**Non-targeted metabolomics data processing and peak annotation：**

The raw data were converted to the mzXML format using ProteoWizard and processed with an in-house program, which was developed using R 3.6.0 and based on XCMS, for peak detection, extraction, alignment, and integration. Then an in-house MS2 database (BiotreeDB) was applied in metabolite annotation. The cutoff for annotation was set at 0.3.

**The program used for peak discrimination, filtering, alignment and CAMERA analysis the in LC-(+)ESI-MS data:**

rm(list=ls(all=TRUE)）

library(Biobase)

library(xcms)

library(multtest)

library(CAMERA)

sessionInfo()

xs<-xcmsSet(profmethod="binlin",method="centWave",ppm=25, peakwidth=c(5,30), snthresh =20,prefilter=c(3,100),integrate=1, mzdiff =0.05)

xs <-group(xs,bw=10,minfrac=0.5,mzwid=0.25)

save(xs,file="xs.Rda")

ret.xs.obiwarp <-retcor(xs,method="obiwarp",plottype="deviation")

ret.xs.obiwarp<-group(ret.xs.obiwarp, bw=10,minfrac=0.5,mzwid=0.25)

ret.xs.obiwarp

fill.ret.xs.obiwarp<-fillPeaks(ret.xs.obiwarp)

fill.ret.xs.obiwarp

save(fill.ret.xs.obiwarp, file="fill.ret.xs.obiwarp.Rda")

an.1<-annotate(fill.ret.xs.obiwarp,sigma=6,perfwhm=0.3,cor\_eic\_th=0.75,maxcharge=3,maxiso=3,mzabs=0.03,multiplier=3,polarity="positive")

peaklist.1<-getPeaklist(an.1)

write.csv(peaklist.1,file='annotated.1.csv')

report.fill.ret.xs.obiwarp<-diffreport(fill.ret.xs.obiwarp,"1","2",eicmax=5000,file="diet")

save(report.fill.ret.xs.obiwarp,file="report.fill.ret.xs.obiwarp.Rad")

**The program used for the LC-(-)ESI-MS data:**

rm(list=ls(all=TRUE)）

library(Biobase)

library(xcms)

library(multtest)

library(CAMERA)

sessionInfo()

xs<-xcmsSet(profmethod="binlin",method="centWave",ppm=25, peakwidth=c(5,30), snthresh =20,prefilter=c(3,100),integrate=1, mzdiff =0.05)

xs <-group(xs,bw=10,minfrac=0.5,mzwid=0.25)

save(xs,file="xs.Rda")

ret.xs.obiwarp <-retcor(xs,method="obiwarp",plottype="deviation")

ret.xs.obiwarp<-group(ret.xs.obiwarp, bw=10,minfrac=0.5,mzwid=0.25)

ret.xs.obiwarp

fill.ret.xs.obiwarp<-fillPeaks(ret.xs.obiwarp)

fill.ret.xs.obiwarp

save(fill.ret.xs.obiwarp, file="fill.ret.xs.obiwarp.Rda")

an.1<-annotate(fill.ret.xs.obiwarp,sigma=6,perfwhm=0.3,cor\_eic\_th=0.75,maxcharge=3,maxiso=3,mzabs=0.03,multiplier=3,polarity="negative")

peaklist.1<-getPeaklist(an.1)

write.csv(peaklist.1,file='annotated.1.csv')

report.fill.ret.xs.obiwarp<-diffreport(fill.ret.xs.obiwarp,"1","2",eicmax=5000,file="diet")

save(report.fill.ret.xs.obiwarp,file="report.fill.ret.xs.obiwarp.Rad")