```
install.packages('pacman')
rm(list = ls())
pacman::p_load(devtools, tidyverse, metafor, patchwork, R.rsp, orchaRd,
emmeans,ape, phytools, flextable)
#-------calculate the effect size measures-----------

#--------------gene knockdown genes----------
  View(Effect_size_cal_Gene_Knockdown)
datakd<-Effect_size_cal_Gene_Knockdown
datakd1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakd)
datakd_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakd1)
summary(datakd_MA)
model_results <- orchaRd::mod_results(datakd_MA, mod = "1", at = NULL,
group = "Author")
model_results
orchaRd::orchard_plot(datakd_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
# use i2_sn function to obtain the total I^2
I2 <- orchaRd::i2_ml(datakd_MA)

setwd("C:/Users/v1lliu34/Downloads")
pp<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 5, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
pp
ggsave('gene_knockdown_overall.pdf',width = 15,height = 10,pp)
or
pdf(file = "gene_knockdown-overall", height=10, width=15)
plot(test)
dev.off()


datakd1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakd)
datakd_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakd1)
datakd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakd1)
datakd_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakd2)
summary(datakd_MR0)
res2 <- orchaRd::mod_results(datakd_MR0, mod = "Species", group = "Author")
res2
p3 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('gene_knockdown_genes_species_moderator.pdf',width = 15,height =
10,p3)
```

```
datakd1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakd)
dataoe_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakd1)
datakd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakd1)
datakd_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = datakd2)
summary(datakd_MR01)
res3 <- orchaRd::mod_results(datakd_MR01, mod = "Group", group = "Author")
res3
p4 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p4
ggsave('gene_knockdown_genes_Group_moderator.pdf',width = 10,height =
13,p4)



###sensitivity analysis
result1=rma(SMD, vSMD, data=datakd1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

--------------gene overexpression genes----------
  View(Effect_size_cal_Gene_Overexpression)
dataoe<-Effect_size_cal_Gene_Overexpression
dataoe1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoe)
dataoe_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoe1)
summary(dataoe_MA)
model_results <- orchaRd::mod_results(dataoe_MA, mod = "1", at = NULL,
group = "Author")
model_results
orchaRd::orchard_plot(dataoe_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
# use i2_sn function to obtain the total I^2
I2 <- orchaRd::i2_ml(dataoe_MA)

setwd("C:/Users/v1lliu34/Downloads")
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 51, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
```

```
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('gene_overexpression_overall.pdf',width = 15,height = 10,p1)



dataoe1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoe)
dataoe_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoe1)
dataoe2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoe1)
dataoe_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataoe2)
summary(dataoe_MR0)
res2 <- orchaRd::mod_results(dataoe_MR0, mod = "Species", group = "Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('gene_overexpression_genes_species_moderator.pdf',width = 15,height
= 10,p2)


dataoe_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataoe2)
summary(dataoe_MR0)
res2 <- orchaRd::mod_results(dataoe_MR0, mod = "Group", group = "Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('gene_overexpression_genes_Group_moderator.pdf',width = 10,height =
13,p2)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataoe1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)




#--------------gene knockdown related genes----------
library(readxl)
  View(Effect_size_cal_Gene_Knockdown_related_gene)
```

```
datakdr<-Effect_size_cal_Gene_Knockdown_related_gene
datakdr1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdr)
datakdr_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdr1)
summary(datakdr_MA)
model_results <- orchaRd::mod_results(datakdr_MA, mod = "1", at = NULL,
group = "Author")
model_results
P1<-orchaRd::orchard_plot(datakdr_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p2<-I2 <- orchaRd::i2_ml(datakdr_MA)

setwd("C:/Users/v1lliu34/Downloads")
test<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 19, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
test
pdf(file = "gene_knockdown_related_genes_overall.pdf", height=10, width=15)
plot(test)
dev.off()
or
ggsave('gene_knockdown_related_genes_overall.pdf',width = 15,height =
10,test)

datakdr_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdr1)
datakdr2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdr1)
datakdr_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakdr2)
summary(datakdr_MR0)
res3 <- orchaRd::mod_results(datakdr_MR0, mod = "Species", group =
"Author")
res3
pkdr <- orchaRd::orchard_plot(res3, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
pkdr
ggsave('gene_knockdown_related_genes_species_omderator.pdf',width =
15,height = 10,pkdr)

datakdr_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdr1)
datakdr2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdr1)
datakdr_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = datakdr2)
summary(datakdr_MR0)
res4 <- orchaRd::mod_results(datakdr_MR0, mod = "Group", group = "Author")
res4
pkdr2 <- orchaRd::orchard_plot(res4, mod = "Group", group = "Author", xlab
= "Standardised mean difference")
```

```
pkdr2
ggsave('gene_knockdown_related_genes_group_omderator wide.pdf',width =
10,height = 30,pkdr2)

###---------------funnel--------------------
datakdr1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdr)
datakdr1
datakdr_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdr1)
p5<-funnel(datakdr_MA)

###sensitivity analysis
result1=rma(SMD, vSMD, data=datakdr1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

pdf(file = "gene_knockdown_related_genes_funnel", height=15, width=19)
plot(p5)
dev.off()
ggsave('gene_knockdown_related_genes_funnel.pdf',width = 15,height = 19,p5)

--------------gene overexpression related genes----------
View(Effect_size_cal_Gene_Overexpression_related_gene)
dataoer<-Effect_size_cal_Gene_Overexpression_related_gene
dataoer1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoer)
dataoer_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoer1)
summary(dataoer_MA)
model_results <- orchaRd::mod_results(dataoer_MA, mod = "1", at = NULL,
group = "Author")
model_results
P1<-orchaRd::orchard_plot(dataoer_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
I2 <- orchaRd::i2_ml(datakdr_MA)

por<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 22, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
por
ggsave('gene_overexpression_related_genes_overall.pdf',width = 15,height =
10,por)
```

```
dataoer2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoer1)
dataoer_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataoer2)
summary(dataoer_MR0)
res2 <- orchaRd::mod_results(dataoer_MR0, mod = "Species", group =
"Author")
res2
pors <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
pors
ggsave('gene_overexpression_related_genes_species_moderator.pdf',width =
15,height = 10,pors)

dataoer3 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean,n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoer1)
dataoer_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataoer3)
summary(dataoer_MR01)
res3 <- orchaRd::mod_results(dataoer_MR01, mod = "Group", group = "Author")
res3
por2 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
por2
ggsave('gene_overexpression_related_genes_Group_moderator wide.pdf',width =
10,height = 30,por2)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataoer1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

--------------gene knockdown proteins----------
View(Effect_size_cal_PROTEIN_Knockdown)
datakdp<-Effect_size_cal_PROTEIN_Knockdown
datakdp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdp)
datakdp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdp1)
summary(datakdp_MA)
model_results <- orchaRd::mod_results(datakdp_MA, mod = "1", at = NULL,
group = "Author")
model_results
P1<-orchaRd::orchard_plot(datakdp_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
```

```
p1

I2 <- orchaRd::i2_ml(datakdp_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.5, y = -2.5, label =
paste0("italic(I)^{2} == ", round(I2[1],4), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('proteins_knockdown_overall.pdf',width = 15,height = 10,p1)


datakdp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdp)
datakdp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdp1)
datakdp2 <- escalc(measure = "CVR",n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdp1)
datakdp_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakdp2)
summary(datakdp_MR0)
res2 <- orchaRd::mod_results(datakdp_MR0, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('proteins_knockdown_species_moderator.pdf',width = 15,height =
10,p2)

datakdp_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = datakdp2)
summary(datakdp_MR0)
res3 <- orchaRd::mod_results(datakdp_MR0, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('proteins_knockdown_Group_moderator.pdf',width = 10,height = 13,p3)
ggsave('proteins_knockdown_Group_moderator wide.pdf',width = 10,height =
30,p3)


# caterpillar plot --------------species
datakdp<-Effect_size_cal_PROTEIN_Knockdown
datakdp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdp)
datakdp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdp1)
datakdp2 <- escalc(measure = "CVR",n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdp1)
datakdp_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakdp2)
summary(datakdp_MR0)
```

```
res2 <- orchaRd::mod_results(datakdp_MR0, mod = "Species", group =
"Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
setwd("C:/Users/v1lliu34/Downloads")
ggsave('gene_knockdown_proteins_Species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
datakdp<-Effect_size_cal_PROTEIN_Knockdown
datakdp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdp)
datakdp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdp1)
datakdp2 <- escalc(measure = "CVR",n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdp1)
datakdp_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = datakdp2)
summary(datakdp_MR0)
res2 <- orchaRd::mod_results(datakdp_MR0, mod = "Group", group = "Author")
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_knockdown_proteins_Group.pdf',width = 15,height = 10,p5)

###sensitivity analysis
result1=rma(SMD, vSMD, data=datakdp, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

--------------gene overexpression proteins----------
View(Effect_size_cal_PROTEIN_Overexpression)
dataoep<-Effect_size_cal_PROTEIN_Overexpression
dataoep1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoep)
dataoep_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoep1)
summary(dataoep_MA)
model_results <- orchaRd::mod_results(dataoep_MA, mod = "1", at = NULL,
group = "Author")
model_results
P1<-orchaRd::orchard_plot(dataoep_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
```

```
p1
I2 <- orchaRd::i2_ml(dataoep_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 23, label =
paste0("italic(I)^{2} == ", round(I2[1],4), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('proteins_overexpression_overall.pdf',width = 15,height = 10,p1)


dataoep1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoep)
dataoep_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoep1)
dataoep2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoep1)
dataoep_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataoep2)
summary(dataoep_MR0)
res2 <- orchaRd::mod_results(dataoep_MR0, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('proteins_overexpression_species_moderator.pdf',width = 15,height =
10,p2)

dataoep_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataoep2)
summary(dataoep_MR01)
res3 <- orchaRd::mod_results(dataoep_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('proteins_overexpression_Group_moderator.pdf',width = 10,height =
13,p3)
ggsave('proteins_overexpression_Group_moderator wide.pdf',width = 10,height
= 13,p3)

# caterpillar plot --------------species
View(Effect_size_cal_PROTEIN_Overexpression)
dataoep1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoep)
dataoep_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoep1)
dataoep2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoep1)
dataoep_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataoep2)
summary(dataoep_MR0)
```

```
res2 <- orchaRd::mod_results(dataoep_MR0, mod = "Species", group =
"Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
setwd("C:/Users/v1lliu34/Downloads")
ggsave('overexpression_proteins_Species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
dataoep1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoep)
dataoep_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoep1)
dataoep2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoep1)
dataoep_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataoep2)
summary(dataoep_MR0)
res2 <- orchaRd::mod_results(dataoep_MR0, mod = "Group", group = "Author")
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('overexpression_proteins_Group.pdf',width = 15,height = 10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataoep1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

--------------related protein of knockdown ----------
  View(Effect_size_cal_PROTEIN_Knockdown_related_protein)
datakdrp<-Effect_size_cal_PROTEIN_Knockdown_related_protein
datakdrp<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdrp)
datakdrp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdrp)
summary(datakdrp_MA)
model_results <- orchaRd::mod_results(datakdrp_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(datakdrp_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
```

```
p1
I2 <- orchaRd::i2_ml(datakdrp_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 22, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
setwd("C:/Users/v1lliu34/Downloads")
ggsave('related_proteins_knockdown_overall.pdf',width = 15,height = 10,p1)


datakdrp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdrp)
datakdrp2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdrp1)
datakdrp_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = datakdrp2)
summary(datakdrp_MR1)
res2 <- orchaRd::mod_results(datakdrp_MR1, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('relaited_proteins_knockdown_species_moderator.pdf',width =
15,height = 10,p2)

datakdrp_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = datakdrp2)
summary(datakdrp_MR01)
res2 <- orchaRd::mod_results(datakdrp_MR01, mod = "Group", group =
"Author")
res2
p3 <- orchaRd::orchard_plot(res2, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('relaited_proteins_knockdown_Group_moderator wide.pdf',width =
10,height = 30,p3)



# caterpillar plot --------------group
View(Effect_size_cal_PROTEIN_Knockdown_related_protein)
datakdrp<-Effect_size_cal_PROTEIN_Knockdown_related_protein
datakdrp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdrp)
datakdrp2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdrp1)
datakdrp_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = datakdrp2)
summary(datakdrp_MR01)
res2 <- orchaRd::mod_results(datakdrp_MR01, mod = "Group", group =
"Author")
```

```
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('knockdown_related_prteions__Group.pdf',width = 15,height = 10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=datakdrp, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

#--------------related protein of overexpression ----------
View(Effect_size_cal_PROTEIN_Overexpression_related_protein)
dataoerp<-Effect_size_cal_PROTEIN_Overexpression_related_protein
dataoerp<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoerp)
dataoerp_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoerp)
summary(dataoerp_MA)
model_results <- orchaRd::mod_results(dataoerp_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataoerp_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataoerp_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 22, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
setwd("C:/Users/v1lliu34/Downloads")
ggsave('related_proteins_overpression_overall.pdf',width = 15,height =
10,p1)


dataoerp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoerp)
dataoerp2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoerp1)
dataoerp_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = dataoerp2)
summary(dataoerp_MR1)
```

```
res3 <- orchaRd::mod_results(dataoerp_MR1, mod = "Species", group =
"Author")
res3
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('relaited_proteins_overexpression_species_moderator.pdf',width =
15,height = 10,p2)

dataoerp_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataoerp2)
summary(dataoerp_MR01)
res2 <- orchaRd::mod_results(dataoerp_MR01, mod = "Group", group =
"Author")
res2
p3 <- orchaRd::orchard_plot(res2, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('relaited_proteins_overexpression_Group_moderator wide.pdf',width =
10,height =30,p3)



# caterpillar plot --------------group
dataoerp<-Effect_size_cal_PROTEIN_Overexpression_related_protein
dataoerp1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoerp)
dataoerp2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoerp1)
dataoerp_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataoerp2)
summary(dataoerp_MR1)
dataoerp_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataoerp2)
summary(dataoerp_MR01)
res2 <- orchaRd::mod_results(dataoerp_MR01, mod = "Group", group =
"Author")
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('overexpression_related_proteins_Group.pdf',width = 15,height =
10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataoerp, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
```

```
res.tf
funnel(res.tf)

#--------------TG of knockdown ----------
View(Effect_size_cal_Knockdown_TG)
dataT1<-Effect_size_cal_Knockdown_TG
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataT2)
summary(dataT_MA)
model_results <- orchaRd::mod_results(dataT_MA, mod = "1", at = NULL, group
= "Author")
model_results
p1<-orchaRd::orchard_plot(dataT_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataT_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 8.3, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('TG_knockdown_overall.pdf',width = 15,height = 10,p1)


dataT1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataT1)
dataT_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1 |
Author, ~1 | ID), data = dataT2)
summary(dataT_MR1)
resT2 <- orchaRd::mod_results(dataT_MR1, mod = "Species", group = "Author")
resT2
p2 <- orchaRd::orchard_plot(resT2, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
p2
ggsave('TG_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

dataT2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataT1)
dataT_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataT2)
summary(dataT_MR01)
res3 <- orchaRd::mod_results(dataT_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('TG_knockdown_Group_moderator wide.pdf',width = 10,height = 20,p3)
```

```
# caterpillar plot --------------overall
dataT1<-Effect_size_cal_Knockdown_TG
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataT2)
summary(dataT_MA)
model_results <- orchaRd::mod_results(dataT_MA, mod = "1", at = NULL, group
= "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_knockdown_TG_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
dataT1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataT1)
dataT_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1 |
Author, ~1 | ID), data = dataT2)
summary(dataT_MR1)
resT2 <- orchaRd::mod_results(dataT_MR1, mod = "Species", group = "Author")
resT2
p6<-orchaRd::caterpillars(resT2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_knockdown_TG_species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
dataT2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataT1)
dataT_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataT2)
summary(dataT_MR01)
res3 <- orchaRd::mod_results(dataT_MR01, mod = "Group", group = "Author")
res3
p5<-orchaRd::caterpillars(res3, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_knockdown_TG_Group.pdf',width = 15,height = 10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataT2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
```

```
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)


#-----------Gene for TG in Knockdown-------------
#--------------SREBP----------
View(KD_gene_SREBP)
dataT1<-KD_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_SREBP.pdf',width = 5,height = 10,p1)
or
pdf(file = "KD_gene_SREBP", height=5, width=10)

------------SREBP----------
  View(KD_gene_SREBP)
dataT1<-KD_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_SREBP.pdf',width = 5,height = 10,p1)
or
pdf(file = "KD_gene_SREBP", height=5, width=10)

------------LD----------
  View(KD_gene_LD)
dataT1<-KD_gene_LD
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_LD.pdf',width = 5,height = 10,p1)

------------PI3K-AKT----------
  View(KD_gene_PI3K_AKT)
dataT1<-KD_gene_PI3K_AKT
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
```

```
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_PI3K_AKT.pdf',width = 5,height = 10,p1)


------------FAs AE----------
  View(KD_gene_FAs_AE)
dataT1<-KD_gene_FAs_AE
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_FAs_AE.pdf',width = 5,height = 10,p1)

-----------PPAR----------
  View(KD_gene_PPAR)
dataT1<-KD_gene_PPAR
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_PPAR.pdf',width = 5,height = 10,p1)


-----------Insulin----------
  View(KD_gene_insulin)
dataT1<-KD_gene_insulin
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_Insulin.pdf',width = 5,height = 10,p1)

--------------TG of overexpression ----------
  View(Effect_size_cal_Overexpression_TG)
dataToe1<-Effect_size_cal_Overexpression_TG
dataToe2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataToe1)
dataToe_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataToe2)
summary(dataToe_MA)
model_results <- orchaRd::mod_results(dataToe_MA, mod = "1", at = NULL,
group = "Author")
model_results
```

```
p1<-orchaRd::orchard_plot(dataToe_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataToe_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 9.5, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('TG_overexpression_overall.pdf',width = 15,height = 10,p1)


dataToe1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataToe1)
dataToe2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataToe1)
dataToe_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataToe2)
summary(dataToe_MR1)
resToe2 <- orchaRd::mod_results(dataToe_MR1, mod = "Species", group =
"Author")
resToe2
p2 <- orchaRd::orchard_plot(resToe2, mod = "Species", group = "Author",
xlab = "Standardised mean difference")
p2
ggsave('TG_overpression_species_moderator.pdf',width = 15,height = 10,p2)

dataToe2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataToe1)
dataToe_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataToe2)
summary(dataToe_MR01)
res3tg <- orchaRd::mod_results(dataToe_MR01, mod = "Group", group =
"Author")
res3tg
p3 <- orchaRd::orchard_plot(res3tg, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('TG_overexpression_Group_moderator wide.pdf',width = 10,height =
25,p3)


# caterpillar plot --------------overall
dataToe1<-Effect_size_cal_Overexpression_TG
dataToe2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataToe1)
dataToe_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataToe2)
summary(dataToe_MA)
model_results <- orchaRd::mod_results(dataToe_MA, mod = "1", at = NULL,
group = "Author")
model_results
```

```
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_overexpression_TG_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
dataToe1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataToe1)
dataToe2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataToe1)
dataToe_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataToe2)
summary(dataToe_MR1)
resToe2 <- orchaRd::mod_results(dataToe_MR1, mod = "Species", group =
"Author")
resToe2
p6<-orchaRd::caterpillars(resToe2, mod = "ManipType", group = "Species",
xlab = "Standardised mean difference")
p6
ggsave('gene_overexpression_TG_species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
dataToe2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataToe1)
dataToe_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataToe2)
summary(dataToe_MR01)
res3tg <- orchaRd::mod_results(dataToe_MR01, mod = "Group", group =
"Author")
res3tg
p5<-orchaRd::caterpillars(res3tg, mod = "ManipType", group = "Group", xlab
= "Standardised mean difference")
p5
ggsave('gene_overexpression_TG_Group.pdf',width = 15,height = 10,p5)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataToe2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

-----------Ubi----------
  View(OE_gene_Ubi)
dataT1<-OE_gene_Ubi
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
```

```
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_Ubi.pdf',width = 5,height = 10,p1)

-----------FAs_AE----------
  View(OE_gene_FAs_AE)
dataT1<-OE_gene_FAs_AE
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_FAs_AE.pdf',width = 5,height = 10,p1)

-----------JAK_STAT----------
  View(OE_gene_JAK_STAT)
dataT1<-OE_gene_JAK_STAT
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_JAK_STAT.pdf',width = 5,height = 10,p1)

-----------LD----------
  View(OE_gene_LD)
dataT1<-OE_gene_LD
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_LD.pdf',width = 5,height = 10,p1)


-----------PPAR----------
  View(OE_gene_PPAR)
dataT1<-OE_gene_PPAR
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
```

```
ggsave('OE_gene_PPAR.pdf',width = 5,height = 10,p1)

-----------SREBP----------
  View(OE_gene_SREBP)
dataT1<-OE_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_SREBP.pdf',width = 5,height = 10,p1)

-----------insulin----------
  View(OE_gene_Insulin)
dataT1<-OE_gene_Insulin
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_Insulin.pdf',width = 5,height = 10,p1)

--------------lipid of knockdown ----------
  View(Effect_size_cal_Knockdown_Lipid)
datakdl<-Effect_size_cal_Knockdown_Lipid
datakdl<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdl)
datakdl_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdl)
summary(datakdl_MA)
model_results <- orchaRd::mod_results(datakdl_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(datakdl_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(datakdl_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 1.8, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
setwd("C:/Users/v1lliu34/Downloads")
ggsave('lipid_knockdown_overall.pdf',width = 15,height = 10,p1)


datakdl1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdl)
```

```
datakdl2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdl1)
datakdl_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakdl2)
summary(datakdl_MR1)
res2 <- orchaRd::mod_results(datakdl_MR1, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('lipid_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

datakdl_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~group, random = list(~1
| Author, ~1 | ID), data = datakdl2)
summary(datakdl_MR01)
res3 <- orchaRd::mod_results(datakdl_MR01, mod = "group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('lipid_knockdown_Group_moderator.pdf',width = 15,height = 10,p3)

# caterpillar plot --------------overall
datakdl<-Effect_size_cal_Knockdown_Lipid
datakdl<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdl)
datakdl_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdl)
summary(datakdl_MA)
model_results <- orchaRd::mod_results(datakdl_MA, mod = "1", at = NULL,
group = "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_knockdown_lipid_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
datakdl1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdl)
datakdl2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdl1)
datakdl_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datakdl2)
summary(datakdl_MR1)
res2 <- orchaRd::mod_results(datakdl_MR1, mod = "Species", group =
"Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_knockdown_lipid_species.pdf',width = 15,height = 10,p6)
```

```
# caterpillar plot --------------group
datakdl_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~group, random = list(~1
| Author, ~1 | ID), data = datakdl2)
summary(datakdl_MR01)
res3 <- orchaRd::mod_results(datakdl_MR01, mod = "group", group = "Author")
res3
p5<-orchaRd::caterpillars(res3, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_knockdown_lipid_Group.pdf',width = 15,height = 10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=datakdl, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

---------LD----------
  View(KD_gene_LD_on_LD)
dataT1<-KD_gene_LD_on_LD
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('kd_gene_LD ON LD.pdf',width = 5,height = 10,p1)

--------------lipid of overexpression ----------
  View(Effect_size_cal_Overexpression_Lipid)
data1<-Effect_size_cal_Overexpression_Lipid
data2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = data1)
data_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = data2)
summary(data_MA)
model_results <- orchaRd::mod_results(data_MA, mod = "1", at = NULL, group
= "Author")
model_results
p1<-orchaRd::orchard_plot(data_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(data_MA)
```

```
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 5.8, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
setwd("C:/Users/v1lliu34/Downloads")
ggsave('lipid_overexpression_overall.pdf',width = 15,height = 10,p1)


data1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = data1)
data2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = data1)
data_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1 |
Author, ~1 | ID), data = data2)
summary(data_MR1)
res2 <- orchaRd::mod_results(data_MR1, mod = "Species", group = "Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('lipid_overexpression_species_moderator.pdf',width = 15,height =
10,p2)

data2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = data1)
data_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = data2)
summary(data_MR01)
res3 <- orchaRd::mod_results(data_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('lipid_overexpression_Group_moderator.pdf',width = 15,height =
10,p3)

# caterpillar plot --------------overall
data1<-Effect_size_cal_Overexpression_Lipid
data2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = data1)
data_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = data2)
summary(data_MA)
model_results <- orchaRd::mod_results(data_MA, mod = "1", at = NULL, group
= "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_overexpression_lipid_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
```

```
data1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = data1)
data2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = data1)
data_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1 |
Author, ~1 | ID), data = data2)
summary(data_MR1)
res2 <- orchaRd::mod_results(data_MR1, mod = "Species", group = "Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_overexpression_lipid_species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
data2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = data1)
data_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = data2)
summary(data_MR01)
res3 <- orchaRd::mod_results(data_MR01, mod = "Group", group = "Author")
res3
p5<-orchaRd::caterpillars(res3, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_overexpression_lipid_Group.pdf',width = 15,height = 10,p5)

###sensitivity analysis
result1=rma(SMD, vSMD, data=data2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

---------SREBP----------
  View(OE_gene_SREBP)
dataT1<-OE_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_SREBP ON LD.pdf',width = 5,height = 10,p1)

#--------------gene knockdown cholesterol----------
```

```
  View(Effect_size_cal_Knockdown_Cholesterol)
datakdcho<-Effect_size_cal_Knockdown_Cholesterol
datakdcho<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdcho)
datakdcho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdcho)
summary(datakdcho_MA)
model_results <- orchaRd::mod_results(datakdcho_MA, mod = "1", at = NULL,
group = "Author")
model_results
P1<-orchaRd::orchard_plot(datakdcho_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(datakdcho_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 6.5, label =
paste0("italic(I)^{2} == ", round(I2[1],4), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
pdf(file = "gene_knockdown_cholesterol_overall", height=10, width=15)
setwd("C:/Users/v1lliu34/Downloads")
ggsave('cholesterol_knockdown_overall.pdf',width = 15,height = 10,p1)


datakdcho1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdcho)
datakdcho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datakdcho1)
datakdcho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdcho1)
datakdcho_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = datakdcho2)
summary(datakdcho_MR0)
res2 <- orchaRd::mod_results(datakdcho_MR0, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('gene_knockdown_chole_species_moderator.pdf',width = 15,height =
10,p2)

datakdcho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random =
list(~1 | Author, ~1 | ID), data = datakdcho2)
summary(datakdcho_MR01)
res2 <- orchaRd::mod_results(datakdcho_MR01, mod = "Group", group =
"Author")
res2
p3 <- orchaRd::orchard_plot(res2, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('gene_knockdown_chole_Group_moderator.pdf',width = 15,height =
10,p3)
```

```
##forest-----------------
library(metafor)
library(readxl)
View(Effect_size_cal_Knockdown_Cholesterol)
datakdcho<-Effect_size_cal_Knockdown_Cholesterol
datakdcho<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdcho)
datakdcho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
Author),data = datakdcho)
forest(datakdcho_MA)

# caterpillar plot --------------overall
model_results <- orchaRd::mod_results(datakdcho_MA, mod = "1", at = NULL,
group = "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
setwd("C:/Users/v1lliu34/Downloads")
library(ggplot2)
ggsave('gene_knockdown_chole_Group_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
datakdcho1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdcho)
datakdcho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdcho1)
datakdcho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = datakdcho2)
summary(datakdcho_MR01)
res2 <- orchaRd::mod_results(datakdcho_MR01, mod = "Species", group =
"Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_knockdown_chole_Species.pdf',width = 8,height = 10,p6)

# caterpillar plot --------------group
datakdcho1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datakdcho)
datakdcho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datakdcho1)
datakdcho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random =
list(~1 | Author, ~1 | Author), data = datakdcho2)
summary(datakdcho_MR01)
res2 <- orchaRd::mod_results(datakdcho_MR01, mod = "Group", group =
"Author")
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_knockdown_chole_Group.pdf',width = 15,height = 10,p5)
```

```
###sensitivity analysis
result1=rma(SMD, vSMD, data=datakdcho1, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

----------insulin----------
  View(KD_gene_Insulin)
dataT1<-KD_gene_Insulin
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_Insulin ON CHO.pdf',width = 5,height = 10,p1)

----------PPAR----------
  View(KD_gene_PPAR)
dataT1<-KD_gene_PPAR
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_PPAR ON CHO.pdf',width = 5,height = 10,p1)

---------SREBP----------
  View(KD_gene_SREBP)
dataT1<-KD_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_SREBP ON CHO.pdf',width = 5,height = 10,p1)
```

```
--------------gene overexpression cholesterol----------
  View(Effect_size_cal_Overexpression_Cholesterol)
dataoecho<-Effect_size_cal_Overexpression_Cholesterol
dataoecho<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoecho)
dataoecho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoecho)
summary(dataoecho_MA)
model_results <- orchaRd::mod_results(dataoecho_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataoecho_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataoecho_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 2, label =
paste0("italic(I)^{2} == ", round(I2[1],4), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
setwd("C:/Users/v1lliu34/Downloads")
ggsave('cholesterol_overexpression_overall.pdf',width = 15,height = 10,p1)


dataoecho1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoecho)
dataoecho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoecho1)
dataoecho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoecho1)
dataoecho_MR0 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = dataoecho2)
summary(dataoecho_MR0)
res2 <- orchaRd::mod_results(dataoecho_MR0, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('cholesterol_overexpression_species_moderator.pdf',width = 15,height
= 10,p2)

dataoecho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random =
list(~1 | Author, ~1 | ID), data = dataoecho2)
summary(dataoecho_MR01)
res2 <- orchaRd::mod_results(dataoecho_MR01, mod = "Group", group =
"Author")
res2
p3 <- orchaRd::orchard_plot(res2, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('cholesterol_overexpression_Group_moderator.pdf',width = 15,height =
10,p3)
```

```
# caterpillar plot --------------overall
dataoecho<-Effect_size_cal_Overexpression_Cholesterol
dataoecho<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoecho)
dataoecho_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataoecho)
summary(dataoecho_MA)
model_results <- orchaRd::mod_results(dataoecho_MA, mod = "1", at = NULL,
group = "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_overexpression_chole_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
dataoecho<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoecho)
dataoecho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoecho)
dataoecho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | Author), data = dataoecho2)
summary(dataoecho_MR01)
res2 <- orchaRd::mod_results(dataoecho_MR01, mod = "Species", group =
"Author")
res2
p6<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_overexpression_chole_species.pdf',width = 8,height = 10,p6)

# caterpillar plot --------------group
dataoecho1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataoecho)
dataoecho2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataoecho1)
dataoecho_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random =
list(~1 | Author, ~1 | Author), data = dataoecho2)
summary(dataoecho_MR01)
res2 <- orchaRd::mod_results(dataoecho_MR01, mod = "Group", group =
"Author")
res2
p5<-orchaRd::caterpillars(res2, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_overexpression_chole_Group.pdf',width = 15,height = 10,p5)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataoecho1, method="REML")
result1
```

```
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

---------Insulin----------
  View(OE_gene_Insulin)
dataT1<-OE_gene_Insulin
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_Insulin ON CHO.pdf',width = 5,height = 10,p1)

---------LD----------
  View(OE_gene_LD)
dataT1<-OE_gene_LD
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_LD ON CHO.pdf',width = 5,height = 10,p1)

---------SREBP----------
  View(OE_gene_SREBP)
dataT1<-OE_gene_SREBP
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_SREBP ON CHO.pdf',width = 5,height = 10,p1)



--------------TFAs of knockdown ----------
  View(Effect_size_cal_Knockdown_TFAs)
dataTFA1<-Effect_size_cal_Knockdown_TFAs
dataTFA2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA1)
```

```
dataTFA_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataTFA2)
summary(dataTFA_MA)
model_results <- orchaRd::mod_results(dataTFA_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataTFA_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataTFA_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 5.8, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('TFAs_knockdown_overall.pdf',width = 15,height = 10,p1)


dataTFA1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA1)
dataTFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataTFA1)
dataTFA_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataTFA2)
summary(dataTFA_MR1)
res2 <- orchaRd::mod_results(dataTFA_MR1, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('TFAs_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

dataTFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataTFA1)
dataTFA_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataTFA2)
summary(dataTFA_MR01)
res3 <- orchaRd::mod_results(dataTFA_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('TFAs_knockdown_Group_moderator.pdf',width = 15,height = 10,p3)

##Forest------------

View(Effect_size_cal_Knockdown_TFAs)
dataTFA1<-Effect_size_cal_Knockdown_TFAs
dataTFA2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA1)
```

```
dataTFA_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataTFA2)
summary(dataTFA_MA)
P4<-forest(dataTFA_MA)
P4
library(ggplot2)
ggsave('TFAs_knockdown_Forest.pdf',width = 15,height = 10,P4)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataTFA2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)



--------------TFAs of overexpression ----------
  View(Effect_size_cal_Overexpression_TFAs)
dataTFA4<-Effect_size_cal_Overexpression_TFAs
dataTFA5<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA4)
dataTFA_MA1 <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataTFA5)
summary(dataTFA_MA1)
model_results1 <- orchaRd::mod_results(dataTFA_MA1, mod = "1", at = NULL,
group = "Author")
model_results1
p1<-orchaRd::orchard_plot(dataTFA_MA1, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataTFA_MA1)
p1<-orchaRd::orchard_plot(model_results1, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 5.8, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('TFAs_knockdown_overall.pdf',width = 15,height = 10,p1)


dataTFA1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA1)
dataTFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataTFA1)
```

```
dataTFA_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataTFA2)
summary(dataTFA_MR1)
res2 <- orchaRd::mod_results(dataTFA_MR1, mod = "Species", group =
"Author")
res2
p2 <- orchaRd::orchard_plot(res2, mod = "Species", group = "Author", xlab =
"Standardised mean difference")
p2
ggsave('TFAs_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

dataTFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataTFA1)
dataTFA_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataTFA2)
summary(dataTFA_MR01)
res3 <- orchaRd::mod_results(dataTFA_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
ggsave('TFAs_knockdown_Group_moderator.pdf',width = 15,height = 10,p3)

##Forest------------

View(Effect_size_cal_Knockdown_TFAs)
dataTFA1<-Effect_size_cal_Knockdown_TFAs
dataTFA2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataTFA1)
dataTFA_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataTFA2)
summary(dataTFA_MA)
P4<-forest(dataTFA_MA)
P4
library(ggplot2)
ggsave('TFAs_knockdown_Forest.pdf',width = 15,height = 10,P4)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataTFA2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)
```

```
--------------UFAs of knockdown ----------
 library(readxl)
Effect_size_cal_Knockdown_UFAs <- read_excel("M:/Meta analysis/2024-05 meta
analysis/参考文???/基因/DATA/Effect_size_cal_Knockdown_UFAs.xlsx")
View(Effect_size_cal_Knockdown_UFAs)
dataT1<-Effect_size_cal_Knockdown_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataT2)
summary(dataT_MA)
model_results <- orchaRd::mod_results(dataT_MA, mod = "1", at = NULL, group
= "Author")
model_results
p1<-orchaRd::orchard_plot(dataT_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataT_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 3.5, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('UFA_knockdown_overall.pdf',width = 15,height = 10,p1)


dataUFA1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataUFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataUFA1)
dataUFA_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataUFA2)
summary(dataUFA_MR1)
resT2 <- orchaRd::mod_results(dataUFA_MR1, mod = "Species", group =
"Author")
resT2
p2 <- orchaRd::orchard_plot(resT2, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
p2
ggsave('UFA_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

dataUFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataUFA1)
dataUFA_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataUFA2)
summary(dataUFA_MR01)
res3 <- orchaRd::mod_results(dataUFA_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
p3
```

```
ggsave('UFA_knockdown_Group_moderator.pdf',width = 15,height = 22,p3)

# caterpillar plot --------------overall
View(Effect_size_cal_Knockdown_UFAs)
dataT1<-Effect_size_cal_Knockdown_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataT2)
summary(dataT_MA)
model_results <- orchaRd::mod_results(dataT_MA, mod = "1", at = NULL, group
= "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_knockdown_UFAs_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
dataUFA1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataUFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataUFA1)
dataUFA_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataUFA2)
summary(dataUFA_MR1)
resT2 <- orchaRd::mod_results(dataUFA_MR1, mod = "Species", group =
"Author")
resT2
p6<-orchaRd::caterpillars(resT2, mod = "ManipType", group = "Species", xlab
= "Standardised mean difference")
p6
ggsave('gene_knockdown_UFAs_species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
dataUFA2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataUFA1)
dataUFA_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataUFA2)
summary(dataUFA_MR01)
res3 <- orchaRd::mod_results(dataUFA_MR01, mod = "Group", group = "Author")
res3
p5<-orchaRd::caterpillars(res3, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_knockdown_UFAs_Group.pdf',width = 15,height = 10,p5)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataT2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
```

```
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

---------LD----------
  View(KD_gene_LD_on_UFAs)
dataT1<-KD_gene_LD_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_LD_on_UFAs.pdf',width = 5,height = 10,p1)

---------LD----------
  View(KD_gene_PPAR_on_UFAs)
dataT1<-KD_gene_PPAR_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_PPAR_on_UFAs.pdf',width = 5,height = 10,p1)

---------PPAR----------
  View(KD_gene_PPAR_on_UFAs)
dataT1<-KD_gene_PPAR_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_PPAR_on_UFAs.pdf',width = 5,height = 10,p1)

---------SREBP----------
  View(KD_gene_SREBP_on_UFAs)
dataT1<-KD_gene_SREBP_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('KD_gene_SREBP_on_UFAs.pdf',width = 5,height = 10,p1)
```

```
--------------UFA of overexpression ----------
  View(Effect_size_cal_Overexpression_UFAs)
dataufa<-Effect_size_cal_Overexpression_UFAs
dataufa2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataufa)
dataufa_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataufa2)
summary(dataufa_MA)
model_results <- orchaRd::mod_results(dataufa_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataufa_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataufa_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 9, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('ufa_overexpression_overall.pdf',width = 15,height = 10,p1)


dataufa1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataufa)
dataufa2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataufa1)
dataufa_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataufa2)
summary(dataufa_MR1)
resufa2 <- orchaRd::mod_results(dataufa_MR1, mod = "Species", group =
"Author")
resufa2
p2 <- orchaRd::orchard_plot(resufa2, mod = "Species", group = "Author",
xlab = "Standardised mean difference")
p2
ggsave('ufa_overpression_species_moderator.pdf',width = 15,height = 10,p2)

dataufa2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataufa1)
dataufa_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataufa2)
summary(dataufa_MR01)
res3 <- orchaRd::mod_results(dataufa_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
ggsave('ufa_overpression_group_moderator.pdf',width = 15,height = 10,p3)
```

```
# caterpillar plot --------------overall
dataufa<-Effect_size_cal_Overexpression_UFAs
dataufa2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataufa)
dataufa_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataufa2)
summary(dataufa_MA)
model_results <- orchaRd::mod_results(dataufa_MA, mod = "1", at = NULL,
group = "Author")
model_results
p4<-orchaRd::caterpillars(model_results, mod = "1", xlab = "Standardised
mean difference")
p4
ggsave('gene_overexpression_UFA_overall.pdf',width = 15,height = 10,p4)

# caterpillar plot --------------species
dataufa1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataufa1)
dataufa2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataufa1)
dataufa_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataufa2)
summary(dataufa_MR1)
resufa2 <- orchaRd::mod_results(dataufa_MR1, mod = "Species", group =
"Author")
resufa2
p6<-orchaRd::caterpillars(resufa2, mod = "ManipType", group = "Species",
xlab = "Standardised mean difference")
p6
ggsave('gene_overexpression_UFA_species.pdf',width = 15,height = 10,p6)

# caterpillar plot --------------group
dataufa2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataufa1)
dataufa_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataufa2)
summary(dataufa_MR01)
res3 <- orchaRd::mod_results(dataufa_MR01, mod = "Group", group = "Author")
res3
p5<-orchaRd::caterpillars(res3, mod = "ManipType", group = "Group", xlab =
"Standardised mean difference")
p5
ggsave('gene_overexpression_UFA_Group.pdf',width = 15,height = 10,p5)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataufa2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")
```

```
## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)



---------LD----------
  View(OE_gene_LD_on_UFAs)
dataT1<-OE_gene_LD_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_LD_on_UFAs.pdf',width = 5,height = 10,p1)

---------PPAR----------
  View(OE_gene_PPAR_on_UFAs)
dataT1<-OE_gene_PPAR_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_PPAR_on_UFAs.pdf',width = 5,height = 10,p1)

---------SREBP----------
  View(OE_gene_SREBP_on_UFAs)
dataT1<-OE_gene_SREBP_on_UFAs
dataT2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataT1)
dataT_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Gene, ~1 |
Gene),data = dataT2)
summary(dataT_MA)
forest(dataT_MA)
p1<-forest(dataT_MA)
ggsave('OE_gene_SREBP_on_UFAs.pdf',width = 5,height = 10,p1)



--------------w3 of knockdown ----------
  View(Effect_size_cal_Knockdown_w3)
dataw3kd1<-Effect_size_cal_Knockdown_w3
dataw3kd2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw3kd1)
dataw3kd_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataw3kd2)
summary(dataw3kd_MA)
```

```
model_results <- orchaRd::mod_results(dataw3kd_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataw3kd_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataw3kd_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.5, y = 0, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('w3_knockdown_overall.pdf',width = 15,height = 10,p1)


dataw3kd1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw3kd1)
dataw3kd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw3kd1)
dataw3kd_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random =
list(~1 | Author, ~1 | ID), data = dataw3kd2)
summary(dataw3kd_MR1)
resw3kd <- orchaRd::mod_results(dataw3kd_MR1, mod = "Species", group =
"Author")
resw3kd
p2 <- orchaRd::orchard_plot(resw3kd, mod = "Species", group = "Author",
xlab = "Standardised mean difference")
p2
ggsave('w3_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

dataw3kd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw3kd1)
dataw3kd_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = dataw3kd2)
summary(dataw3kd_MR01)
resw3kd3 <- orchaRd::mod_results(dataw3kd_MR01, mod = "Group", group =
"Author")
resw3kd3
p3 <- orchaRd::orchard_plot(resw3kd3, mod = "Group", group = "Author", xlab
= "Standardised mean difference")
p3
ggsave('w3_knockdown_Group_moderator.pdf',width = 15,height = 10,p3)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataw3kd2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
```

```
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)


#--------------w3 of overexpression ----------
  View(Effect_size_cal_Overexpression_w3)
dataw3<-Effect_size_cal_Overexpression_w3
dataw32<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw3)
dataw3_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataw32)
summary(dataw3_MA)
model_results <- orchaRd::mod_results(dataw3_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataw3_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataw3_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 9, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('w3_overexpression_overall.pdf',width = 15,height = 10,p1)


dataw31<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw3)
dataw32 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw31)
dataw3_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataw32)
summary(dataw3_MR1)
resw32 <- orchaRd::mod_results(dataw3_MR1, mod = "Species", group =
"Author")
resw32
p2 <- orchaRd::orchard_plot(resw32, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
p2
ggsave('w3_overpression_species_moderator.pdf',width = 15,height = 10,p2)

dataw32 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw31)
dataw3_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataw32)
summary(dataw3_MR01)
res3 <- orchaRd::mod_results(dataw3_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
```

```
ggsave('w3_overpression_group_moderator.pdf',width = 15,height = 10,p3)


###sensitivity analysis
result1=rma(SMD, vSMD, data=dataw32, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)


--------------w6 of knockdown ----------
  View(Effect_size_cal_Knockdown_w6)
datawkd1<-Effect_size_cal_Knockdown_w6
datawkd2<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datawkd1)
datawkd_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = datawkd2)
summary(datawkd_MA)
model_results <- orchaRd::mod_results(datawkd_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(datawkd_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(datawkd_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 1.2, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('w6_knockdown_overall.pdf',width = 15,height = 10,p1)


datawkd1<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = datawkd1)
datawkd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datawkd1)
datawkd_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = datawkd2)
summary(datawkd_MR1)
reswkd2 <- orchaRd::mod_results(datawkd_MR1, mod = "Species", group =
"Author")
reswkd2
p2 <- orchaRd::orchard_plot(reswkd2, mod = "Species", group = "Author",
xlab = "Standardised mean difference")
```

```
p2
ggsave('w6_knockdown_species_moderator.pdf',width = 15,height = 10,p2)

datawkd2 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = datawkd1)
datawkd_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1
| Author, ~1 | ID), data = datawkd2)
summary(datawkd_MR01)
reswkd3 <- orchaRd::mod_results(datawkd_MR01, mod = "Group", group =
"Author")
reswkd3
p3 <- orchaRd::orchard_plot(reswkd3, mod = "Group", group = "Author", xlab
= "Standardised mean difference")
p3
ggsave('w6_knockdown_Group_moderator.pdf',width = 15,height = 10,p3)


###sensitivity analysis
result1=rma(SMD, vSMD, data=datawkd2, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

--------------w6 of overexpression ----------
  View(Effect_size_cal_Overexpression_w6)
dataw6<-Effect_size_cal_Overexpression_w6
dataw62<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw6)
dataw6_MA <- rma.mv(yi = SMD, V = vSMD, random = list(~1 | Author, ~1 |
ID),data = dataw62)
summary(dataw6_MA)
model_results <- orchaRd::mod_results(dataw6_MA, mod = "1", at = NULL,
group = "Author")
model_results
p1<-orchaRd::orchard_plot(dataw6_MA, mod = "1", group = "Author", xlab =
"Standardised mean difference",transfm = "none", twig.size = 0.5,
trunk.size = 1)
p1
I2 <- orchaRd::i2_ml(dataw6_MA)
p1<-orchaRd::orchard_plot(model_results, mod = "1", xlab = "Standardised
mean difference") +annotate(geom = "text", x = 0.8, y = 6.5, label =
paste0("italic(I)^{2} == ", round(I2[1],2), "*\"%\""), color = "black",
parse = TRUE, size = 5) + scale_fill_manual(values = "#ea5c6f") +
  scale_colour_manual(values = "#ea5c6f")
p1
ggsave('w6_overexpression_overall.pdf',width = 15,height = 10,p1)
```

```
dataw61<-escalc(measure = "SMD", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("SMD", "vSMD"), data = dataw6)
dataw62 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw61)
dataw6_MR1 <- rma.mv(yi = SMD, V = vSMD, mods = ~Species, random = list(~1
| Author, ~1 | ID), data = dataw62)
summary(dataw6_MR1)
resw62 <- orchaRd::mod_results(dataw6_MR1, mod = "Species", group =
"Author")
resw62
p2 <- orchaRd::orchard_plot(resw62, mod = "Species", group = "Author", xlab
= "Standardised mean difference")
p2
ggsave('w6_overpression_species_moderator.pdf',width = 15,height = 10,p2)

dataw62 <- escalc(measure = "CVR", n1i = treat_n, sd1i = treat_sd, m1i =
treat_mean, n2i = control_n, sd2i = control_sd, m2i = control_mean,
var.names = c("lnCVR", "vlnCVR"),data = dataw61)
dataw6_MR01 <- rma.mv(yi = SMD, V = vSMD, mods = ~Group, random = list(~1 |
Author, ~1 | ID), data = dataw62)
summary(dataw6_MR01)
res3 <- orchaRd::mod_results(dataw6_MR01, mod = "Group", group = "Author")
res3
p3 <- orchaRd::orchard_plot(res3, mod = "Group", group = "Author", xlab =
"Standardised mean difference")
ggsave('w6_overpression_group_moderator.pdf',width = 15,height = 10,p3)

###sensitivity analysis
result1=rma(SMD, vSMD, data=dataw62, method="REML")
result1
inf<-influence(result1)
plot(inf)#red points indicates outliers

##conduct classical Egger's test regression analysis
regtest(result1, model="lm")

## conduct trim and fill analysis
res.tf <- trimfill(result1)
res.tf
funnel(res.tf)

#----------circle for genes-----------
library(ggraph)
library(tidygraph)
library(tidyverse)
library(readxl)
Edges <- read_excel("G:/liulily/文章/SCI/2024-05 meta analysis/Meta-
analysis of genes regulating milk fat synthesis in ruminants/data/环状网
络???/Edges.xlsx")
View(Edges)
The_whole_genes_in_articles <- read_excel("G:/liulily/文章/SCI/2024-05 meta
analysis/Meta-analysis of genes regulating milk fat synthesis in ruminants/
data/环状网络???/The whole genes in articles.xlsx")
View(The_whole_genes_in_articles)
length(unique(Edges$From))
length(unique(Edges$to))
```

```
length(unique(The_whole_genes_in_articles$Gene_name))
length(unique(The_whole_genes_in_articles$Group))
length(unique(The_whole_genes_in_articles$Level))


edges=Edges
nodes=Nodes
gene_graph<-tbl_graph(nodes=nodes, edges=edges)
gene_graph

#Edges$From<-as.character(Edges$From)
#Edges$to<-as.character(Edges$to)
#names(Edges)<-c('from','to')
#Edges<-Edges %>%
 # filter(to %in% c('AMPK',"ACACA",'COX2','RPS6KB1') )
#The_whole_genes_in_articles$Correlation <-
as.character(The_whole_genes_in_articles$Correlation)
#names(The_whole_genes_in_articles)<-
c('node_name','node_branch','Correlation','node_level')
#The_whole_genes_in_articles<-The_whole_genes_in_articles %>%
 # filter( node_branch %in%c('AMPK signalling pathway','De novo Fatty acids
metabolism')) %>%
 # filter(node_name %in% c('AMPK',"ACACA",'COX2','RPS6KB1','AMPK signalling
pathway','De novo Fatty acids metabolism') )

gene_graph<-tbl_graph(nodes=Nodes, edges=Edges)

pal=c('#df0307','#fc81be','#05b4ea','#00884e','#8e0180','#a24f20','#073966','#e28006','

p1<-ggraph(gene_graph,layout = 'dendrogram',circular = TRUE) +
# 画网络图的边
  geom_edge_diagonal(aes(color=node1.Group), alpha=0.5, linewidth=0.1) +
# 画网络图d节点
  geom_node_point(aes(size=Counts, color=Group), alpha=0.35) +
##文字标注
  geom_node_text(aes(x = x*1.05, y = y*1.05, label=Gene_name,
angle=node_angle(x, y),filter = leaf, color = Group),size = 2, hjust =
'outward')+
  geom_node_text(aes(label=Gene_name,  filter = !leaf, color =
Group),fontface="bold", size=3.5) +
  scale_size(range = c(2.5, 35)) +  scale_color_manual(values = pal) +
scale_edge_color_manual(values = pal) +
  scale_x_continuous(limits = c(-1.35, 1.35)) +  scale_y_continuous(limits
= c(-1.25, 1.25)) +
  coord_fixed() +
  theme_void() +
  theme(legend.position = "none",
                                        plot.background =
element_rect(fill = "white", color = "white"))

ggsave('Circle_Genes_Pathway.pdf',width = 15,height = 12,p1)
```