library(enrichR)
#Find all DEGs between 5xFAD+APC and 5xFAD regardless of cell-type
global1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA")

#Find DEGs in each cell-type between 5xFAD+APC and 5xFAD
astrocyte1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "Astrocyte")
endothelial1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "Endothelial")
microglia1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "Microglia")
neuron1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "Neuron")
oligodendrocyte1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "Oligodendrocyte")
opc1 <- FindMarkers(ywt_fad_apc, ident.1 = "apc", ident.2 = "fad", group.by = "treatment", assay = "RNA", subset.ident = "OPC")

#Find all DEGs between 5xFAD and WT regardless of cell-type
global2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA")

#Find DEGs in each cell-type between 5xFAD and WT
astrocyte2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "Astrocyte")
endothelial2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "Endothelial")
microglia2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "Microglia")
neuron2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "Neuron")
oligodendrocyte2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "Oligodendrocyte")
opc2 <- FindMarkers(ywt_fad_apc, ident.1 = "fad", ident.2 = "ywt", group.by = "treatment", assay = "RNA", subset.ident = "OPC")

#Enrichment of 5xFAD+APC and 5xFAD Differential expression data
setEnrichrSite("Enrichr")
listEnrichrDbs()
dbs <- listEnrichrDbs()
dbs <- c("GO_Biological_Process_2021")

#Astrocyte Upregulated, Removing all terms with adjusted p-value >0.05
Astro <- astrocyte1
Astrou <- Astro[Astro$avg_log2FC >= 0,]
eAstrou <- enrichr(Astrou$X, dbs)
threshold0 <- eAstrou$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eAstrou$GO_Biological_Process_2021$threshold <- threshold0
eAstrou$GO_Biological_Process_2021 <-
eAstrou$GO_Biological_Process_2021[!grepl("FALSE", eAstrou$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eAstrou$GO_Biological_Process_2021 <-
eAstrou$GO_Biological_Process_2021[, !names(eAstrou$GO_Biological_Process_2021) %in% remove.col, drop = F]
# Enriched terms in eAstrou$GO_Biological_Process_2021
# Astrocyte Downregulated, Removing all terms with adjusted p-value >0.05
Astrod <- Astro[Astro$avg_log2FC <= 0,]
eAstrod <- enrichr(Astrod$X, dbs)
threshold0 <- eAstrod$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eAstrod$GO_Biological_Process_2021$threshold <- threshold0
eAstrod$GO_Biological_Process_2021 <-
eAstrod$GO_Biological_Process_2021[!grepl("FALSE", eAstrod$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eAstrod$GO_Biological_Process_2021 <-
eAstrod$GO_Biological_Process_2021[, !names(eAstrod$GO_Biological_Process_2021) %in% remove.col, drop = F]
# Enriched terms in eAstrod$GO_Biological_Process_2021
# Endothelial Upregulated, Removing all terms with adjusted p-value >0.05
Endou <- endothelial1
Endou <- Endou[Endou$avg_log2FC >= 0,]
eEndou <- enrichr(Endou$X, dbs)
threshold0 <- eEndou$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eEndou$GO_Biological_Process_2021$threshold <- threshold0
eEndou$GO_Biological_Process_2021 <-
eEndou$GO_Biological_Process_2021[!grepl("FALSE", eEndou$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eEndou$GO_Biological_Process_2021 <-
eEndou$GO_Biological_Process_2021[, !names(eEndou$GO_Biological_Process_2021) %in% remove.col, drop = F]
# Enriched terms in eEndou$GO_Biological_Process_2021
# Endothelial Downregulated, Removing all terms with adjusted p-value >0.05
Endod <- Endou[Endou$avg_log2FC <= 0,]
eEndod <- enrichr(Endod$X, dbs)
threshold0 <- eEndod$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eEndod$GO_Biological_Process_2021$threshold <- threshold0
#Enriched terms in eEndod$GO_Biological_Process_2021
#Microglia Upregulated, Removing all terms with adjusted p-value >0.05

Micro <- microglia1
Microu <- Micro[Micro$avg_log2FC >=0, ]
eMicrou <- enrichr(Microu$X, dbs)
threshold0 <- eMicrou$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eMicrou$GO_Biological_Process_2021$threshold <- threshold0
eMicrou$GO_Biological_Process_2021[!grepl("FALSE", eMicrou$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eMicrou$GO_Biological_Process_2021[,,!names(eMicrou$GO_Biological_Process_2021) %in% remove.col, drop = F]

#Enriched terms in e-endod$GO_Biological_Process_2021
#Microglia Downregulated, Removing all terms with adjusted p-value >0.05

Microd <- Micro[Micro$avg_log2FC <=0, ]
eMicrod <- enrichr(Microd$X, dbs)
threshold0 <- eMicrod$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eMicrod$GO_Biological_Process_2021$threshold <- threshold0
eMicrod$GO_Biological_Process_2021[!grepl("FALSE", eMicrod$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eMicrod$GO_Biological_Process_2021[,,!names(eMicrod$GO_Biological_Process_2021) %in% remove.col, drop = F]

#Enriched terms in eNeuro$GO_Biological_Process_2021
#Neuron Upregulated, Removing all terms with adjusted p-value >0.05

Neuro <- neuron1
Neurou <- Neuro[Neuro$avg_log2FC >=0, ]
eNeurou <- enrichr(Neurou$X, dbs)
threshold0 <- eNeurou$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eNeurou$GO_Biological_Process_2021$threshold <- threshold0
eNeurou$GO_Biological_Process_2021[!grepl("FALSE", eNeurou$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eNeurou$GO_Biological_Process_2021[,,!names(eNeurou$GO_Biological_Process_2021) %in% remove.col, drop = F]
eNeurou$GO_Biological_Process_2021[,!names(eNeurou$GO_Biological_Process_2021) %in% remove.col, drop = F]

# Enriched terms in eNeurou$GO_Biological_Process_2021
# Neuron Downregulated, Removing all terms with adjusted p-value >0.05
Neurod <- Neuro[Neuro$avg_log2FC <=0, ]
eNeurod <- enrichr(NeurodX,dbs)
threshold0 <- eNeurod$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eNeurod$GO_Biological_Process_2021$threshold <- threshold0
eNeurod$GO_Biological_Process_2021 <- eNeurod$GO_Biological_Process_2021[!grepl("FALSE",eNeurod$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eNeurod$GO_Biological_Process_2021 <- eNeurod$GO_Biological_Process_2021[,!names(eNeurod$GO_Biological_Process_2021) %in% remove.col, drop = F]

# Enriched terms in eNeurod$GO_Biological_Process_2021
# Oligodendrocyte Upregulated, Removing all terms with adjusted p-value >0.05
Oligo <- oligodendrocyte1
Oligou <- Oligo[Oligo$avg_log2FC >=0, ]
eOligou <- enrichr(OligouX,dbs)
threshold0 <- eOligou$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eOligou$GO_Biological_Process_2021$threshold <- threshold0
eOligou$GO_Biological_Process_2021 <- eOligou$GO_Biological_Process_2021[!grepl("FALSE",eOligou$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eOligou$GO_Biological_Process_2021 <- eOligou$GO_Biological_Process_2021[,!names(eOligou$GO_Biological_Process_2021) %in% remove.col, drop = F]

# Enriched terms in eOligou$GO_Biological_Process_2021
# Oligodendrocyte Downregulated, Removing all terms with adjusted p-value >0.05
Oligod <- Oligo[Oligo$avg_log2FC <=0, ]
eOligod <- enrichr(OligodX,dbs)
threshold0 <- eOligod$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eOligod$GO_Biological_Process_2021$threshold <- threshold0
eOligod$GO_Biological_Process_2021 <- eOligod$GO_Biological_Process_2021[!grepl("FALSE",eOligod$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eOligod$GO_Biological_Process_2021 <- eOligod$GO_Biological_Process_2021[,!names(eOligod$GO_Biological_Process_2021) %in% remove.col, drop = F]

# Enriched terms in eOligod$GO_Biological_Process_2021
# OPC Upregulated, Removing all terms with adjusted p-value >0.05
OPC <- opc1
OPCu <- OPC[OPC$avg_log2FC >=0, ]
eOPCu <- enrichr(OPCu$X,dbs)
threshold0 <- eOPCu$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eOPCu$GO_Biological_Process_2021$threshold <- threshold0
eOPCu$GO_Biological_Process_2021[!grepl("FALSE",eOPCu$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eOPCu$GO_Biological_Process_2021[,
!names(eOPCu$GO_Biological_Process_2021) %in% remove.col, drop = F]
#Enriched terms in eOPCu$GO_Biological_Process_2021

#OPC Downregulated, Removing all terms with adjusted p-value >0.05
OPCd <- OPC[OPC$avg_log2FC <=0, ]
eOPCd <- enrichr(OPCd$X,dbs)
threshold0 <- eOPCd$GO_Biological_Process_2021$Adjusted.P.value < 0.05
eOPCd$GO_Biological_Process_2021$threshold <- threshold0
eOPCd$GO_Biological_Process_2021[!grepl("FALSE",eOPCd$GO_Biological_Process_2021$threshold),]
remove.col <- "threshold"
eOPCd$GO_Biological_Process_2021[,
!names(eOPCd$GO_Biological_Process_2021) %in% remove.col, drop = F]
#Enriched terms in eOPCd$GO_Biological_Process_2021
#Clean Environment
rm(Astro, Endo, Micro, Neuro, Oligo, OPC, Astrod, Astrou, dbs,
   Endod, Endou, Microd, Microu, Neurod, Neurou, Oligod, Oligou, OPCd, OPCu, remove.col, threshold0)