnit("Mb")
rs6565653_GENES
```

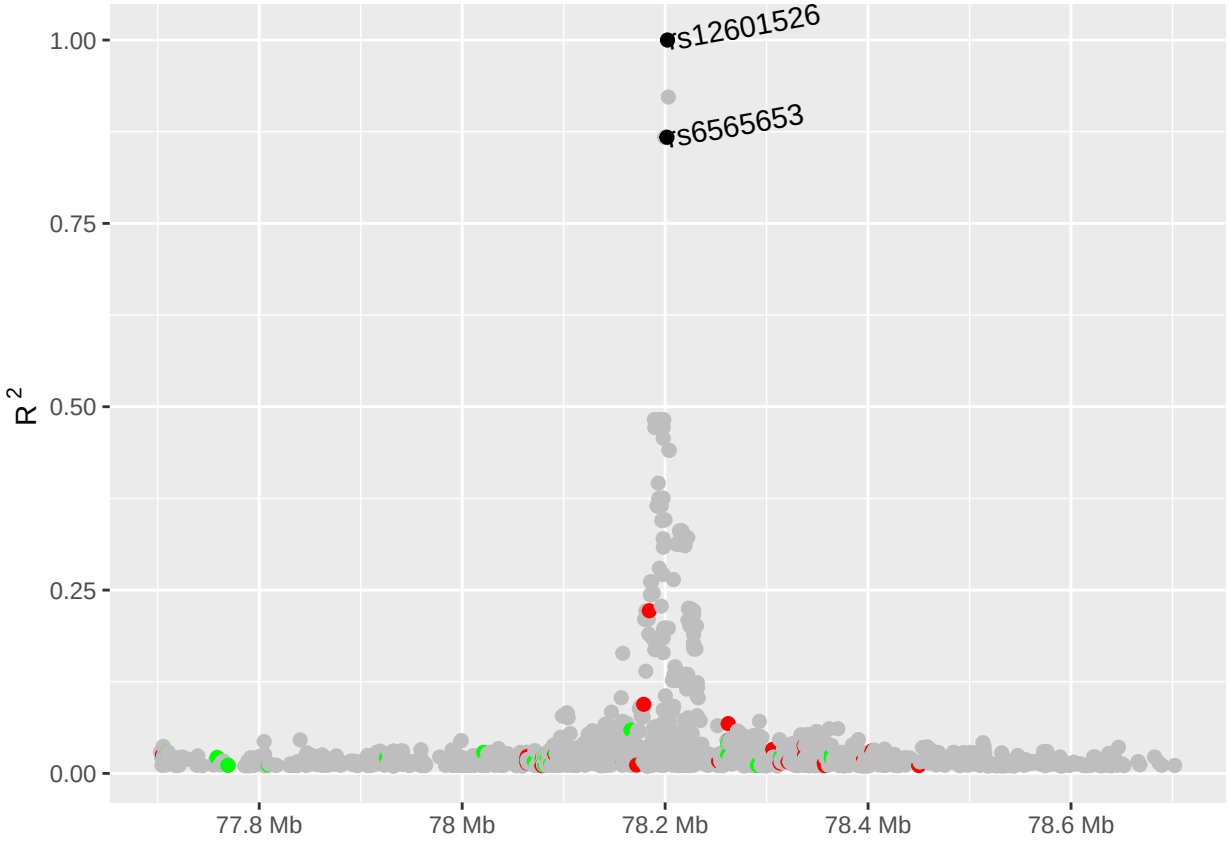



```
fixed (rs6565653_GENES) <- TRUE

rs6565653_GENES.gg <- rs6565653_GENES@ggplot
rs6565653_GENES.gg
```

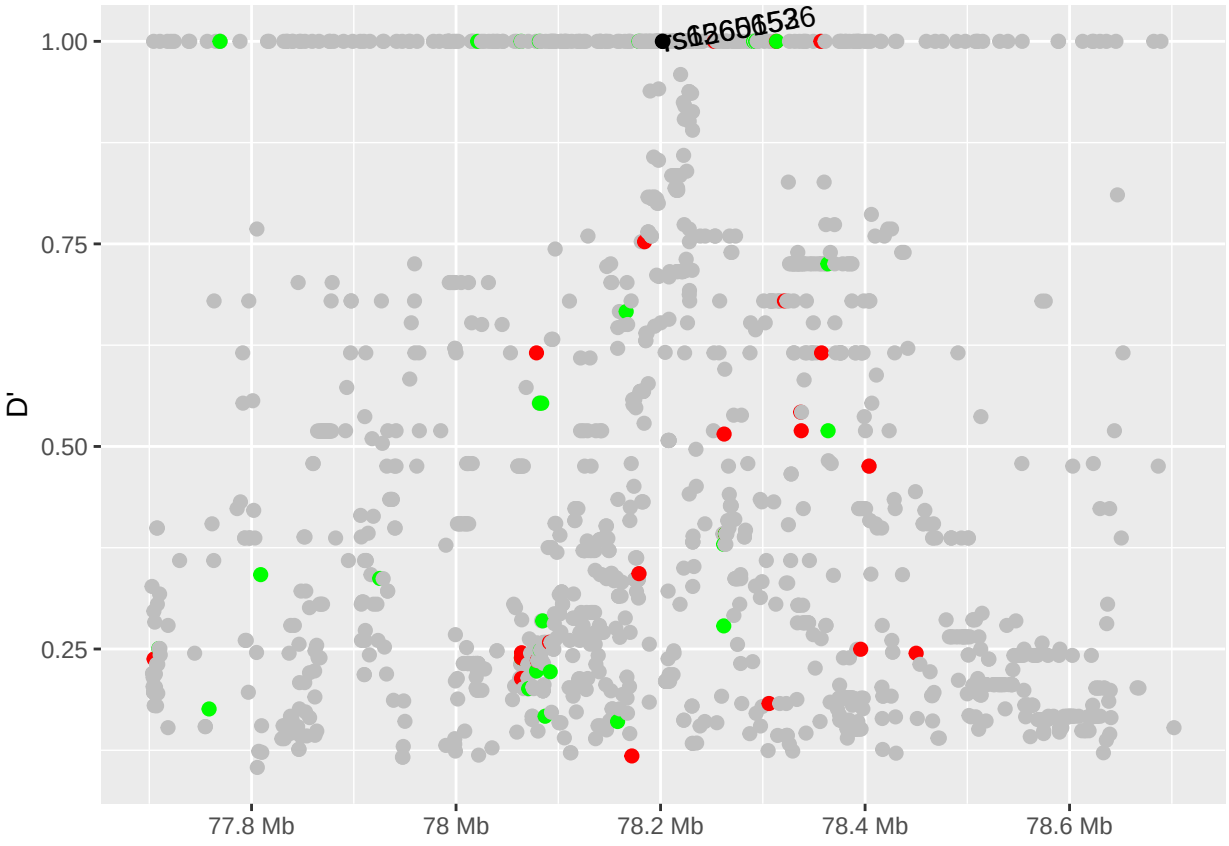



```
# Plots for rs12601526 in CEU population
CEU_12601526_df <- as.data.frame(read.table("input_files/CEU_files/Proxy SNPs rs12601526 CEU population.
                                            sep = "\t", header = TRUE, na.strings = c(".", "NA"),
                                            stringsAsFactors = FALSE))

CEU_12601526_df$Function[is.na(CEU_12601526_df$Function)] <- "N/A"

range_start<-head(CEU_12601526_df$Start,n=1)
range_end<-tail(CEU_12601526_df$Start,n=1)
scale_combined <- GRanges('chr17', IRanges(start = range_start, end = range_end))

legend_title <- "SNP function"

y_lab_r <- as.expression(bquote('R'^{~2}~''))

rs12601526_r <- ggplot(CEU_12601526_df, aes(Start,R2)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(CEU_12601526_df, DisplayName == "Y"),
                   aes(Start, R2), color = "black") +
        geom_text(data=subset(CEU_12601526_df, DisplayName == "Y"),
                  aes(Start, R2,label=ID, hjust = 0, angle = 10)) +
        labs(y = y_lab_r, color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "synonymous"),
                           values = c("red", "grey", "green")) +
```

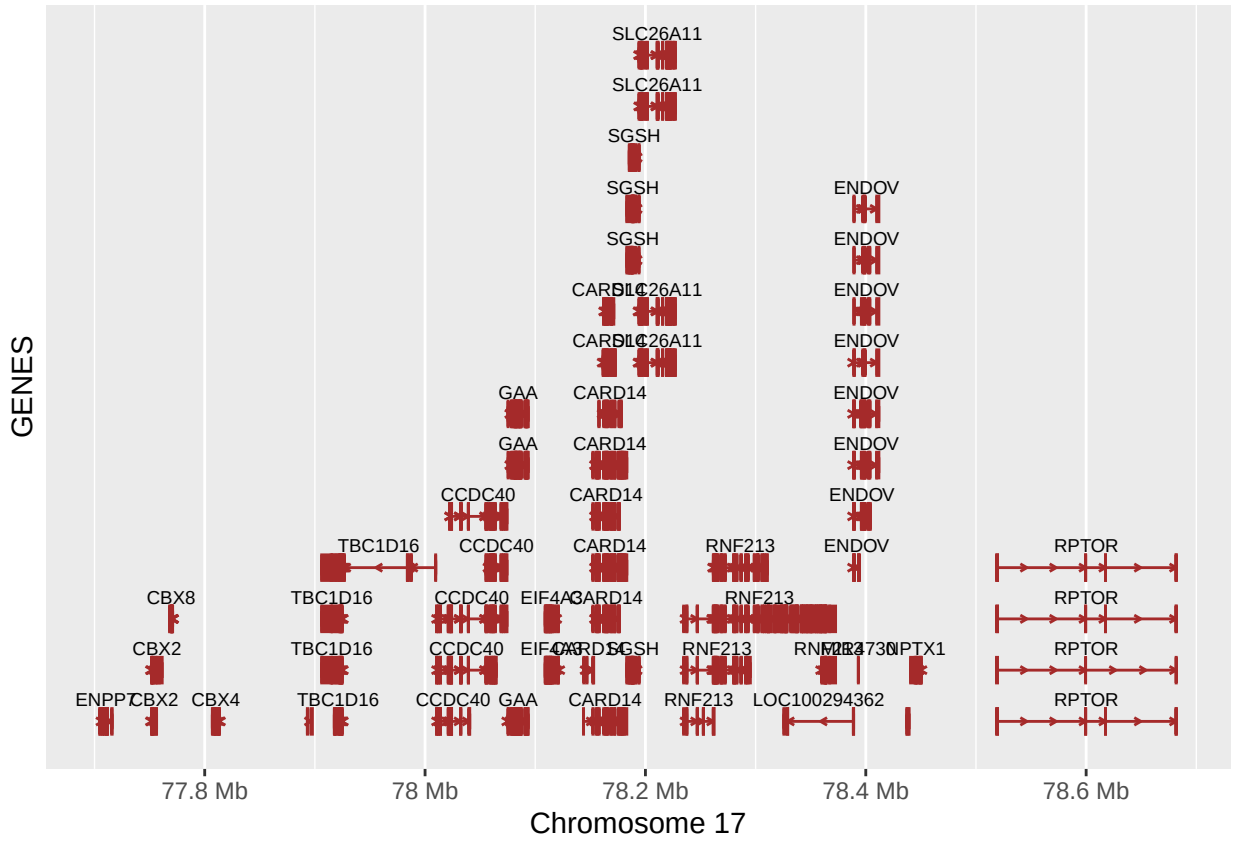
```
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs12601526_r) <- TRUE
rs12601526_r
```



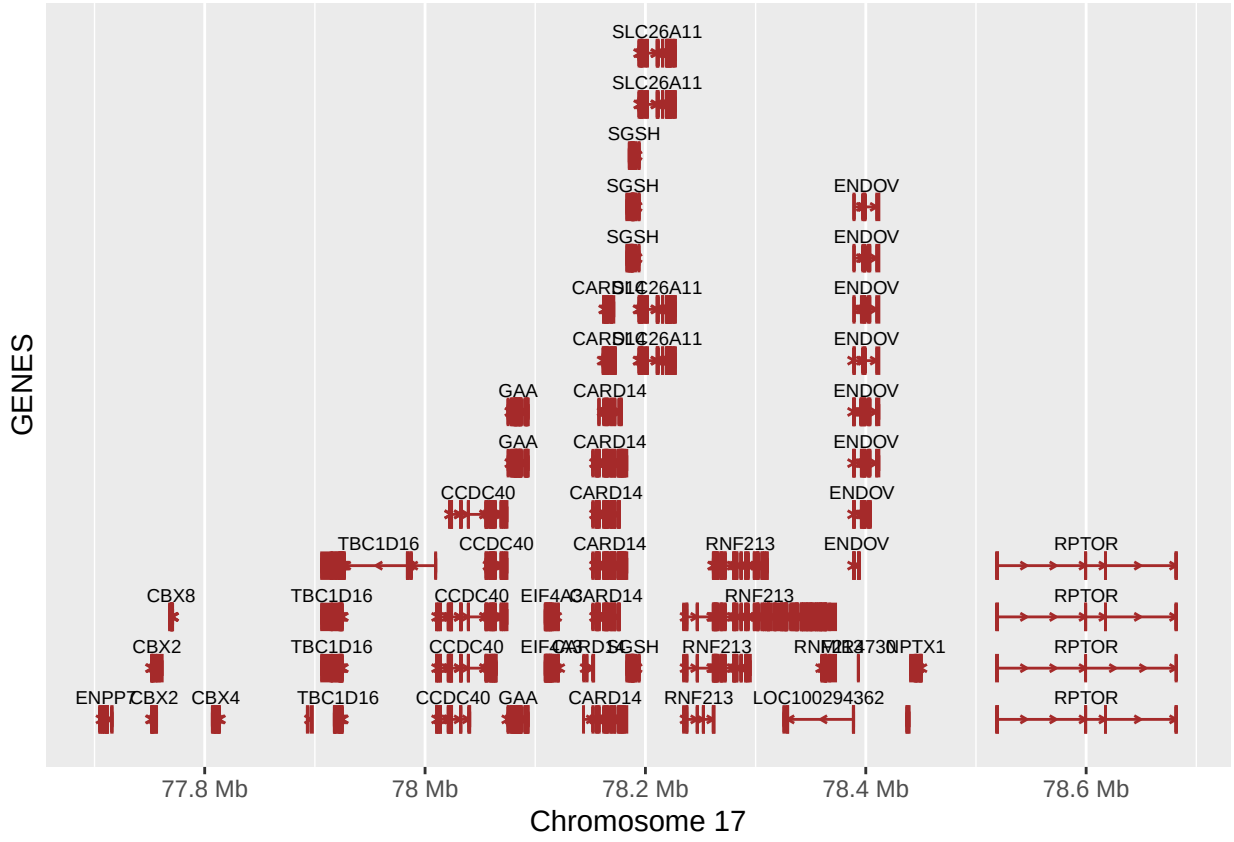

```
rs12601526_D <- ggplot(CEU_12601526_df, aes(Start,Dprime)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(CEU_12601526_df, DisplayName == "Y"),
                   aes(Start, Dprime), color = "black") +
        geom_text(data=subset(CEU_12601526_df, DisplayName == "Y"),
                  aes(Start, Dprime,label=ID, hjust = 0, angle = 10)) +
        labs(y = "D\'", color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "synonymous"),
                           values = c("red", "grey", "green")) +
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs12601526_D) <- TRUE
rs12601526_D
```



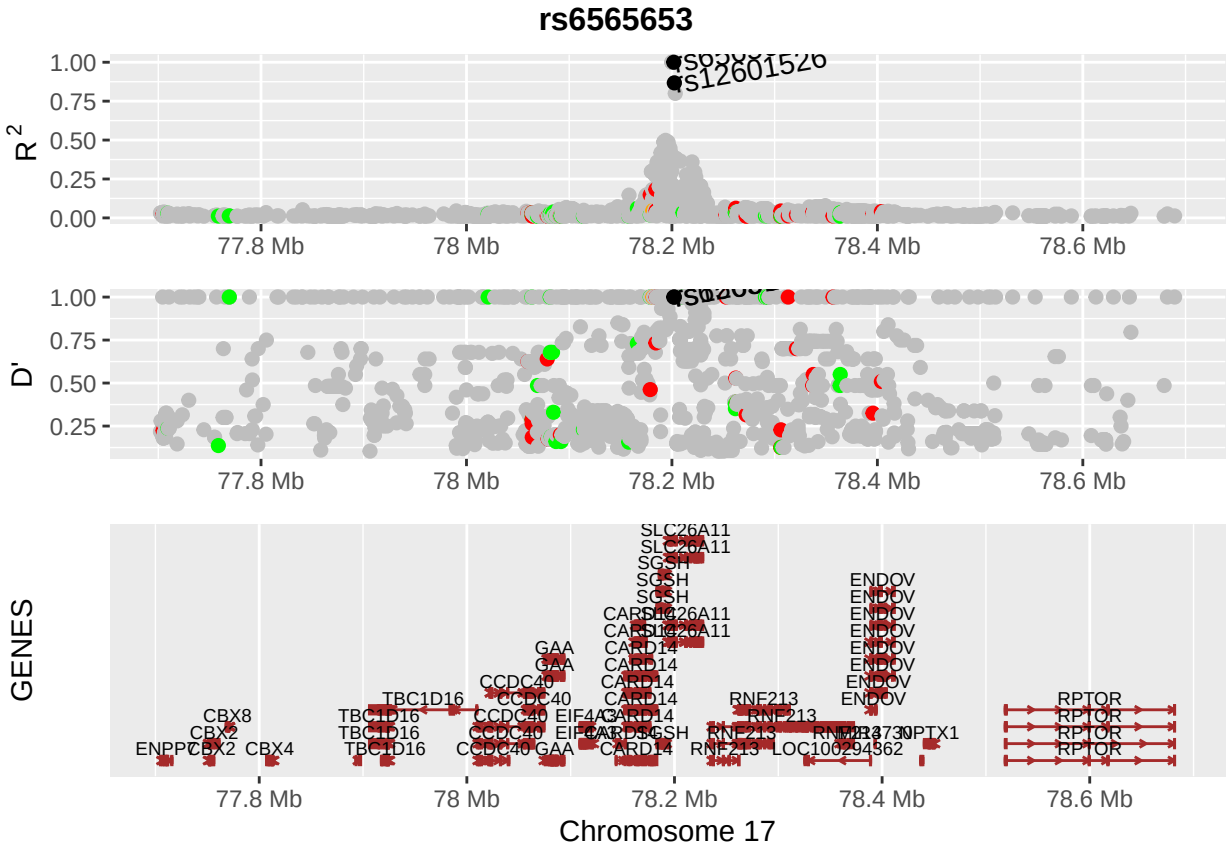

```
# Missing genes: "LOC101928766", "LOC101928738", "MIR4730"

data(genesymbol, package = "biovizBase")
wh <- genesymbol[c("ENPP7", "RPTOR")]
wh <- range(wh, ignore.strand = TRUE)

rs12601526_GENES <- autoplot(Homo.sapiens, which = wh, xlab = "Chromosome 17", ylab = "GENES",
                             label.color = "black", color = "brown",
                             fill = "brown", columns = c("ALIAS", "GO"), scale = "Mb") +
        xlim (scale_combined) +
        scale_x_sequnit("Mb")
rs12601526_GENES
```



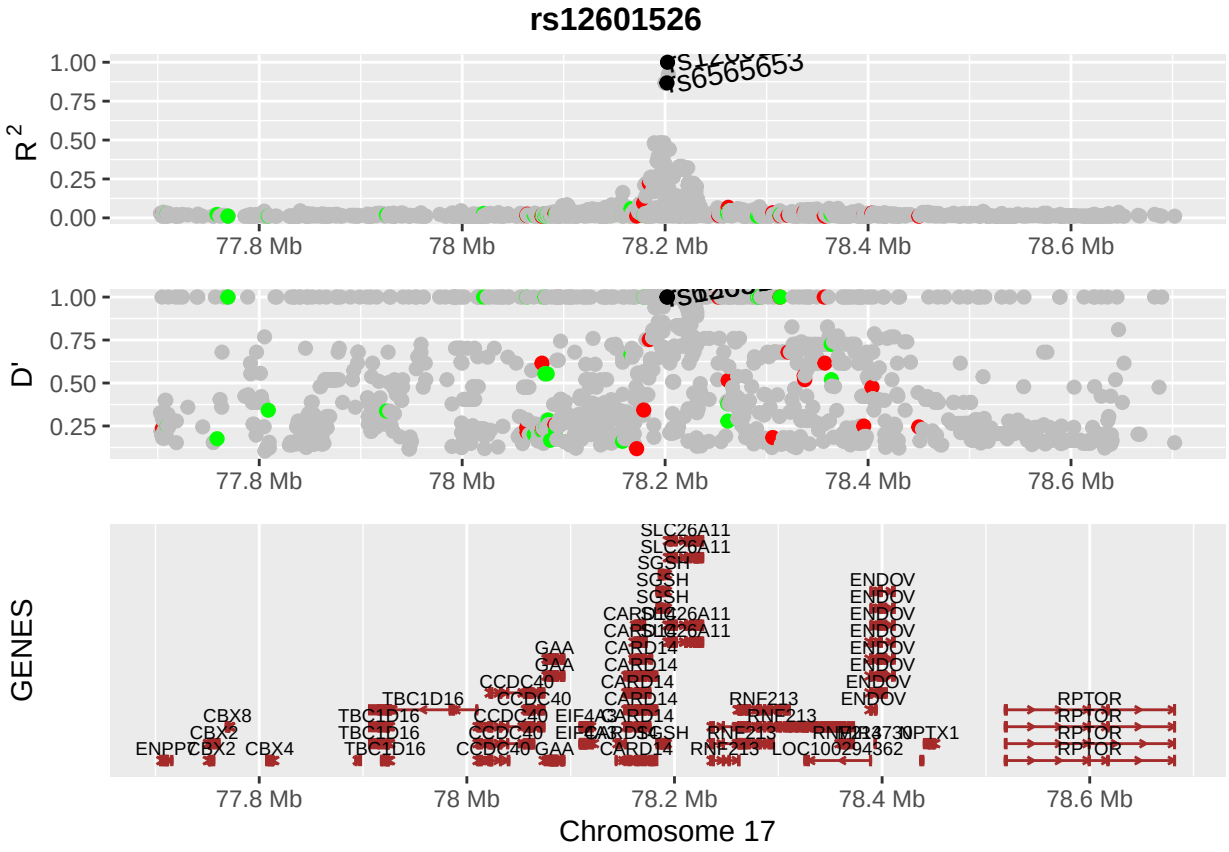

```
fixed (rs12601526_GENES) <- TRUE

rs12601526_GENES.gg <- rs12601526_GENES@ggplot
rs12601526_GENES.gg
```




```
# Get the gtables
gA <- ggplotGrob (rs6565653_r)
gB <- ggplotGrob (rs6565653_D)
gC <- ggplotGrob (rs6565653_GENES.gg)

gD <- ggplotGrob (rs12601526_r)
gE <- ggplotGrob (rs12601526_D)
gF <- ggplotGrob (rs12601526_GENES.gg)

# Set the widths
gB$widths <- gA$widths
gC$widths <- gA$widths

gE$widths <- gD$widths
gF$widths <- gD$widths

# Arrange the three charts
rs6565653_title = textGrob("rs6565653", gp=gpar(fontsize=12, font = 2))
grid.newpage()
CEU_plot_rs6565653 <- grid.arrange(gA, gB, gC,  heights = c(4,4,6), top = rs6565653_title)
```



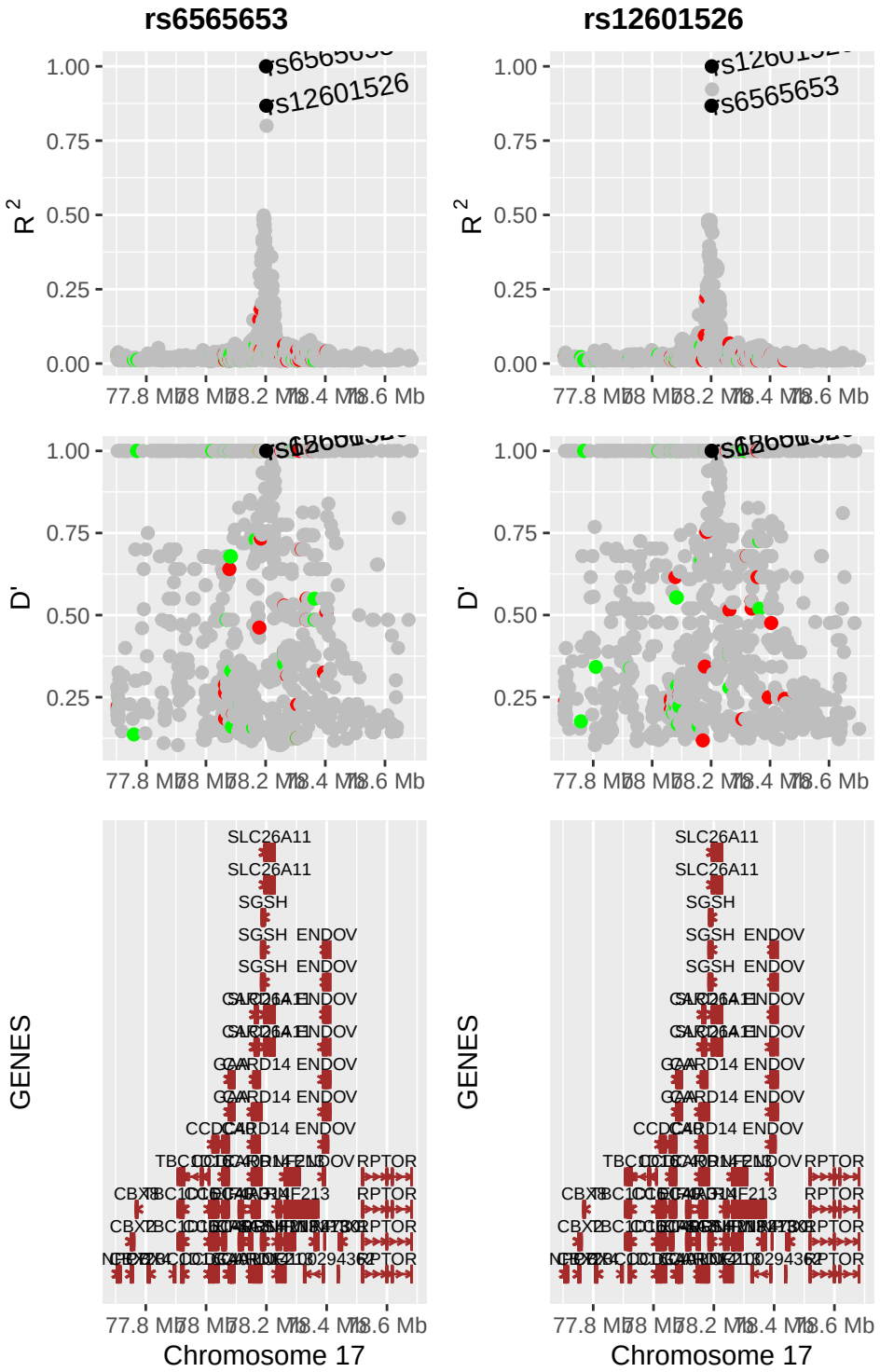

```
rs12601526_title = textGrob("rs12601526", gp=gpar(fontsize=12, font = 2))
grid.newpage()
CEU_plot_rs12601526 <- grid.arrange(gD, gE, gF, heights = c(4,4,6), top = rs12601526_title)
```




```
main_title = textGrob("rs6565653 and rs12601526 proxy SNPs in CEU population",
                      gp=gpar(fontsize=16, font = 2))
grid.newpage()
```

Supplemntary Figure 2 - Plot "rs6565653 and rs12601526 proxy SNPs in CEU population"

```
FINAL_PLOT_CEU <- grid.arrange(CEU_plot_rs6565653, CEU_plot_rs12601526, ncol = 2, top =
                               main_title)
```



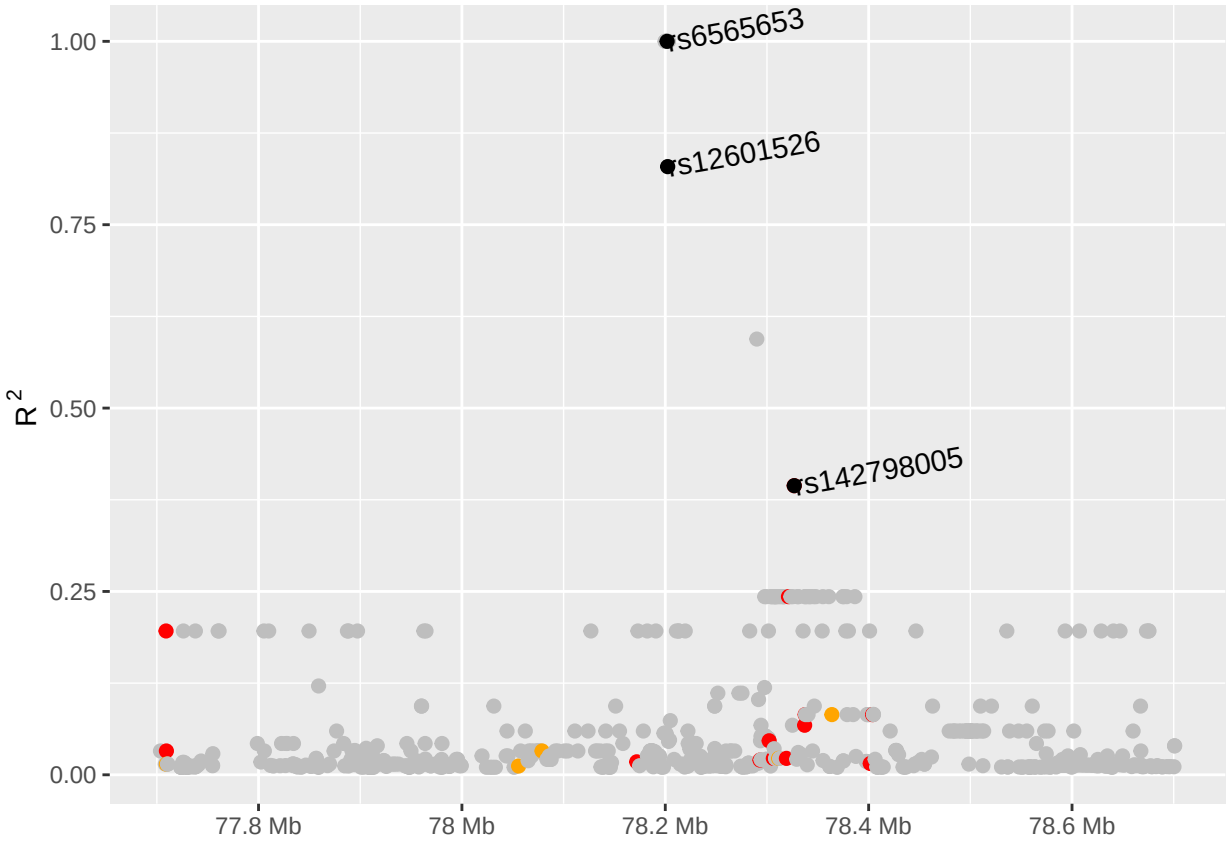

```
dev.off()
```

```
## null device
##           1
```

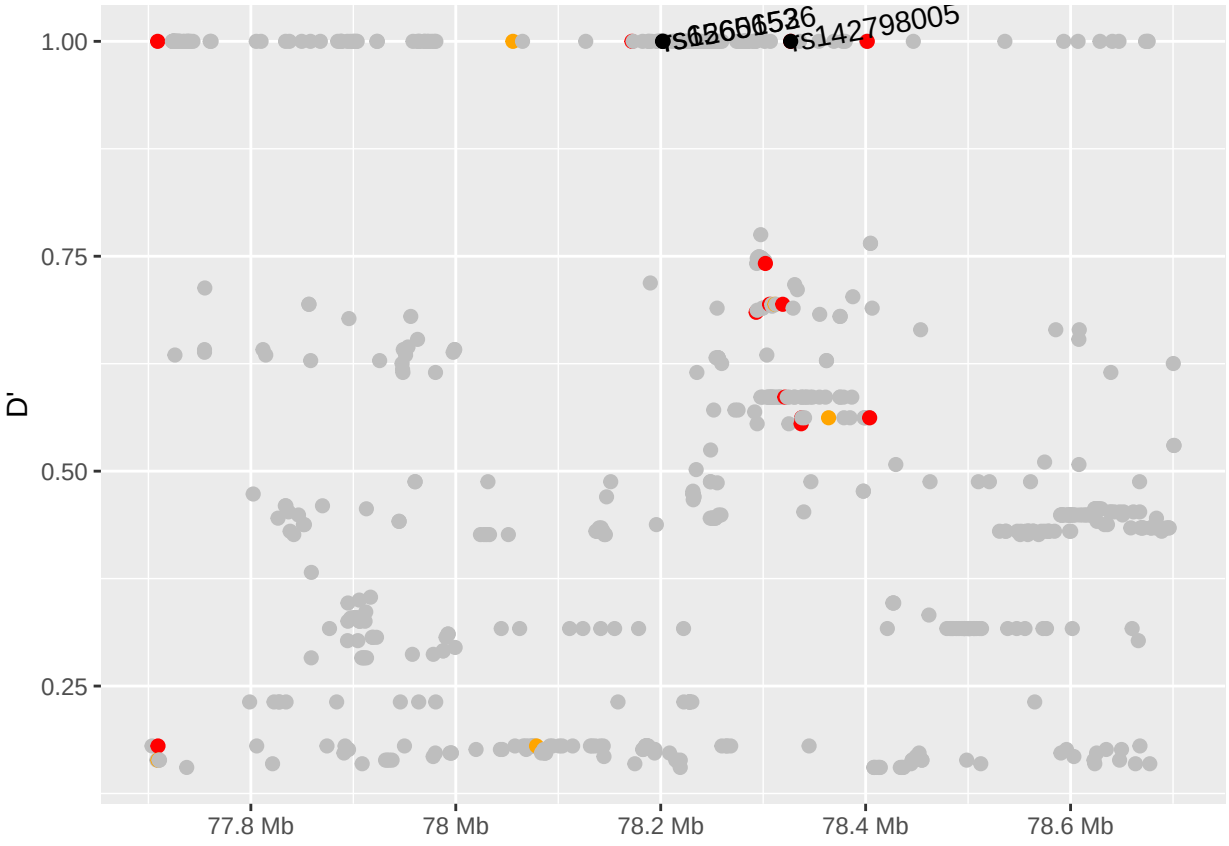
Proxy SNPs for JPT population

Get proxy SNPs for JPT population for rs6565653 and rs12601526

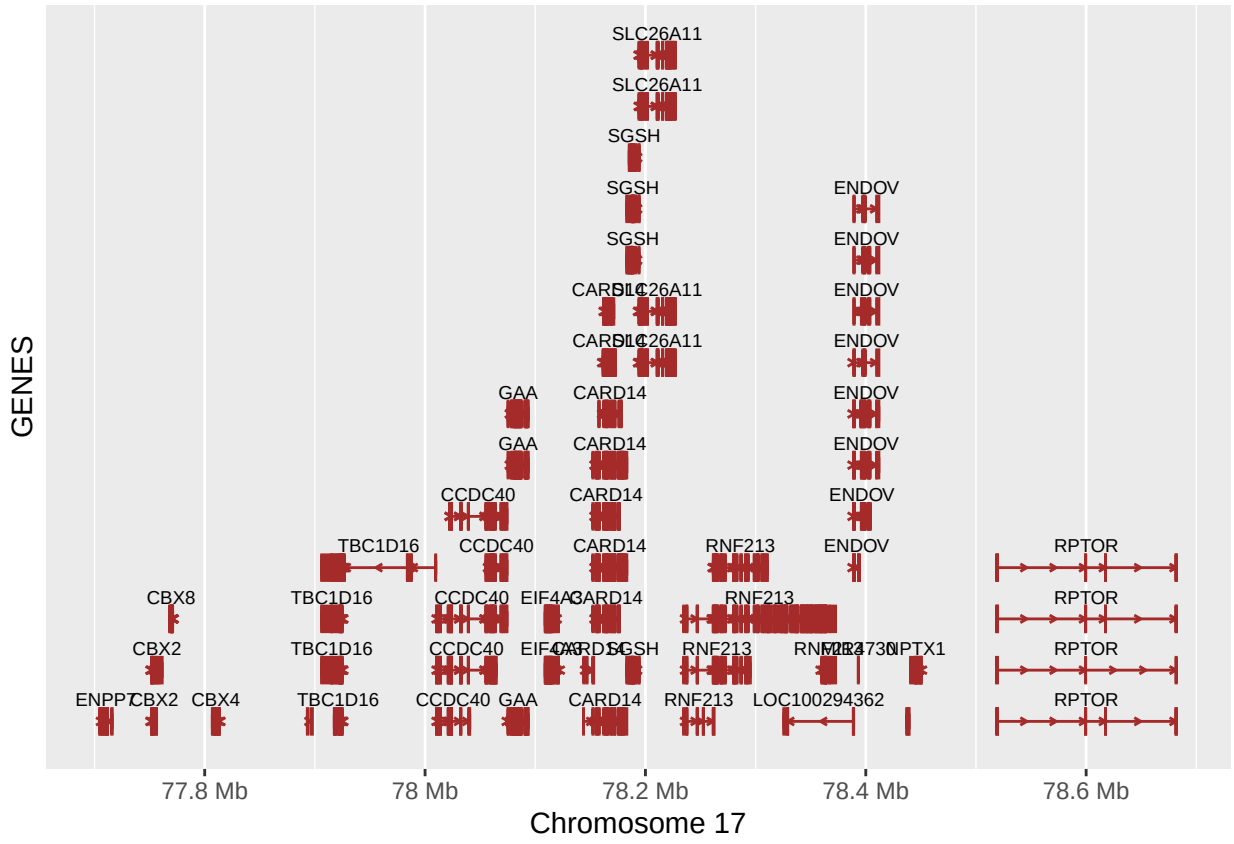
```
# JPT population rs6565653 proxy SNPs
dirname <- getwd()
setwd(dirname)


# Plots for rs6565653 in JPT population
JPT_6565653_df <- as.data.frame(read.table("input_files/JPT_files/Proxy SNPs rs6565653 JPT population.tx
                                           sep = "\t", header = TRUE, na.strings = c(".", "NA"),
                                           stringsAsFactors = FALSE))

JPT_6565653_df$Function[is.na(JPT_6565653_df$Function)] <- "N/A"

range_start<-head(JPT_6565653_df$Start,n=1)
range_end<-tail(JPT_6565653_df$Start,n=1)
scale_combined <- GRanges('chr17', IRanges(start = range_start, end = range_end))


legend_title <- "SNP function"

y_lab_r <- as.expression(bquote('R'^{~2}~''))

rs6565653_r <- ggplot(JPT_6565653_df, aes(Start,R2)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(JPT_6565653_df, DisplayName == "Y"),
                   aes(Start, R2), color = "black") +
        geom_text(data=subset(JPT_6565653_df, DisplayName == "Y"),
                  aes(Start, R2,label=ID, hjust = 0, angle = 10)) +
        labs(y = y_lab_r, color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "nonsense", "synonymous"),
                           values = c("red", "grey", "orange", "green")) +
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs6565653_r) <- TRUE
rs6565653_r
```



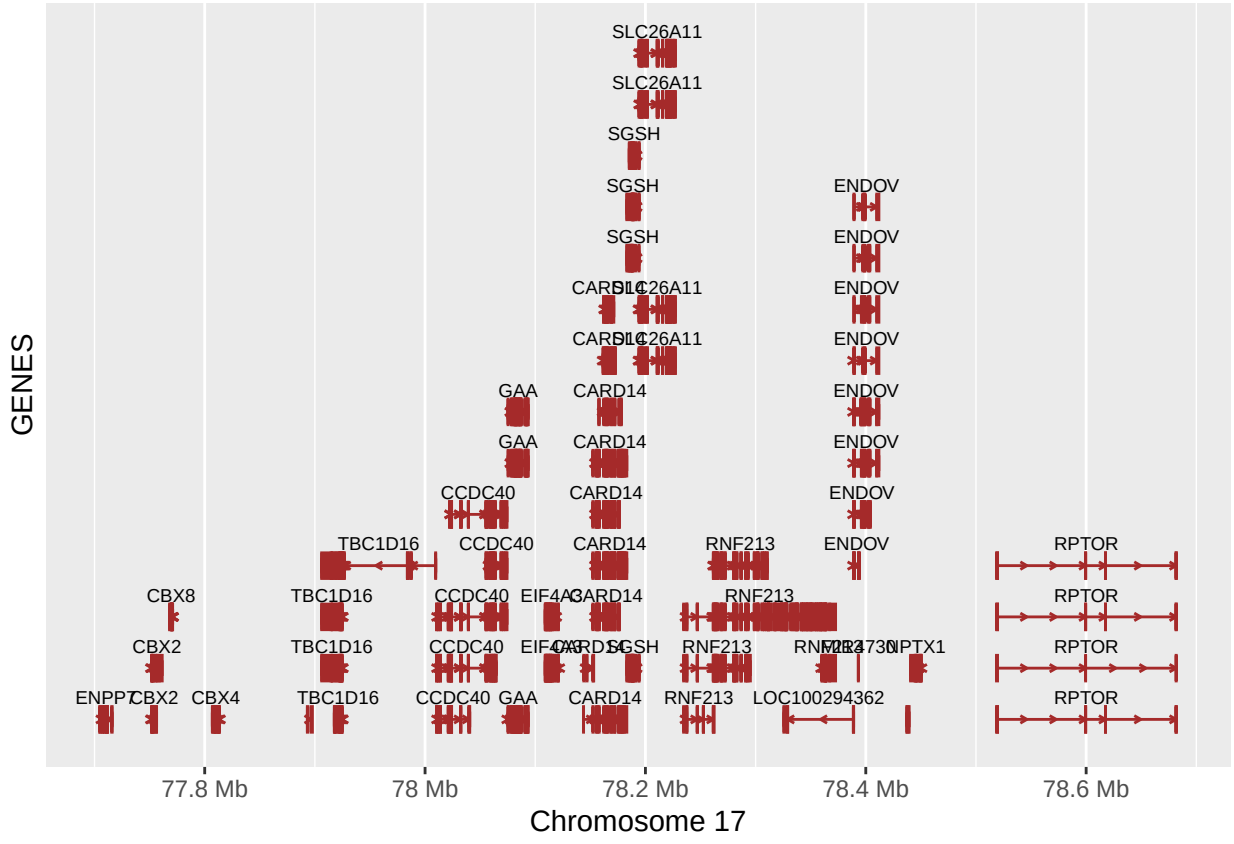

```
rs6565653_D <- ggplot(JPT_6565653_df, aes(Start,Dprime)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(JPT_6565653_df, DisplayName == "Y"),
                   aes(Start, Dprime), color = "black") +
        geom_text(data=subset(JPT_6565653_df, DisplayName == "Y"),
                  aes(Start, Dprime,label=ID, hjust = 0, angle = 10)) +
        labs(y = "D\'", color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "nonsense", "synonymous"),
                           values = c("red", "grey", "orange", "green")) +
        scale_x_sequnit("Mb")+
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs6565653_D) <- TRUE
rs6565653_D
```




```
# Missing genes: "LOC101928766", "LOC101928738", "MIR4730"

data(genesymbol, package = "biovizBase")
wh <- genesymbol[c("ENPP7", "RPTOR")]
wh <- range(wh, ignore.strand = TRUE)

rs6565653_GENES <- autoplot(Homo.sapiens, which = wh, xlab = "Chromosome 17", ylab = "GENES",
                            label.color = "black", color = "brown", fill = "brown", columns =
                              c("ALIAS", "GO"), scale = "Mb")+
        xlim (scale_combined) +
        scale_x_sequnit("Mb")
rs6565653_GENES
```

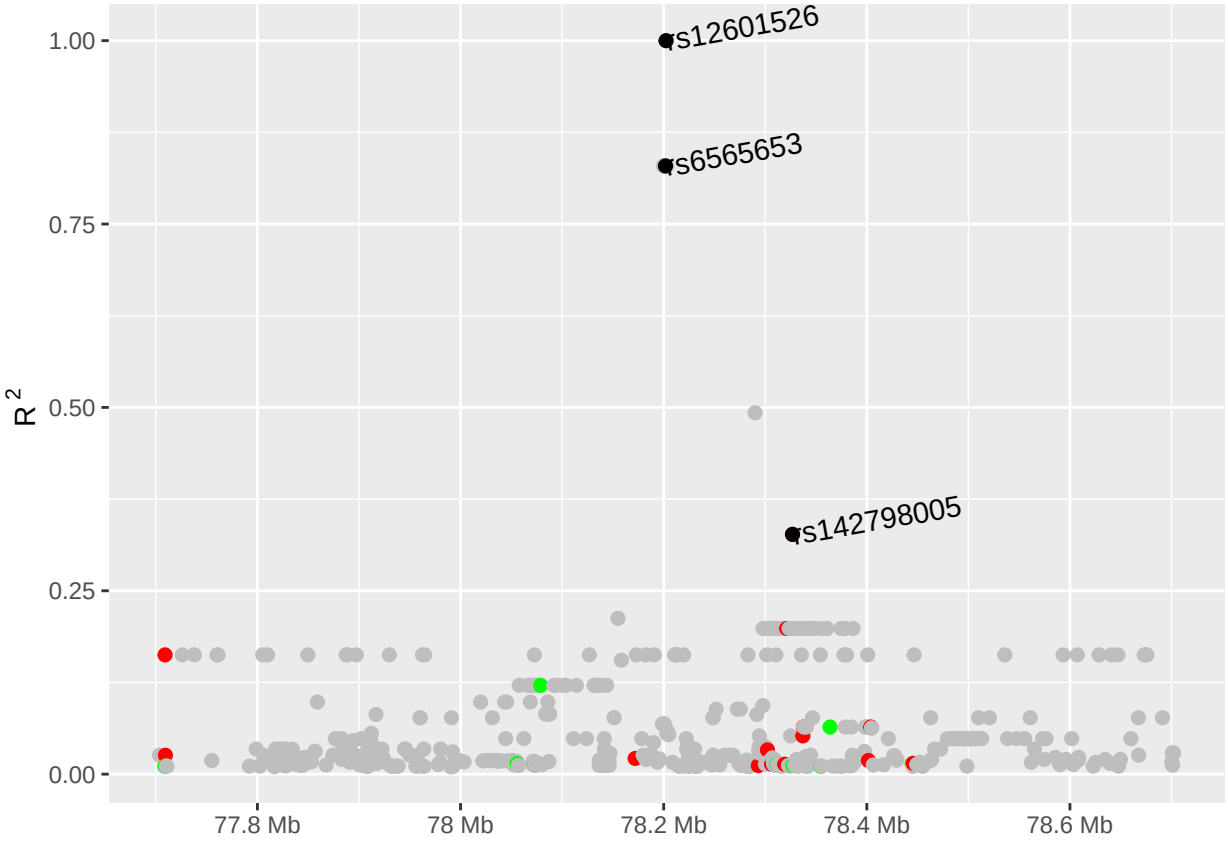



```
fixed (rs6565653_GENES) <- TRUE

rs6565653_GENES.gg <- rs6565653_GENES@ggplot
rs6565653_GENES.gg
```

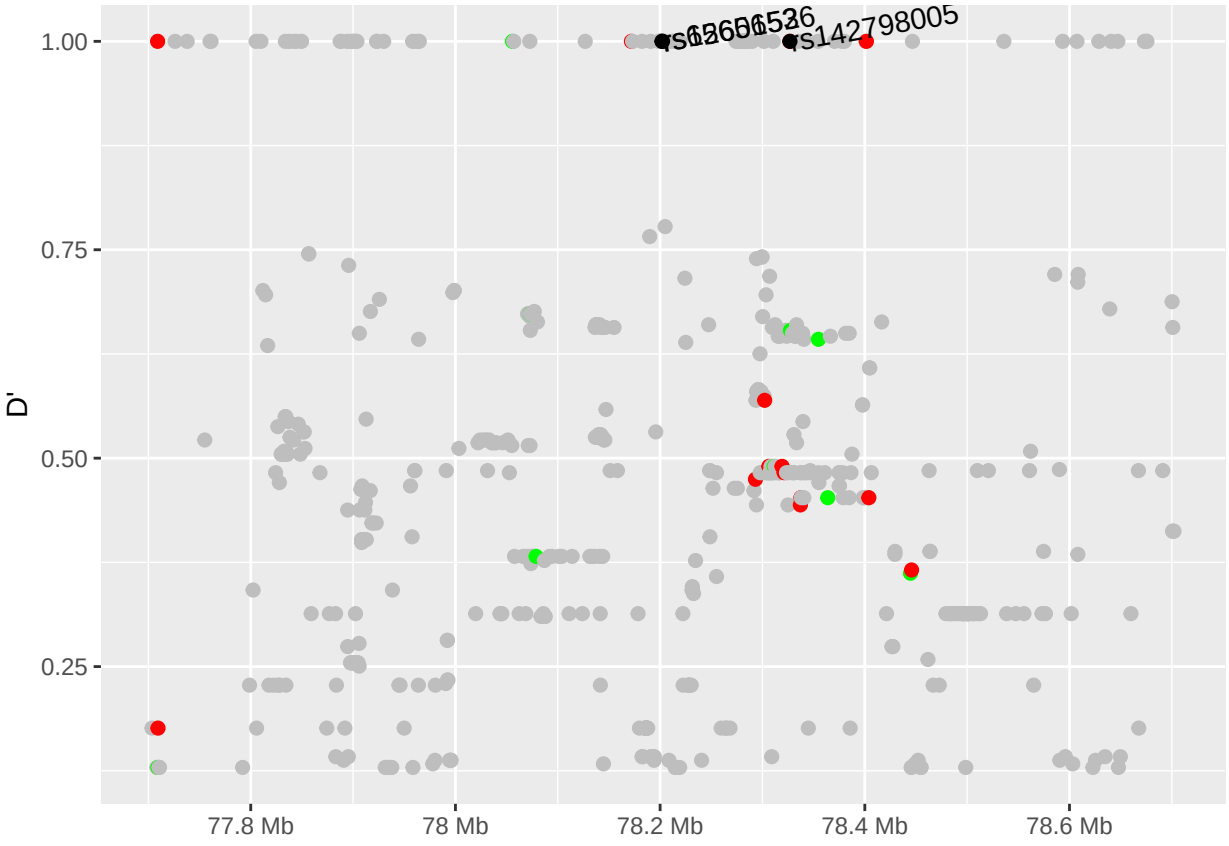



```
############################################################

# Plots for rs12601526 in JPT population
JPT_12601526_df <- as.data.frame(read.table("input_files/JPT_files/Proxy SNPs rs12601526 JPT population.
                                            sep = "\t", header = TRUE, na.strings = c(".", "NA"),
                                            stringsAsFactors = FALSE))

JPT_12601526_df$Function[is.na(JPT_12601526_df$Function)] <- "N/A"

range_start<-head(JPT_12601526_df$Start,n=1)
range_end<-tail(JPT_12601526_df$Start,n=1)
scale_combined <- GRanges('chr17', IRanges(start = range_start, end = range_end))


legend_title <- "SNP function"

y_lab_r <- as.expression(bquote('R'^{~2}~''))

rs12601526_r <- ggplot(JPT_12601526_df, aes(Start,R2)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(JPT_12601526_df, DisplayName == "Y"),
                   aes(Start, R2), color = "black") +
        geom_text(data=subset(JPT_12601526_df, DisplayName == "Y"),
                  aes(Start, R2,label=ID, hjust = 0, angle = 10)) +
```

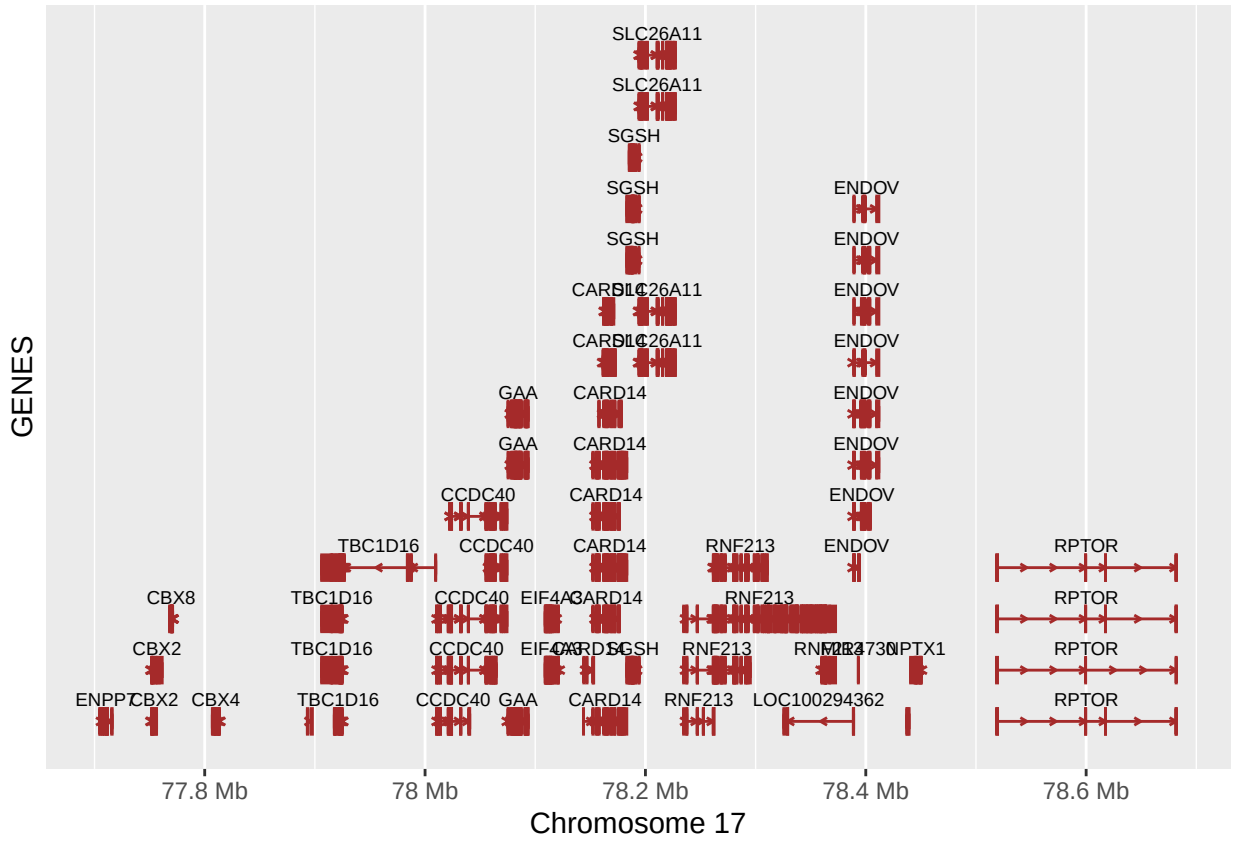
```
        labs(y = y_lab_r, color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "synonymous"),
                           values = c("red", "grey", "green")) +
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs12601526_r) <- TRUE
rs12601526_r
```



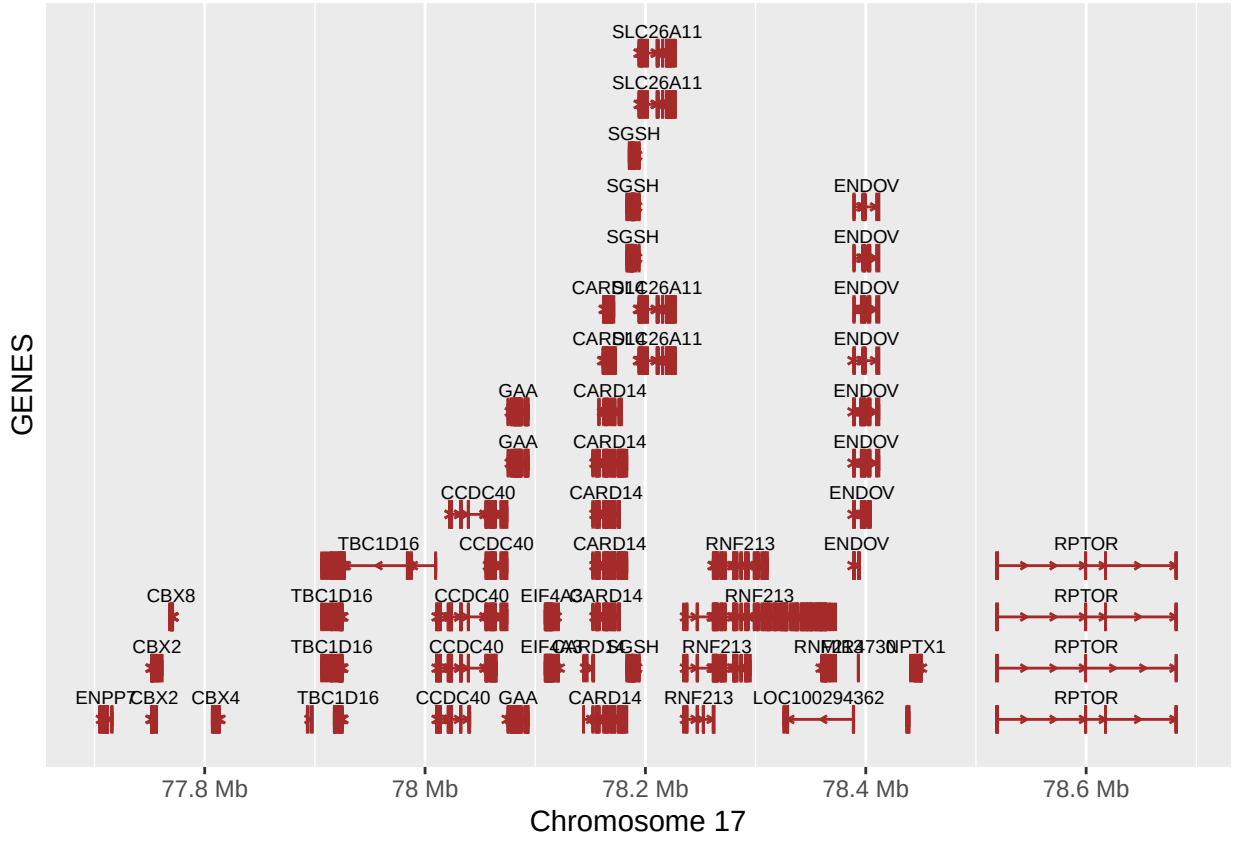

```
rs12601526_D <- ggplot(JPT_12601526_df, aes(Start,Dprime)) +
        xlim (scale_combined) +
        geom_point(size = 2, aes(colour = Function)) +
        geom_point(size = 2, data=subset(JPT_12601526_df, DisplayName == "Y"),
                   aes(Start, Dprime), color = "black") +
        geom_text(data=subset(JPT_12601526_df, DisplayName == "Y"),
                  aes(Start, Dprime,label=ID, hjust = 0, angle = 10)) +
        labs(y = "D\'", color = "SNP Function\n") +
        scale_color_manual(labels = c("missense", "unkwnown", "synonymous"),
                           values = c("red", "grey", "green")) +
        scale_x_sequnit("Mb") +
        theme(axis.title.x = element_blank (), legend.position = "none")
fixed(rs12601526_D) <- TRUE
rs12601526_D
```



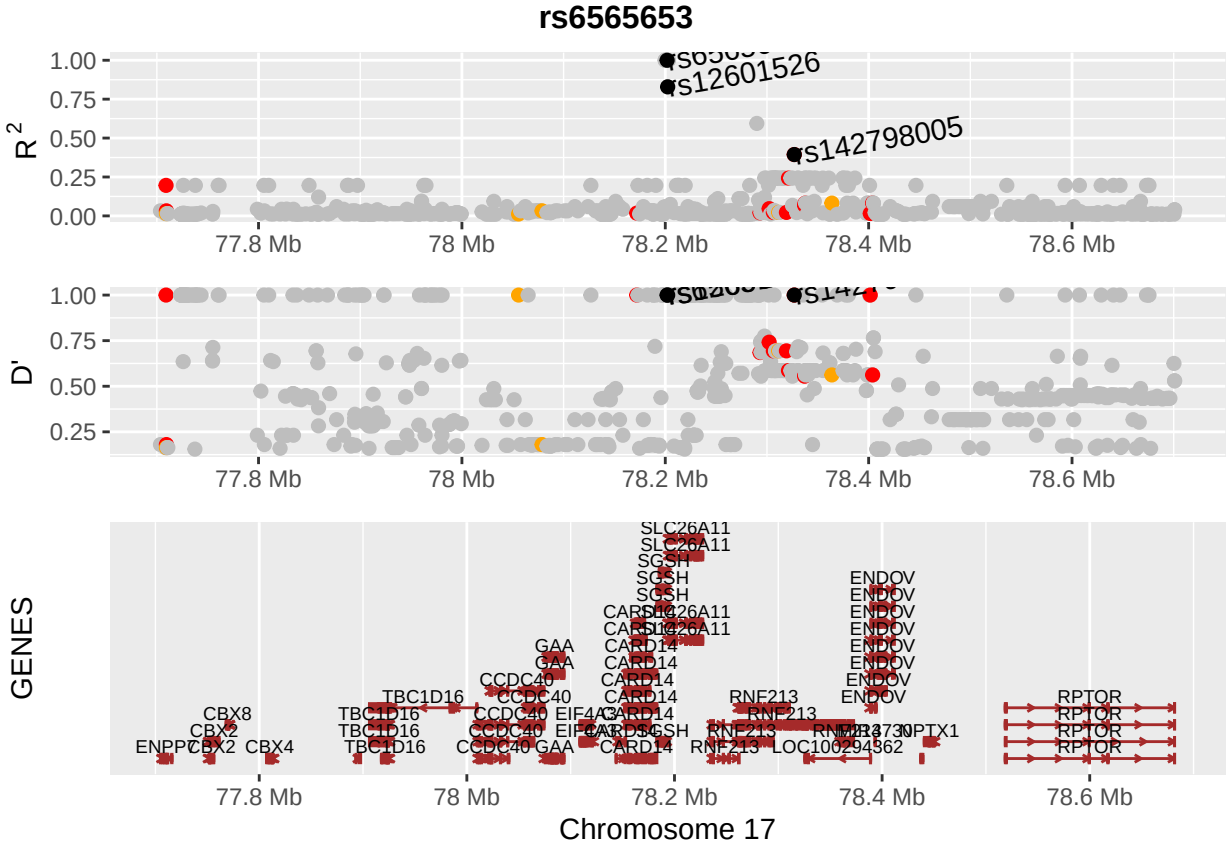

```
# Missing genes: "LOC101928766", "LOC101928738", "MIR4730"

data(genesymbol, package = "biovizBase")
wh <- genesymbol[c("ENPP7", "RPTOR")]
wh <- range(wh, ignore.strand = TRUE)

rs12601526_GENES <- autoplot(Homo.sapiens, which = wh, xlab = "Chromosome 17", ylab = "GENES",
                             label.color = "black", color = "brown",
                             fill = "brown", columns = c("ALIAS", "GO"), scale = "Mb") +
        xlim (scale_combined) +
        scale_x_sequnit("Mb")
rs12601526_GENES
```



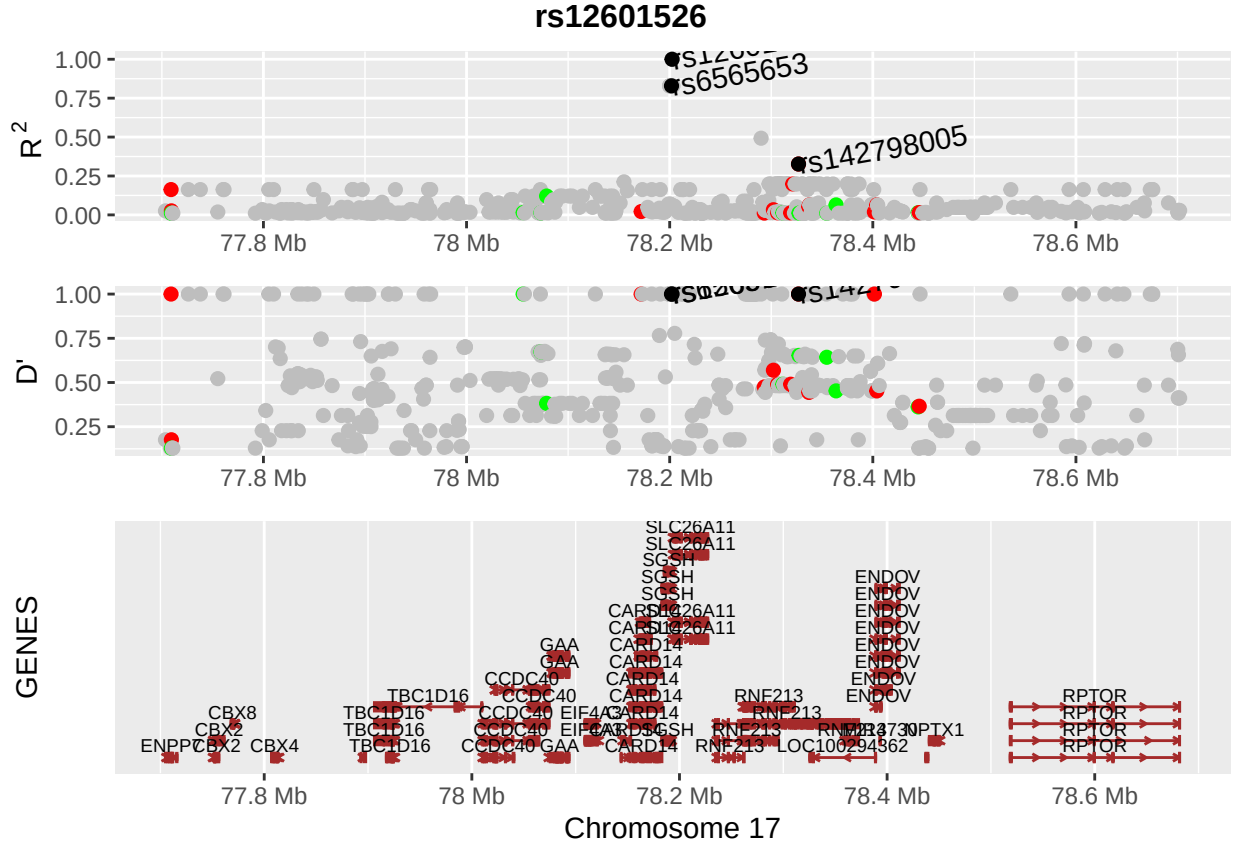

```
fixed (rs12601526_GENES) <- TRUE

rs12601526_GENES.gg <- rs12601526_GENES@ggplot
rs12601526_GENES.gg
```




```
# Get the gtables
gA <- ggplotGrob (rs6565653_r)
gB <- ggplotGrob (rs6565653_D)
gC <- ggplotGrob (rs6565653_GENES.gg)

gD <- ggplotGrob (rs12601526_r)
gE <- ggplotGrob (rs12601526_D)
gF <- ggplotGrob (rs12601526_GENES.gg)

# Set the widths
gB$widths <- gA$widths
gC$widths <- gA$widths

gE$widths <- gD$widths
gF$widths <- gD$widths

# Arrange the three charts
rs6565653_title = textGrob("rs6565653", gp=gpar(fontsize=12, font = 2))
grid.newpage()
JPT_plot_rs6565653 <- grid.arrange(gA, gB, gC,  heights = c(4,4,6), top = rs6565653_title)
```



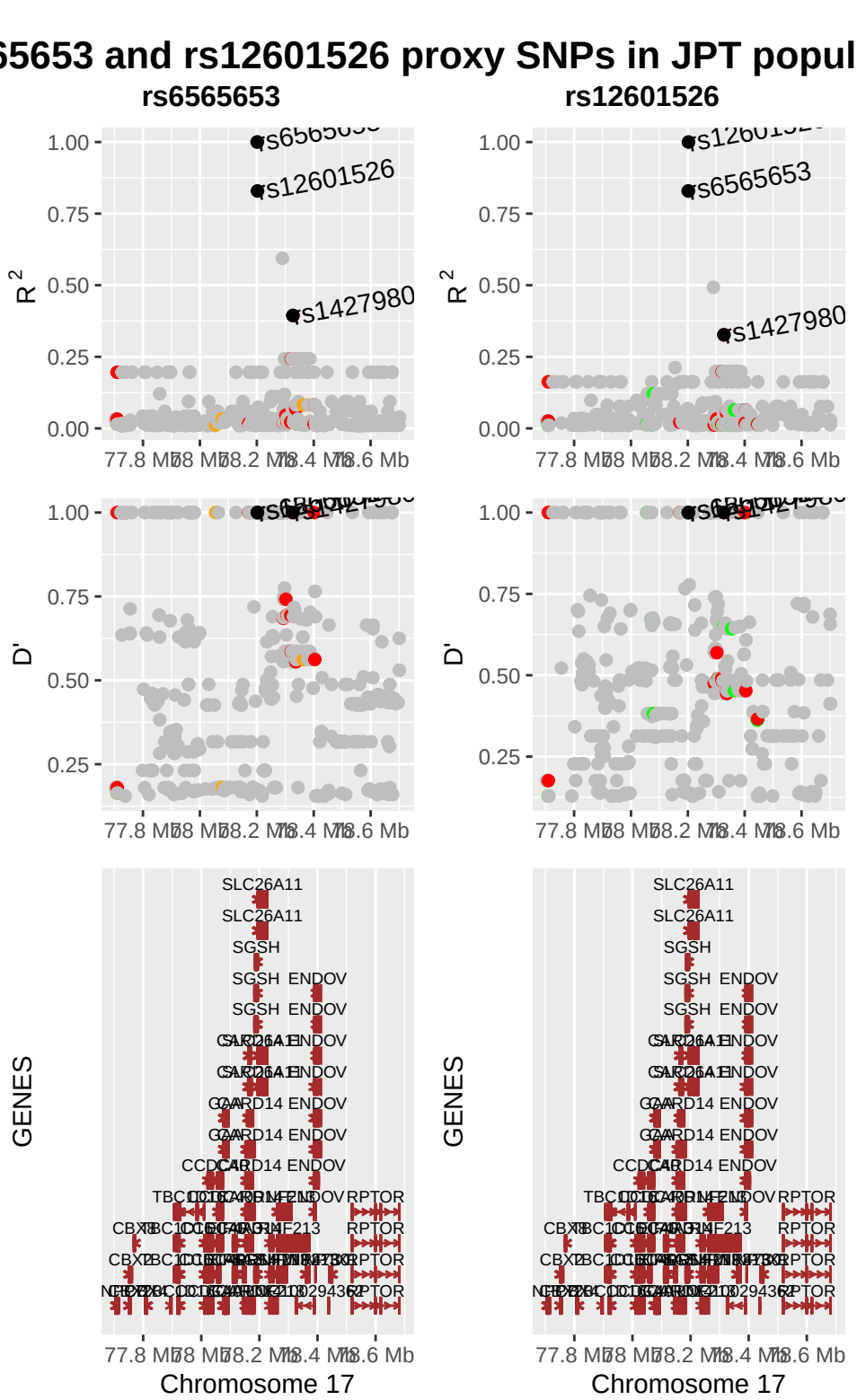

```
rs12601526_title = textGrob("rs12601526", gp=gpar(fontsize=12, font = 2))
grid.newpage()
JPT_plot_rs12601526 <- grid.arrange(gD, gE, gF, heights = c(4,4,6), top = rs12601526_title)
```




```
main_title = textGrob("rs6565653 and rs12601526 proxy SNPs in JPT population",
                      gp=gpar(fontsize=16, font = 2))
grid.newpage()
```

Supplementary Figure 3 - Plot "rs6565653 and rs12601526 proxy SNPs in JPT population"

```
FINAL_PLOT_JPT <- grid.arrange(JPT_plot_rs6565653, JPT_plot_rs12601526, ncol = 2, top =
                               main_title)
```

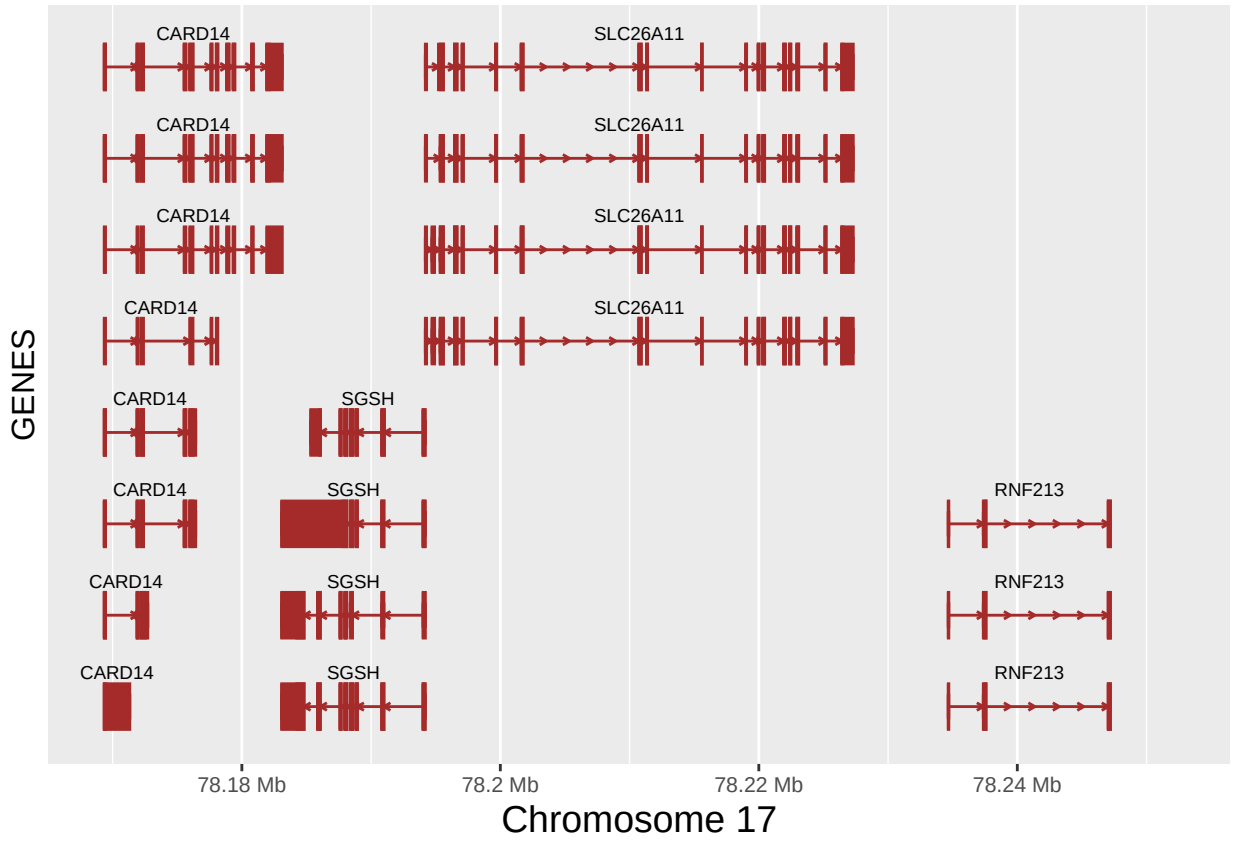



```
dev.off()
```

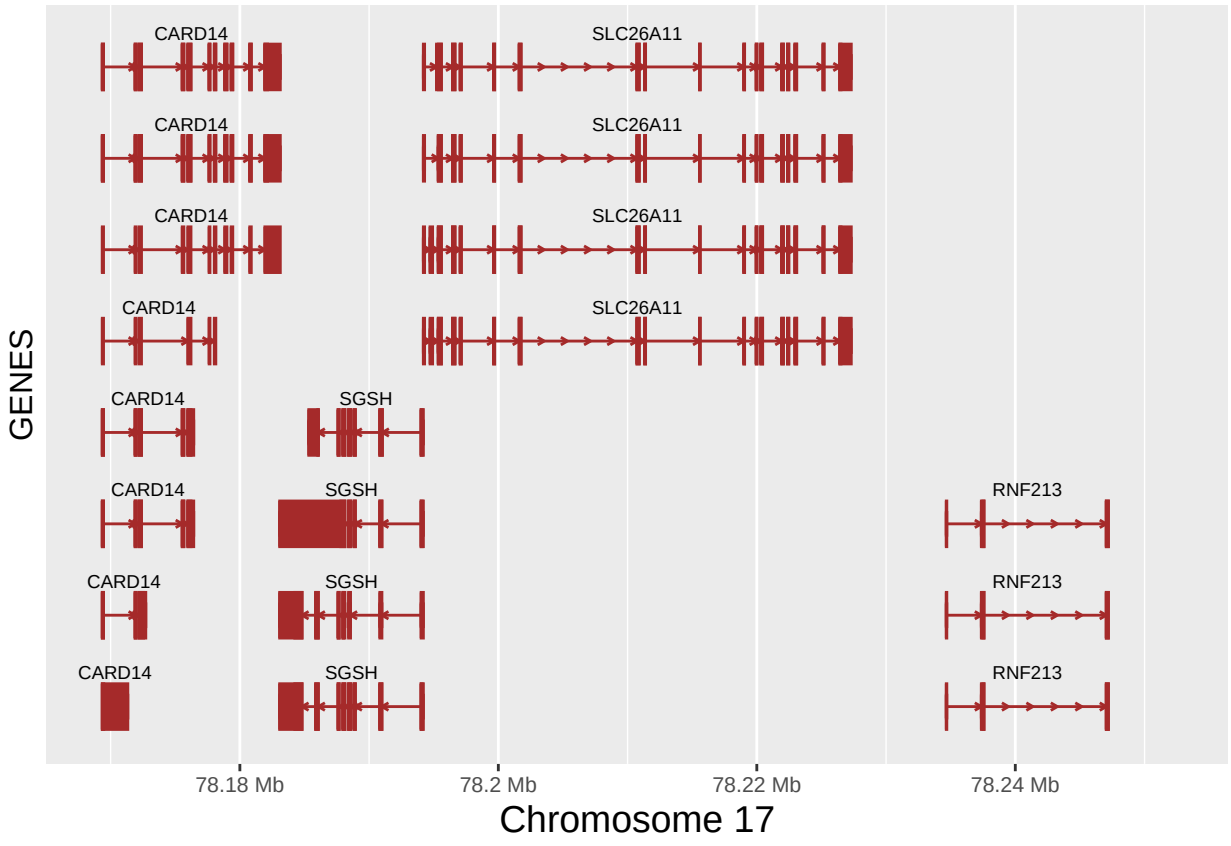
```
## null device
##           1
```

Artery__eQTL__values__RNF213__SLC26A1

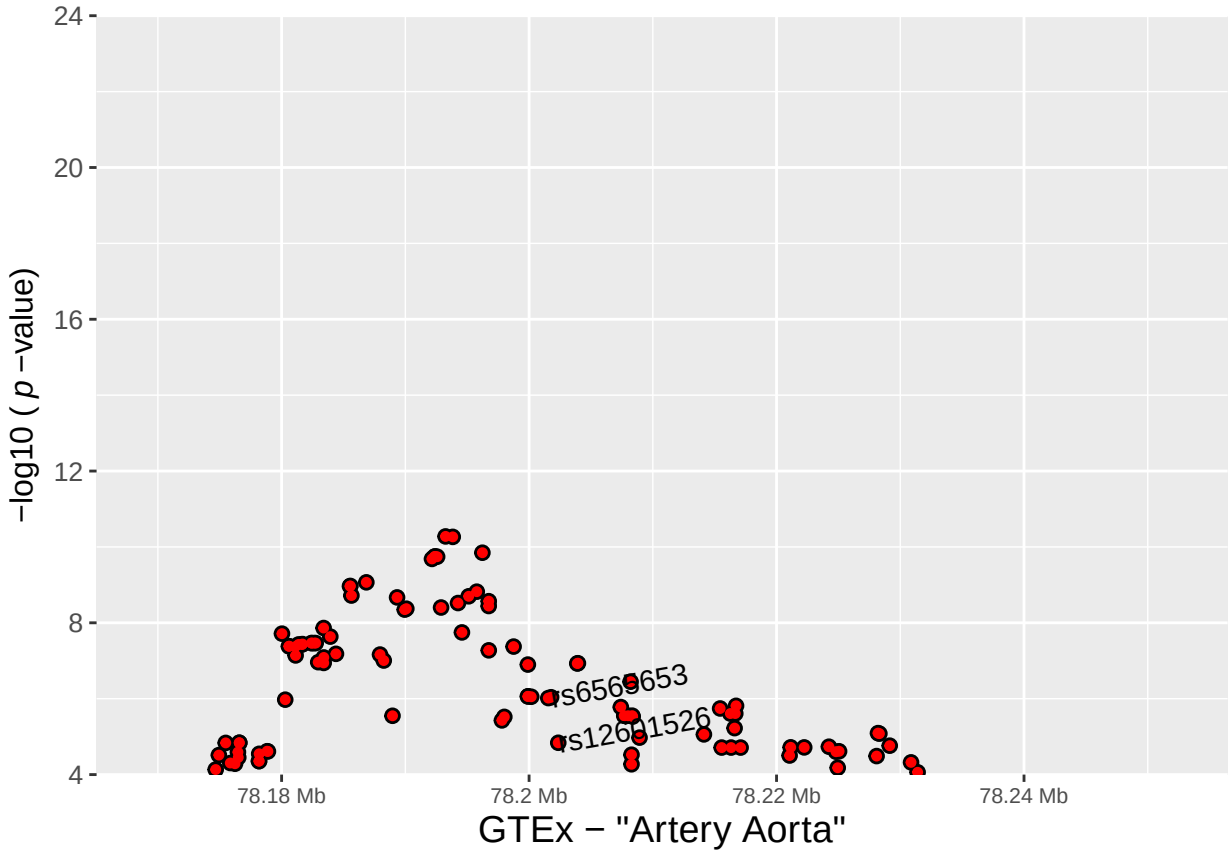
```
data(hg19IdeogramCyto, package = "biovizBase")
data(hg19Ideogram, package = "biovizBase")
data(genesymbol, package = "biovizBase")

hg19 <- keepSeqlevels(hg19IdeogramCyto, paste0("chr", c(1:22, "X", "Y")))

# RNF213_SLC26A11_eQTL_association_files
x_lab_aorta <- "GTEx - \"Artery Aorta\""
x_lab_coronary <- "GTEx - \"Artery Coronary\""
x_lab_tibial <- "GTEx - \"Artery Tibial\""
y_lab <- as.expression(bquote('-log10 ('~italic(p)~'-value)'), fontsize=8, font = 2)


# Plots for SLC26A11 significant eQTL SNPs
# SLC26A11 Genes Plot
wh_SLC26A11 <- genesymbol[c("SLC26A11")]
SLC26A11_start <- as.vector(slot(wh_SLC26A11@ranges, "start") - 25000)
SLC26A11_end <- as.vector(slot(wh_SLC26A11@ranges, "start") + slot (wh_SLC26A11@ranges,
                                                                    "width") - 1 + 25000)
SLC26A11_range <- GRanges('chr17', IRanges(start = SLC26A11_start, end = SLC26A11_end))
wh_SLC26A11 <- range(SLC26A11_range, ignore.strand = TRUE)


SLC26A11_GENES <- autoplot(Homo.sapiens, which = wh_SLC26A11, xlab = "Chromosome 17", ylab =
                             "GENES", label.color = "black", color = "brown", fill = "brown",
                           columns = c("ALIAS", "GO"), scale = "Mb")+
        xlim (SLC26A11_range) +
        scale_x_sequnit("Mb") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
SLC26A11_GENES
```



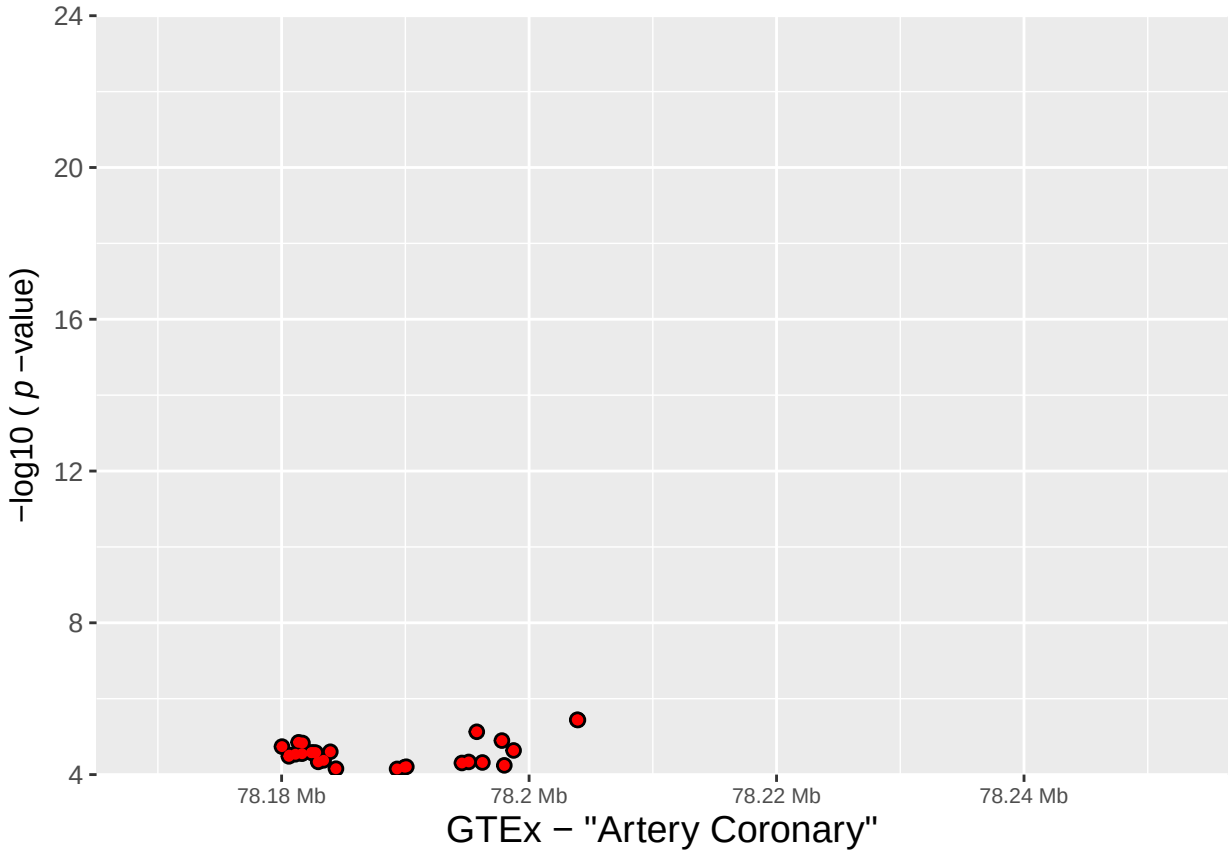

```
fixed (SLC26A11_GENES) <- TRUE

SLC26A11_GENES.gg <- SLC26A11_GENES@ggplot
SLC26A11_GENES.gg
```



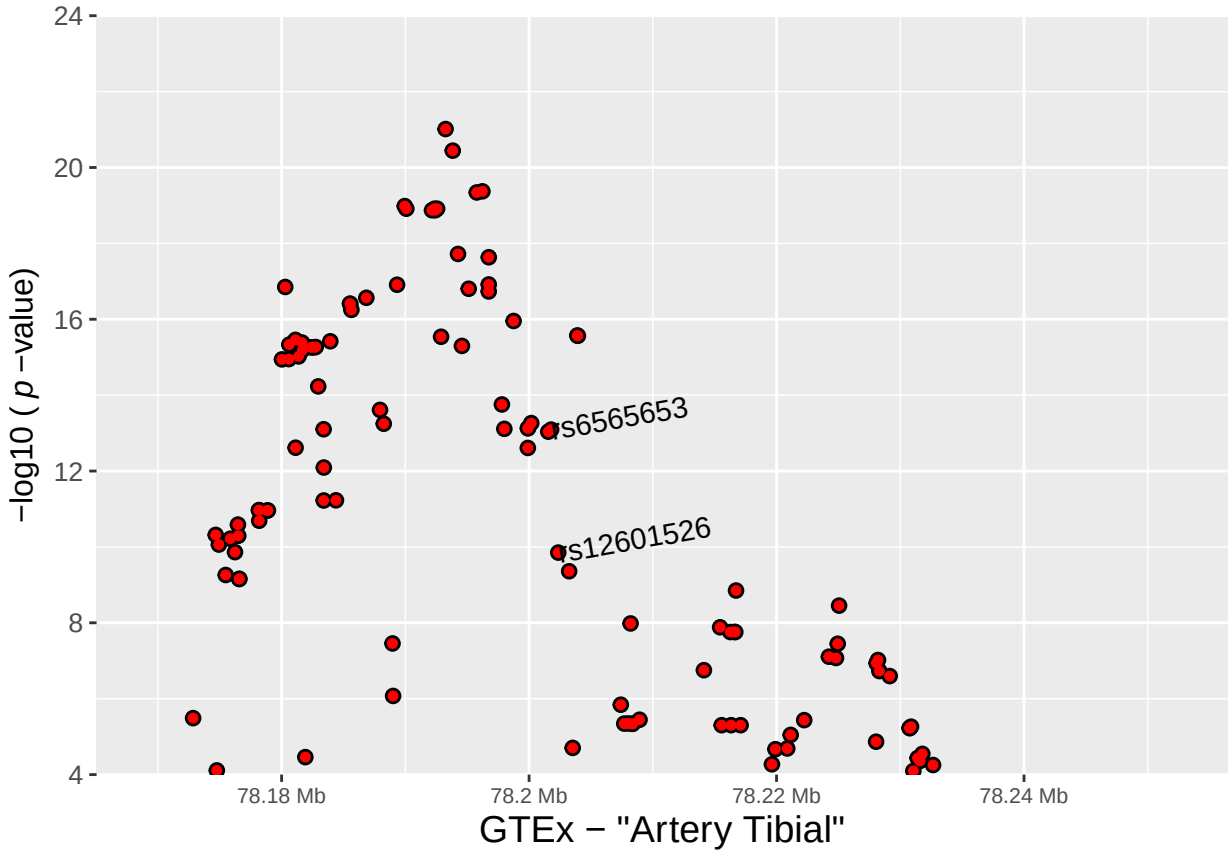

```
# AORTA
SLC26A11_aorta_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_aorta.txt",
                                              sep = "\t", header = TRUE,
                                              na.strings = c(".", "NA"),
                                              stringsAsFactors = FALSE))

SLC26A11_aorta <- ggplot(SLC26A11_aorta_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (SLC26A11_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(SLC26A11_aorta_df,
                                            -log10(SLC26A11_aorta_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(SLC26A11_aorta_df,
                                            -log10(SLC26A11_aorta_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        geom_text(data=subset(SLC26A11_aorta_df, Include == "Y"),
                  aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_aorta, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(SLC26A11_aorta) <- TRUE
SLC26A11_aorta
```



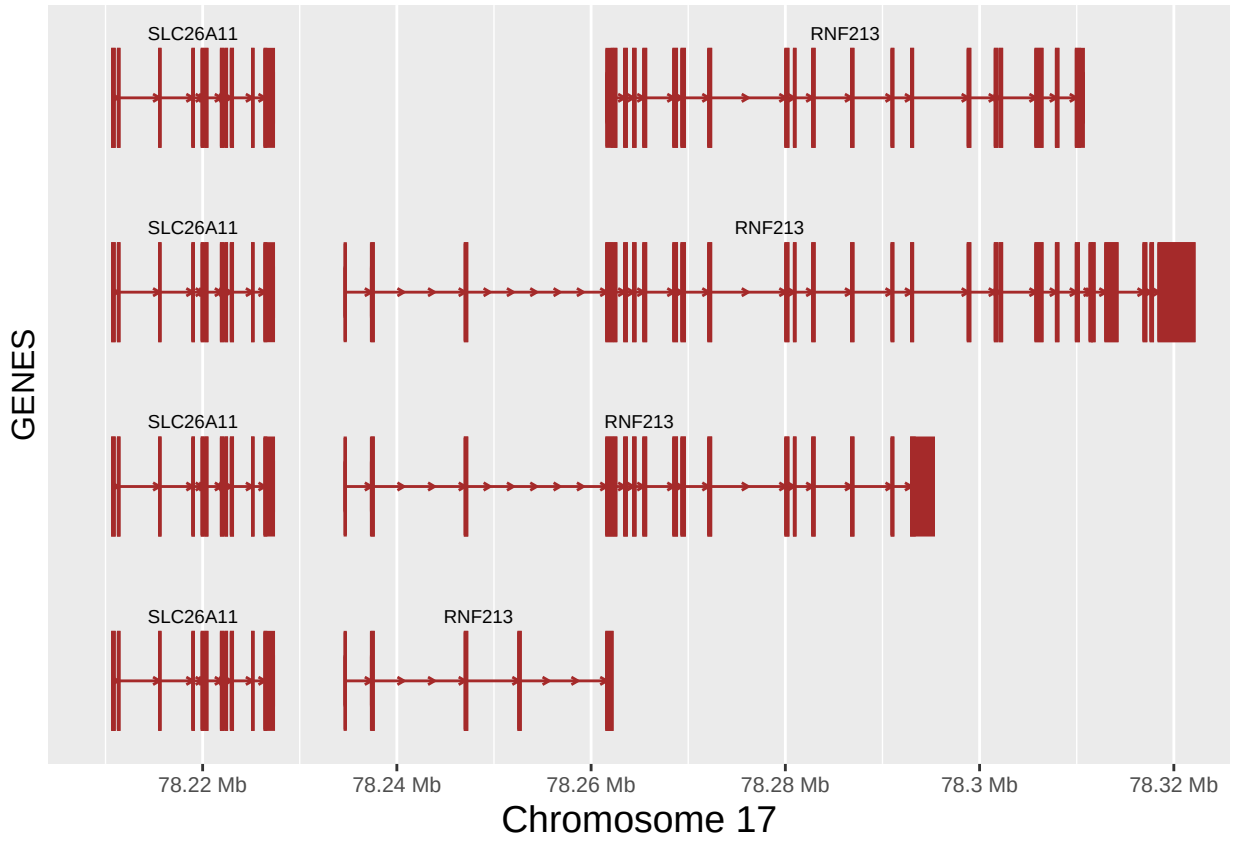

```
# CORONARY
SLC26A11_coronary_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_coronary.txt",
                                                 sep = "\t", header = TRUE,
                                                 na.strings = c(".", "NA"),
                                                 stringsAsFactors = FALSE))

SLC26A11_coronary <- ggplot(SLC26A11_coronary_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (SLC26A11_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(SLC26A11_coronary_df,
                                            -log10(SLC26A11_coronary_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(SLC26A11_coronary_df,
                                            -log10(SLC26A11_coronary_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        ##geom_text(data=subset(SLC26A11_coronary_df, Include == "Y"),
        ##          aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_coronary, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(SLC26A11_coronary) <- TRUE
SLC26A11_coronary
```



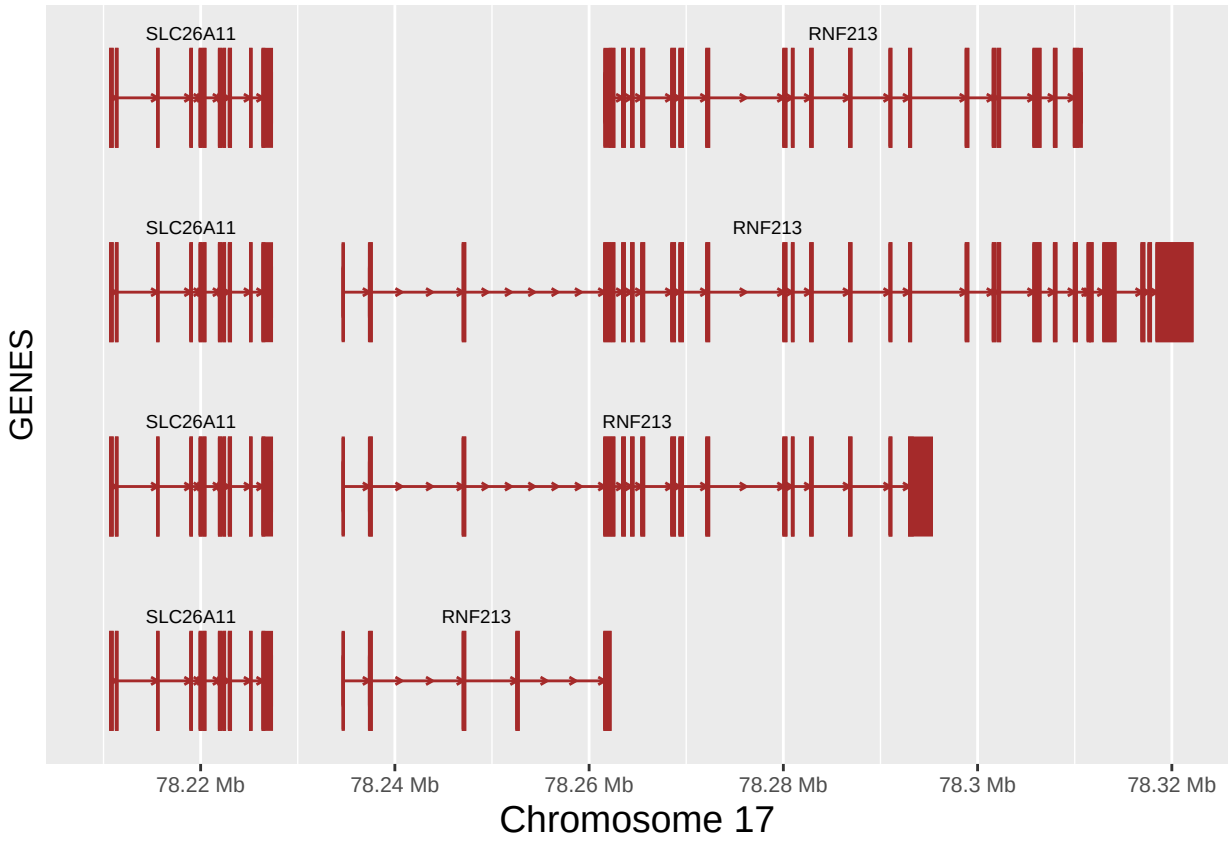

```
# TIBIAL
SLC26A11_tibial_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_tibial.txt",
                                               sep = "\t", header = TRUE,
                                               na.strings = c(".", "NA"),
                                               stringsAsFactors = FALSE))

SLC26A11_tibial <- ggplot(SLC26A11_tibial_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (SLC26A11_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(SLC26A11_tibial_df,
                                            -log10(SLC26A11_tibial_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(SLC26A11_tibial_df,
                                            -log10(SLC26A11_tibial_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        geom_text(data=subset(SLC26A11_tibial_df, Include == "Y"),
                  aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_tibial, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(SLC26A11_tibial) <- TRUE
SLC26A11_tibial
```



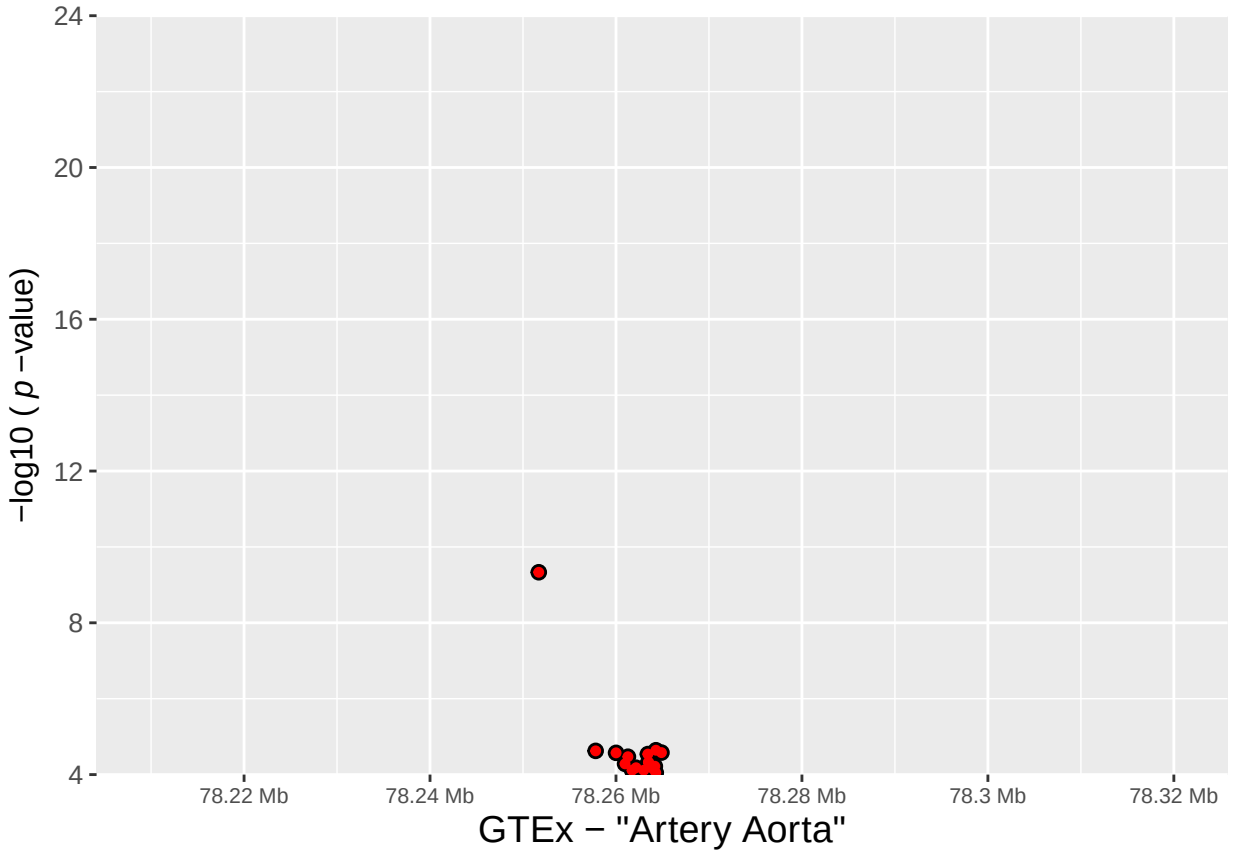

```
# Plots for RNF213 significant eQTL SNPs
# RNF213 Genes Plot
wh_RNF213 <- genesymbol[c("RNF213")]
RNF213_start <- as.vector(slot(wh_RNF213@ranges, "start") - 25000)
RNF213_end <- as.vector(slot(wh_RNF213@ranges, "start") +
                          slot (wh_RNF213@ranges, "width") - 1 + 25000)
RNF213_range <- GRanges('chr17', IRanges(start = RNF213_start, end = RNF213_end))
wh_RNF213 <- range(RNF213_range, ignore.strand = TRUE)


RNF213_GENES <- autoplot(Homo.sapiens, which = wh_RNF213,
                         xlab = "Chromosome 17", ylab = "GENES",
                         label.color = "black", color = "brown", fill = "brown",
                         columns = c("ALIAS", "GO"), scale = "Mb") +
        xlim (RNF213_range) +
        scale_x_sequnit("Mb") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
RNF213_GENES
```



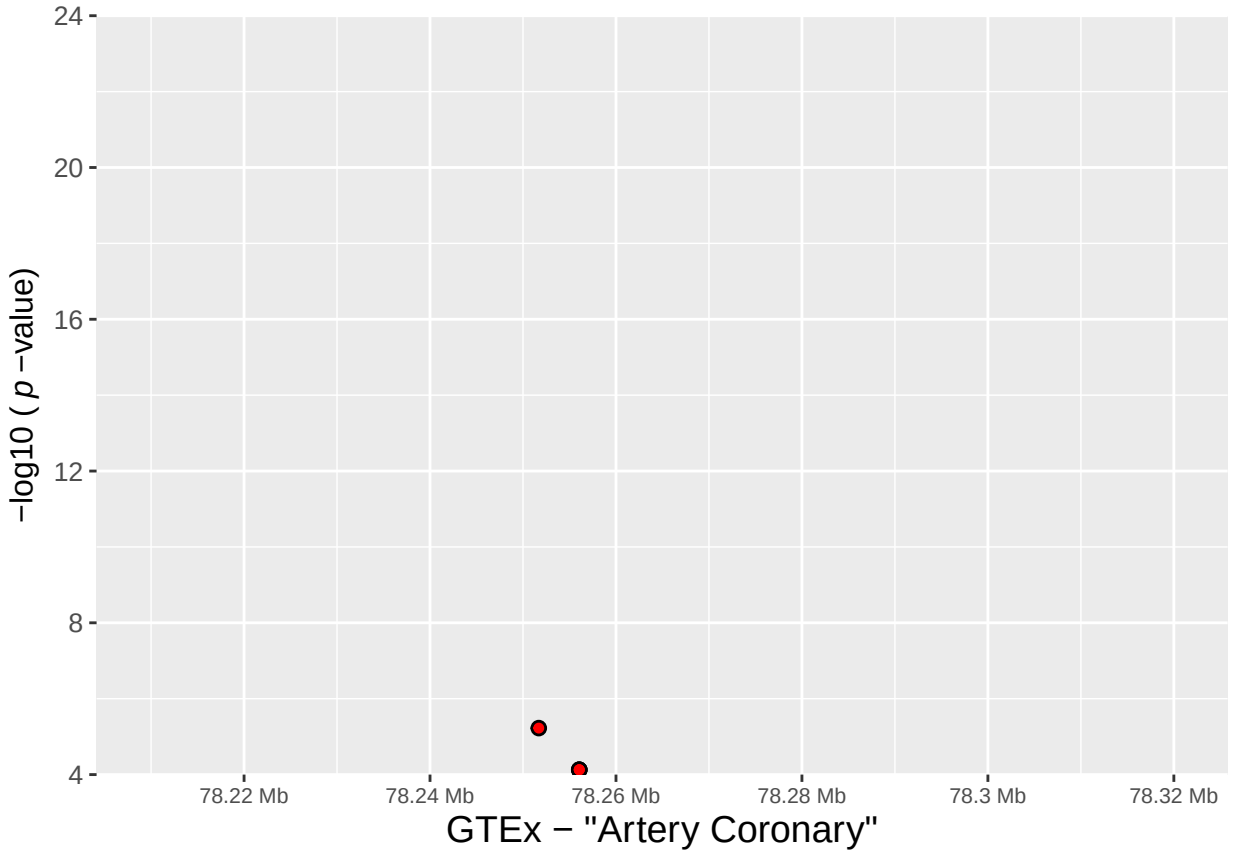

```
fixed (RNF213_GENES) <- TRUE

RNF213_GENES.gg <- RNF213_GENES@ggplot
RNF213_GENES.gg
```



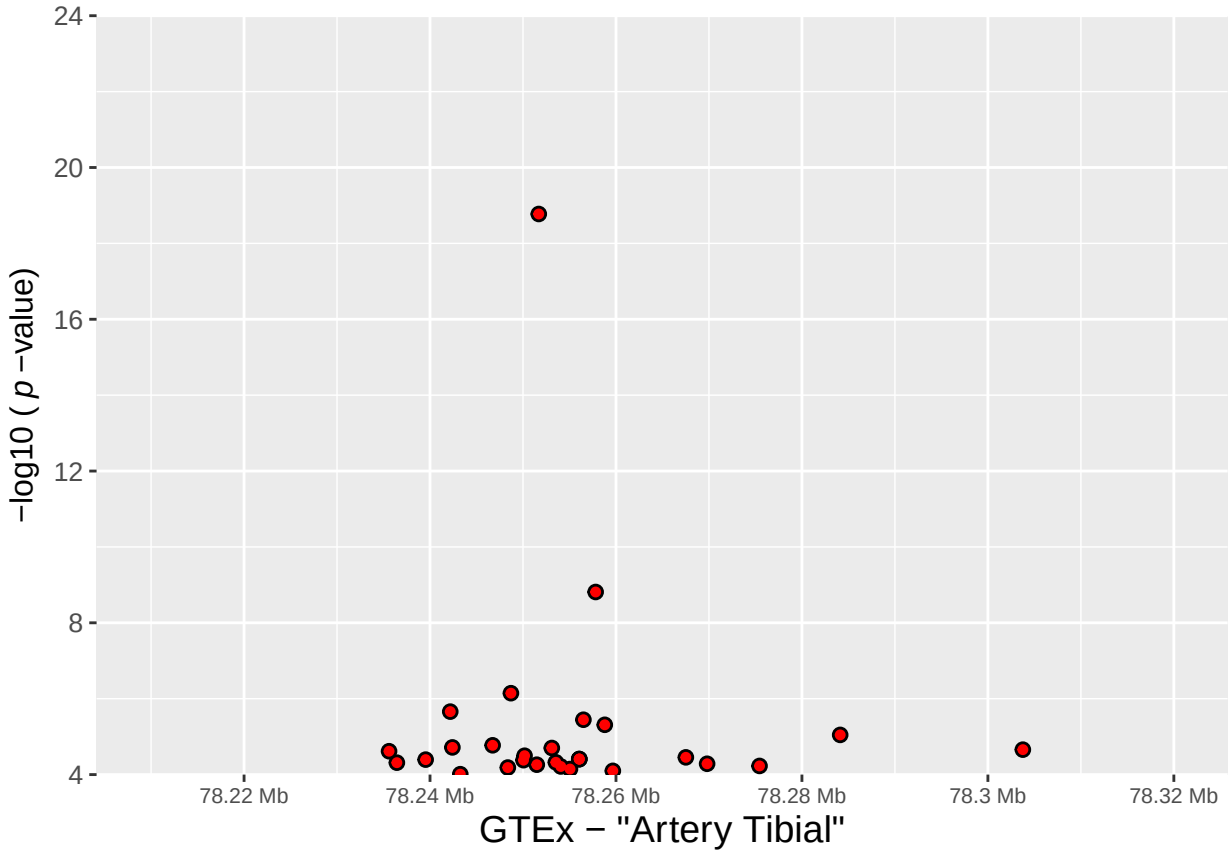

```
# AORTA
RNF213_aorta_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_aorta.txt",
                                            sep = "\t", header = TRUE,
                                            na.strings = c(".", "NA"), stringsAsFactors = FALSE))

RNF213_aorta <- ggplot(RNF213_aorta_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (RNF213_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(RNF213_aorta_df,
                                            -log10(RNF213_aorta_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(RNF213_aorta_df,
                                            -log10(RNF213_aorta_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        ##geom_text(data=subset(RNF213_aorta_df, Include == "Y"),
        ##          aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_aorta, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(RNF213_aorta) <- TRUE
RNF213_aorta
```



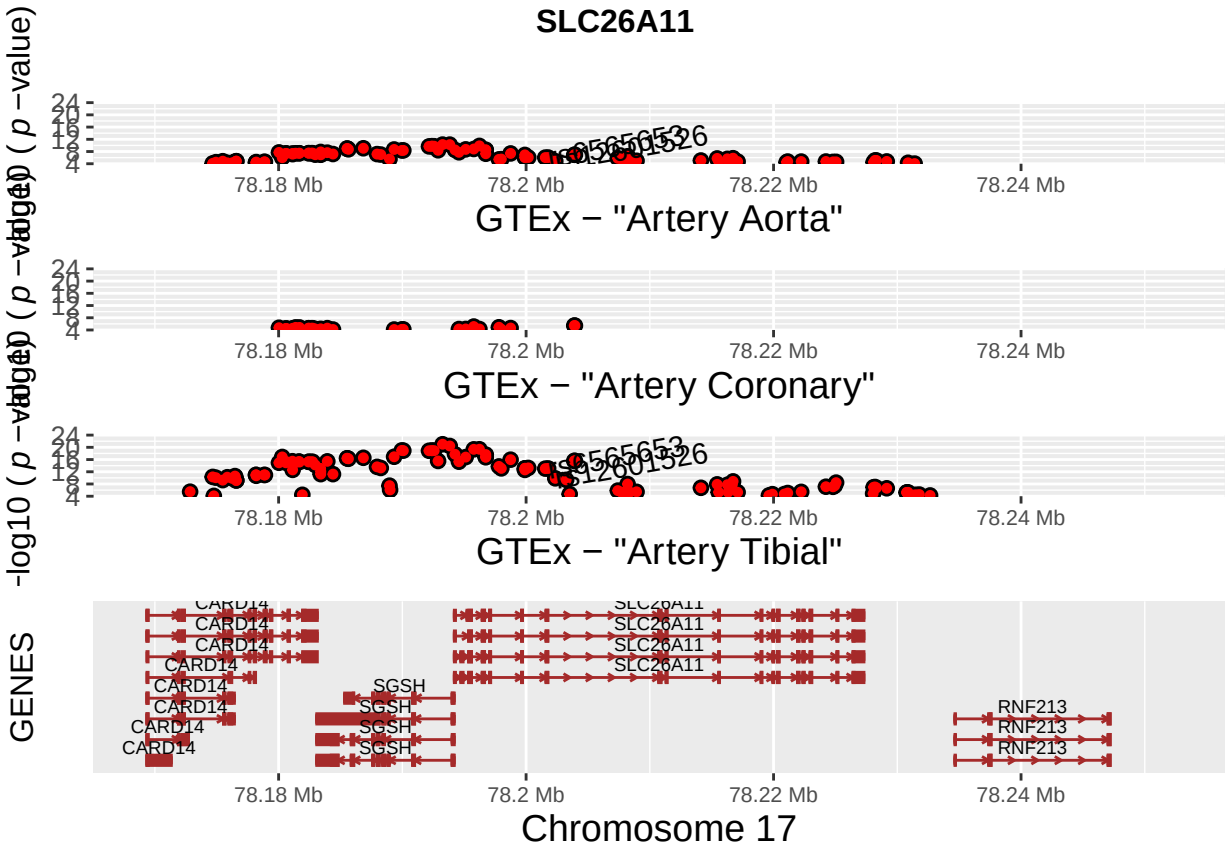

```
# CORONARY
RNF213_coronary_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_coronary.txt",
                                               sep = "\t", header = TRUE,
                                               na.strings = c(".", "NA"),
                                               stringsAsFactors = FALSE))

RNF213_coronary <- ggplot(RNF213_coronary_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (RNF213_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(RNF213_coronary_df,
                                            -log10(RNF213_coronary_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(RNF213_coronary_df,
                                            -log10(RNF213_coronary_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        ##geom_text(data=subset(RNF213_coronary_df, Include == "Y"),
        ##          aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_coronary, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(RNF213_coronary) <- TRUE
RNF213_coronary
```



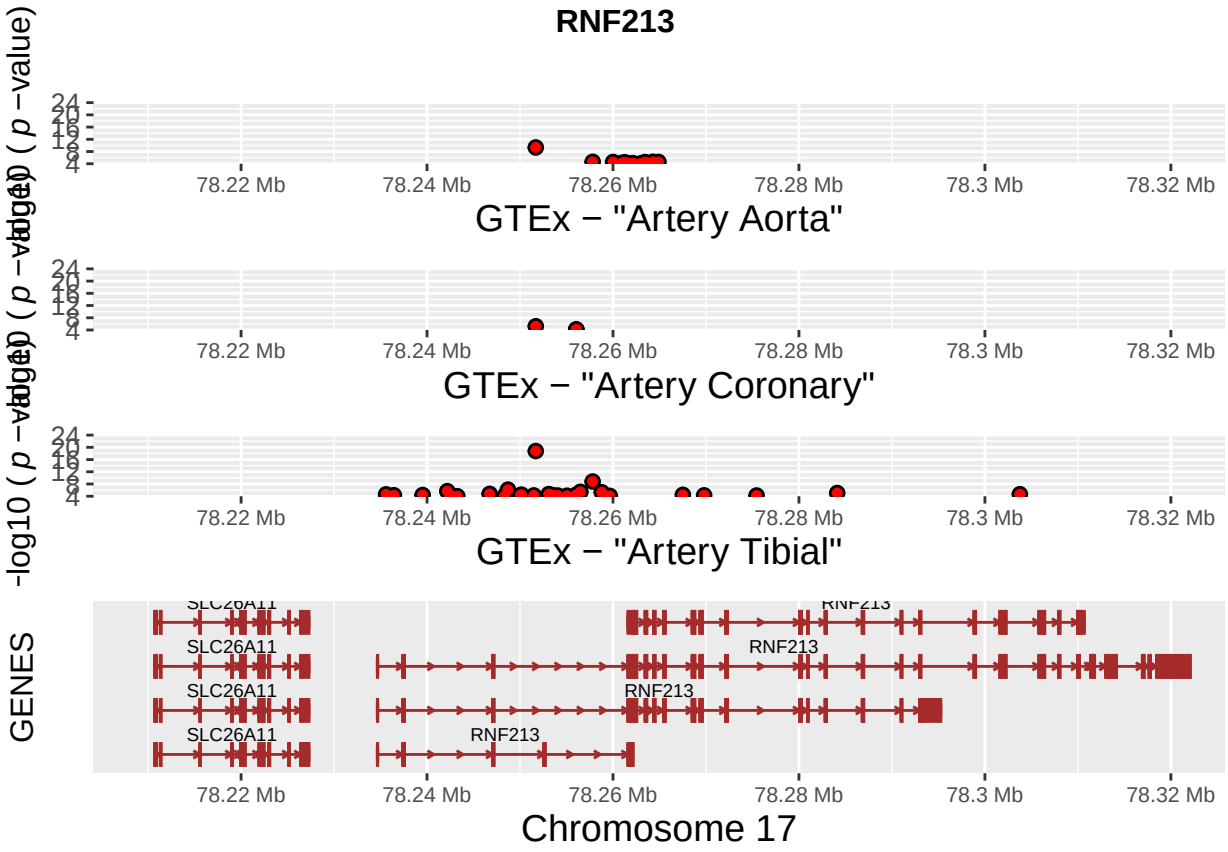

```
# TIBIAL
RNF213_tibial_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_tibial.txt",
                                             sep = "\t", header = TRUE,
                                             na.strings = c(".", "NA"),
                                             stringsAsFactors = FALSE))

RNF213_tibial <- ggplot(RNF213_tibial_df, aes(x = position, y = -log10(pval_nominal))) +
        xlim (RNF213_range) +
        scale_y_continuous(limits = c(4,24), breaks=seq(4,24,4), expand = c(0,0)) +
        geom_point(size = 2.25, data=subset(RNF213_tibial_df,
                                            -log10(RNF213_tibial_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "black") +
        geom_point(size = 1.25, data=subset(RNF213_tibial_df,
                                            -log10(RNF213_tibial_df$pval_nominal)>4),
                   aes(position, -log10(pval_nominal)), color = "red") +
        ##geom_text(data=subset(RNF213_tibial_df, Include == "Y"),
        ##          aes(position, -log10(pval_nominal),label=SNP_ID, hjust = 0, angle = 10)) +
        scale_x_sequnit("Mb") +
        labs(x = x_lab_tibial, y = y_lab) +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
fixed(RNF213_tibial) <- TRUE
RNF213_tibial
```




```
# Get the gtables
gA <- ggplotGrob (SLC26A11_aorta)
gB <- ggplotGrob (SLC26A11_coronary)
gC <- ggplotGrob (SLC26A11_tibial)
gD <- ggplotGrob (RNF213_aorta)
gE <- ggplotGrob (RNF213_coronary)
gF <- ggplotGrob (RNF213_tibial)
gG <- ggplotGrob (SLC26A11_GENES.gg)
gH <- ggplotGrob (RNF213_GENES.gg)

# Set the widths
gA$widths <- gC$widths
gB$widths <- gC$widths
gD$widths <- gC$widths
gE$widths <- gC$widths
gF$widths <- gC$widths
gG$widths <- gC$widths
gH$widths <- gC$widths

# Arrange the SLC26A11 charts
SLC26A11_title = textGrob("SLC26A11\n", gp=gpar(fontsize=12, font = 2))
grid.newpage()
SLC26A11_plot <- grid.arrange(gA, gB, gC, gG, heights = c(6,6,6,10), top =SLC26A11_title)
```



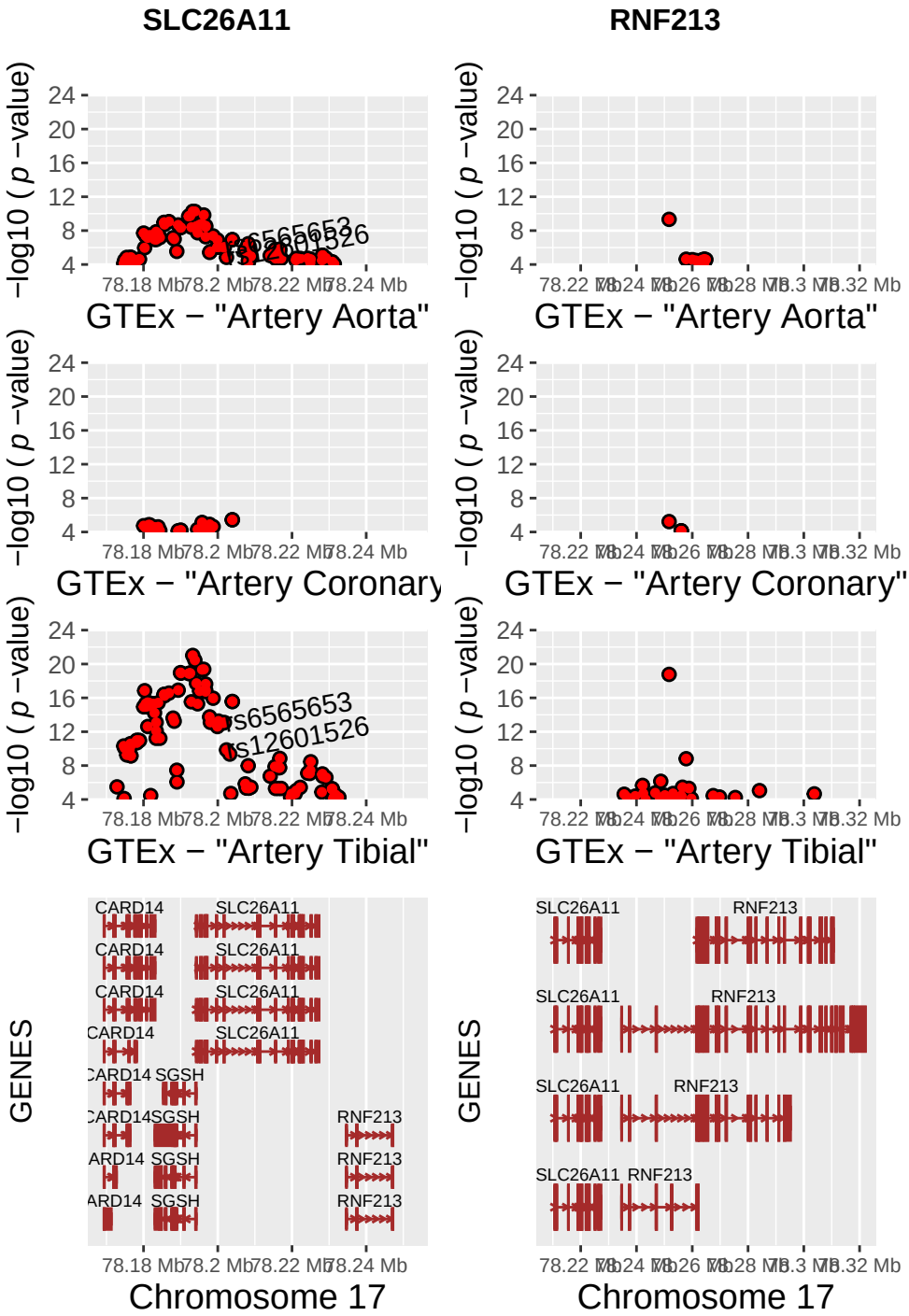

```
# Arrange the RNF213 charts
RNF213_title = textGrob("RNF213\n", gp=gpar(fontsize=12, font = 2))
grid.newpage()
RNF213_plot <- grid.arrange(gD, gE, gF, gH, heights = c(6,6,6,10), top =RNF213_title)
```



Supplementary Figure 4

```
# Arrange SLC26A11 - RNF213 plots together
main_title = textGrob("Arterial tissue cis-eQTL data for SLC26A11 and RNF213 SNPs and their expression\n
                      gp=gpar(fontsize=16, font = 2))
grid.newpage()
FINAL_PLOT <- grid.arrange(SLC26A11_plot, RNF213_plot, ncol = 2, top = main_title)
```

Arterial tissue cis−eQTL data for SLC26A11 and RNF213 SNPs and their expression



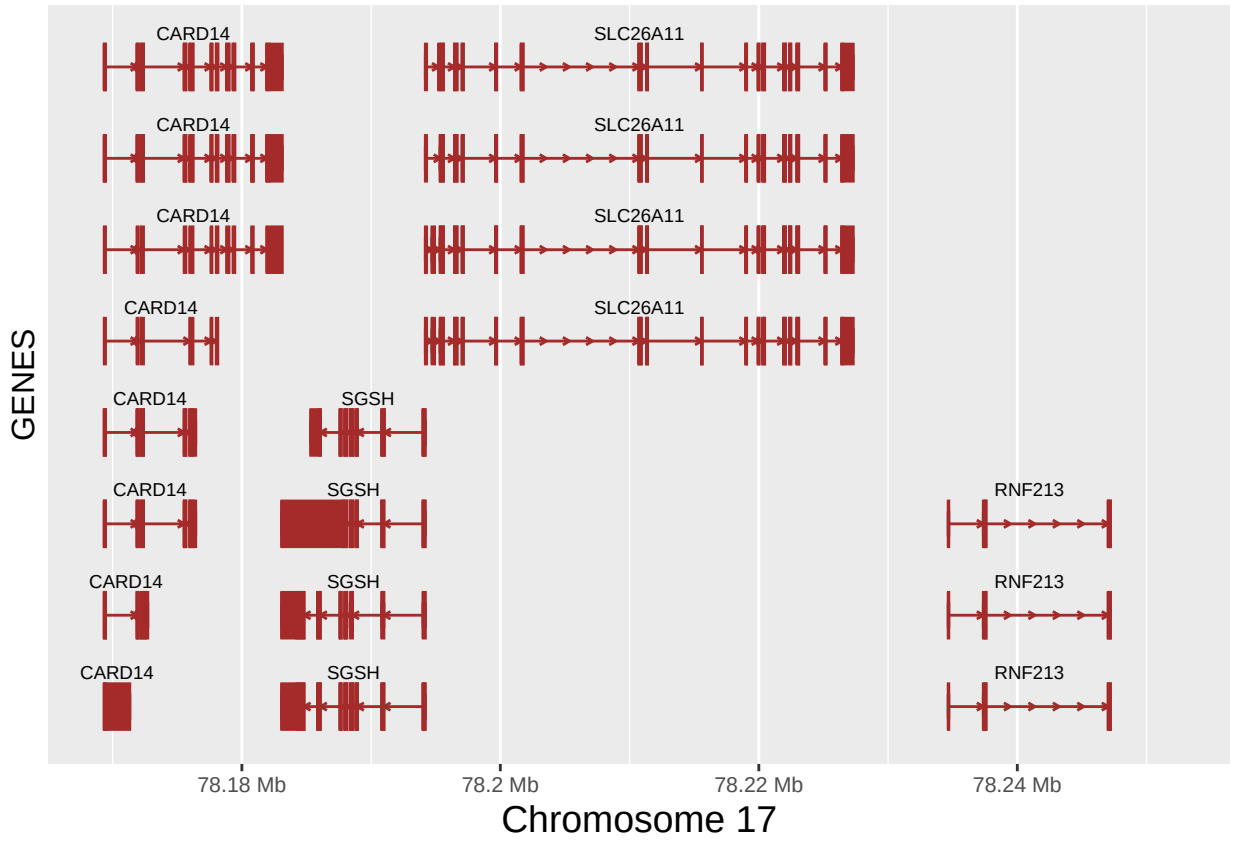

```
dev.off()
```

```
## null device
##           1
```

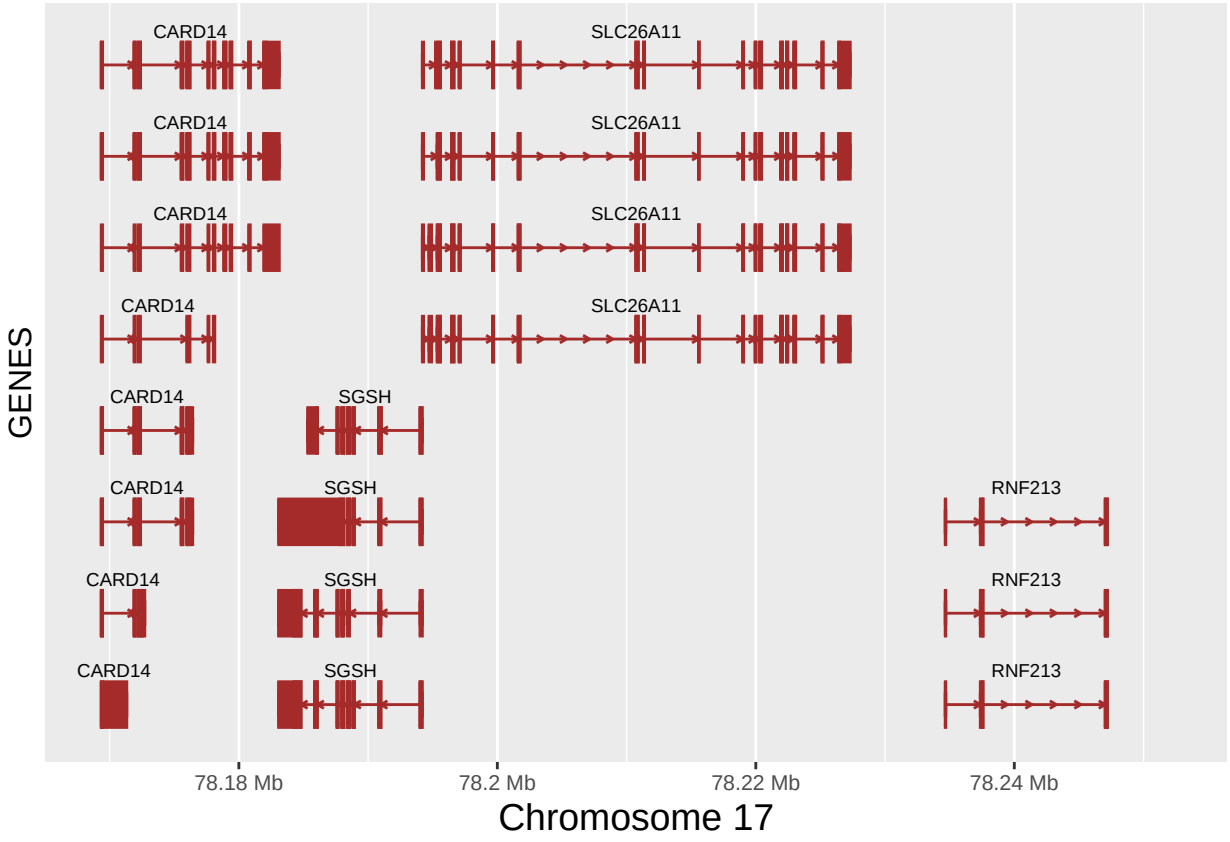
Artery__expression__changes__RNF213__SLC26A11

Data extracted from the GTEx database

```
data(hg19IdeogramCyto, package = "biovizBase")
data(hg19Ideogram, package = "biovizBase")
data(genesymbol, package = "biovizBase")

hg19 <- keepSeqlevels(hg19IdeogramCyto, paste0("chr", c(1:22, "X", "Y")))

# RNF213_SLC26A11_eQTL_association_files

x_lab_aorta <- "GTEx - \"Artery Aorta\""
x_lab_coronary <- "GTEx - \"Artery Coronary\""
x_lab_tibial <- "GTEx - \"Artery Tibial\""
y_lab <- as.expression("Expression variation in %", fontsize=6, font = 2)
size_label = bquote("Magnitude of association\n-log10("*italic(p)*"-value)")

# Plots for SLC26A11 significant expression changes

# SLC26A11 Genes Plot
wh_SLC26A11 <- genesymbol[c("SLC26A11")]
SLC26A11_start <- as.vector(slot(wh_SLC26A11@ranges, "start") - 25000)
SLC26A11_end <- as.vector(slot(wh_SLC26A11@ranges, "start") +
                            slot (wh_SLC26A11@ranges, "width") - 1 + 25000)
SLC26A11_range <- GRanges('chr17', IRanges(start = SLC26A11_start, end = SLC26A11_end))
wh_SLC26A11 <- range(SLC26A11_range, ignore.strand = TRUE)


SLC26A11_GENES <- autoplot(Homo.sapiens, which = wh_SLC26A11, xlab = "Chromosome 17",
                           ylab = "GENES",
                           label.color = "black", color = "brown", fill = "brown",
                           columns = c("ALIAS", "GO"), scale = "Mb") +
        xlim (SLC26A11_range) +
        scale_x_sequnit("Mb") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
SLC26A11_GENES
```

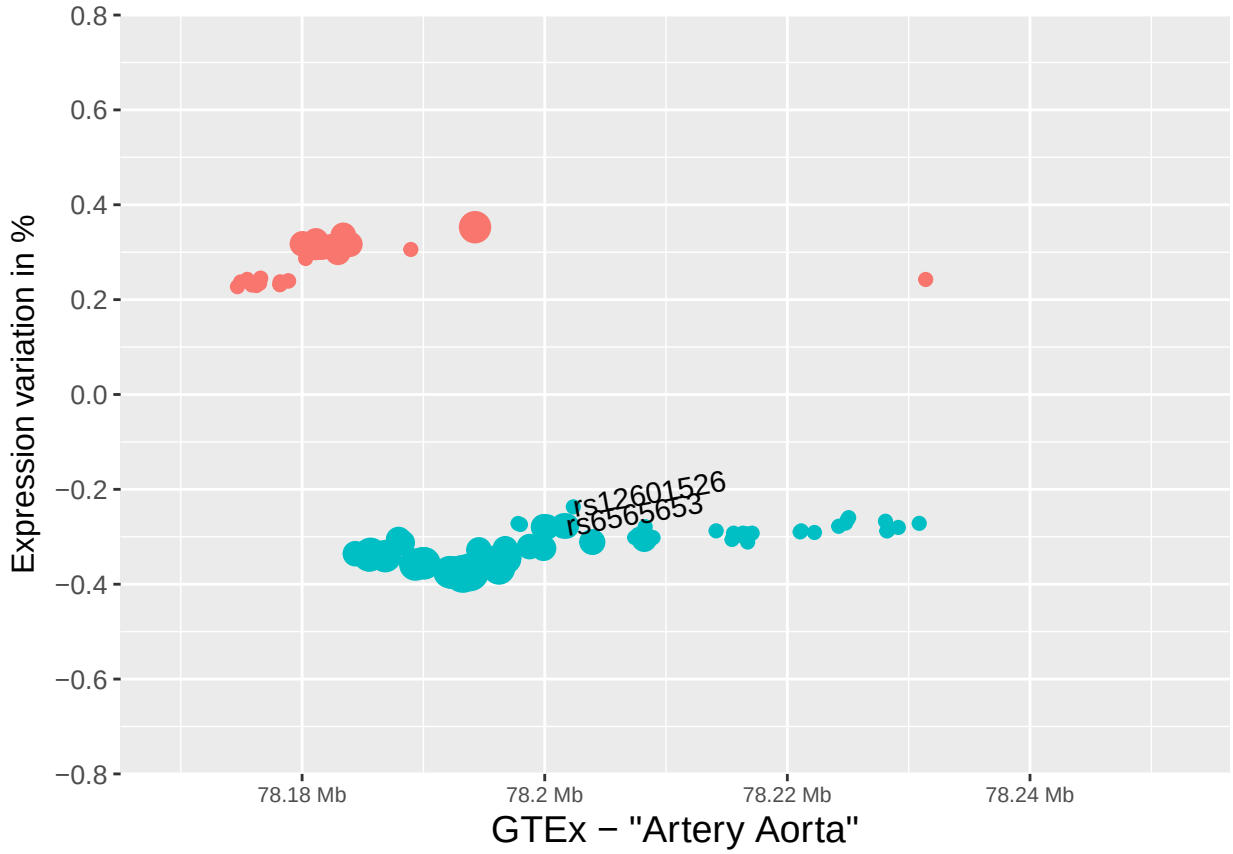



```
fixed (SLC26A11_GENES) <- TRUE

SLC26A11_GENES.gg <- SLC26A11_GENES@ggplot
SLC26A11_GENES.gg
```



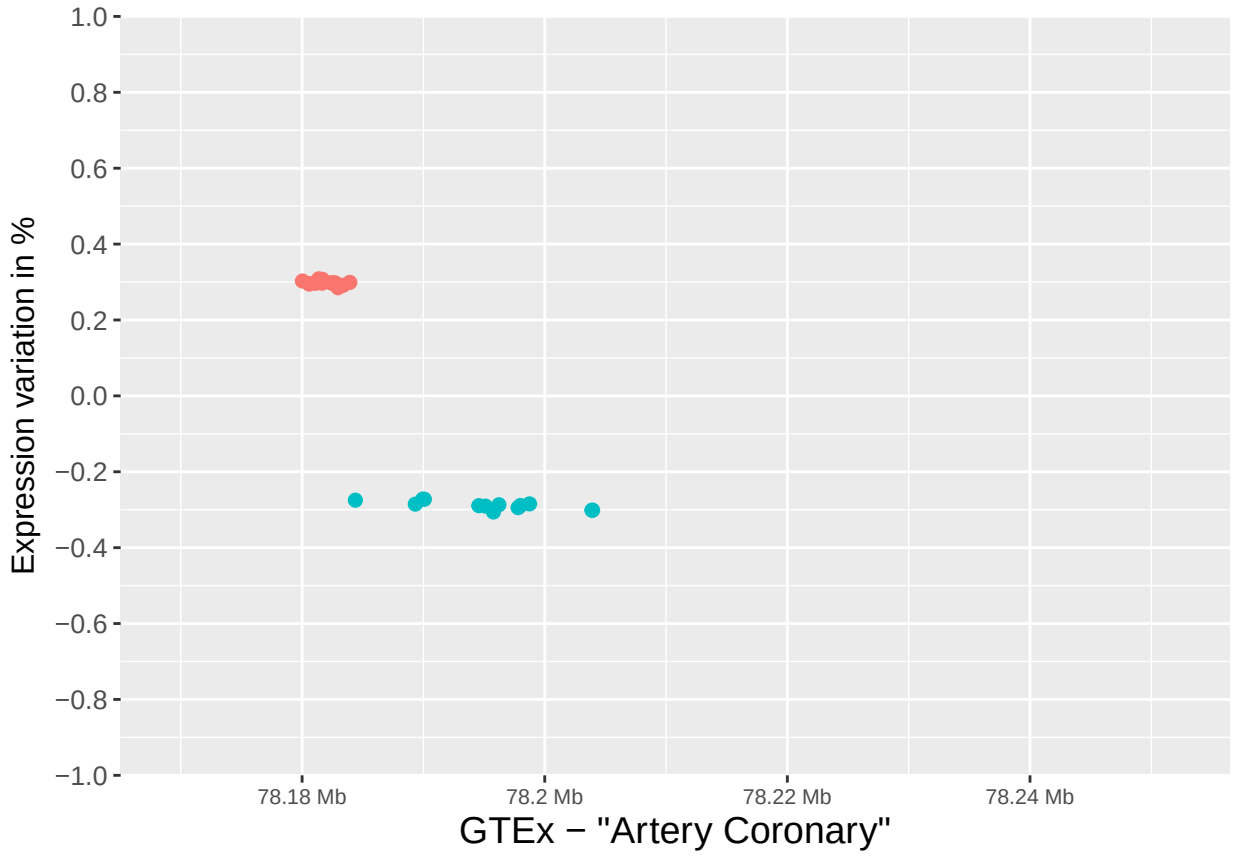

```
# SLC26A11 expression changes
# AORTA
SLC26A11_aorta_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_aorta.txt",
                                              sep = "\t", header = TRUE,
                                              na.strings = c(".", "NA"),
                                              stringsAsFactors = FALSE))

Sign_eQTLs_SAo <- subset(SLC26A11_aorta_df,-log10(SLC26A11_aorta_df$pval_nominal)>4)
Sign_eQTLs_SAo$log10 <- -log10(Sign_eQTLs_SAo$pval_nominal)
Sign_eQTLs_SAo$ranges <- cut(Sign_eQTLs_SAo$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_SAo$color <- ifelse(Sign_eQTLs_SAo$slope<0, "Underexpression","Overespression")


SLC26A11_aorta_ex <- ggplot(Sign_eQTLs_SAo) +
        xlim (SLC26A11_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-0.8,0.8),
                           breaks=c(-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8), expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_SAo$ranges,
                       color =Sign_eQTLs_SAo$color)) +
        geom_text(data=subset(SLC26A11_aorta_df, Include == "Y"),
                  aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
```

```
        labs(x = x_lab_aorta, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(SLC26A11_aorta_ex) <- TRUE
SLC26A11_aorta_ex
```



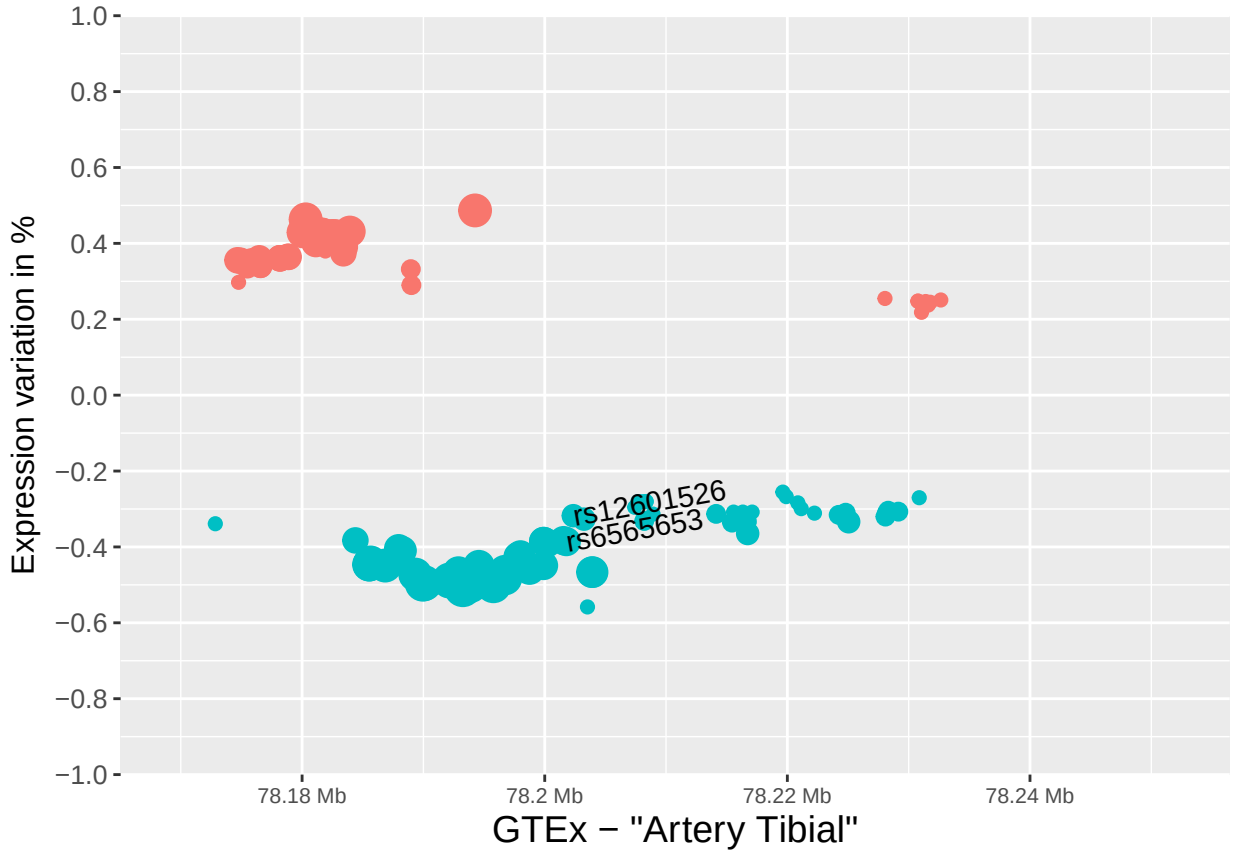

```
# CORONARY
SLC26A11_coronary_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_coronary.txt",
                                                 sep = "\t", header = TRUE,
                                                 na.strings = c(".", "NA"),
                                                 stringsAsFactors = FALSE))

Sign_eQTLs_SCo <- subset(SLC26A11_coronary_df,-log10(SLC26A11_coronary_df$pval_nominal)>4)
Sign_eQTLs_SCo$log10 <- -log10(Sign_eQTLs_SCo$pval_nominal)
Sign_eQTLs_SCo$ranges <- cut(Sign_eQTLs_SCo$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_SCo$color <- ifelse(Sign_eQTLs_SCo$slope<0, "Underexpression","Overespression")


SLC26A11_coronary_ex <- ggplot(Sign_eQTLs_SCo) +
```

```
        xlim (SLC26A11_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-1,1),
                           breaks=c(-1.0,-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8,1.0),
                           expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_SCo$ranges,
                       color =Sign_eQTLs_SCo$color)) +
        geom_text(data=subset(SLC26A11_coronary_df, Include == "Y"),
                  aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
        labs(x = x_lab_coronary, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(SLC26A11_coronary_ex) <- TRUE
SLC26A11_coronary_ex
```

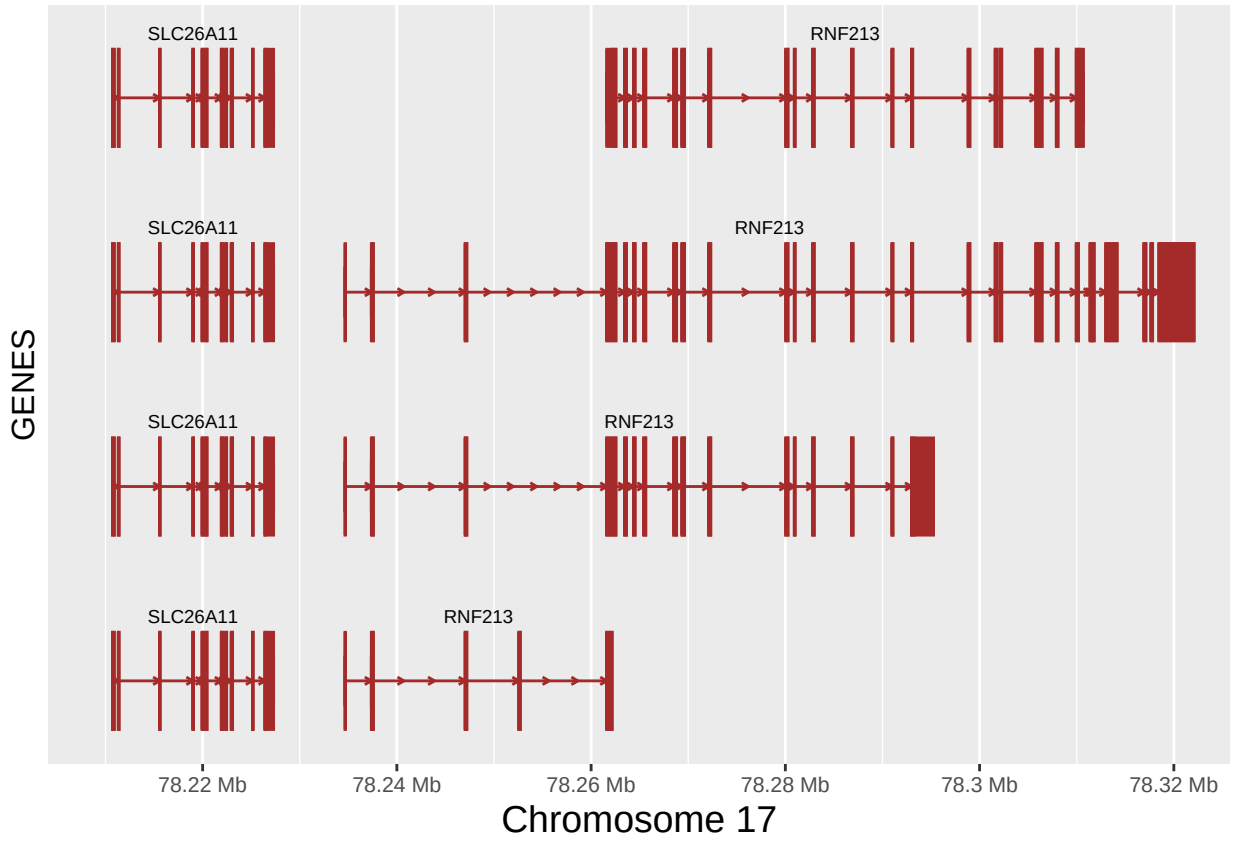



```
# TIBIAL
SLC26A11_tibial_df <- as.data.frame(read.table("input_files/GTEx_files/SLC26A11_tibial.txt",
                                               sep = "\t", header = TRUE,
                                               na.strings = c(".", "NA"),
                                               stringsAsFactors = FALSE))

Sign_eQTLs_STi <- subset(SLC26A11_tibial_df,-log10(SLC26A11_tibial_df$pval_nominal)>4)
```

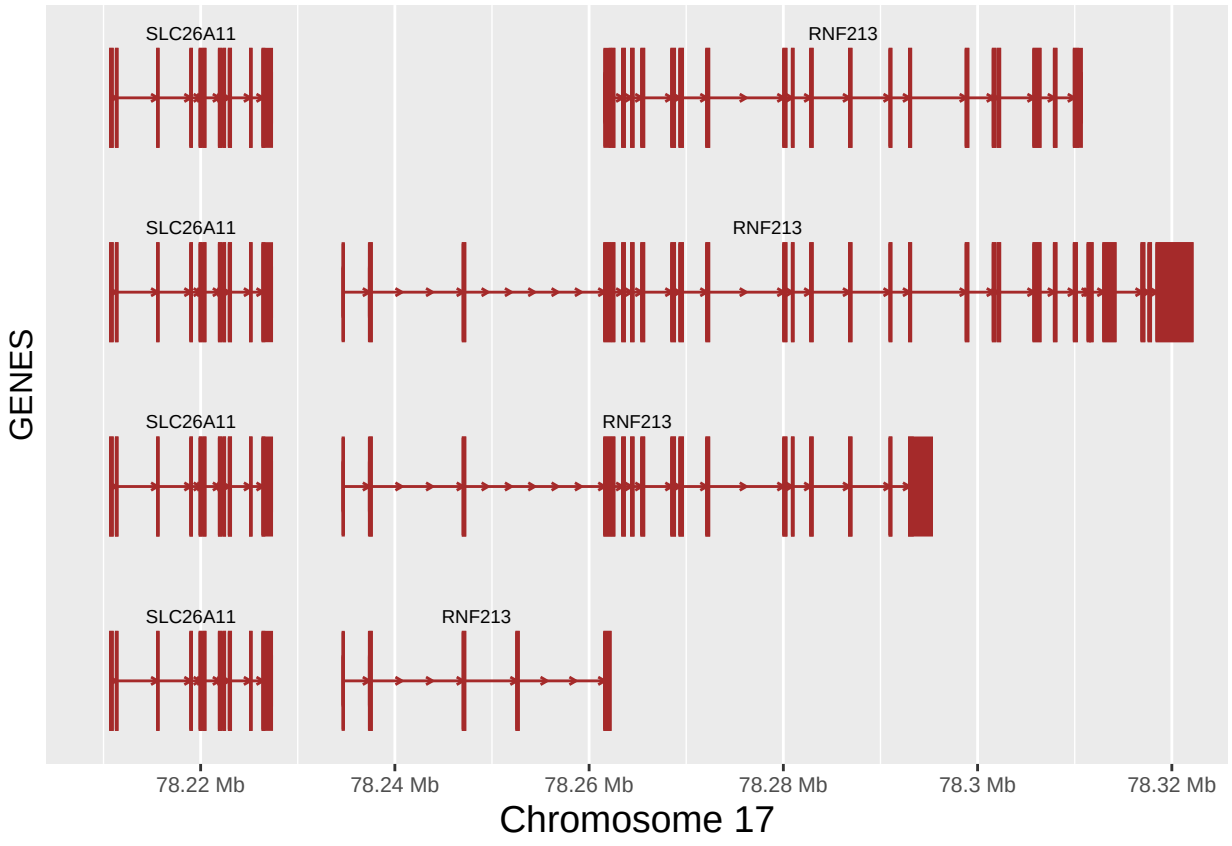
```
Sign_eQTLs_STi$log10 <- -log10(Sign_eQTLs_STi$pval_nominal)
Sign_eQTLs_STi$ranges <- cut(Sign_eQTLs_STi$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_STi$color <- ifelse(Sign_eQTLs_STi$slope<0, "Underexpression","Overespression")


SLC26A11_tibial_ex <- ggplot(Sign_eQTLs_STi) +
        xlim (SLC26A11_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-1,1),
                           breaks=c(-1.0,-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8,1.0),
                           expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_STi$ranges,
                       color =Sign_eQTLs_STi$color)) +
        geom_text(data=subset(SLC26A11_tibial_df, Include == "Y"),
                  aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
        labs(x = x_lab_tibial, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(SLC26A11_tibial_ex) <- TRUE
SLC26A11_tibial_ex
```




```
# Plots for RNF213 significant expression changes
# RNF213 Genes Plot
wh_RNF213 <- genesymbol[c("RNF213")]
RNF213_start <- as.vector(slot(wh_RNF213@ranges, "start") - 25000)
RNF213_end <- as.vector(slot(wh_RNF213@ranges, "start") +
                          slot (wh_RNF213@ranges, "width") - 1 + 25000)
RNF213_range <- GRanges('chr17', IRanges(start = RNF213_start, end = RNF213_end))
wh_RNF213 <- range(RNF213_range, ignore.strand = TRUE)


RNF213_GENES <- autoplot(Homo.sapiens, which = wh_RNF213,
                         xlab = "Chromosome 17", ylab = "GENES",
                         label.color = "black", color = "brown", fill = "brown",
                         columns = c("ALIAS", "GO"), scale = "Mb")+
        xlim (RNF213_range) +
        scale_x_sequnit("Mb") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12))
RNF213_GENES
```

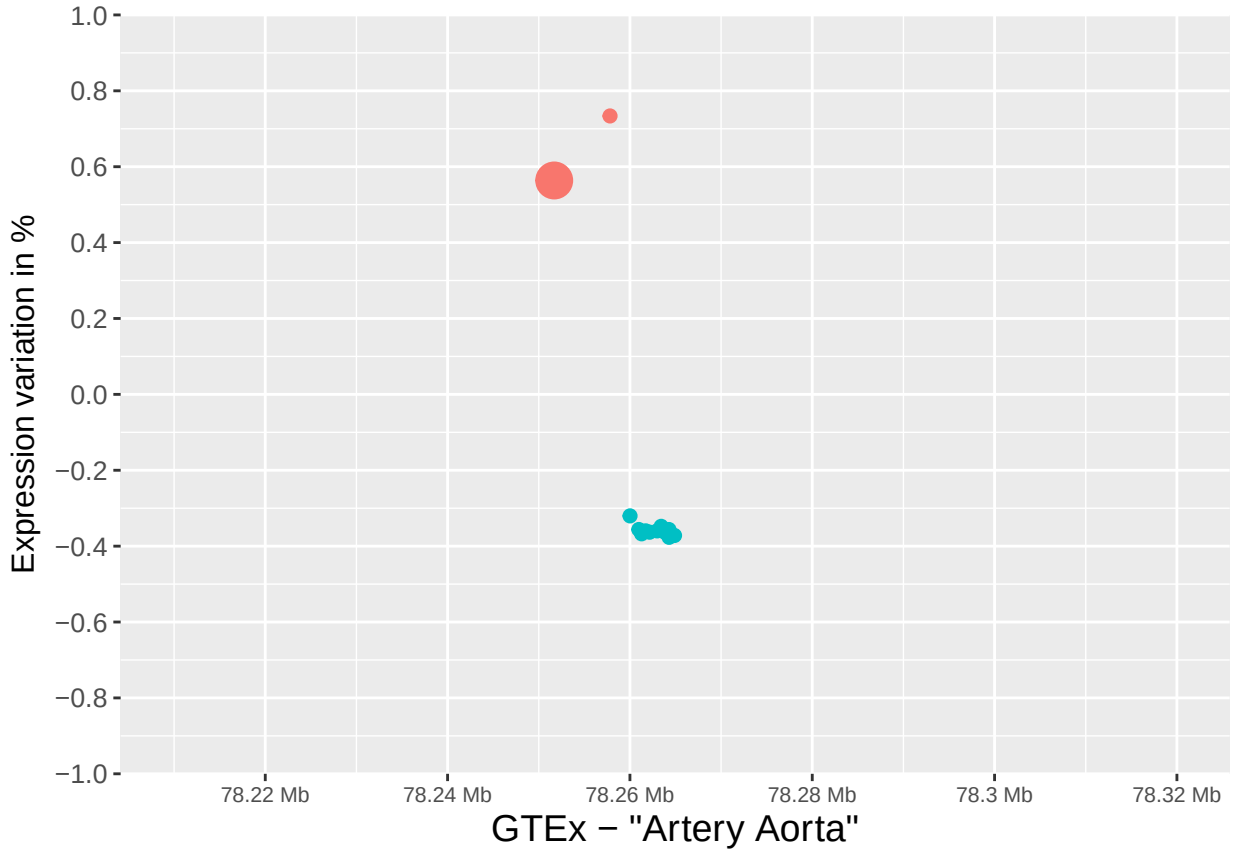



```
fixed (RNF213_GENES) <- TRUE

RNF213_GENES.gg <- RNF213_GENES@ggplot
RNF213_GENES.gg
```



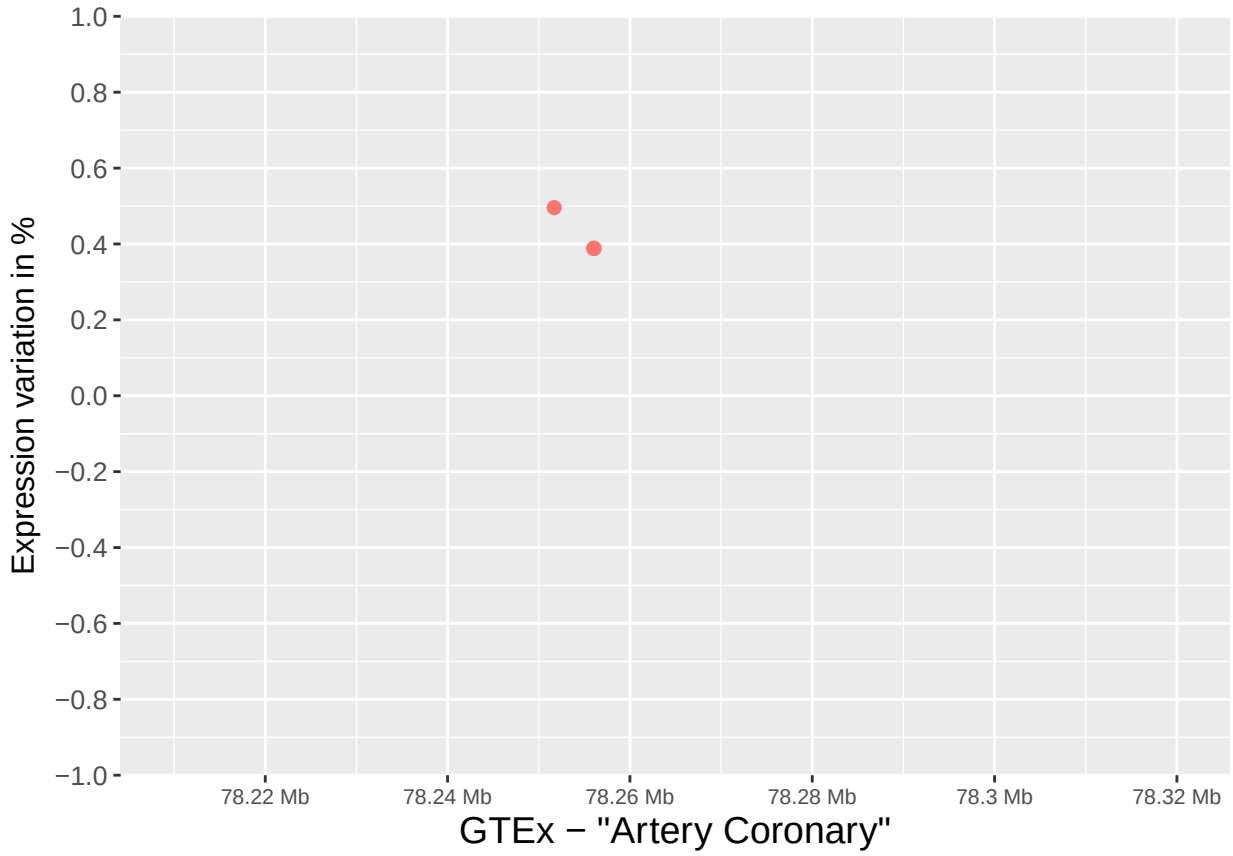

```
# RNF213 expression changes
# AORTA
RNF213_aorta_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_aorta.txt",
                                            sep = "\t", header = TRUE,
                                            na.strings = c(".", "NA"),
                                            stringsAsFactors = FALSE))

Sign_eQTLs_RAo <- subset(RNF213_aorta_df,-log10(RNF213_aorta_df$pval_nominal)>4)
Sign_eQTLs_RAo$log10 <- -log10(Sign_eQTLs_RAo$pval_nominal)
Sign_eQTLs_RAo$ranges <- cut(Sign_eQTLs_RAo$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_RAo$color <- ifelse(Sign_eQTLs_RAo$slope<0, "Underexpression","Overespression")


RNF213_aorta_ex <- ggplot(Sign_eQTLs_RAo) +
        xlim (RNF213_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-1,1),
                           breaks=c(-1.0,-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8,1.0),
                           expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_RAo$ranges,
                       color =Sign_eQTLs_RAo$color)) +
        #geom_text(data=subset(RNF213_aorta_df, Include == "Y"),
```

```
        #          aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
        labs(x = x_lab_aorta, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(RNF213_aorta_ex) <- TRUE
RNF213_aorta_ex
```



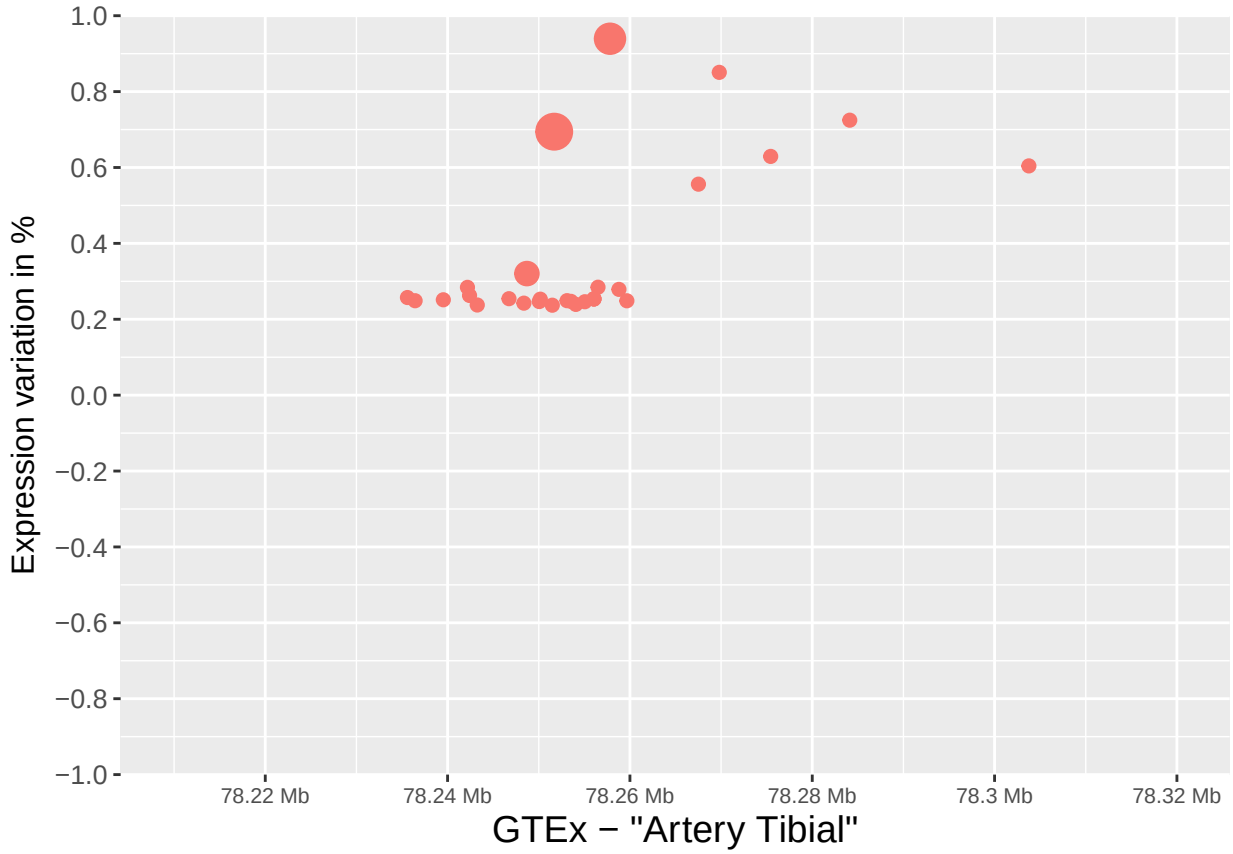

```
# CORONARY
RNF213_coronary_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_coronary.txt",
                                               sep = "\t", header = TRUE,
                                               na.strings = c(".", "NA"),
                                               stringsAsFactors = FALSE))

Sign_eQTLs_RCo <- subset(RNF213_coronary_df,-log10(RNF213_coronary_df$pval_nominal)>4)
Sign_eQTLs_RCo$log10 <- -log10(Sign_eQTLs_RCo$pval_nominal)
Sign_eQTLs_RCo$ranges <- cut(Sign_eQTLs_RCo$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_RCo$color <- ifelse(Sign_eQTLs_RCo$slope<0, "Underexpression","Overespression")
```

```
RNF213_coronary_ex <- ggplot(Sign_eQTLs_RCo) +
        xlim (RNF213_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-1,1),
                           breaks=c(-1.0,-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8,1.0),
                           expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_RCo$ranges,
                       color =Sign_eQTLs_RCo$color)) +
        #geom_text(data=subset(RNF213_coronary_df, Include == "Y"),
        #          aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
        labs(x = x_lab_coronary, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(RNF213_coronary_ex) <- TRUE
RNF213_coronary_ex
```

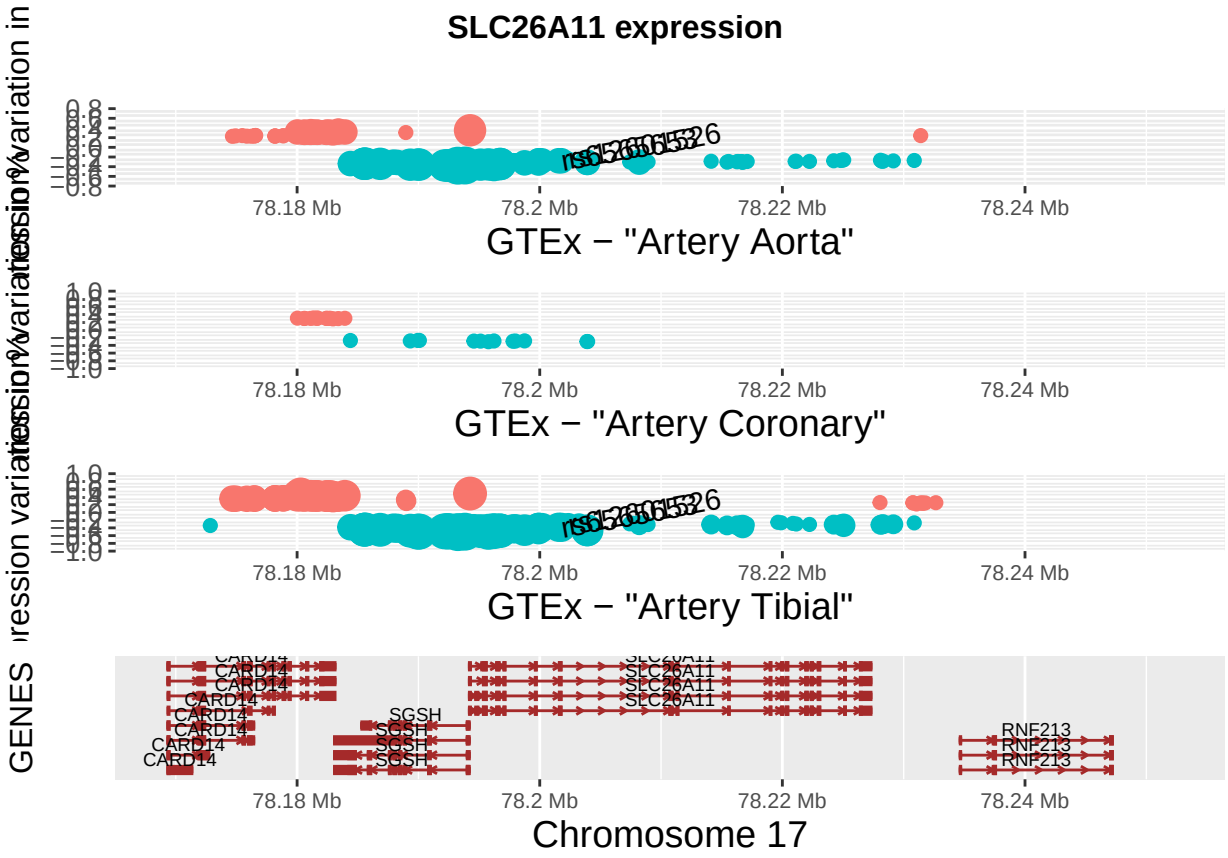



```
# TIBIAL
RNF213_tibial_df <- as.data.frame(read.table("input_files/GTEx_files/RNF213_tibial.txt",
                                             sep = "\t", header = TRUE,
                                             na.strings = c(".", "NA"),
                                             stringsAsFactors = FALSE))
```

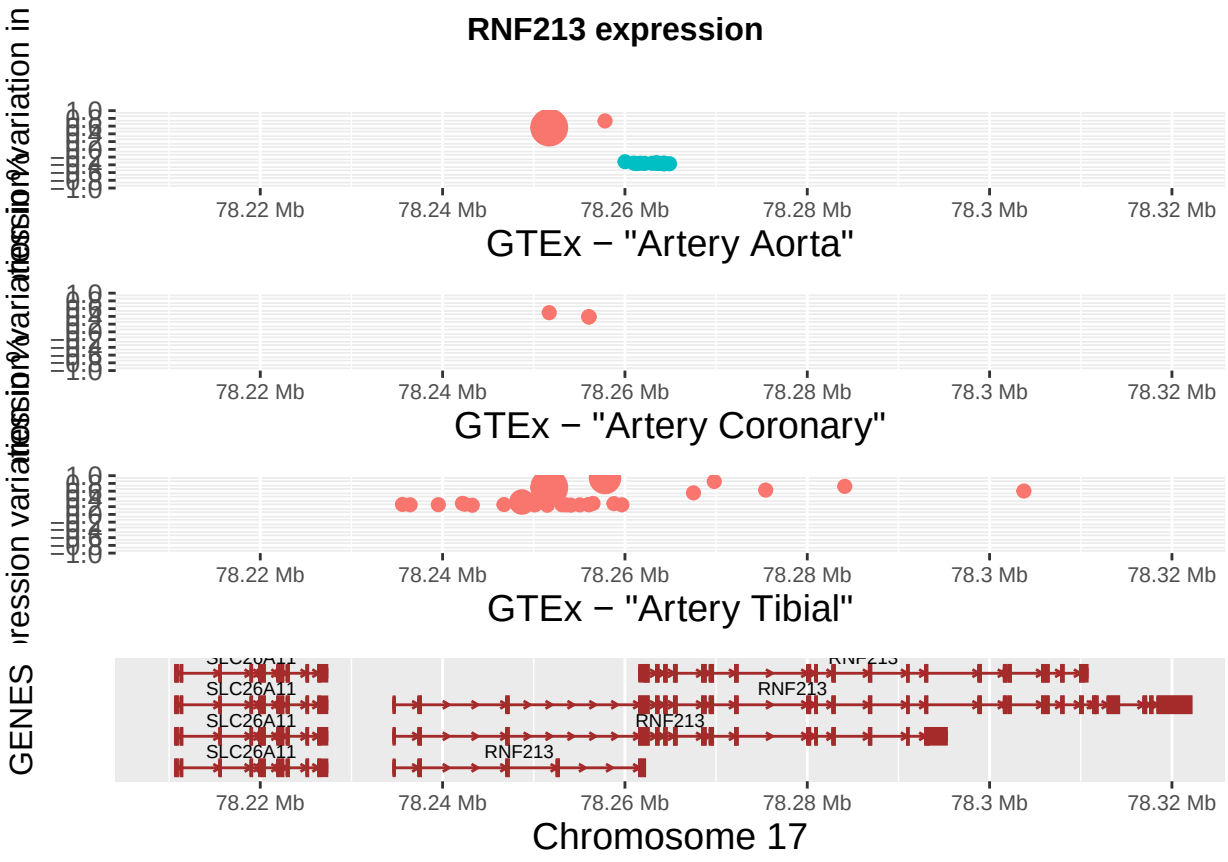
```
Sign_eQTLs_RTi <- subset(RNF213_tibial_df,-log10(RNF213_tibial_df$pval_nominal)>4)
Sign_eQTLs_RTi$log10 <- -log10(Sign_eQTLs_RTi$pval_nominal)
Sign_eQTLs_RTi$ranges <- cut(Sign_eQTLs_RTi$log10, seq(4,24,2),
                             labels = c("4 - 5.99","6 - 7.99","8 - 9.99","10 - 11.99",
                                        "12 - 13.99","14 - 15.99","16 - 17.99","18 - 19.99",
                                        "20 - 21.99","22 - 24"))
Sign_eQTLs_RTi$color <- ifelse(Sign_eQTLs_RTi$slope<0, "Underexpression","Overespression")


RNF213_tibial_ex <- ggplot(Sign_eQTLs_RTi) +
        xlim (RNF213_range) +
        scale_x_sequnit("Mb") +
        scale_y_continuous(limits = c(-1,1),
                           breaks=c(-1.0,-0.8,-0.6,-0.4,-0.2,0,0.2,0.4,0.6,0.8,1.0),
                           expand = c(0,0)) +
        geom_point(aes(position, slope, size = Sign_eQTLs_RTi$ranges,
                       color =Sign_eQTLs_RTi$color)) +
        geom_text(data=subset(RNF213_tibial_df, Include == "Y"),
                  aes( x= position, y = slope, label = SNP_ID), hjust = 0, angle = 10) +
        labs(x = x_lab_tibial, y = y_lab, size = size_label,
             color = "Expression change") +
        theme(axis.text.x = element_text(size=8), axis.text.y = element_text(size=10),
              axis.title.x = element_text(size=14), axis.title.y = element_text(size=12)) +
        theme(legend.position="none")
fixed(RNF213_tibial_ex) <- TRUE
RNF213_tibial_ex
```




```
# Get the gtables
gA <- ggplotGrob (SLC26A11_aorta_ex)
gB <- ggplotGrob (SLC26A11_coronary_ex)
gC <- ggplotGrob (SLC26A11_tibial_ex)
gD <- ggplotGrob (RNF213_aorta_ex)
gE <- ggplotGrob (RNF213_coronary_ex)
gF <- ggplotGrob (RNF213_tibial_ex)
gG <- ggplotGrob (SLC26A11_GENES.gg)
gH <- ggplotGrob (RNF213_GENES.gg)

# Set the widths
gA$widths <- gC$widths
gB$widths <- gC$widths
gD$widths <- gC$widths
gE$widths <- gC$widths
gF$widths <- gC$widths
gG$widths <- gC$widths
gH$widths <- gC$widths

# Arrange the SLC26A11 charts
SLC26A11_title = textGrob("SLC26A11 expression\n", gp=gpar(fontsize=12, font = 2))
grid.newpage()
SLC26A11_plot <- grid.arrange(gA, gB, gC, gG, heights = c(8,8,8,10), top =SLC26A11_title)
```



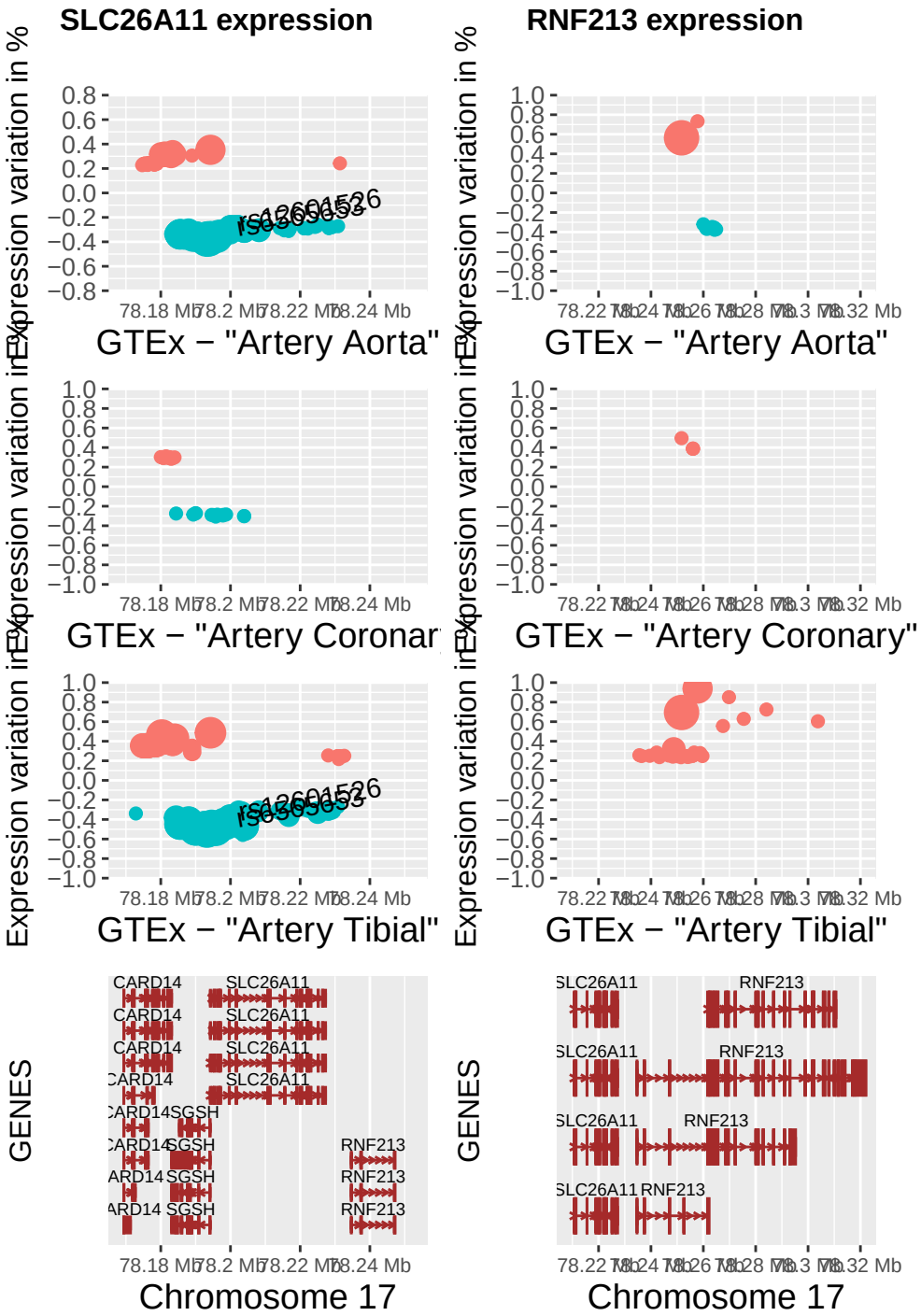

```
# Arrange the RNF213 charts
RNF213_title = textGrob("RNF213 expression\n", gp=gpar(fontsize=12, font = 2))
grid.newpage()
RNF213_plot <- grid.arrange(gD, gE, gF, gH, heights = c(8,8,8,10), top =RNF213_title)
```



Supplementary Figure 5

```
# Arrange SLC26A11 - RNF213 plots together
main_title = textGrob("Arterial tissue expression changes due to the SLC26A11 and RNF213 variation\n",
                      gp=gpar(fontsize=16, font = 2))
grid.newpage()

FINAL_PLOT <- grid.arrange(SLC26A11_plot, RNF213_plot, ncol = 2, top = main_title)
```

Arterial tissue expression changes due to the SLC26A11 and RNF213 variation




```
dev.off()
```

```
## null device
##           1
```

```
sessionInfo()
```

```
## R version 3.5.1 (2018-07-02)
## Platform: x86_64-apple-darwin15.6.0 (64-bit)
## Running under: macOS High Sierra 10.13.6
##
## Matrix products: default
## BLAS: /Library/Frameworks/R.framework/Versions/3.5/Resources/lib/libRblas.0.dylib
## LAPACK: /Library/Frameworks/R.framework/Versions/3.5/Resources/lib/libRlapack.dylib
##
## locale:
## [1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8
##
## attached base packages:
##  [1] stats4    grid      parallel  stats     graphics  grDevices utils
##  [8] datasets  methods   base
##
## other attached packages:
##  [1] VariantAnnotation_1.28.13
##  [2] SummarizedExperiment_1.12.0
##  [3] DelayedArray_0.8.0
##  [4] BiocParallel_1.16.6
##  [5] matrixStats_0.55.0
##  [6] scales_1.1.0
##  [7] Rsamtools_1.34.1
##  [8] reshape_0.8.8
##  [9] raster_3.0-7
## [10] sp_1.3-2
## [11] plyr_1.8.5
## [12] LDheatmap_0.99-7
## [13] BSgenome.Hsapiens.UCSC.hg19_1.4.0
## [14] BSgenome_1.50.0
## [15] rtracklayer_1.42.2
## [16] Biostrings_2.50.2
## [17] XVector_0.22.0
## [18] Homo.sapiens_1.3.1
## [19] TxDb.Hsapiens.UCSC.hg19.knownGene_3.2.2
## [20] org.Hs.eg.db_3.7.0
## [21] GO.db_3.7.0
## [22] OrganismDbi_1.24.0
## [23] genetics_1.3.8.1.2
## [24] mvtnorm_1.0-11
## [25] MASS_7.3-51.5
## [26] gtools_3.8.1
## [27] gdata_2.18.0
## [28] combinat_0.0-8
## [29] ensembldb_2.6.8
## [30] AnnotationFilter_1.6.0
## [31] GenomicFeatures_1.34.8
## [32] AnnotationDbi_1.44.0
## [33] Biobase_2.42.0
## [34] GenomicRanges_1.34.0
```

```
## [35] GenomeInfoDb_1.18.2
## [36] IRanges_2.16.0
## [37] S4Vectors_0.20.1
## [38] cowplot_1.0.0
## [39] gtable_0.3.0
## [40] png_0.1-7
## [41] gridExtra_2.3
## [42] ggbio_1.30.0
## [43] BiocGenerics_0.28.0
## [44] extrafont_0.17
## [45] ggplot2_3.2.1
##
## loaded via a namespace (and not attached):
##  [1] colorspace_1.4-1         biovizBase_1.30.1        htmlTable_1.13.3
##  [4] base64enc_0.1-3          dichromat_2.0-0          rstudioapi_0.10
##  [7] farver_2.0.1             bit64_0.9-7              codetools_0.2-16
## [10] splines_3.5.1            knitr_1.26               zeallot_0.1.0
## [13] Formula_1.2-3            Rttf2pt1_1.3.7           cluster_2.1.0
## [16] graph_1.60.0             BiocManager_1.30.10      compiler_3.5.1
## [19] httr_1.4.1               backports_1.1.5          assertthat_0.2.1
## [22] Matrix_1.2-18            lazyeval_0.2.2           acepack_1.4.1
## [25] htmltools_0.4.0          prettyunits_1.0.2        tools_3.5.1
## [28] glue_1.3.1               GenomeInfoDbData_1.2.0   reshape2_1.4.3
## [31] dplyr_0.8.3              Rcpp_1.0.3               vctrs_0.2.1
## [34] extrafontdb_1.0          xfun_0.11                stringr_1.4.0
## [37] lifecycle_0.1.0          XML_3.98-1.20            zlibbioc_1.28.0
## [40] hms_0.5.2                ProtGenerics_1.14.0      RBGL_1.58.2
## [43] RColorBrewer_1.1-2       yaml_2.2.0               curl_4.3
## [46] memoise_1.1.0            biomaRt_2.38.0           rpart_4.1-15
## [49] latticeExtra_0.6-28      stringi_1.4.3            RSQLite_2.1.5
## [52] checkmate_1.9.4          rlang_0.4.2              pkgconfig_2.0.3
## [55] bitops_1.0-6             evaluate_0.14            lattice_0.20-38
## [58] purrr_0.3.3              labeling_0.3             GenomicAlignments_1.18.1
## [61] htmlwidgets_1.5.1        bit_1.1-14               tidyselect_0.2.5
## [64] GGally_1.4.0             magrittr_1.5             R6_2.4.1
## [67] Hmisc_4.3-0              DBI_1.1.0                pillar_1.4.3
## [70] foreign_0.8-74           withr_2.1.2              survival_3.1-8
## [73] RCurl_1.95-4.12          nnet_7.3-12              tibble_2.1.3
## [76] crayon_1.3.4             rmarkdown_2.0            progress_1.2.2
## [79] data.table_1.12.8        blob_1.2.0               digest_0.6.23
## [82] munsell_0.5.0
```