

main

July 9, 2021

1 Boxplot of top five up- and downregulated genes

```
[1]: library(ggpubr)
library(ggsignif)
library(tidyverse)
```

Loading required package: ggplot2

```
Attaching packages: tidyverse
1.3.1
```

```
tibble 3.1.2    dplyr  1.0.7
tidyr  1.1.3    stringr 1.4.0
readr  1.4.0    forcats 0.5.1
purrr  0.3.4
```

Conflicts

```
tidyverse_conflicts()
dplyr::filter() masks stats::filter()
dplyr::lag()    masks stats::lag()
```

1.1 Functions

```
[2]: add_symnum <- function(res){
  symnum.args <- list(cutpoints = c(0, 0.0001, 0.001, 0.01, 0.05, 1),
                     symbols = c("****", "***", "**", "*", "ns"))
  symnum.args$x <- res$adj.P.Val
  pvalue.signif <- do.call(stats::symnum, symnum.args) %>%
    as.character()
  pvalue.format <- format.pval(res$adj.P.Val, digits = 2)
  res <- res %>%
    dplyr::ungroup() %>%
    mutate(FDR = pvalue.format, p.signif = pvalue.signif)
  return(res)
}

save_ggplots <- function(fn, p, w, h){
```

```

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

```

1.2 All genes

1.2.1 Differential expressed genes

```

[3]: genes = read.delim('../_m/genes/diffExpr_maleVfemale_full.txt')
genes = genes %>% filter(adj.P.Val < 0.05) %>%
  select(gencodeID, ensemblID, Symbol, logFC, t, adj.P.Val)
genes = add_symnum(genes)

up_genes = genes %>% filter(t > 0) %>% mutate('Direction'='Male Bias') %>%
  head(5)
down_genes = genes %>% filter(t < 0) %>% mutate('Direction'='Female Bias') %>%
  head(5)

sig_genes = bind_rows(up_genes, down_genes) %>% mutate_at(vars(Direction), as.
  factor)

for(xx in seq_along(sig_genes$Symbol)){
  sig_genes$New_ID[xx] <- ifelse(sig_genes$Symbol[xx] == '',
    as.character(sig_genes$ensemblID[xx]),
    as.character(sig_genes$Symbol[xx]))
}

sig_genes

```

A data.frame: 10 × 10

	gencodeID <chr>	ensemblID <chr>	Symbol <chr>	logFC <dbl>	t <dbl>	adj.P.Val <dbl>
	ENSG00000114374.12	ENSG00000114374	USP9Y	8.6836787	100.18087	1.9536
	ENSG00000183878.15	ENSG00000183878	UTY	8.5971522	88.46621	8.1331
	ENSG00000012817.15	ENSG00000012817	KDM5D	8.6930099	88.03682	3.5934
	ENSG00000067048.16	ENSG00000067048	DDX3Y	8.5878028	86.79686	5.0351
	ENSG00000067646.11	ENSG00000067646	ZFY	8.5329011	81.80364	9.1060
	ENSG00000229807.10	ENSG00000229807	XIST	-9.2961371	-100.35608	1.9536
	ENSG00000005889.15	ENSG00000005889	ZFX	-0.6315196	-46.06126	3.8877
	ENSG00000147050.14	ENSG00000147050	KDM6A	-0.5283117	-31.99315	3.0178
	ENSG00000126012.11	ENSG00000126012	KDM5C	-0.4877813	-31.52353	1.7667
	ENSG00000130021.13	ENSG00000130021	PUDP	-0.5965470	-27.93309	1.6502

1.2.2 Load residualized expression

```
[4]: res_file = '../_m/genes/residualized_expression.tsv'
tmp_df = data.table::fread(res_file, data.table=F)

resdf0 = tmp_df %>% filter(V1 %in% sig_genes$gencodeID) %>%
  ↪column_to_rownames("V1")
resdf0 <- data.frame(t(resdf0))
resdf0[1:2, 1:5]
```

Warning message in data.table::fread(res_file, data.table = F):
 "Detected 393 column names but the data has 394 columns (i.e. invalid file).
 Added 1 extra default column name for the first column which is guessed to be
 row names or an index. Use setnames() afterwards if this guess is not correct,
 or fix the file write command that created the file to create a valid file."

A data.frame: 2 × 5		ENSG00000130021.13	ENSG00000005889.15	ENSG00000147050.14	ENSG00000147050.14
		<dbl>	<dbl>	<dbl>	<dbl>
	R12864	1.7296843	2.2011553	0.7197812	0.777743
	R12865	-0.6949843	-0.7467199	-0.5590480	-0.342652

1.2.3 Load pheno data

```
[5]: pheno_file = '/ceph/projects/v3_phase3_paper/inputs/phenotypes/_m/
  ↪caudate_phenotypes.csv'
pheno <- data.table::fread(pheno_file) %>%
  mutate_if(is.character, as.factor) %>%
  column_to_rownames("V1")
levels(pheno$Sex) <- c("Female", "Male")
head(pheno, 2)
```

A data.frame: 2 × 8		BrNum	RNum	Region	RIN	Age	Sex	Race	Dx
		<fct>	<fct>	<fct>	<dbl>	<dbl>	<fct>	<fct>	<fct>
	R12864	Br1303	R12864	Caudate	9.6	42.98	Female	AA	Schizo
	R12865	Br1320	R12865	Caudate	9.5	53.12	Male	AA	Schizo

1.2.4 Merge dataframe

```
[6]: resdf <- inner_join(rownames_to_column(pheno),
  ↪rownames_to_column(resdf0),
  ↪by="rowname")
dim(resdf)
resdf[1:2, 1:10]
```

1. 393 2. 19

A data.frame: 2 × 10		rowname	BrNum	RNum	Region	RIN	Age	Sex	Race	Dx
		<chr>	<fct>	<fct>	<fct>	<dbl>	<dbl>	<fct>	<fct>	<fct>
	1	R12864	Br1303	R12864	Caudate	9.6	42.98	Female	AA	Schizo
	2	R12865	Br1320	R12865	Caudate	9.5	53.12	Male	AA	Schizo

1.2.5 Melt data frame

```
[7]: df = resdf %>% select(c('rowname', 'Sex', starts_with('ENSG'))) %>%
  pivot_longer(-c(rowname, Sex), names_to = "gencodeID", values_to = "Res")
  #>%
  inner_join(sig_genes, by='gencodeID') %>% mutate_at(vars("New_ID",
  #>"Symbol", "gencodeID"), as.factor)

df$New_ID = with(df, reorder(New_ID, adj.P.Val, median))
head(df, 2)
```

A tibble: 2 × 13

	rowname	Sex	gencodeID	Res	ensemblID	Symbol	logFC
	<chr>	<fct>	<fct>	<dbl>	<chr>	<fct>	<dbl>
	R12864	Female	ENSG000000130021.13	1.729684	ENSG000000130021	PUDP	-0.59654
	R12864	Female	ENSG00000005889.15	2.201155	ENSG00000005889	ZFX	-0.63151

1.2.6 Initial ggplot with ggpubr

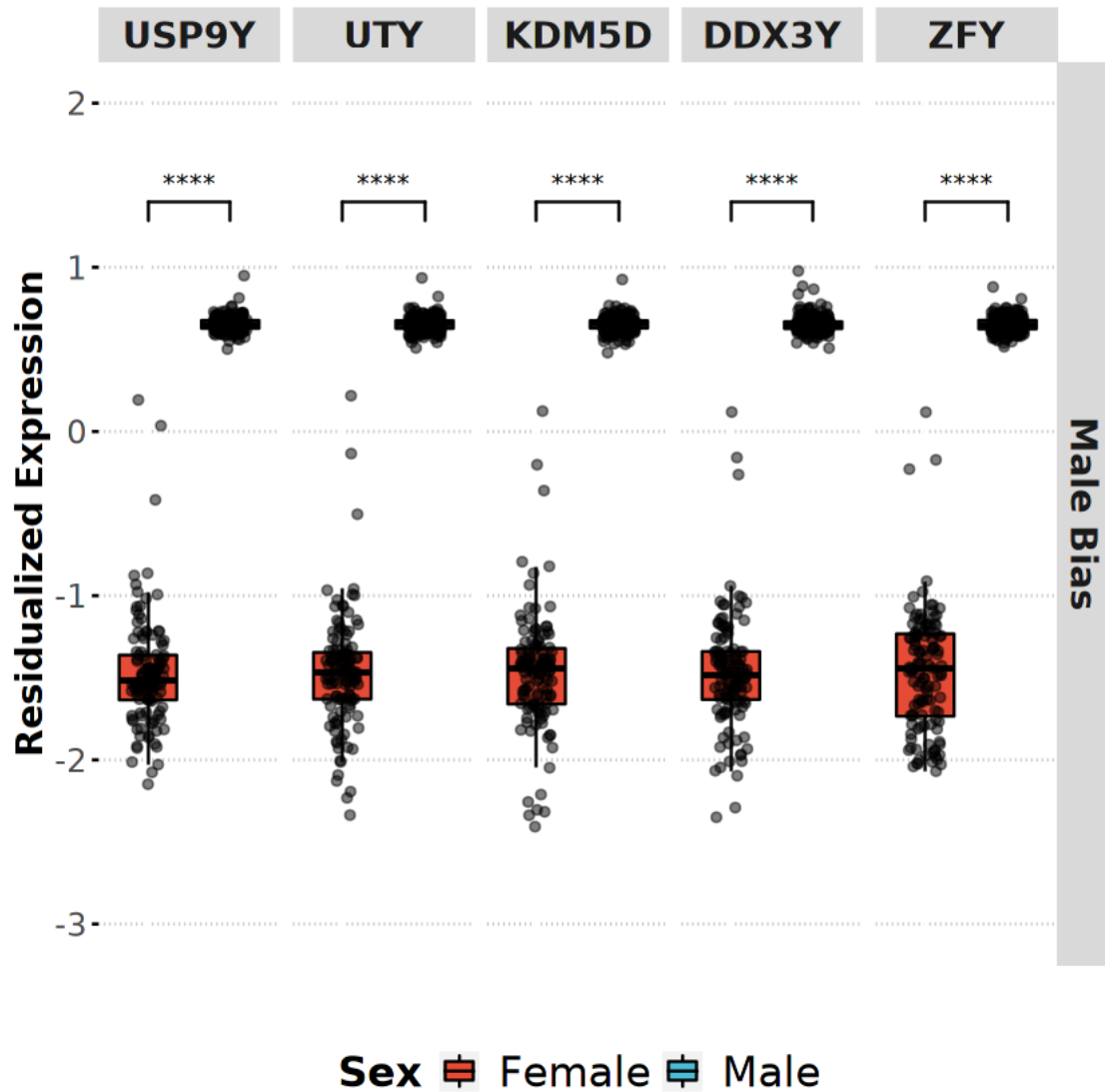
```
[8]: tmp = sig_genes %>% mutate(group1='Female', group2='Male', y_pos=1.4) %>%
  #>filter(Direction == 'Male Bias') %>%
  mutate_if(is.character, as.factor)

bxp_up <- df %>% filter(Direction=="Male Bias") %>%
  ggboxplot(x="Sex", y="Res", facet.by=c("Direction", "New_ID"),
  #>fill="Sex", xlab='',
  panel.labs.font=list(face='bold', size = 16), palette="npg",
  #>outlier.shape=NA,
  ylab='Residualized Expression', add='jitter', ylim=c(-3, 2),
  add.params=list(alpha=0.5), legend="bottom",
  #>ggtheme=theme_pubclean()) +
  geom_signif(data=tmp,
  aes(xmin=group1, xmax=group2, annotations=p.signif,
  #>y_position = y_pos),
  manual=TRUE) +
  font("xy.title", size=16, face="bold") + font("xy.text", size=14) +
  font("legend.title", size=18, face="bold") +
  font("legend.text", size=18) + rremove("x.text") + rremove("x.ticks")

bxp_up
```

Warning message:

"Ignoring unknown aesthetics: xmin, xmax, annotations, y_position"



```
[9]: tmp = sig_genes %>% mutate(group1='Female', group2='Male', y_pos=3.4) %>%
  filter(Direction == 'Female Bias') %>%
  mutate_if(is.character, as.factor)

bxp_down <- df %>% filter(Direction=='Female Bias') %>%
  ggboxplot(x="Sex", y="Res", fill="Sex", palette="npg", xlab='', outlier.
  ↳ shape=NA,
  facet.by=c("Direction", "New_ID"), panel.labs.
  ↳ font=list(face='bold', size = 16),
  ylab='Residualized Expression', add='jitter', ylim=c(-3, 4),
  add.params=list(alpha=0.5), legend="bottom",
  ↳ ggtheme=theme_pubclean()) +
```

```

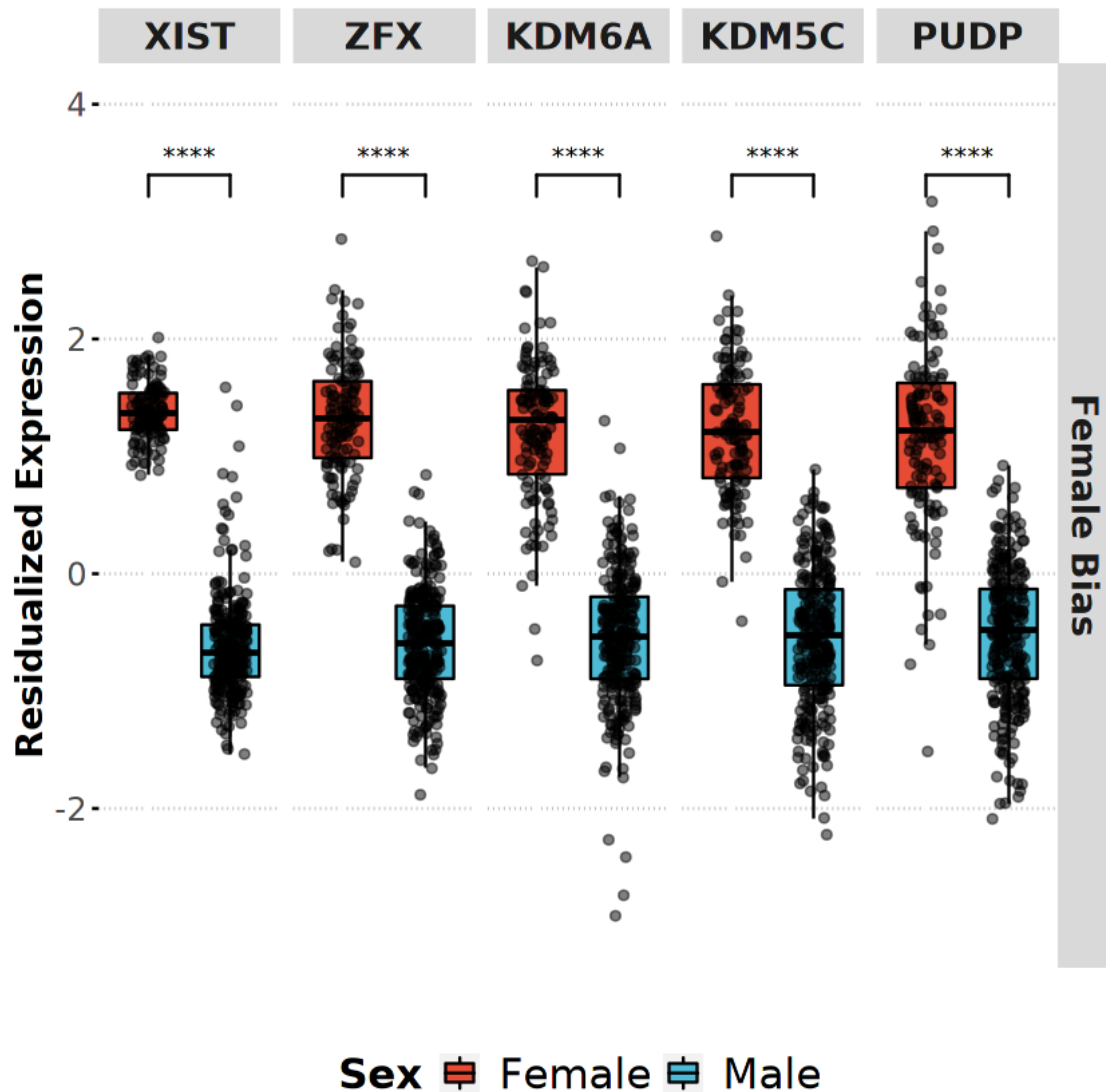
geom_signif(data=tmp,
            aes(xmin=group1, xmax=group2, annotations=p.signif,
→ y_position = y_pos),
            manual=TRUE) +
font("xy.title", size=16, face="bold") + font("xy.text", size=14) +
font("legend.title", size=18, face="bold") +
font("legend.text", size=18) + rremove("x.text") + rremove("x.ticks")

```

bxp_down

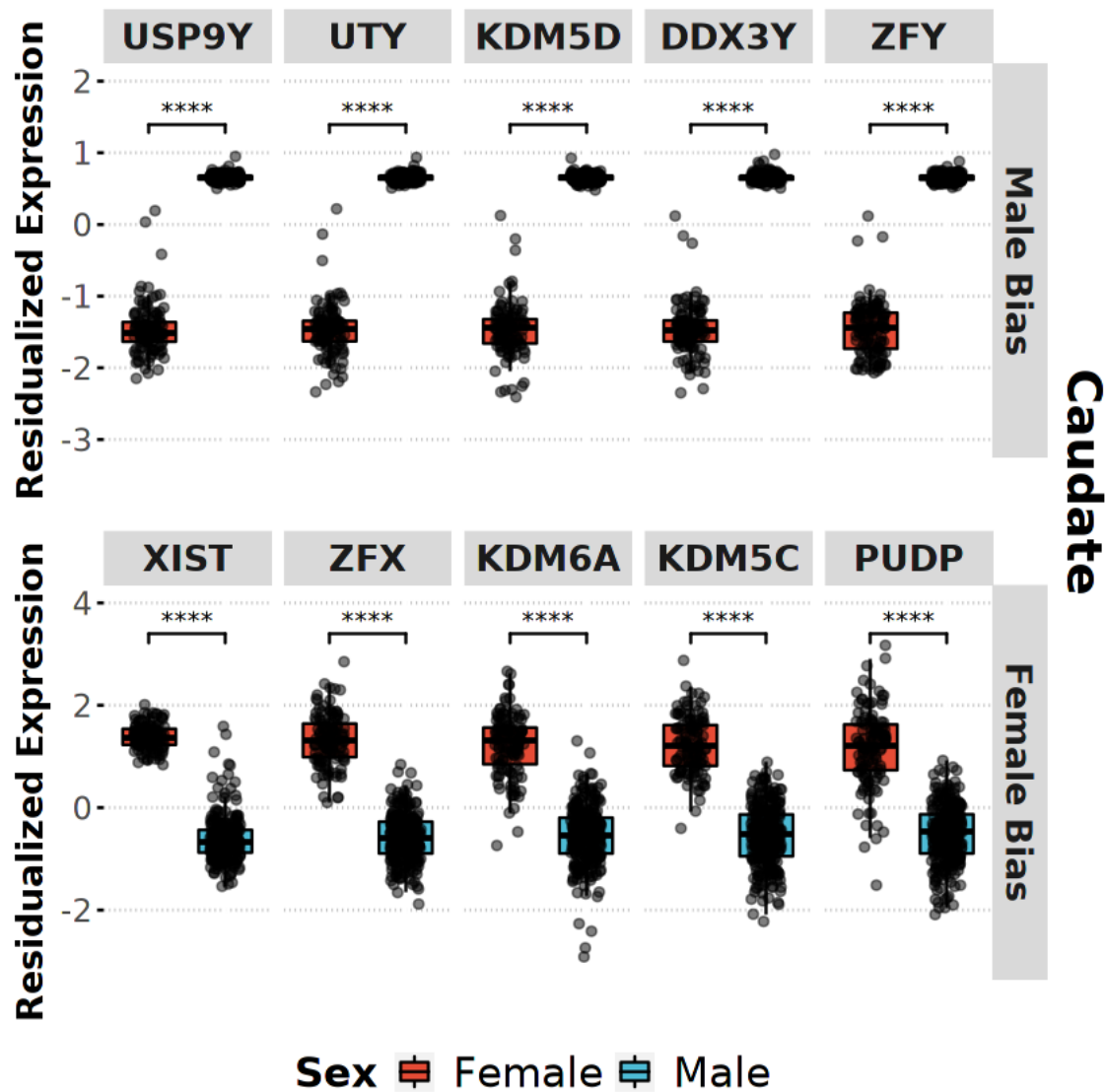
Warning message:

"Ignoring unknown aesthetics: xmin, xmax, annotations, y_position"



1.2.7 Annotate figure

```
[10]: figure <- ggarrange(bxp_up, bxp_down, ncol = 1, nrow=2, common.legend=TRUE,
  ↳ legend='bottom')
figure <- annotate_figure(figure,
  right=text_grob("Caudate", size=22, rot=-90,
  ↳ face='bold', hjust=0.8))
figure
```



```
[11]: save_ggplots('caudate_topSig_boxplot', figure, 12, 8)
```

1.3 Autosomal only

1.3.1 Differential expressed genes

```
[12]: genes = read.csv('.././metrics_summary/_m/autosomal_DEG.csv')
genes = genes %>% rename("gencodeID" = "Feature") %>%
  filter(adj.P.Val < 0.05) %>%
  select(gencodeID, ensemblID, Symbol, logFC, adj.P.Val)
genes = add_symnum(genes)

up_genes = genes %>% filter(logFC > 0) %>% mutate('Direction'='Male Bias') %>%
  head(5)
down_genes = genes %>% filter(logFC < 0) %>% mutate('Direction'='Female Bias')
  head(5)

sig_genes = bind_rows(up_genes, down_genes) %>% mutate_at(vars(Direction), as.
  factor)

for(xx in seq_along(sig_genes$Symbol)){
  sig_genes$New_ID[xx] <- ifelse(as.character(sig_genes$Symbol[xx]) == '',
    as.character(sig_genes$ensemblID[xx]),
    as.character(sig_genes$Symbol[xx]))
}
sig_genes
```

	gencodeID <chr>	ensemblID <chr>	Symbol <chr>	logFC <dbl>	adj.P.Val <dbl>	FD <c
A data.frame: 10 × 9	ENSG00000205611.4	ENSG00000205611	LINC01597	1.3079897	6.877867e-20	< 2
	ENSG00000283443.1	ENSG00000283443		1.4162533	2.838705e-18	< 2
	ENSG00000149531.15	ENSG00000149531	FRG1BP	0.6715762	1.190836e-17	< 2
	ENSG00000282826.1	ENSG00000282826	FRG1CP	0.5551378	1.474014e-15	1.5
	ENSG00000258484.3	ENSG00000258484	SPESP1	0.7304981	4.974455e-12	5.0
	ENSG00000095932.6	ENSG00000095932	SMIM24	-0.9013291	1.022672e-15	1.0
	ENSG00000261600.1	ENSG00000261600		-0.9681869	3.921912e-13	3.9
	ENSG00000236698.1	ENSG00000236698	EIF1AXP1	-0.2509585	2.863151e-12	2.9
	ENSG00000241532.1	ENSG00000241532	AGGF1P3	-0.7277903	8.886125e-11	8.9
	ENSG00000180574.3	ENSG00000180574		-0.2318311	9.268579e-11	9.3

1.3.2 Load residualized expression

```
[13]: resdf0 = tmp_df %>% filter(V1 %in% sig_genes$gencodeID) %>%
  column_to_rownames("V1")
resdf0 <- data.frame(t(resdf0))
resdf0[1:2, 1:5]
```

A data.frame: 2 × 5		ENSG00000236698.1 <dbl>	ENSG00000261600.1 <dbl>	ENSG00000241532.1 <dbl>	ENSG00000180574.3 <dbl>
	R12864	-0.0355813	0.4617652	0.05548178	2.0144561
	R12865	-1.1127706	-1.1681747	0.50413144	-0.5880534

1.3.3 Merge dataframe

```
[14]: resdf <- inner_join(rownames_to_column(pheno),
                        rownames_to_column(resdf0),
                        by="rowname")

dim(resdf)
resdf[1:2, 1:10]
```

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	rowname	BrNum	RNum	Region	RIN	Age	Sex	Race	Dx	
A data.frame: 2 × 10	<chr>	<fct>	<fct>	<fct>	<dbl>	<dbl>	<fct>	<fct>	<fct>	
	1	R12864	Br1303	R12864	Caudate	9.6	42.98	Female	AA	Schizo
	2	R12865	Br1320	R12865	Caudate	9.5	53.12	Male	AA	Schizo

1.3.4 Melt data frame

```
[15]: df = resdf %>% select(c('rowname', 'Sex', starts_with('ENSG')) %>%
  pivot_longer(-c(rowname, Sex), names_to = "gencodeID", values_to = "Res")
  %>%
  mutate_if(is.character, as.factor) %>% inner_join(sig_genes,
  by='gencodeID') %>%
  mutate_at(vars("New_ID", "Symbol", "gencodeID"), as.factor)

df$New_ID = with(df, reorder(New_ID, adj.P.Val, median))
head(df, 2)
```

	rowname	Sex	gencodeID	Res	ensemblID	Symbol	logP
	<fct>	<fct>	<fct>	<dbl>	<chr>	<fct>	<dbl>
A tibble: 2 × 12	R12864	Female	ENSG00000236698.1	-0.0355813	ENSG00000236698	EIF1AXP1	-0.2
	R12864	Female	ENSG00000261600.1	0.4617652	ENSG00000261600		-0.9

1.3.5 Initial ggplot with ggpubr

```
[16]: tmp = sig_genes %>% mutate(group1='Female', group2='Male', y_pos=3.5) %>%
  filter(Direction == 'Male Bias') %>%
  mutate_if(is.character, as.factor)

bxp_up <- df %>% filter(Direction == "Male Bias") %>%
  ggboxplot(x="Sex", y="Res", fill="Sex", palette="npg", xlab='', outlier.
  shape=NA,
            facet.by=c("Direction", "New_ID"), panel.labs.
  font=list(face='bold', size = 16),
            ylab='Residualized Expression', add='jitter', ylim=c(-6.5,
  5),
            add.params=list(alpha=0.5), legend="bottom",
  theme=theme_pubclean()) +
  geom_signif(data=tmp,
```

```

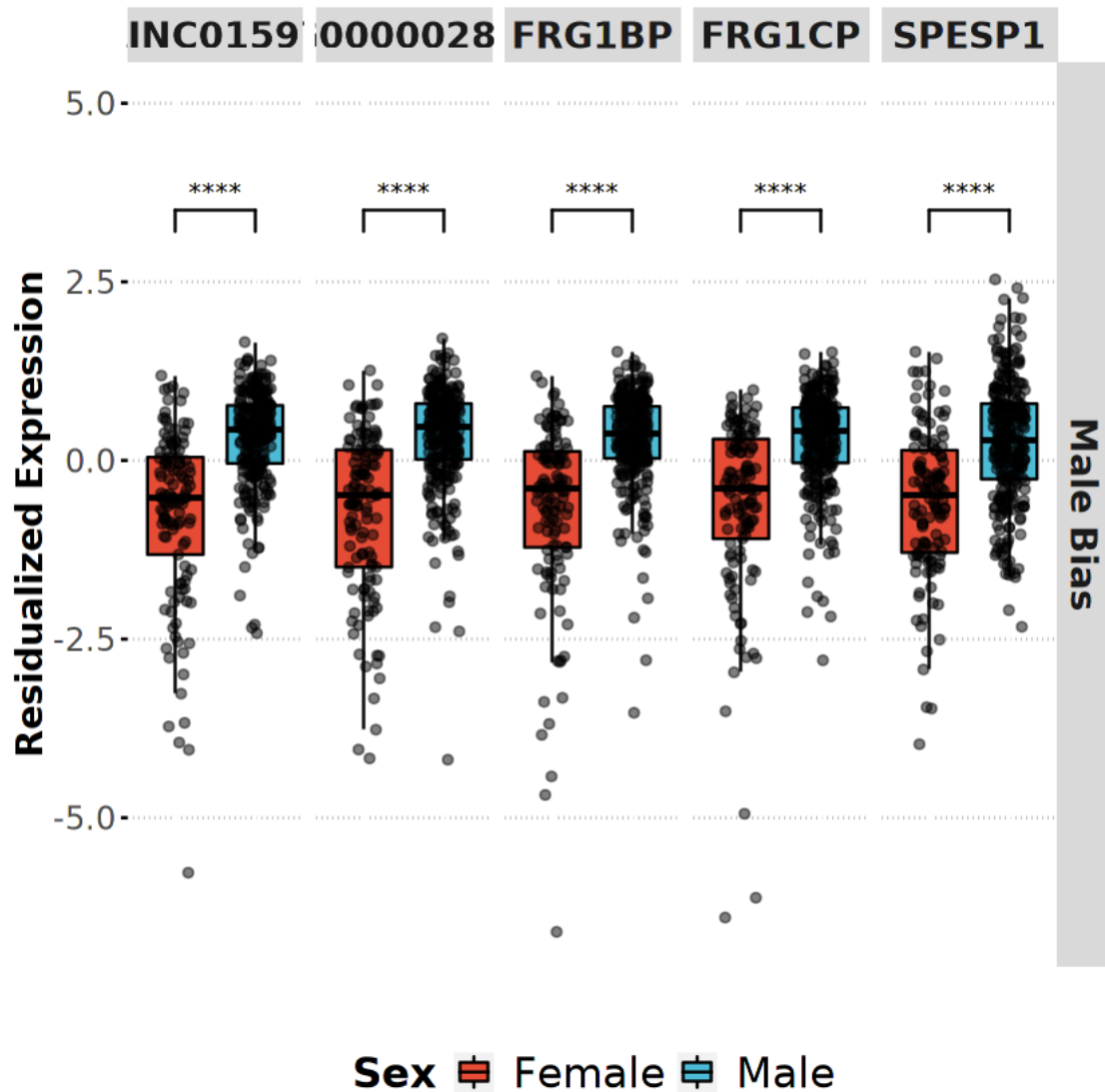
aes(xmin=group1, xmax=group2, annotations=p.signif,
↪y_position = y_pos),
manual=TRUE) +
font("xy.title", size=16, face="bold") + font("xy.text", size=14) +
font("legend.title", size=18, face="bold") +
font("legend.text", size=18) + rremove("x.text") + rremove("x.ticks")

```

bxp_up

Warning message:

"Ignoring unknown aesthetics: xmin, xmax, annotations, y_position"



```

[17]: tmp = sig_genes %>% mutate(group1='Female', group2='Male', y_pos=4.5) %>%
      filter(Direction == 'Female Bias') %>%
      mutate_if(is.character, as.factor)

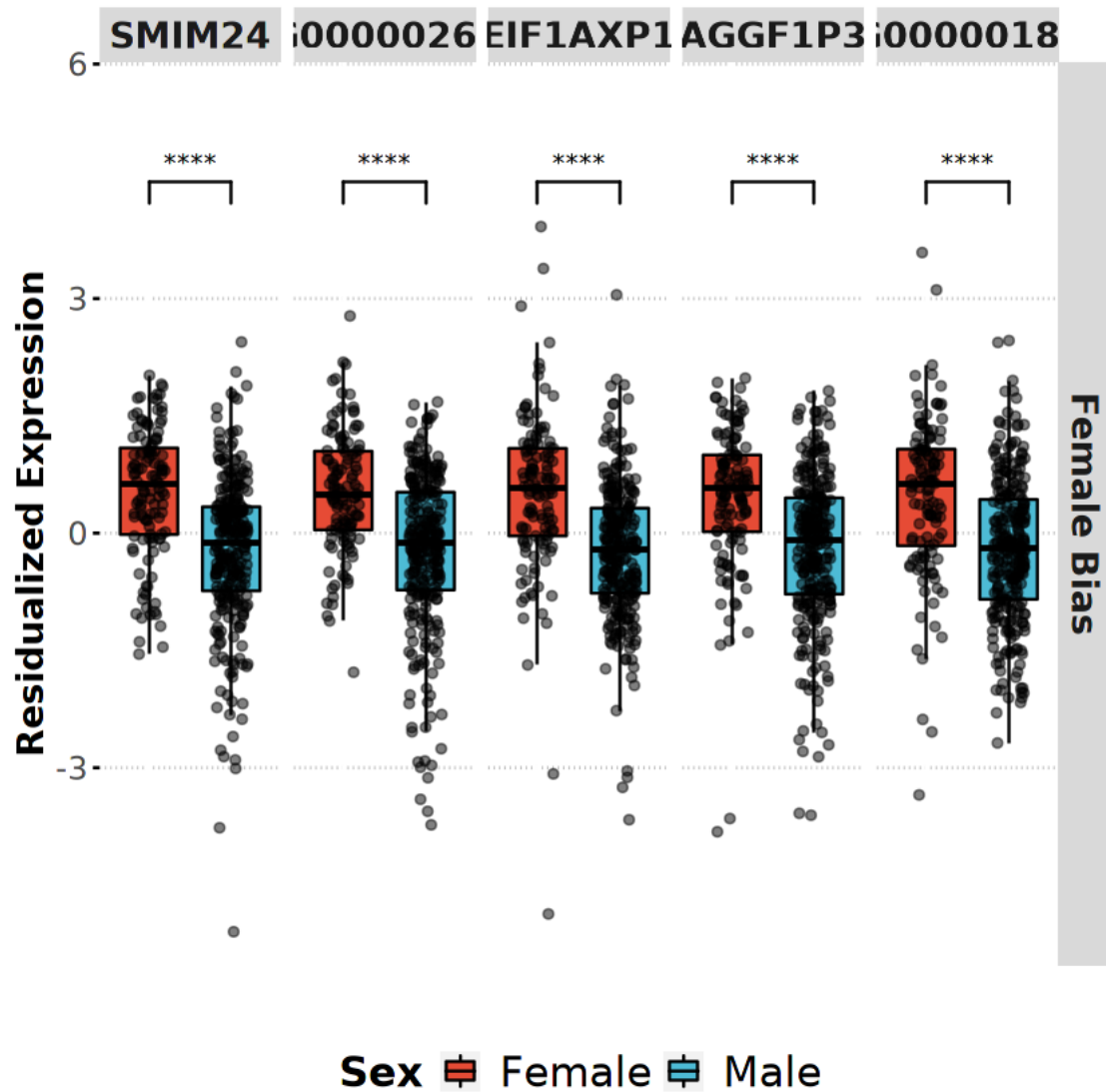
bxp_down <- df %>% filter(Direction=="Female Bias") %>%
      ggboxplot(x="Sex", y="Res", fill="Sex", palette="npg", xlab='', outlier.
      ↪shape=NA,
              facet.by=c("Direction", "New_ID"),
              panel.labs.font=list(face='bold', size = 16),
              ylab='Residualized Expression', add='jitter', ylim=c(-5, 5.5),
              add.params=list(alpha=0.5), legend="bottom",
      ↪ggtheme=theme_pubclean()) +
      geom_signif(data=tmp,
                  aes(xmin=group1, xmax=group2, annotations=p.signif,
      ↪y_position = y_pos),
                  manual=TRUE) +
      font("xy.title", size=16, face="bold") + font("xy.text", size=14) +
      font("legend.title", size=18, face="bold") +
      font("legend.text", size=18) + rremove("x.text") + rremove("x.ticks")

bxp_down

```

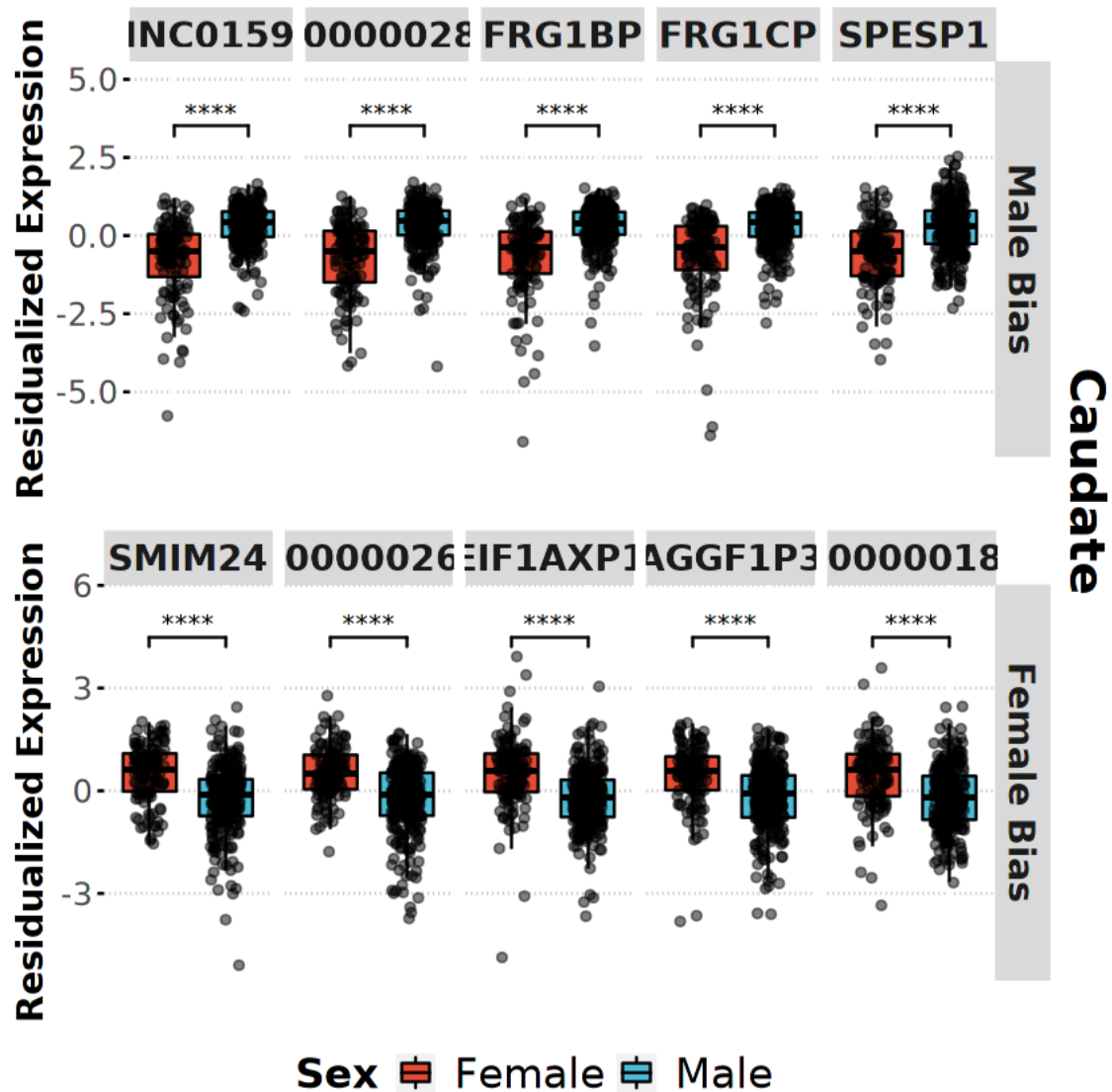
Warning message:

"Ignoring unknown aesthetics: xmin, xmax, annotations, y_position"



1.3.6 Annotate figure

```
[18]: figure2 <- ggarrange(bxp_up, bxp_down, ncol=1, nrow=2, common.legend=TRUE,
  ↪ legend='bottom')
figure2 <- annotate_figure(figure2,
  ↪ right=text_grob("Caudate", size=22, rot=-90,
  ↪ face='bold', hjust=0.8))
figure2
```



```
[19]: save_ggplots('caudate_topSig_autosomal_boxplot', figure2, 12, 8)
```

1.4 Session Info

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

```
[1] "2021-07-09 20:49:18 EDT"
```

```
user system elapsed
21.941 1.930 22.776
```

```

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     2021-07-09

```

```

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         0.7.8     2021-06-24 [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           3.0.0     2021-06-30 [1] CRAN (R 4.0.3)
colorspace    2.0-2     2021-06-24 [1] CRAN (R 4.0.3)
cowplot       1.1.1     2020-12-30 [1] CRAN (R 4.0.2)
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)
fans          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)
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)
ggsci         2.9       2018-05-14 [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)
gridExtra     2.3       2017-09-09 [1] CRAN (R 4.0.2)
gtable        0.3.0     2019-03-25 [1] CRAN (R 4.0.2)

```

haven	2.4.1	2021-04-23	[1]	CRAN	(R 4.0.3)
hms	1.1.0	2021-05-17	[1]	CRAN	(R 4.0.3)
htmltools	0.5.1.1	2021-01-22	[1]	CRAN	(R 4.0.2)
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)
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	1.6.1	2021-05-16	[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)
R6	2.5.0	2020-10-28	[1]	CRAN	(R 4.0.2)
Rcpp	1.0.7	2021-07-07	[1]	CRAN	(R 4.0.3)
readr	* 1.4.0	2020-10-05	[1]	CRAN	(R 4.0.2)
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	2.0.0	2021-04-02	[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	1.0.0	2021-03-09	[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	1.6.2	2021-05-17	[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	* 3.1.2	2021-05-16	[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)
utf8	1.2.1	2021-03-12	[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)

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

[2] /usr/lib/R/library