

Radiomic features parallel RNA-seq analysis and enrichment

Carla Casanova

2022-06-13

```
library(limma)
library(sva)
library(ggplot2)
library(org.Hs.eg.db)
library(annotate)
library(hgu133plus2.db)
library(clusterProfiler)
library(enrichplot)
```

This analysis will be performed with counts from **sputum samples**:

```
load("/Users/carlacasanovasuarez/Documents/Master Bioinformatics UAB/Prácticas Radiomics/Radiomic features")
load("/Users/carlacasanovasuarez/Documents/Master Bioinformatics UAB/Prácticas Radiomics/Radiomic features")
load("/Users/carlacasanovasuarez/Documents/Master Bioinformatics UAB/Prácticas Radiomics/Radiomic features")

variables_interest <- data.frame(Sex = as.factor(phenoDataFrame$SEX), Age = phenoDataFrame$AGE,
  Dwalk = phenoDataFrame$DWALK, BMI = phenoDataFrame$BMI, Smoke_history = phenoDataFrame$SUSMHS,
  Years_smoke = phenoDataFrame$SUSMYR, Cough = as.factor(phenoDataFrame$COUGH),
  ex_first_year = phenoDataFrame$Y1EXBS, Group = as.factor(phenoDataFrame$GROUP_bin),
  N_cigarette_day = phenoDataFrame$SUCGSMDY, Cr_bronchitis = as.factor(phenoDataFrame$CBRONCH),
  Cr_wheezeeng = as.factor(phenoDataFrame$ATS3EG), history_asthma = as.factor(phenoDataFrame$ATS5G),
  fume_expose = as.factor(phenoDataFrame$ATS6C), dusty_expose = as.factor(phenoDataFrame$ATS6B),
  phlegm = as.factor(phenoDataFrame$PHLEGM), heart_failure = as.factor(phenoDataFrame$ATS8F),
  stroke = as.factor(phenoDataFrame$ATS8E), diabetes = as.factor(phenoDataFrame$ATS8L),
  osteoporosis = as.factor(phenoDataFrame$ATS8H), FEVVCVD = phenoDataFrame$FEVVCVD,
  FEV1PSPC = phenoDataFrame$FEV1PSPC, TLC = phenoDataFrame$TLC, FRC = phenoDataFrame$FRC,
  Low_percentile = phenoDataFrame$LOW15PCT, row.names = rownames(phenoDataFrame))

# Code for removing columns with some NA
variables_interest <- variables_interest[, apply(variables_interest, 2, function(x) !any(is.na(x)))]
```

Add radiomic features without grouping them

```
identical(colnames(rdr_assay), rownames(variables_interest))
```

[1] TRUE

```
variables_interest <- cbind(variables_interest, t(rdr_assay))
```

Select counts

```
countData <- counts.ok[rowSums(counts.ok) > 10, ]
```

count unique values for each variable

```
sapply(lapply(variables_interest, unique), length)
```

```

##                               Sex
##                               2
##                               Age
##                               25
##                               Dwalk
##                               98
##                               BMI
##                               124
##                               Smoke_history
##                               1
##                               Years_smoke
##                               37
##                               Cough
##                               2
##                               Group
##                               2
##                               N_cigarrete_day
##                               18
##                               Cr_bronchitis
##                               2
##                               Cr_wheezeng
##                               2
##                               history_asthma
##                               2
##                               fume_expose
##                               2
##                               dusty_expose
##                               2
##                               phlegm
##                               2
##                               heart_failure
##                               2
##                               stroke
##                               2
##                               diabetes
##                               2
##                               osteoporosis
##                               2
##                               FEVVCVD
##                               47
##                               FEV1PSPC
##                               115
##                               Elongation.original
##                               125
##                               Flatness.original
##                               125
##                               LeastAxisLength.original
##                               125
##                               MajorAxisLength.original
##                               125
##                               Maximum2DDiameterColumn.original
##                               125
##                               Maximum2DDiameterRow.original
##                               125

```

```

##           Maximum2DDiameterSlice.original      125
##           Maximum3DDiameter.original        125
##           MeshVolume.original            125
##           MinorAxisLength.original       125
##           Sphericity.original          125
##           SurfaceArea.original         125
##           SurfaceVolumeRatio.original   125
##           VoxelVolume.original         125
##           10Percentile.original        125
##           90Percentile.original        125
##           Energy.original             125
##           Entropy.original            125
##           InterquartileRange.original  125
##           Kurtosis.original           125
##           Maximum.original            125
##           MeanAbsoluteDeviation.original 125
##           Mean.original               125
##           Median.original              125
##           Minimum.original             125
##           Range.original               125
##           RobustMeanAbsoluteDeviation.original 125
##           RootMeanSquared.original     125
##           Skewness.original            125
##           TotalEnergy.original          125
##           Uniformity.original          125
##           Variance.original             125
##           Autocorrelation.original      125

```

```

##           ClusterProminence.original      125
##           ClusterShade.original        125
##           ClusterTendency.original     125
##           Contrast.original         125
##           Correlation.original       125
##           DifferenceAverage.original  125
##           DifferenceEntropy.original 125
##           DifferenceVariance.original 125
##           Id.original              125
##           Idm.original             125
##           Idmn.original            125
##           Idn.original             125
##           Imc1.original            125
##           Imc2.original            125
##           InverseVariance.original   125
##           JointAverage.original     125
##           JointEnergy.original      125
##           JointEntropy.original     125
##           MCC.original             125
##           MaximumProbability.original 125
##           SumAverage.original       125
##           SumEntropy.original        125
##           SumSquares.original        125
##           GrayLevelNonUniformity.original 125
##           GrayLevelNonUniformityNormalized.original 125
##           GrayLevelVariance.original    125
##           HighGrayLevelRunEmphasis.original 125

```

```

##          LongRunEmphasis.original      125
##          LongRunHighGrayLevelEmphasis.original      125
##          LongRunLowGrayLevelEmphasis.original      125
##          LowGrayLevelRunEmphasis.original      125
##          RunEntropy.original      125
##          RunLengthNonUniformity.original      125
##          RunLengthNonUniformityNormalized.original      125
##          RunPercentage.original      125
##          RunVariance.original      125
##          ShortRunEmphasis.original      125
##          ShortRunHighGrayLevelEmphasis.original      125
##          ShortRunLowGrayLevelEmphasis.original      125
##          HighGrayLevelZoneEmphasis.original      125
##          LargeAreaEmphasis.original      125
##          LargeAreaHighGrayLevelEmphasis.original      125
##          LargeAreaLowGrayLevelEmphasis.original      125
##          LowGrayLevelZoneEmphasis.original      125
##          SizeZoneNonUniformity.original      125
##          SizeZoneNonUniformityNormalized.original      125
##          SmallAreaEmphasis.original      125
##          SmallAreaHighGrayLevelEmphasis.original      125
##          SmallAreaLowGrayLevelEmphasis.original      125
##          ZoneEntropy.original      125
##          ZonePercentage.original      125
##          ZoneVariance.original      125
##          DependenceEntropy.original      125
##          DependenceNonUniformity.original      125

```

```

##      DependenceNonUniformityNormalized.original
##                                         125
##      DependenceVariance.original
##                                         125
##      HighGrayLevelEmphasis.original
##                                         125
##      LargeDependenceEmphasis.original
##                                         125
## LargeDependenceHighGrayLevelEmphasis.original
##                                         125
## LargeDependenceLowGrayLevelEmphasis.original
##                                         125
##      LowGrayLevelEmphasis.original
##                                         125
##      SmallDependenceEmphasis.original
##                                         125
## SmallDependenceHighGrayLevelEmphasis.original
##                                         125
## SmallDependenceLowGrayLevelEmphasis.original
##                                         125
##      Busyness.original
##                                         125
##      Coarseness.original
##                                         125
##      Complexity.original
##                                         125
##      Strength.original
##                                         125
##  

# Remove variables with just one factor
variables_interest[, "Smoke_history"] <- NULL  

r.features <- rownames(rdr_assay)
# Features que faltan por calcular small.r.features <- r.features[25]  

# Prepare data in object: variables_interest
names(variables_interest)[names(variables_interest) == "10Percentile.original"] <- "X10Percentile.original"
names(variables_interest)[names(variables_interest) == "90Percentile.original"] <- "X90Percentile.original"  

# Prepare data in object: small.r.features
r.features[15] <- "X10Percentile.original"
r.features[16] <- "X90Percentile.original"

```

Compute analysis for individual features by iterating (code parallelize):

```

library(parallel)  

# Use the detectCores() function to find the number of cores in system
no_cores <- detectCores()  

# Setup cluster: good practice not to use all the cores Don't use all the cores
# at ISGlobal's cluster!!
clust <- makeCluster(no_cores - 3) #This line will take time  

# Export objects from global environment

```

```

clusterExport(cl = clust, varlist = c("variables_interest", "countData", "r.features"))

# Export packages to use
clusterEvalQ(clust, {
  library(tidyverse)
  library(limma)
  library(sva)
})

de_radiomic_features_indv <- function(x) {

  # Null formula
  m.model <- "~ Group + Sex + Age + Dwalk + FEV1PSPC + fume_expose + dusty_expose + history_asthma + Cough + BMI + Cr_wheezeng"

  # -----SVA----- Create a model with the feature and a null model
  mod1 <- model.matrix(formula(paste(m.model, x, sep = "+")), data = variables_interest)
  mod0 <- model.matrix(~Group + Sex + Age + Dwalk + FEV1PSPC + fume_expose + dusty_expose +
    history_asthma + Cough + BMI + Cr_wheezeng, data = variables_interest)

  # This estimates the required number of surrogate variables
  res <- svaseq(countData, mod1, mod0)
  # Add SVs to column data information
  variables_interest_sva <- data.frame(variables_interest, res$sv)

  # Add sva names to formula
  sva.names <- colnames(variables_interest_sva[, (ncol(variables_interest_sva) +
    1 - res$n.sv):ncol(variables_interest_sva)])
  sva.collapsed <- paste(sva.names, collapse = "+")

  # -----VOOM----- Normalize data with voom and add tumor stage as
  # covariate in design
  design <- model.matrix(formula(paste(m.model, x, sva.collapsed, sep = "+")),
    data = variables_interest_sva)
  v <- voom(countData, design = design, plot = FALSE)

  # fit the model
  fit <- lmFit(v, design)
  fit <- eBayes(fit)

  # Store the object
  save(fit, file = paste("/Users/carlacasanovasuzarez/Desktop/Radiomic features models (indiv)/",
    x, ".rda", sep = ""))
}

# With parallel
system.time(result <- parLapply(clust, r.features, de_radiomic_features_indv))
# Good practise to do that at the end
stopCluster(clust)

```

Results DE of individual radiomic features

Check summaries of voom results for each feature:

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Elongation.original.rda")

summa.fit.elongation <- decideTests(fit)

summary(summa.fit.elongation)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           555          0    75     0     0       0             0
## NotSig        22926        48525 48393 48525 48523     48525         48525
## Up            25044          0   57     0     2       0             0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0           0             0             0       0             0
## NotSig        48525        48525          48525       48525         48525
## Up            0           0             0             0       0             0
##          Elongation.original   X1      X2      X3      X4      X5      X6      X7      X8
## Down           0 18468 16189 14065 12406 10547 10701 7086 7190
## NotSig        48525 12772 19790 21872 25064 26823 28379 32507 33637
## Up            0 17285 12546 12588 11055 11155 9445 8932 7698
##          X9      X10     X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down          8179 7918 8317 5548 5382 5633 4567 4149 3123 2597 2755
## NotSig      32403 32542 33291 36394 36443 37176 38873 40133 41220 43549 43252
## Up            7943 8065 6917 6583 6700 5716 5085 4243 4182 2379 2518

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Flatness.original.rda")

summa.fit.flatness <- decideTests(fit)
summary(summa.fit.flatness)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           606          0    87     0     0       0             0
## NotSig        22749        48525 48388 48525 48523     48525         48525
## Up            25170          0   50     0     2       0             0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0           0             0             0       0             0
## NotSig        48525        48525          48525       48525         48525
## Up            0           0             0             0       0             0
##          Flatness.original   X1      X2      X3      X4      X5      X6      X7      X8      X9
## Down           0 18540 16224 14047 12129 10471 10708 7176 7291 8163
## NotSig        48525 12702 19698 21934 25785 27074 28395 32428 33398 32420
## Up            0 17283 12603 12544 10611 10980 9422 8921 7836 7942
##          X10     X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down          7838 8316 5592 5342 5604 4579 4298 2838 2672 2637
## NotSig      32645 33281 36281 36438 37275 39014 39929 41713 43501 43186
## Up            8042 6928 6652 6745 5646 4932 4298 3974 2352 2702

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LeastAxisLength.original.rda")

summa.fit.leastAxis <- decideTests(fit)
summary(summa.fit.leastAxis)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           580          0    68     0     0       0             0
## NotSig        22923        48525 48419 48525 48523     48525         48525
## Up            25022          0   38     0     2       0             0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY

```

```

## Down 0 0 0 0 0
## NotSig 48525 48525 48525 48525 48525
## Up 0 0 0 0 0
## LeastAxisLength.original X1 X2 X3 X4 X5 X6 X7 X8
## Down 0 18561 16207 14003 12204 10448 10671 6930 7270
## NotSig 48525 12691 19717 22008 25625 27104 28445 32808 33491
## Up 0 17273 12601 12514 10696 10973 9409 8787 7764
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down 8133 7845 8316 5581 5317 5627 4645 4347 2835 2673 2610
## NotSig 32421 32677 33271 36288 36499 37220 38844 39838 41731 43448 43221
## Up 7971 8003 6938 6656 6709 5678 5036 4340 3959 2404 2694

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/MajorAxisLength.original.rda")

summa.fit.majorAxis <- decideTests(fit)
summary(summa.fit.majorAxis)

## (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down 580 0 48 0 1 0 0
## NotSig 22782 48525 48443 48525 48522 48525 48525
## Up 25163 0 34 0 2 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down 0 0 0 0 0 0
## NotSig 48525 48525 48525 48525 48525 48525
## Up 0 0 0 0 0 0
## MajorAxisLength.original X1 X2 X3 X4 X5 X6 X7 X8
## Down 0 18406 16187 14057 12345 10543 10726 6985 7184
## NotSig 48525 12893 19711 21898 25231 26851 28320 32860 33563
## Up 0 17226 12627 12570 10949 11131 9479 8680 7778
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down 8127 7798 8295 5575 5362 5604 4680 4332 2939 2652 2583
## NotSig 32475 32742 33312 36363 36429 37264 38721 39875 41581 43487 43227
## Up 7923 7985 6918 6587 6734 5657 5124 4318 4005 2386 2715

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum2DDiameterColumn.original.rda")

summa.fit.2ddCol <- decideTests(fit)
summary(summa.fit.2ddCol)

## (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down 565 0 53 0 0 0 0
## NotSig 22755 48525 48439 48525 48523 48525 48525
## Up 25205 0 33 0 2 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down 0 0 0 0 0 0
## NotSig 48525 48525 48525 48525 48525 48525
## Up 0 0 0 0 0 0
## Maximum2DDiameterColumn.original X1 X2 X3 X4 X5 X6
## Down 0 18555 16166 13981 12471 10515 10711
## NotSig 48525 12764 19831 22041 24983 26919 28254
## Up 0 17206 12528 12503 11071 11091 9560
## X7 X8 X9 X10 X11 X12 X13 X14 X15 X16 X17 X18
## Down 6706 7370 8065 7879 8325 5499 5432 5597 4588 4756 2893 2547
## NotSig 33300 33377 32565 32428 33381 36498 36353 37347 38895 39019 41589 43706
## Up 8519 7778 7895 8218 6819 6528 6740 5581 5042 4750 4043 2272

```

```

##          X19
## Down    2556
## NotSig 43204
## Up     2765
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum2DDiameterRow.original

summa.fit.2ddRow <- decideTests(fit)
summary(summa.fit.2ddRow)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down      592           0     81     0     1       0           0
## NotSig   22690         48525 48402 48525 48522     48525       48525
## Up       25243           0     42     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0             0           0           0       0       0           0
## NotSig   48525         48525           48525       48525       48525       48525
## Up       0             0           0           0       0       0           0
##          Maximum2DDiameterRow.original   X1     X2     X3     X4     X5     X6     X7
## Down      0 18523 16188 14021 12381 10564 10716 7088
## NotSig   48525 12760 19772 21968 25195 26853 28329 32590
## Up       0 17242 12565 12536 10949 11108 9480 8847
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down     7270 8119 7833 8233 5571 5354 5537 4617 4327 2936 2708 2552
## NotSig  33472 32440 32730 33479 36310 36434 37433 38811 39896 41597 43391 43294
## Up      7783 7966 7962 6813 6644 6737 5555 5097 4302 3992 2426 2679
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum2DDiameterSlice.original

summa.fit.2ddSlic <- decideTests(fit)
summary(summa.fit.2ddSlic)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down      567           0     38     0     1       0           0
## NotSig   23001         48525 48455 48525 48522     48525       48525
## Up       24957           0     32     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0             0           0           0       0       0           0
## NotSig   48525         48525           48525       48525       48525       48525
## Up       0             0           0           0       0       0           0
##          Maximum2DDiameterSlice.original   X1     X2     X3     X4     X5     X6
## Down      0 18491 16203 14033 12319 10479 10710
## NotSig   48525 12786 19674 21966 25222 26967 28332
## Up       0 17248 12648 12526 10984 11079 9483
##          X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down     6963 7173 8117 7871 8270 5582 5355 5613 4708 4360 2971 2688
## NotSig  32904 33581 32503 32595 33410 36318 36443 37269 38630 39843 41500 43415
## Up      8658 7771 7905 8059 6845 6625 6727 5643 5187 4322 4054 2422
##          X19
## Down     2563
## NotSig  43274
## Up      2688
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum3DDiameter.original.rda

summa.fit.3ddDia <- decideTests(fit)

```

```

summary(summa.fit.3ddDia)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           573          0    55     0     0       0           0
## NotSig        22729        48525 48437 48525 48523     48525       48525
## Up            25223          0    33     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0           0           0           0       0       0           0
## NotSig        48525        48525          48525       48525       48525       48525
## Up             0           0           0           0       0       0           0
##          Maximum3DDiameter.original X1     X2     X3     X4     X5     X6     X7
## Down           0 18502 16192 13983 12467 10558 10732 6809
## NotSig        48525 12827 19732 22055 24995 26848 28232 33285
## Up             0 17196 12601 12487 11063 11119 9561 8431
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7305 8070 7918 8364 5487 5426 5608 4690 4729 2849 2594 2607
## NotSig        33415 32634 32338 33376 36537 36361 37319 38670 39090 41687 43624 43143
## Up            7805 7821 8269 6785 6501 6738 5598 5165 4706 3989 2307 2775

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/MeshVolume.original.rda")

summa.fit.MeshVol <- decideTests(fit)
summary(summa.fit.MeshVol)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           587          0    62     0     0       0           0
## NotSig        22685        48525 48428 48525 48523     48525       48525
## Up            25253          0    35     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0           0           0           0       0       0           0
## NotSig        48525        48525          48525       48525       48525       48525
## Up             0           0           0           0       0       0           0
##          MeshVolume.original X1     X2     X3     X4     X5     X6     X7     X8
## Down           0 18515 16187 13928 12386 10569 10688 6677 7205
## NotSig        48525 12794 19795 22171 25162 26849 28376 33349 33553
## Up             0 17216 12543 12426 10977 11107 9461 8499 7767
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          8121 7780 8272 5534 5356 5645 4661 4308 2904 2665 2632
## NotSig        32446 32791 33410 36415 36426 37214 38738 39932 41621 43453 43138
## Up            7958 7954 6843 6576 6743 5666 5126 4285 4000 2407 2755

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/MinorAxisLength.original.rda")

summa.fit.MinAxis <- decideTests(fit)
summary(summa.fit.MinAxis)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           571          0    74     0     0       0           0
## NotSig        22780        48525 48415 48525 48523     48525       48525
## Up            25174          0    36     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0           0           0           0       0       0           0
## NotSig        48525        48525          48525       48525       48525       48525
## Up             0           0           0           0       0       0           0
##          MinorAxisLength.original X1     X2     X3     X4     X5     X6     X7     X8

```

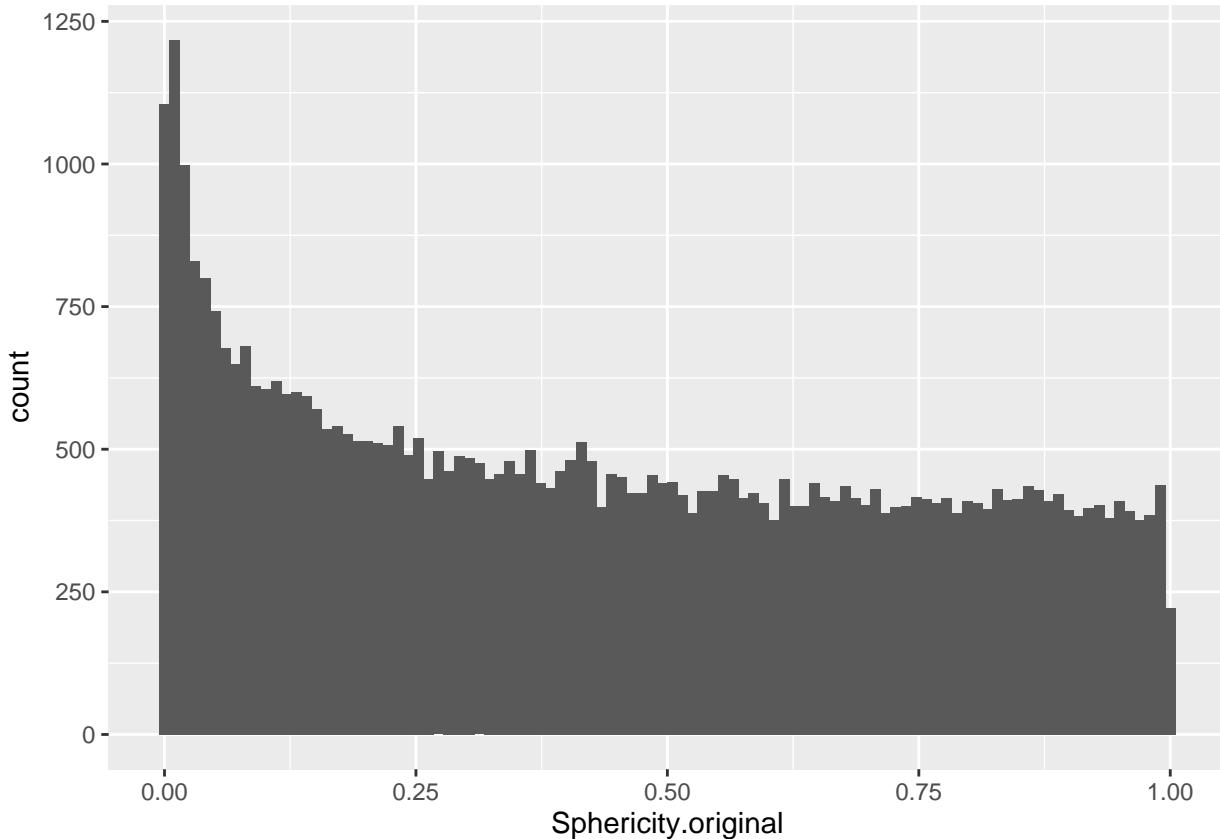
```

## Down          0 18580 16214 14034 12440 10541 10767 7103 7316
## NotSig       48525 12671 19722 21952 25012 26889 28194 32621 33457
## Up           0 17274 12589 12539 11073 11095 9564 8801 7752
## X9    X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down     8092  7828  8339  5558  5397  5624  4523  4730  2823  2611  2798
## NotSig   32600 32510 33403 36339 36407 37291 38961 39030 41766 43602 43115
## Up      7833  8187  6783  6628  6721  5610  5041  4765  3936  2312  2612
load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/Sphericity.original.rda")

# Store: toptable, p.value, summary
summa.fit.sphe <- decideTests(fit)
toptable.sphericity <- topTable(fit, coef = "Sphericity.original", number = dim(counts.ok)[1])
toptable.sphericity <- toptable.sphericity[order(toptable.sphericity$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Sphericity.original)) + geom_histogram(bins = 100)

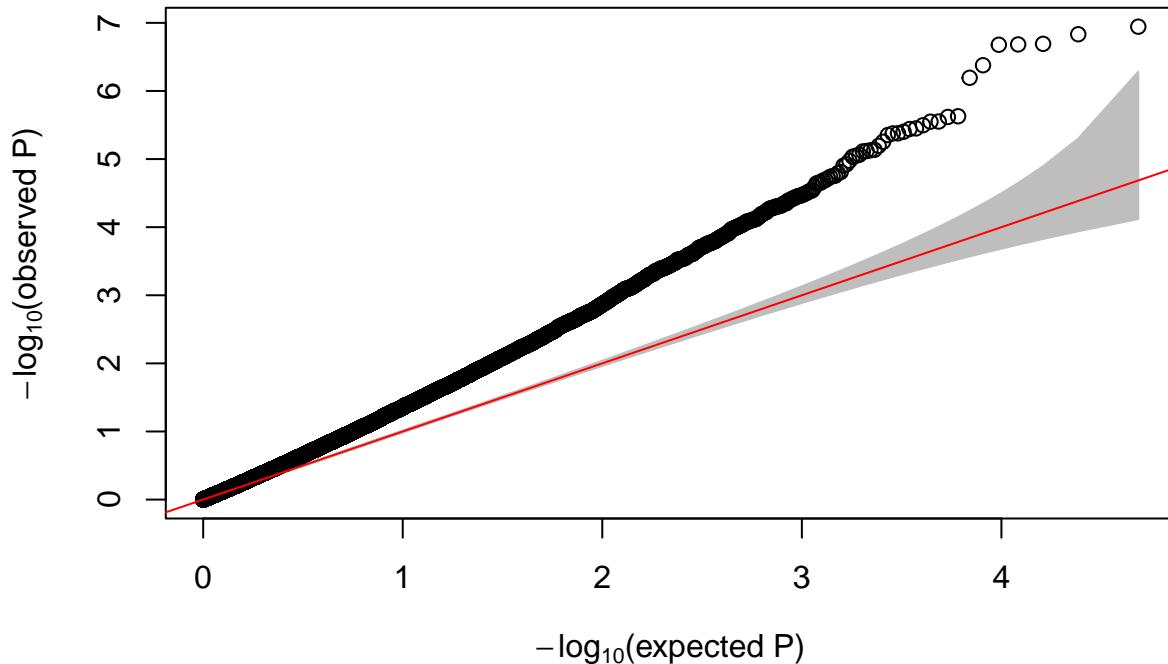
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Sphericity.original)

```



```
summary(summa.fit.sphe)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           500          0   130     0     0      0            0
## NotSig        23022        48525 48282 48525 48523    48525        48525
## Up            25003          0   113     0     2      0            0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezeY
## Down           0            0            0            0            0            0
## NotSig        48525        48525        48525        48525        48525        48525
## Up             0            0            0            0            0            0
##             Sphericity.original X1     X2     X3     X4     X5     X6     X7     X8
## Down           86 18681 15874 14235 12480 10421 10540 6860 7272
## NotSig        48414 12567 20346 21614 25021 26716 28648 32886 33745
## Up            25 17277 12305 12676 11024 11388 9337 8779 7508
##             X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19    X20
## Down          8143 8132 8371 5316 5138 5969 4365 3482 3769 2635 2796 1970
## NotSig       32580 31672 33332 36846 36642 36838 39232 41338 40182 43758 43165 44578
## Up            7802 8721 6822 6363 6745 5718 4928 3705 4574 2132 2564 1977
```

```
head(toptable.sphericity, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val
## 1555057_at	-0.18032328	0.85211268	-5.722587	1.138012e-07	0.002034577
## 233228_at	-0.12628292	4.49382735	-5.664443	1.470117e-07	0.002034577
## 221916_at	-0.19080840	-0.28687457	-5.590379	2.033555e-07	0.002034577
## 1561614_at	-0.18130158	0.64172140	-5.585920	2.073542e-07	0.002034577
## 1560222_at	-0.12313331	0.64394774	-5.583406	2.096421e-07	0.002034577
## 1557566_at	-0.23298881	-0.05812328	-5.423649	4.190543e-07	0.003389102
## 239013_at	-0.16685800	0.44993298	-5.324787	6.401800e-07	0.004437819
## 1570266_x_at	0.09218518	4.64450556	5.015030	2.354072e-06	0.011973303
## 215067_x_at	0.05211018	4.21705911	5.009535	2.408199e-06	0.011973303
## 244579_at	-0.13792111	4.39056355	-4.972056	2.811154e-06	0.011973303
	B				

```

## 1555057_at    7.194662
## 233228_at    7.191464
## 221916_at    6.396601
## 1561614_at    6.590057
## 1560222_at    6.603401
## 1557566_at    5.845504
## 239013_at    5.590874
## 1570266_x_at 4.592324
## 215067_x_at  4.574267
## 244579_at    4.405476

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SurfaceArea.original.rda")

summa.fit.surAr <- decideTests(fit)
summary(summa.fit.surAr)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           591          0    76     0     0      0          0          0
## NotSig        22773        48525  48403  48525  48523    48525        48525
## Up            25161          0   46     0     2      0          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           1             0          0          0          0          0          0
## NotSig        48524        48525          0        48525    48525        48525
## Up             0             0          0          0          0          0          0
##          SurfaceArea.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           0 18548 16219 13907 12381 10567 10596 6790 7183
## NotSig        48525 12705 19622 22171 25112 26807 28572 33361 33597
## Up            0 17272 12684 12447 11032 11151 9357 8374 7745
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         8048  7916  8262  5579  5356  5612  4706  4322  2860  2722  2642
## NotSig      32732  32317 33547 36361 36439 37258 38666 39909 41784 43397 43088
## Up          7745  8292  6716  6585  6730  5655  5153  4294  3881  2406  2795

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SurfaceVolumeRatio.original.rda")

summa.fit.surVol <- decideTests(fit)
summary(summa.fit.surVol)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           565          0    76     0     0      0          0          0
## NotSig        22786        48525  48405  48525  48523    48525        48525
## Up            25174          0   44     0     2      0          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0
## NotSig        48525        48525          0        48525    48525        48525
## Up             0             0          0          0          0          0          0
##          SurfaceVolumeRatio.original   X1     X2     X3     X4     X5     X6     X7
## Down           0 18582 15977 14200 12400 10459 10640 7015
## NotSig        48525 12763 20135 21757 25162 26868 28424 32713
## Up            0 17180 12413 12568 10963 11198 9461 8797
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         7193  8056  7942  8260  5468  5162  5625  4585  3684  3345  2570  2580
## NotSig      33680  32720 32226 33550 36521 36670 37298 38885 41037 40893 43770 43488
## Up          7652  7749  8357  6715  6536  6693  5602  5055  3804  4287  2185  2457

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/VoxelVolume.original.rda")

summa.fit.voxVol <- decideTests(fit)
summary(summa.fit.voxVol)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           587          0     62      0      0          0          0
## NotSig        22686        48525 48428 48525 48523        48525        48525
## Up            25252          0     35      0      2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0
## NotSig        48525        48525          48525        48525        48525
## Up            0             0          0          0          0          0
##          VoxelVolume.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           0 18515 16187 13929 12386 10570 10691 6679 7205
## NotSig        48525 12794 19795 22170 25162 26848 28372 33348 33551
## Up            0 17216 12543 12426 10977 11107 9462 8498 7769
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          8121 7780 8272 5534 5355 5645 4661 4308 2904 2666 2632
## NotSig       32446 32790 33411 36417 36427 37214 38738 39932 41621 43451 43137
## Up            7958 7955 6842 6574 6743 5666 5126 4285 4000 2408 2756

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/TotalEnergy.original.rda")

summa.fit.totEn <- decideTests(fit)
summary(summa.fit.totEn)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           573          0     94      0      0          0          0
## NotSig        22882        48525 48365 48525 48523        48525        48525
## Up            25070          0     66      0      2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0
## NotSig        48525        48525          48525        48525        48525
## Up            0             0          0          0          0          0
##          TotalEnergy.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           0 18574 16147 14064 12374 10380 10553 7149 7284
## NotSig        48525 12669 19782 21911 25142 27199 28702 32542 33419
## Up            0 17282 12596 12550 11009 10946 9270 8834 7822
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          8024 7887 8237 5602 5351 5626 4653 4267 2722 2709 2606
## NotSig       32579 32561 33456 36222 36452 37166 38678 40039 42047 43353 43155
## Up            7922 8077 6832 6701 6722 5733 5194 4219 3756 2463 2764

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Uniformity.original.rda")

summa.fit.unif <- decideTests(fit)
summary(summa.fit.unif)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           607          0     94      0      0          0          0
## NotSig        22618        48525 48365 48525 48524        48525        48525
## Up            25300          0     66      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0

```

```

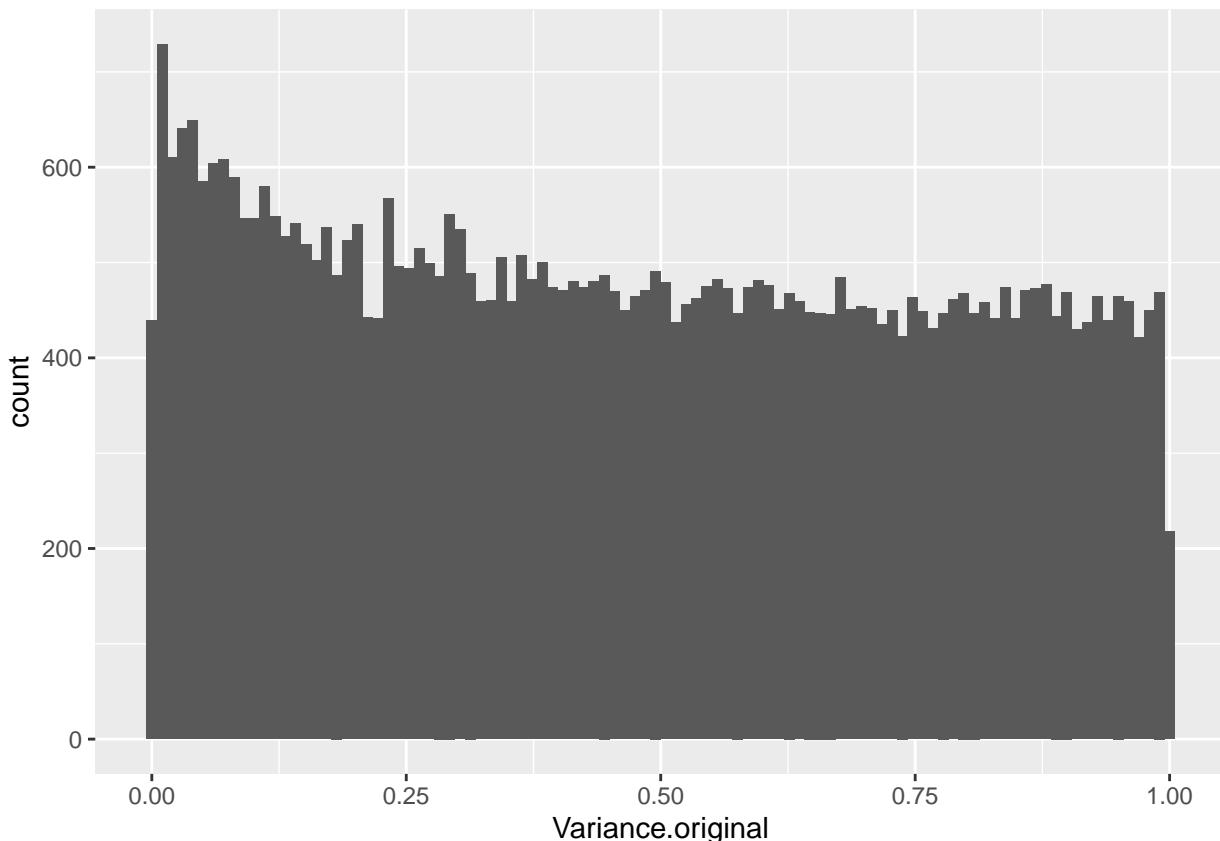
## NotSig          48525          48525          48525 48525          48525
## Up              0              0              0      0      0
##     Uniformity.original   X1    X2    X3    X4    X5    X6    X7    X8
## Down             0 18449 16231 13871 12294 10569 10674 7213 7277
## NotSig          48525 12794 19564 22308 25347 26862 28383 32572 33553
## Up               0 17282 12730 12346 10884 11094 9468 8740 7695
##     X9    X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down            7930  7844  8232  5437  5271  5681  4552  4022  3211  2659  2551
## NotSig         32799 32551 33503 36562 36547 37452 38877 40427 41125 43505 43321
## Up              7796  8130  6790  6526  6707  5392  5096  4076  4189  2361  2653

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Variance.original.rda")

# Store toptable, p-value, summary
summa.fit.var <- decideTests(fit)
toptable.variance <- topTable(fit, coef = "Variance.original", number = dim(counts.ok)[1])
toptable.variance <- toptable.variance[order(toptable.variance$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Variance.original)) + geom_histogram(bins = 100)

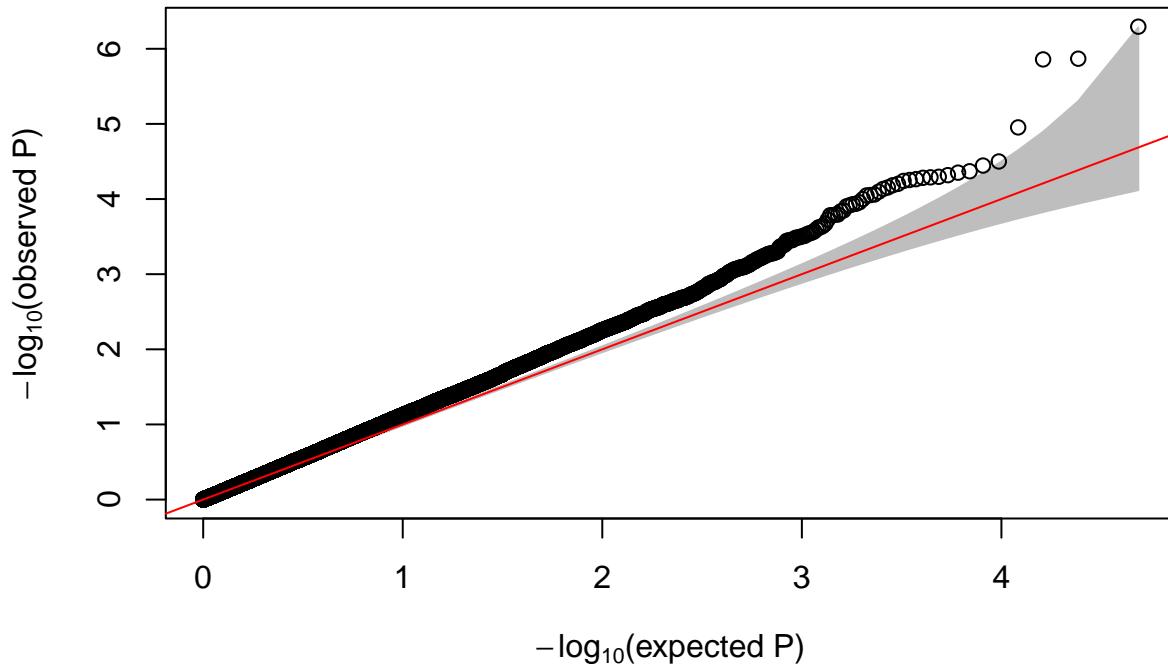
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Variance.original)

```



```
summary(summa.fit.var)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           581          0   93     0     0      0          0
## NotSig        22641        48525 48374 48525 48523    48525        48525
## Up            25303          0   58     0     2      0          0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0           0          0          0      0      0          0
## NotSig        48525        48525        48525    48525 48525        48525
## Up             0           0          0          0      0      0          0
##          Variance.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18594 16125 13922 12288 10645 10712 7001 7320 8312
## NotSig        48522 12667 19907 22015 25311 26644 28474 32655 33596 31952
## Up            3 17264 12493 12588 10926 11236 9339 8869 7609 8261
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19    X20
## Down          7980  8279  5459  5339  5808  4778  4459  2873  2826  2569  2484
## NotSig       32469 33183 36614 36413 36920 38429 39564 41754 43095 43577 43751
## Up            8076  7063  6452  6773  5797  5318  4502  3898  2604  2379  2290
```

```
head(toptable.variance, 10)
```

```
##          logFC     AveExpr      t     P.Value adj.P.Val      B
## 202814_s_at  0.6658893 5.2711632 5.378782 5.081299e-07 0.02241816 5.8538935
## 230825_at    1.2771613 1.0470995 5.147504 1.355389e-06 0.02241816 3.5878362
## 1561431_at   2.1071332 -1.1572903 5.142183 1.385976e-06 0.02241816 1.4751377
## 226699_at    0.8492466 0.8434641 4.631707 1.112736e-05 0.13498877 1.8331468
## 214695_at    0.5861018 4.6285243 4.363720 3.161172e-05 0.18558027 2.1360437
## 239956_at    1.2178626 -0.4591442 4.330883 3.583608e-05 0.18558027 0.2660508
## 242813_at    0.6891639 1.1519933 4.284791 4.269379e-05 0.18558027 1.1798952
## 224964_s_at  -0.6557059 6.4588815 -4.273537 4.455118e-05 0.18558027 1.9024151
## 1562112_at   1.1245873 0.1564666 4.253369 4.807603e-05 0.18558027 0.6249239
## 227981_at    0.5553706 3.4721749 4.240004 5.055810e-05 0.18558027 1.5584154
```

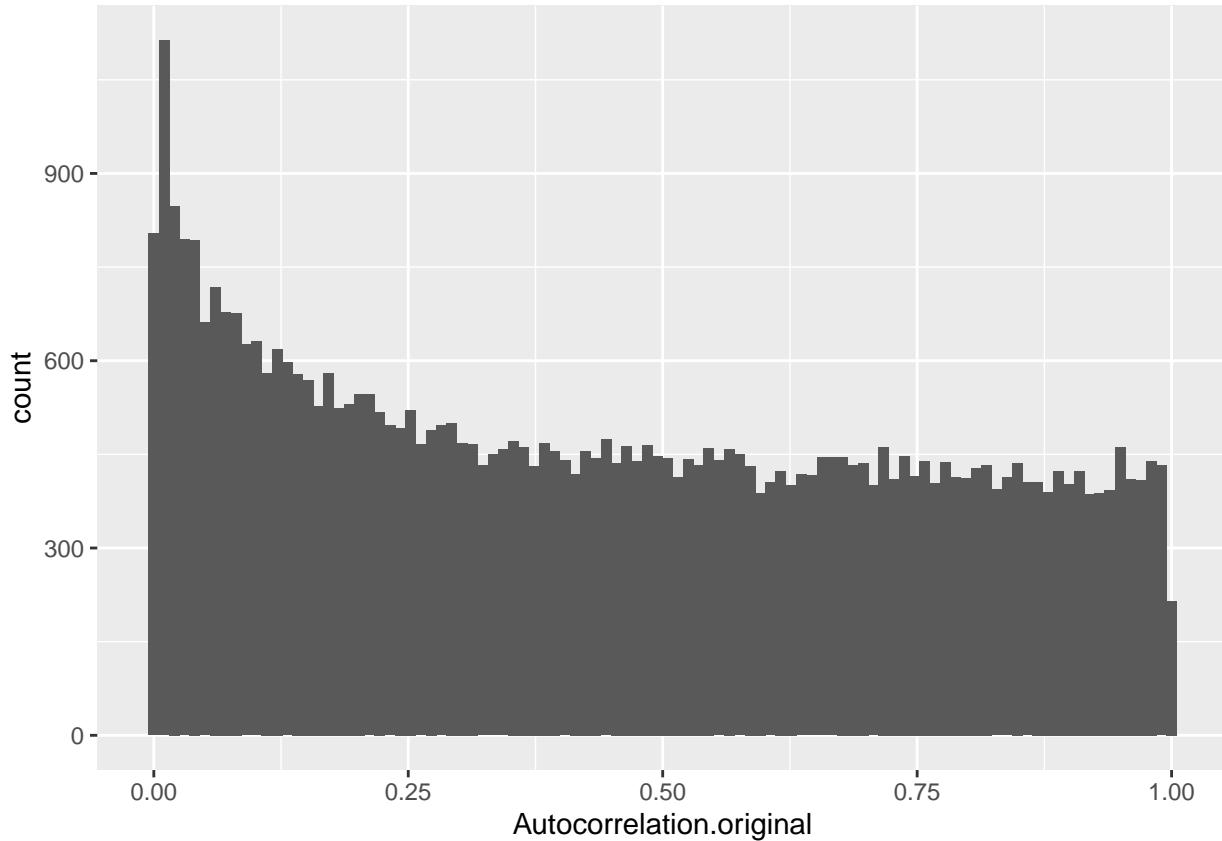
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Autocorrelation.original.rda")

# Store toptable, p.value, summary
summa.fit.auto <- decideTests(fit)
toptable.autoc <- topTable(fit, coef = "Autocorrelation.original", number = dim(counts.ok)[1])
toptable.autoc <- toptable.autoc[order(toptable.autoc$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Autocorrelation.original)) + geom_histogram(bins = 100)

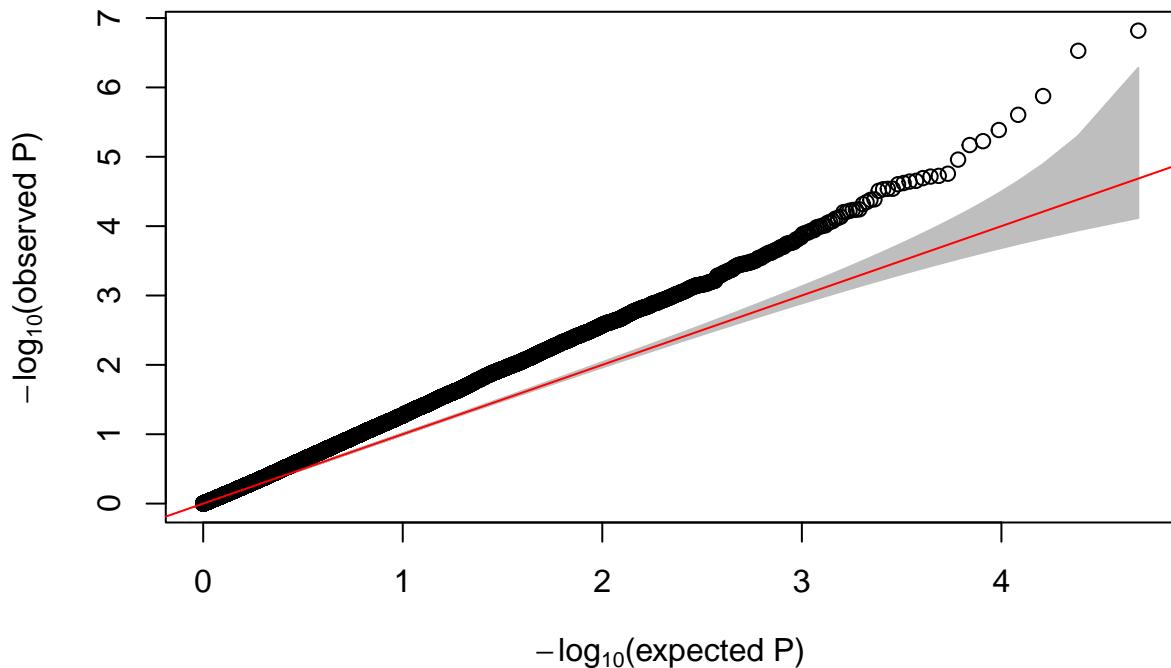
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Autocorrelation.original)

```



```
summary(summa.fit.auto)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           655          0   134     0     0      0            0
## NotSig        22381        48525 48281 48525 48523    48525        48525
## Up            25489          0   110     0     2      0            0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0             0          0          0      0            0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0             0          0          0      0            0
##          Autocorrelation.original X1     X2     X3     X4     X5     X6     X7     X8
## Down           4 18449 16216 13769 12119 10405 9202 8846 7174
## NotSig        48518 12837 19852 22241 25530 26816 28801 32485 34509
## Up            3 17239 12457 12515 10876 11304 10522 7194 6842
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7871  8319  6705  6469  6520  5524  4800  3768  3855  2140  2484
## NotSig       32528 32400 33888 36700 36944 37330 39295 41141 41712 43711 43571
## Up            8126  7806  7932  5356  5061  5671  4430  3616  2958  2674  2470
```

```
head(toptable.autoc, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 212329_at	0.2140579	3.046026	5.652212	1.519904e-07	0.00719515	6.850449
## 227973_at	-0.1569479	4.812141	-5.499370	2.965543e-07	0.00719515	6.501359
## 230036_at	-0.2491051	5.626065	-5.148172	1.331450e-06	0.02153620	5.126485
## 212764_at	-0.2346671	5.362327	-4.998864	2.482641e-06	0.03011754	4.549247
## 218986_s_at	-0.2669902	5.501943	-4.876164	4.112468e-06	0.03991150	4.075728
## 212916_at	0.1046100	5.425691	4.785150	5.953396e-06	0.04695797	3.741335
## 221687_s_at	0.2593628	1.217924	4.753158	6.773947e-06	0.04695797	3.143012
## 239988_at	-0.3690031	2.447993	-4.632331	1.098311e-05	0.06661941	3.075849
## 220238_s_at	-0.1701855	3.591236	-4.513544	1.754084e-05	0.07504312	2.729188
## 228185_at	-0.1254877	4.257772	-4.495131	1.884922e-05	0.07504312	2.687036

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ClusterProminence.original.rda")

summa.fit.clustPro <- decideTests(fit)
summary(summa.fit.clustPro)

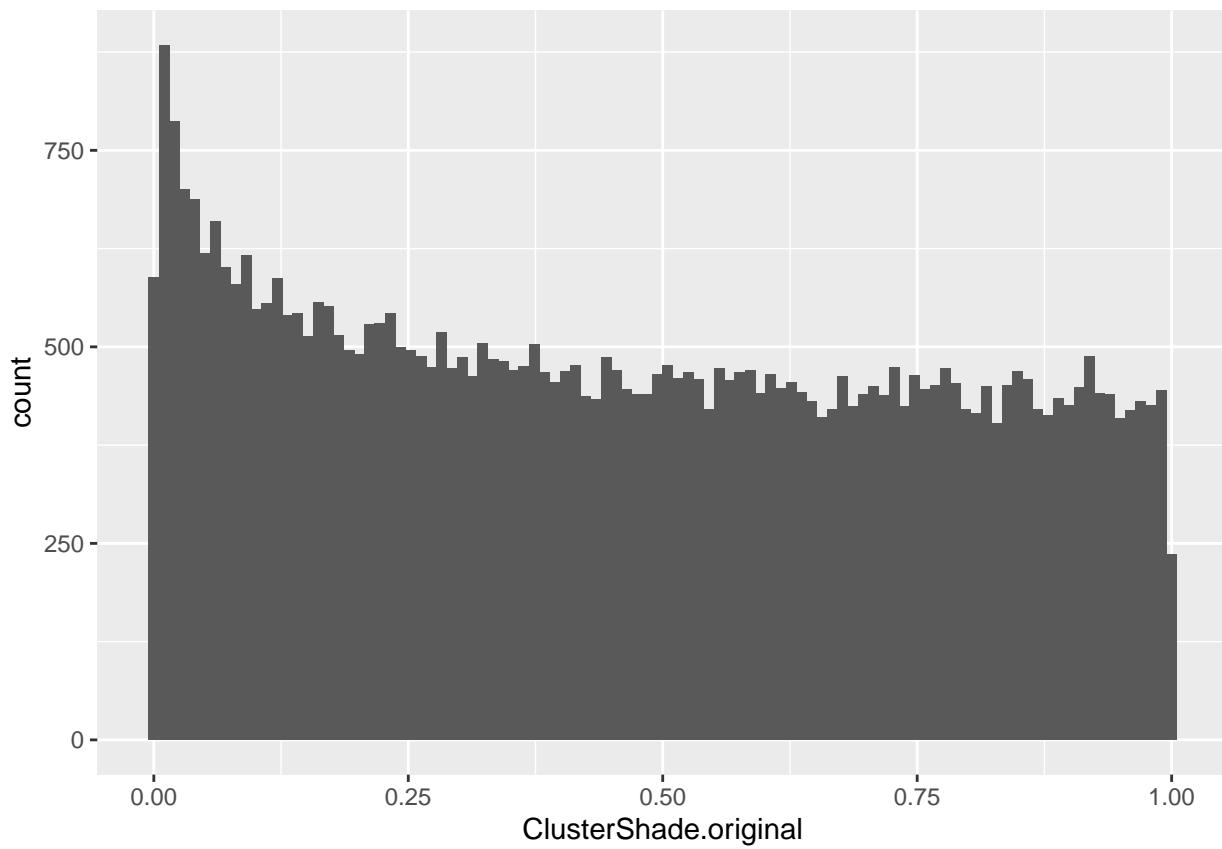
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           595          0    92     0     0          0          0
## NotSig        22639        48525 48365 48525 48524        48525        48525
## Up            25291          0    68     0     1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough      BMI Cr_wheezengY
## Down           0            0          0          0          0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0            0          0          0          0          0
##          ClusterProminence.original   X1     X2     X3     X4     X5     X6     X7
## Down           0 18481 16176 13873 12364 10528  9427  8586
## NotSig        48525 12747 19725 22241 25249 26922 28481 32960
## Up             0 17297 12624 12411 10912 11075 10617  6979
##          X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7666 7944 8062 6956 6537 6723 5551 5092 3940 4197 2313 2653
## NotSig       33668 32557 32555 33257 36521 36572 37200 38791 40648 41079 43646 43366
## Up            7191 8024 7908 8312 5467 5230 5774 4642 3937 3249 2566 2506

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ClusterShade.original.rda")

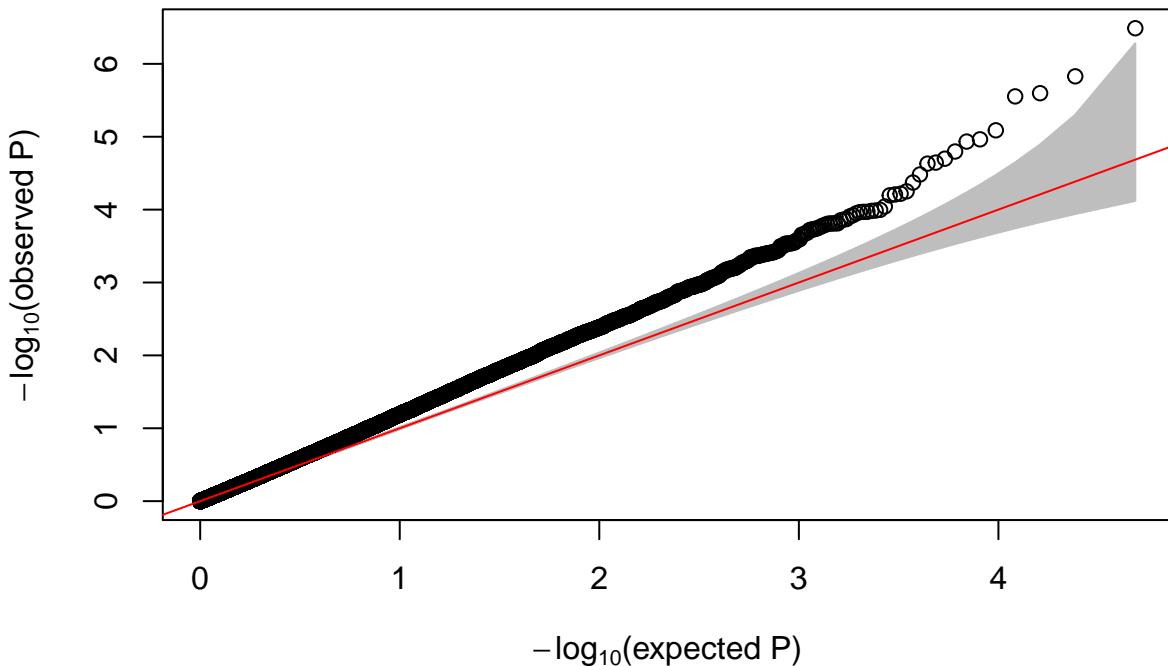
summa.fit.clustSh <- decideTests(fit)
toptable.clustSh <- topTable(fit, coef = "ClusterShade.original", number = dim(counts.ok)[1])
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = ClusterShade.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$ClusterShade.original)
```



```
summary(summa.fit.clustSh)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      592      0 101 0 0 0 0
## NotSig   22818 48525 48341 48525 48523 48525 48525
## Up       25115 0 83 0 2 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## ClusterShade.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      2 18574 16044 13738 12291 10588 9076 8809 7484
## NotSig   48521 12688 20150 22431 25240 26588 29113 32992 33781
## Up       2 17263 12331 12356 10994 11349 10336 6724 7260
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    7806 8462 6781 6468 6642 5556 5134 4077 4141 2482 2525
## NotSig  32697 32179 33679 36651 36496 37445 38763 40531 41197 43138 43224
## Up      8022 7884 8065 5406 5387 5524 4628 3917 3187 2905 2776
head(toptable.clustSh, 10)

##          logFC     AveExpr      t     P.Value adj.P.Val      B
## 214027_x_at  0.17161563 0.6872062 5.478815 3.246790e-07 0.01575505 5.643635
## 239081_at   -0.16362161 2.3837066 -5.122579 1.484159e-06 0.03393020 4.832180
## 204233_s_at  0.20349264 3.0075886 4.994830 2.527017e-06 0.03393020 4.427936
## 213564_x_at  0.09183282 6.5682690 4.706900 8.164235e-06 0.07923390 3.345018
## 201030_x_at  0.08763818 6.2130525 4.617732 1.164706e-05 0.08073908 3.045538
## 233092_s_at -0.35824461 -0.5402662 -4.970275 2.796925e-06 0.03393020 3.013439
## 230774_at   -0.19153535 1.0816671 -4.635558 1.085185e-05 0.08073908 2.878926
## 210681_s_at  0.07254418 7.0264442 4.537919 1.595499e-05 0.09677700 2.662140
## 225855_at   -0.17640895 1.9816101 -4.480038 2.000575e-05 0.10315918 2.513144
## 218983_at   -0.09082771 5.8726308 -4.439856 2.338487e-05 0.10315918 2.425140

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ClusterTendency.original.rda")

summa.fit.clustTen <- decideTests(fit)
summary(summa.fit.clustTen)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      598 0 99 0 0 0 0
## NotSig   22654 48525 48359 48525 48524 48525 48525
## Up       25273 0 67 0 1 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## ClusterTendency.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      0 18452 16230 13851 12265 10553 10670 7220 7250
## NotSig   48525 12794 19606 22325 25391 26901 28384 32551 33566
## Up       0 17279 12689 12349 10869 11071 9471 8754 7709
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    7950 7860 8213 5460 5270 5631 4583 4042 3187 2675 2542
## NotSig  32745 32548 33534 36517 36548 37525 38821 40410 41180 43464 43347
## Up      7830 8117 6778 6548 6707 5369 5121 4073 4158 2386 2636
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Contrast.original.rda")

# Store toptable, p.value, summary
summa.fit.cont <- decideTests(fit)

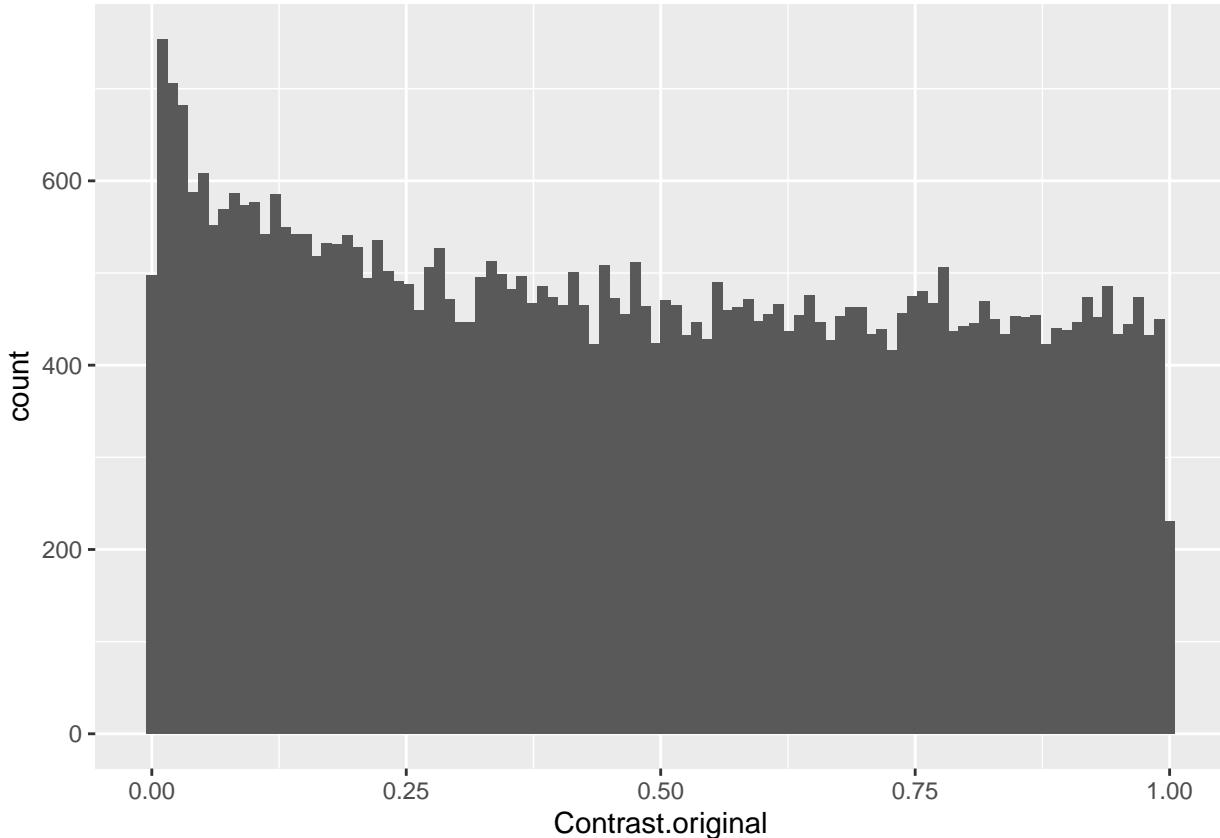
```

```

toptable.cont <- topTable(fit, coef = "Contrast.original", number = dim(counts.ok)[1])
toptable.cont <- toptable.cont[order(toptable.cont$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Contrast.original)) + geom_histogram(bins = 100)

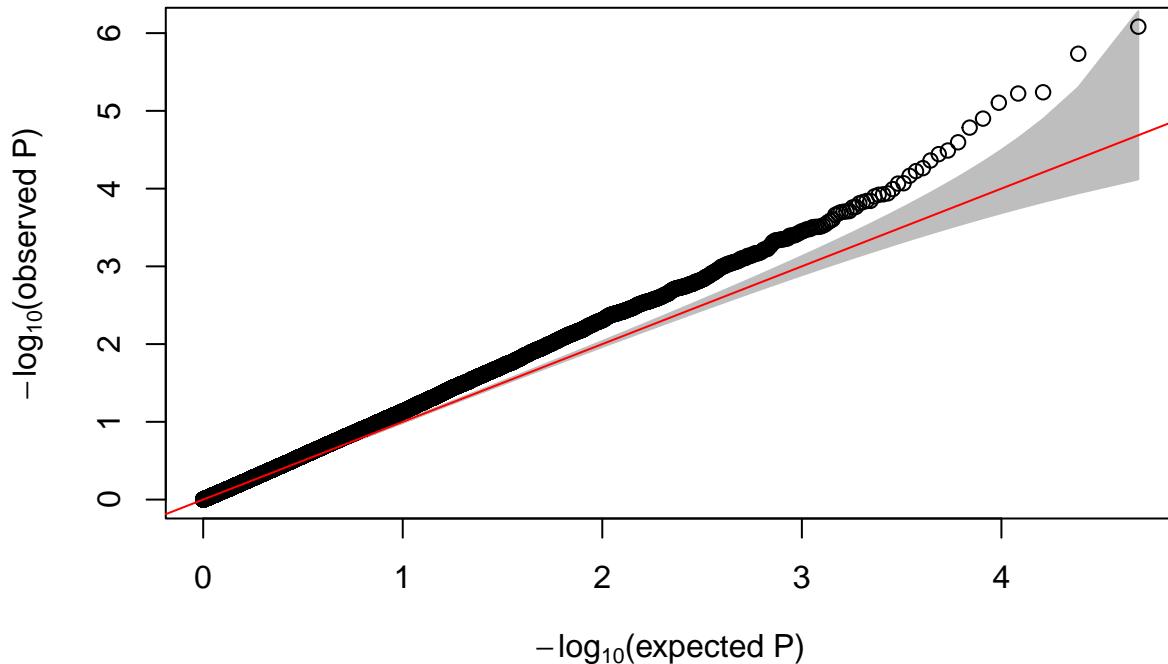
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Contrast.original)

```



```
summary(summa.fit.cont)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           601          0     89      0      0          0          0
## NotSig        22631        48525 48368 48525 48524        48525        48525
## Up            25293          0     68      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0          0
##          Contrast.original   X1      X2      X3      X4      X5      X6      X7      X8      X9
## Down           1 18458 16255 13932 12369 10607 10670 7127 7268 7937
## NotSig        48523 12783 19492 22225 25214 26772 28368 32682 33558 32750
## Up            1 17284 12778 12368 10942 11146 9487 8716 7699 7838
##          X10     X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down          7845  8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig       32626 33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up            8054  6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.cont, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	-0.10041678	5.0379308	-5.261247	8.262337e-07	0.04009299	5.554520
## 1554830_a_at	0.19493497	2.6289573	5.071015	1.840997e-06	0.04466720	4.581840
## 1555229_a_at	0.39799402	0.6820437	4.793267	5.765254e-06	0.07258511	3.111078
## 1562121_at	0.17768900	0.1193435	4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	0.20693649	-0.3358964	4.716413	7.857573e-06	0.07625775	2.217700
## 201645_at	0.26341444	1.8007395	4.598154	1.258368e-05	0.10177048	2.811716
## 219675_s_at	0.09225380	5.0965517	4.530517	1.642267e-05	0.11384429	2.813061
## 224785_at	-0.15288095	3.6686028	-4.418797	2.536640e-05	0.15386309	2.382161
## 217279_x_at	0.21058986	0.8980683	4.355435	3.236753e-05	0.17451493	1.784988
## 218315_s_at	-0.09320256	3.2742864	-4.327517	3.601302e-05	0.17475318	2.058275

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum2DDiameterColumn.original.rda")

summa.fit.corr <- decideTests(fit)
summary(summa.fit.corr)

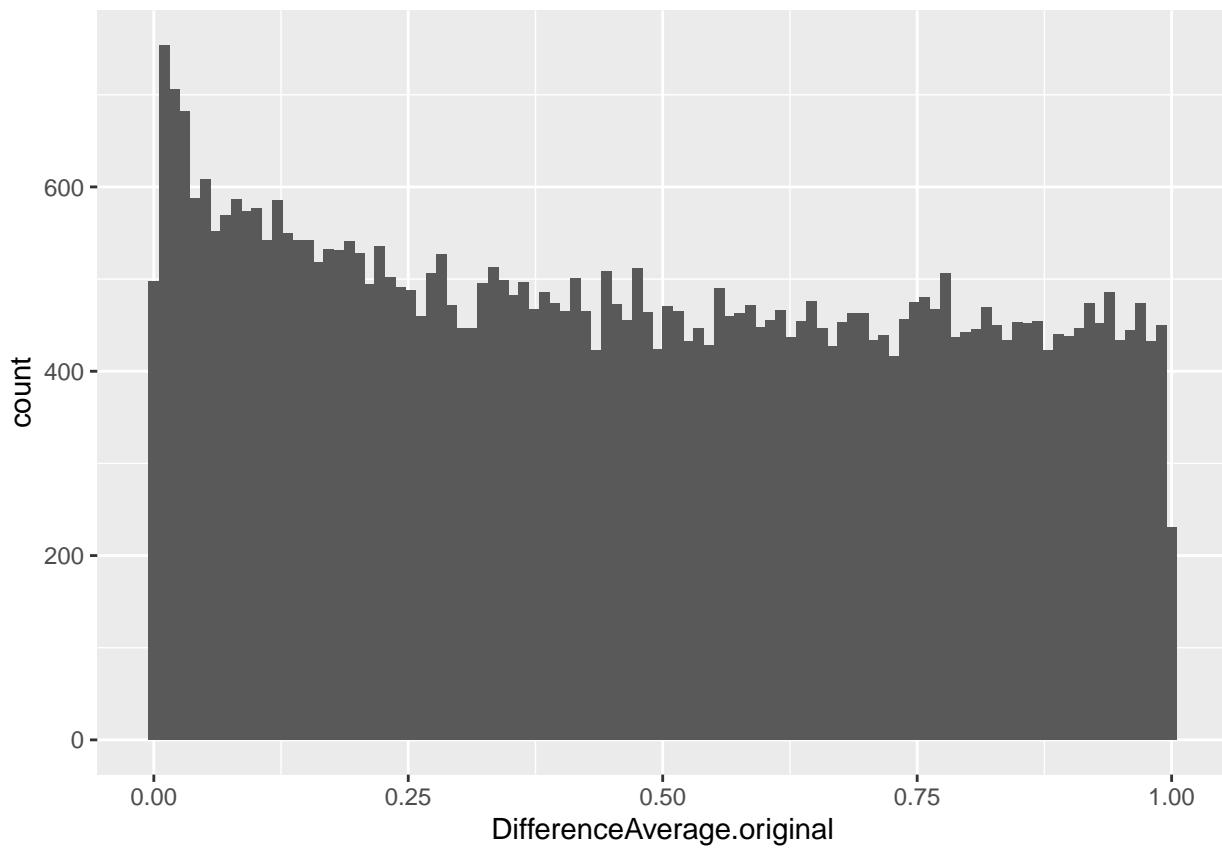
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           565          0     53      0     0          0          0
## NotSig        22755        48525 48439 48525 48523        48525        48525
## Up            25205          0    33      0     2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezeNgeY
## Down           0             0          0          0          0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0             0          0          0          0          0
##          Maximum2DDiameterColumn.original   X1     X2     X3     X4     X5     X6
## Down           0 18555 16166 13981 12471 10515 10711
## NotSig        48525 12764 19831 22041 24983 26919 28254
## Up             0 17206 12528 12503 11071 11091  9560
##          X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down          6706  7370  8065  7879  8325  5499  5432  5597  4588  4756  2893  2547
## NotSig       33300 33377 32565 32428 33381 36498 36353 37347 38895 39019 41589 43706
## Up            8519  7778  7895  8218  6819  6528  6740  5581  5042  4750  4043  2272
##          X19
## Down          2556
## NotSig       43204
## Up            2765

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/DifferenceAverage.original.rda"

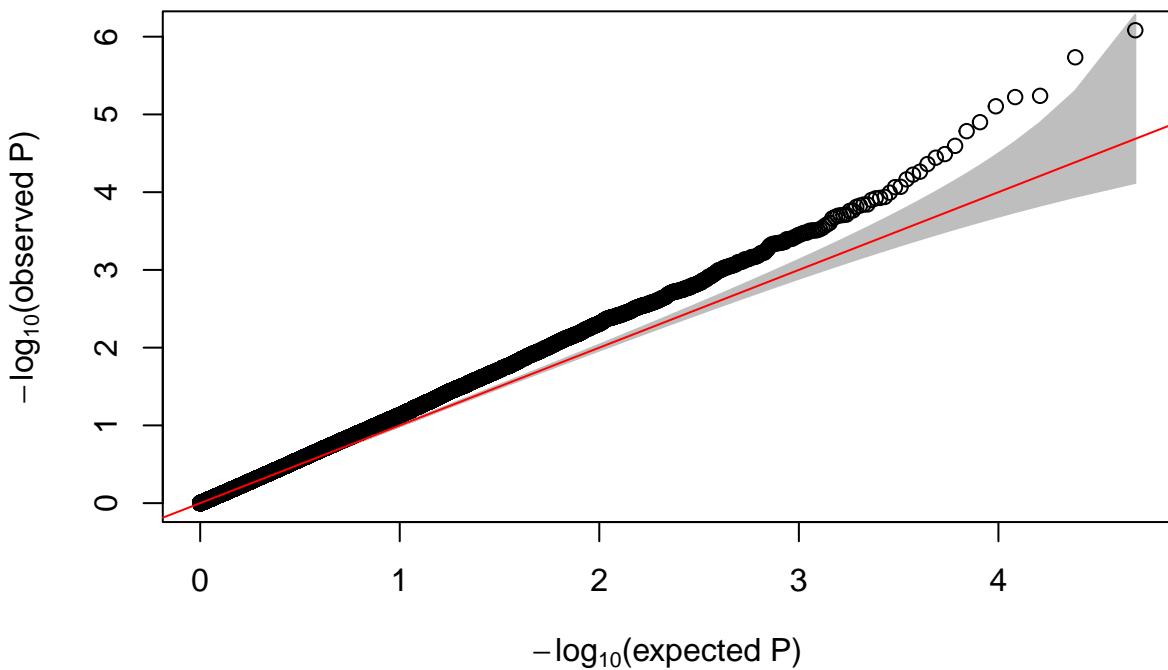
# Store toptable, p.value, summary
summa.fit.diffAv <- decideTests(fit)
toptable.diffAv <- topTable(fit, coef = "DifferenceAverage.original", number = dim(counts.ok)[1])
toptable.diffAv <- toptable.diffAv[order(toptable.diffAv$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = DifferenceAverage.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$DifferenceAverage.original)
```



```
summary(summa.fit.diffAv)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      601      0     89      0      0      0      0
## NotSig   22631    48525  48368  48525  48524    48525    48525
## Up       25293      0     68      0      1      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##      DifferenceAverage.original   X1     X2     X3     X4     X5     X6     X7
## Down      1 18458 16255 13932 12369 10607 10670 7127
## NotSig   48523 12783 19492 22225 25214 26772 28368 32682
## Up       1 17284 12778 12368 10942 11146 9487 8716
##      X8     X9    X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down    7268  7937  7845  8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig 33558 32750 32626 33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up      7699  7838  8054  6853  6442  6712  5434  5070  4076  4204  2364  2674
head(toptable.diffAv, 10)

```

```

##          logFC     AveExpr        t     P.Value adj.P.Val      B
## 203893_at -0.10041678 5.0379308 -5.261247 8.262337e-07 0.04009299 5.554520
## 1554830_a_at 0.19493497 2.6289573 5.071015 1.840997e-06 0.04466720 4.581840
## 1555229_a_at 0.39799402 0.6820437 4.793267 5.765254e-06 0.07258511 3.111078
## 1562121_at  0.17768900 0.1193435 4.784088 5.983317e-06 0.07258511 2.725248
## 216922_x_at  0.20693649 -0.3358964 4.716413 7.857573e-06 0.07625775 2.217700
## 201645_at   0.26341444 1.8007395 4.598154 1.258368e-05 0.10177048 2.811716
## 219675_s_at  0.09225380 5.0965517 4.530517 1.642267e-05 0.11384429 2.813061
## 224785_at   -0.15288095 3.6686028 -4.418797 2.536640e-05 0.15386309 2.382161
## 217279_x_at  0.21058986 0.8980683 4.355435 3.236753e-05 0.17451493 1.784988
## 218315_s_at -0.09320256 3.2742864 -4.327517 3.601302e-05 0.17475318 2.058275

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/DifferenceEntropy.original.rda"

summa.fit.diffEnt <- decideTests(fit)
summary(summa.fit.diffEnt)

```

```

##      (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      600      0     89      0      0      0      0
## NotSig   22633    48525  48367  48525  48524    48525    48525
## Up       25292      0     69      0      1      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##      DifferenceEntropy.original   X1     X2     X3     X4     X5     X6     X7
## Down      0 18475 16251 13944 12398 10546 10653 6907
## NotSig   48525 12748 19558 22145 25175 26911 28418 32988
## Up       0 17302 12716 12436 10952 11068 9454 8630
##      X8     X9    X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down    7258  8056  7883  8297  5419  5293  5682  4508  3924  3383  2647  2560
## NotSig 33524 32507 32643 33288 36666 36495 37383 38965 40591 40862 43494 43264
## Up      7743  7962  7999  6940  6440  6737  5460  5052  4010  4280  2384  2701

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/DifferenceVariance.original.rda"

```

```

summa.fit.diffVar <- decideTests(fit)
summary(summa.fit.diffVar)

```

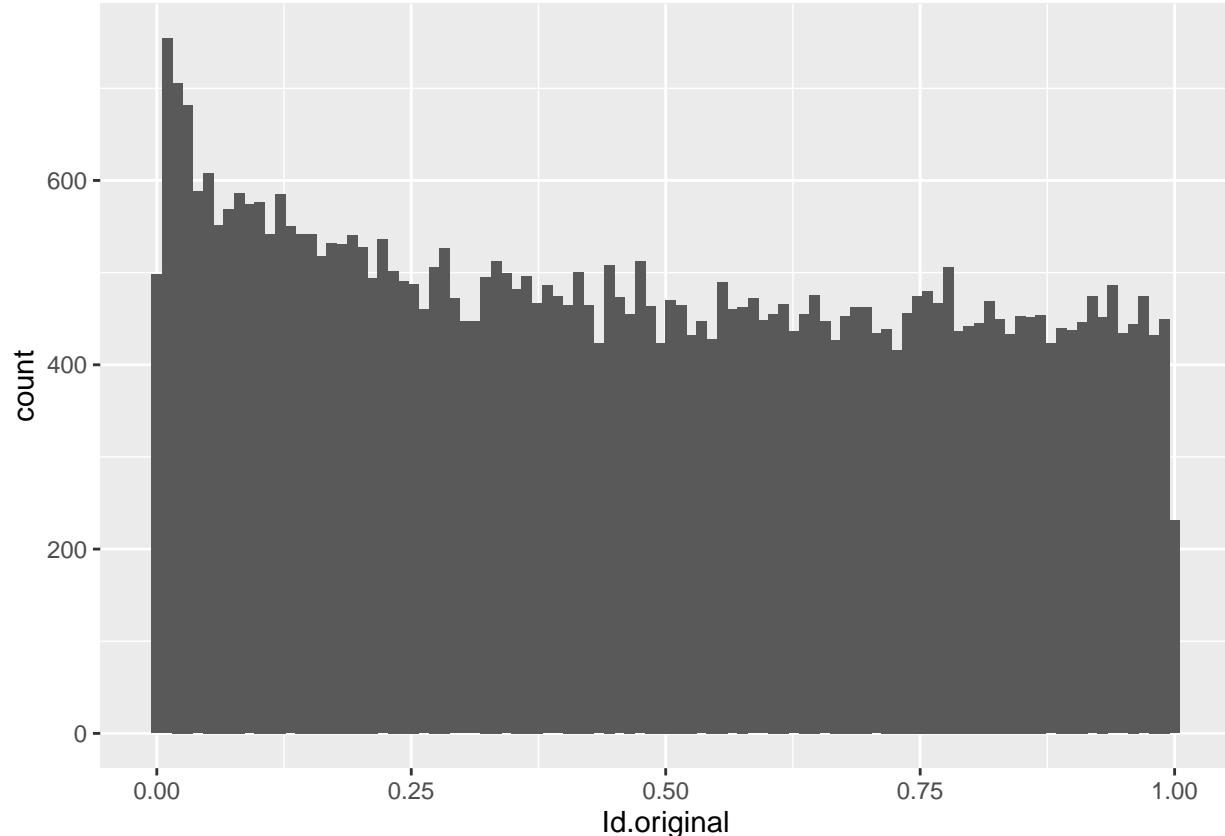
```

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           604            0     90      0     0            0            0
## NotSig        22626        48525  48364  48525  48524        48525        48525
## Up            25295            0     71      0     1            0            0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezyngY
## Down           0            0            0            0            0            0
## NotSig        48525            48525            48525        48525        48525        48525
## Up             0            0            0            0            0            0
##          DifferenceVariance.original   X1     X2     X3     X4     X5     X6     X7
## Down           0 18475 16251 13943 12375 10603 10661 7001
## NotSig        48525 12755 19526 22183 25206 26802 28384 32887
## Up             0 17295 12748 12399 10944 11120  9480  8637
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         7271 7998 7848 8261 5389 5270 5734 4521 3939 3354 2646 2537
## NotSig      33563 32644 32643 33359 36707 36537 37329 38946 40566 40924 43517 43308
## Up          7691 7883 8034 6905 6429 6718 5462 5058 4020 4247 2362 2680
load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Id.original.rda")

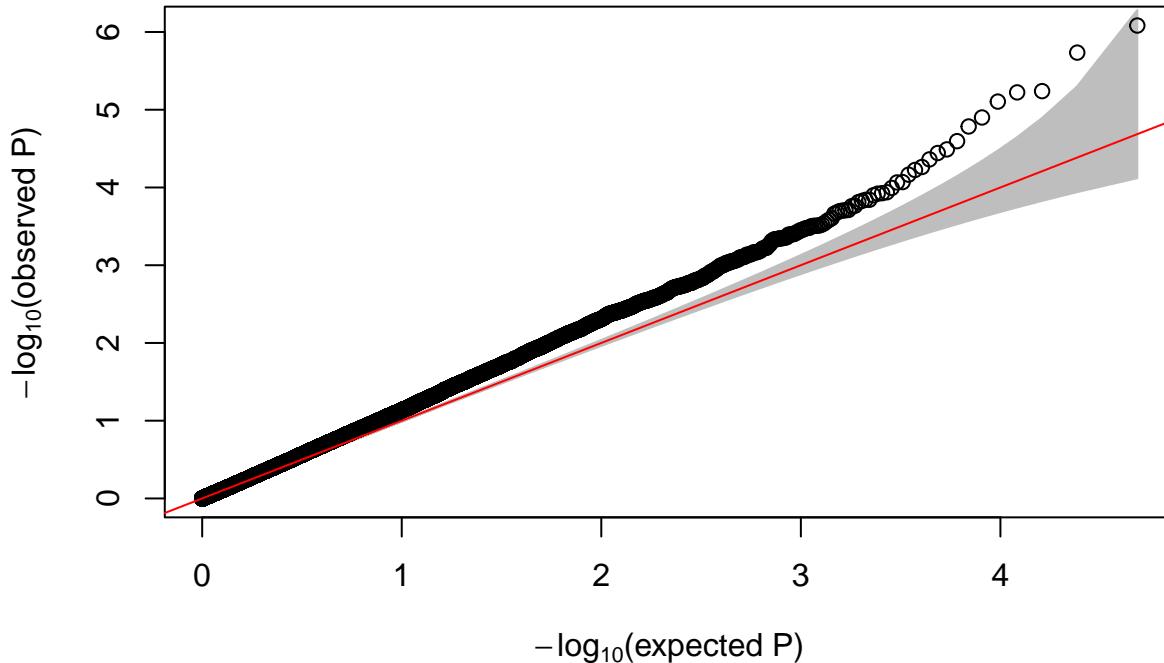
# Store toptable, p.value, summary
summa.fit.id0 <- decideTests(fit)
toptable.id0 <- topTable(fit, coef = "Id.original", number = dim(counts.ok)[1])
toptable.id0 <- toptable.id0[order(toptable.id0$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Id.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Id.original)
```



```
summary(summa.fit.id0)
```

```
##             (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down           601          0    89   0    0      0          0
## NotSig        22631        48525 48368 48525 48524     48525        48525
## Up            25293          0    68   0    1      0          0
##             dusty_exposeY history_asthmaY CoughNo chronic cough      BMI Cr_wheezengY
## Down           0            0          0          0      0      0          0
## NotSig        48525        48525          0          0     48525 48525        48525
## Up             0            0          0          0      0      0          0
##             Id.original X1     X2     X3     X4     X5     X6     X7     X8     X9     X10
## Down           1 18458 16255 13932 12369 10607 10670 7127 7268 7937 7845
## NotSig        48523 12783 19492 22225 25214 26772 28368 32682 33558 32750 32626
## Up            1 17284 12778 12368 10942 11146 9487 8716 7699 7838 8054
##             X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig       33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up          6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.id0, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	0.10041678	5.0379308	5.261247	8.262333e-07	0.04009297	5.554521
## 1554830_a_at	-0.19493497	2.6289573	-5.071015	1.840998e-06	0.04466722	4.581839
## 1555229_a_at	-0.39799402	0.6820437	-4.793267	5.765255e-06	0.07258511	3.111078
## 1562121_at	-0.17768899	0.1193435	-4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	-0.20693649	-0.3358964	-4.716413	7.857575e-06	0.07625776	2.217700
## 201645_at	-0.26341443	1.8007395	-4.598154	1.258368e-05	0.10177053	2.811715
## 219675_s_at	-0.09225380	5.0965517	-4.530517	1.642267e-05	0.11384431	2.813060
## 224785_at	0.15288095	3.6686028	4.418797	2.536641e-05	0.15386312	2.382161

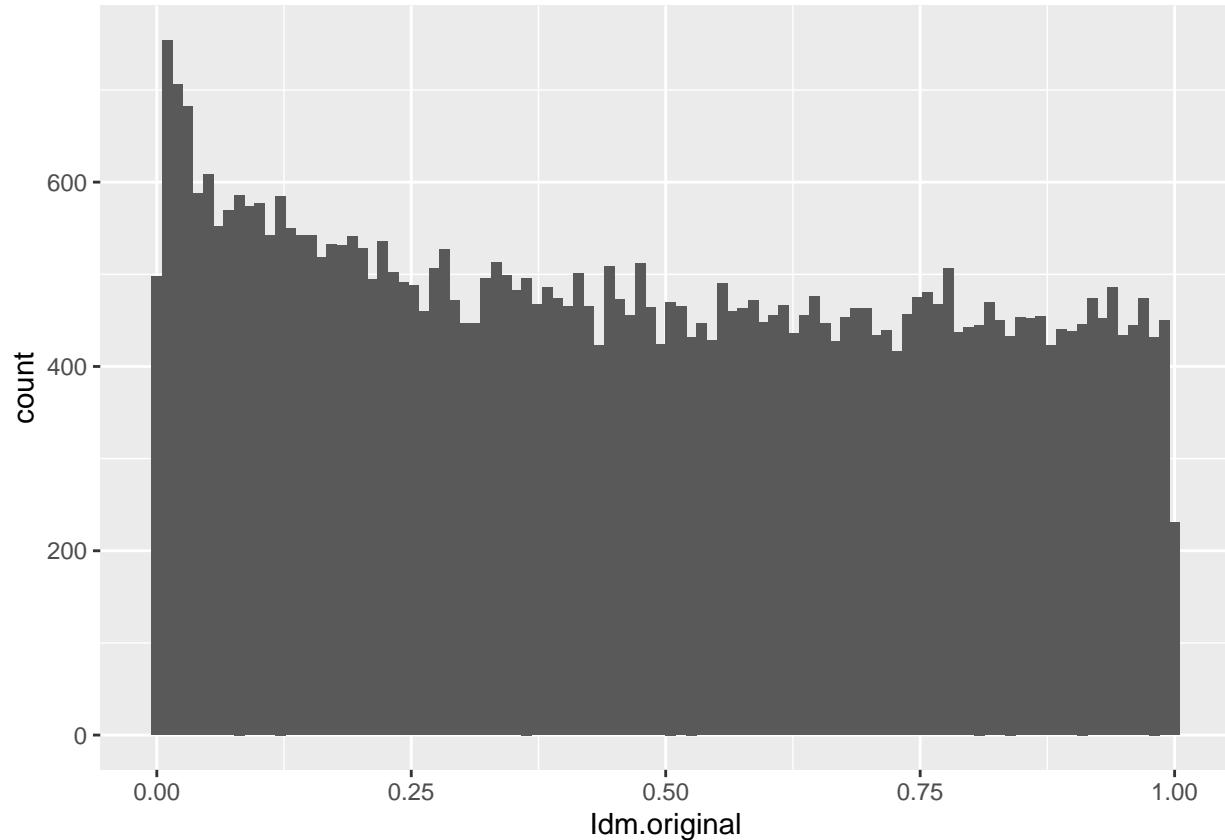
```

## 217279_x_at -0.21058986 0.8980683 -4.355435 3.236753e-05 0.17451491 1.784988
## 218315_s_at 0.09320257 3.2742864 4.327517 3.601304e-05 0.17475327 2.058275
load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Idm.original.rda")

# Store toptable, p.value, summary
summa.fit.idm0 <- decideTests(fit)
toptable.idm0 <- topTable(fit, coef = "Idm.original", number = dim(counts.ok)[1])
toptable.idm0 <- toptable.idm0[order(toptable.idm0$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Idm.original)) + geom_histogram(bins = 100)

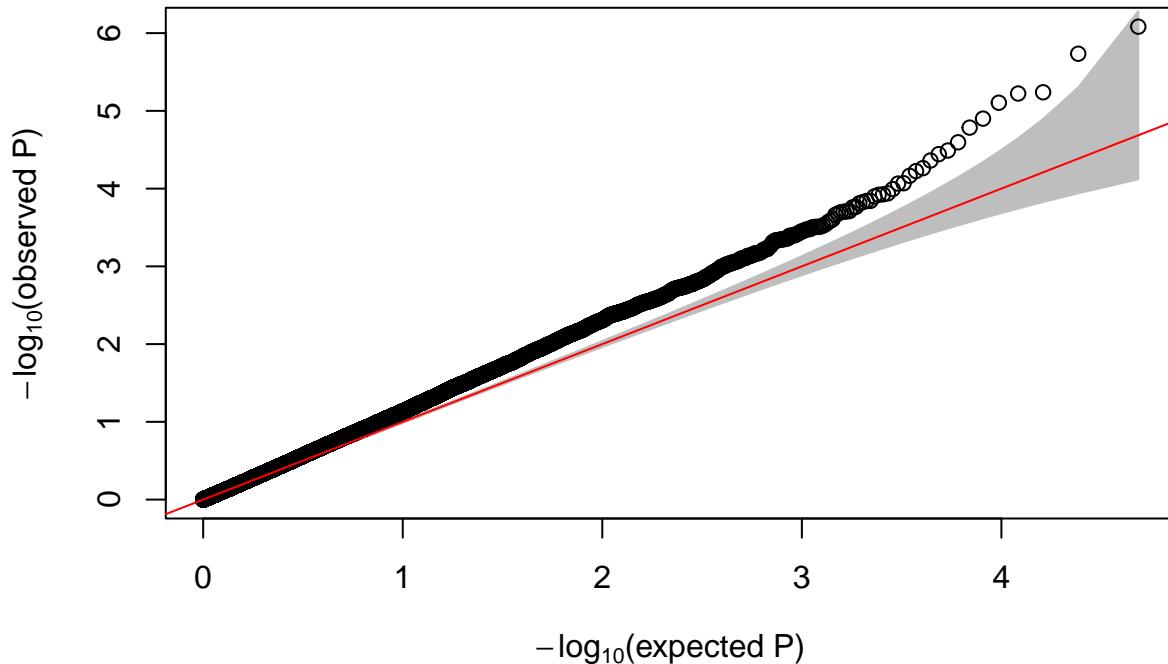
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Idm.original)

```



```
summary(summa.fit.idm0)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           601          0     89      0      0      0          0
## NotSig        22631        48525 48368 48525 48524 48525        48525
## Up            25293          0    68      0      1      0          0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0      0      0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0            0          0          0      0      0          0
##             Idm.original   X1      X2      X3      X4      X5      X6      X7      X8      X9      X10
## Down           1 18458 16255 13932 12369 10607 10670 7127 7268 7937 7845
## NotSig        48523 12783 19492 22225 25214 26772 28368 32682 33558 32750 32626
## Up             1 17284 12778 12368 10942 11146 9487 8716 7699 7838 8054
##             X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down           8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig       33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up            6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.idm0, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	0.10041678	5.0379308	5.261247	8.262333e-07	0.04009297	5.554521
## 1554830_a_at	-0.19493497	2.6289573	-5.071015	1.840998e-06	0.04466722	4.581839
## 1555229_a_at	-0.39799402	0.6820437	-4.793267	5.765255e-06	0.07258511	3.111078
## 1562121_at	-0.17768899	0.1193435	-4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	-0.20693649	-0.3358964	-4.716413	7.857575e-06	0.07625776	2.217700
## 201645_at	-0.26341443	1.8007395	-4.598154	1.258368e-05	0.10177053	2.811715
## 219675_s_at	-0.09225380	5.0965517	-4.530517	1.642267e-05	0.11384431	2.813060
## 224785_at	0.15288095	3.6686028	4.418797	2.536641e-05	0.15386312	2.382161
## 217279_x_at	-0.21058986	0.8980683	-4.355435	3.236753e-05	0.17451491	1.784988
## 218315_s_at	0.09320257	3.2742864	4.327517	3.601304e-05	0.17475327	2.058275

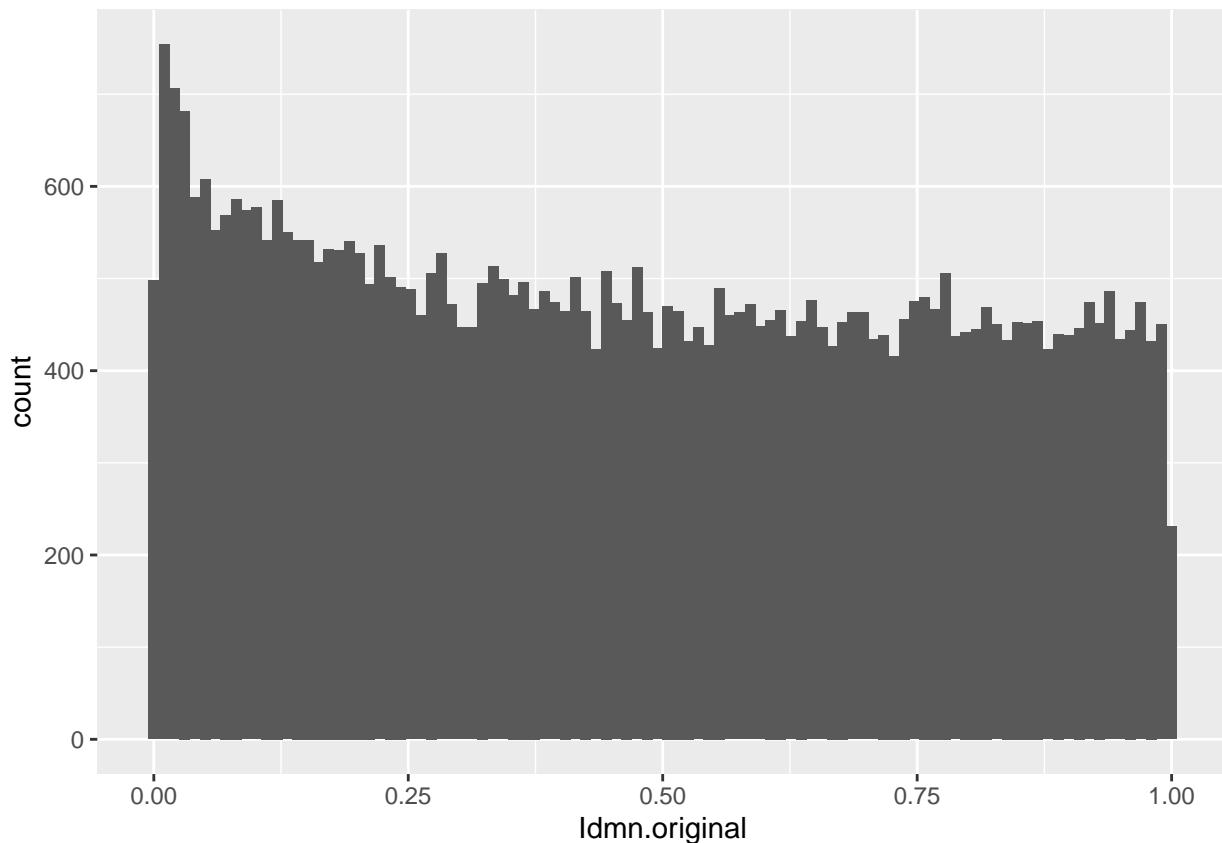
```

load("/Users/carlacasanovasuzarez/Desktop/Radiomic features models (indiv)/Idmn.original.rda")

# Store toptable, p.value, summary
summa.fit.idmn0 <- decideTests(fit)
toptable.idmn0 <- topTable(fit, coef = "Idmn.original", number = dim(counts.ok)[1])
toptable.idmn0 <- toptable.idmn0[order(toptable.idmn0$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Idmn.original)) + geom_histogram(bins = 100)

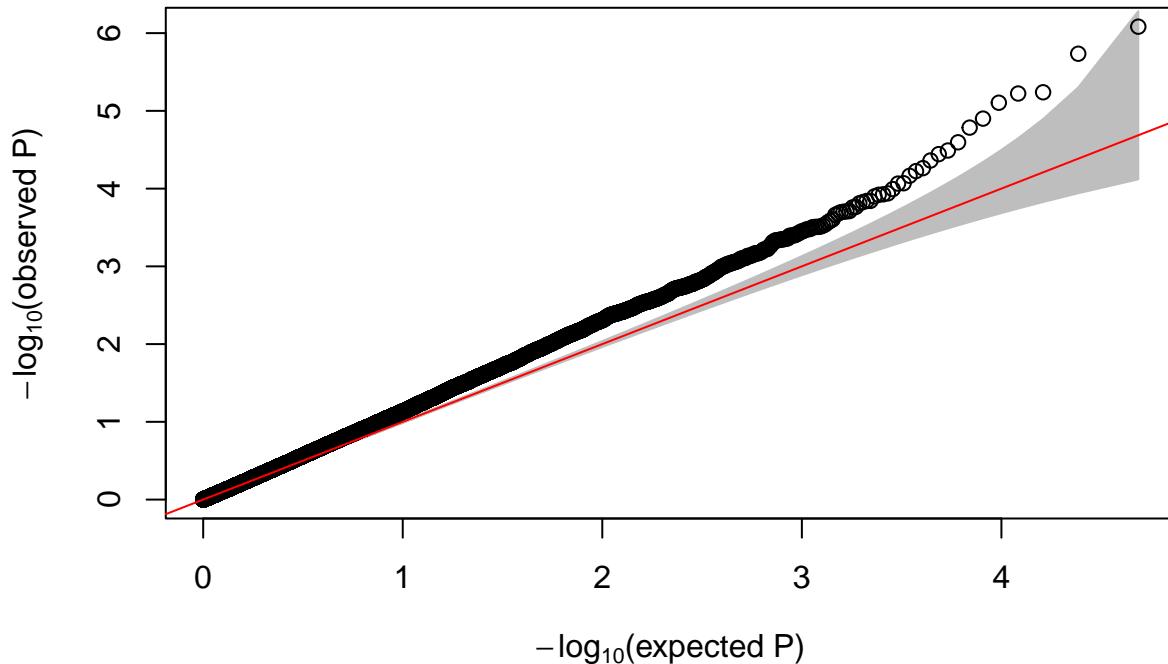
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Idmn.original)

```



```
summary(summa.fit.idmn0)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           601          0     89      0      0      0          0
## NotSig        22631        48525 48368 48525 48524 48525        48525
## Up            25293          0    68      0      1      0          0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0          0          0          0
## NotSig        48525        48525        48525        48525        48525        48525
## Up             0            0          0          0          0          0          0
##             Idmn.original   X1      X2      X3      X4      X5      X6      X7      X8      X9
## Down           1 18458 16255 13932 12369 10607 10670 7127 7268 7937
## NotSig        48523 12783 19492 22225 25214 26772 28368 32682 33558 32750
## Up            1 17284 12778 12368 10942 11146 9487 8716 7699 7838
##             X10     X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down          7845  8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig       32626 33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up            8054  6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.idmn0, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	0.10041678	5.0379308	5.261247	8.262337e-07	0.04009299	5.554520
## 1554830_a_at	-0.19493497	2.6289573	-5.071015	1.840997e-06	0.04466720	4.581840
## 1555229_a_at	-0.39799402	0.6820437	-4.793267	5.765254e-06	0.07258511	3.111078
## 1562121_at	-0.17768900	0.1193435	-4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	-0.20693649	-0.3358964	-4.716413	7.857573e-06	0.07625775	2.217700
## 201645_at	-0.26341444	1.8007395	-4.598154	1.258368e-05	0.10177048	2.811716
## 219675_s_at	-0.09225380	5.0965517	-4.530517	1.642267e-05	0.11384429	2.813061
## 224785_at	0.15288095	3.6686028	4.418797	2.536640e-05	0.15386309	2.382161
## 217279_x_at	-0.21058986	0.8980683	-4.355435	3.236753e-05	0.17451493	1.784988
## 218315_s_at	0.09320256	3.2742864	4.327517	3.601302e-05	0.17475318	2.058275

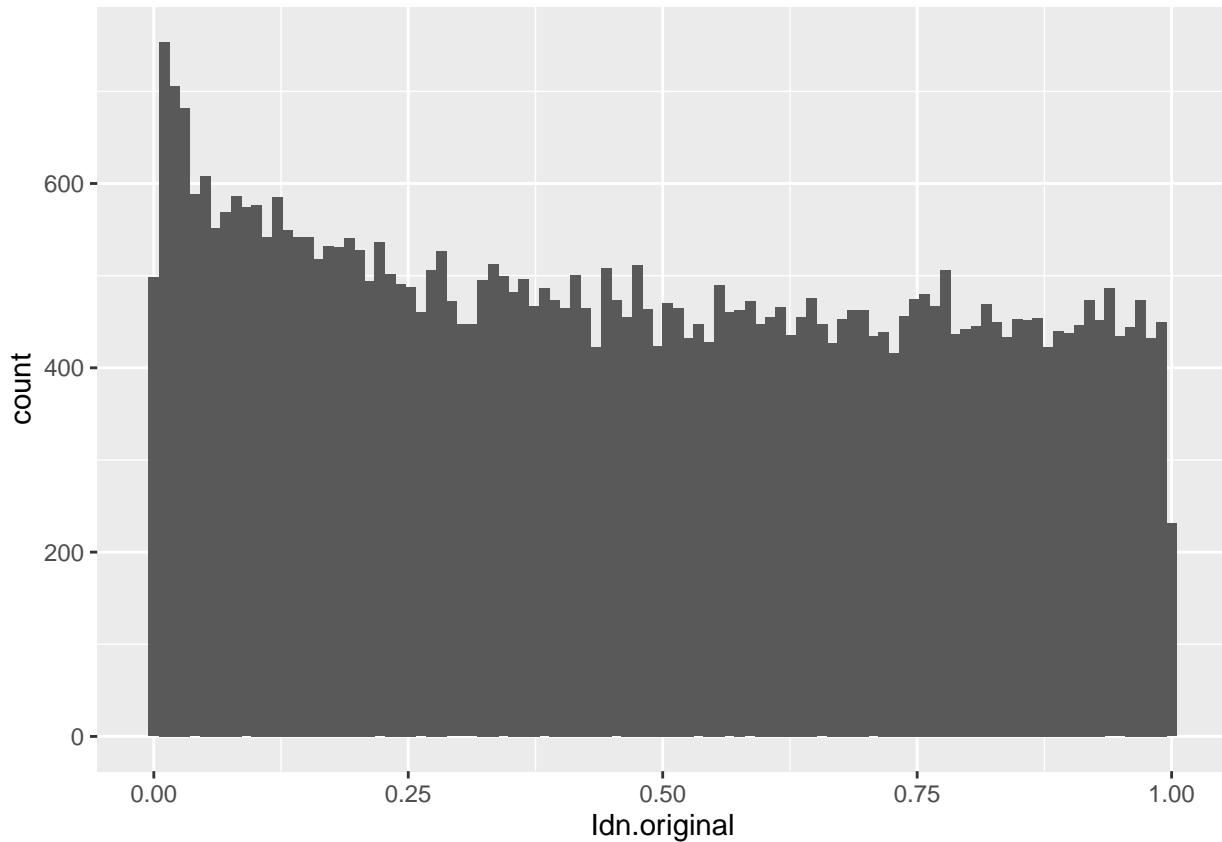
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Idn.original.rda")

summa.fit.idn0 <- decideTests(fit)
toptable.idn0 <- topTable(fit, coef = "Idn.original", number = dim(counts.ok)[1])
toptable.idn0 <- toptable.idn0[order(toptable.idn0$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Idn.original)) + geom_histogram(bins = 100)

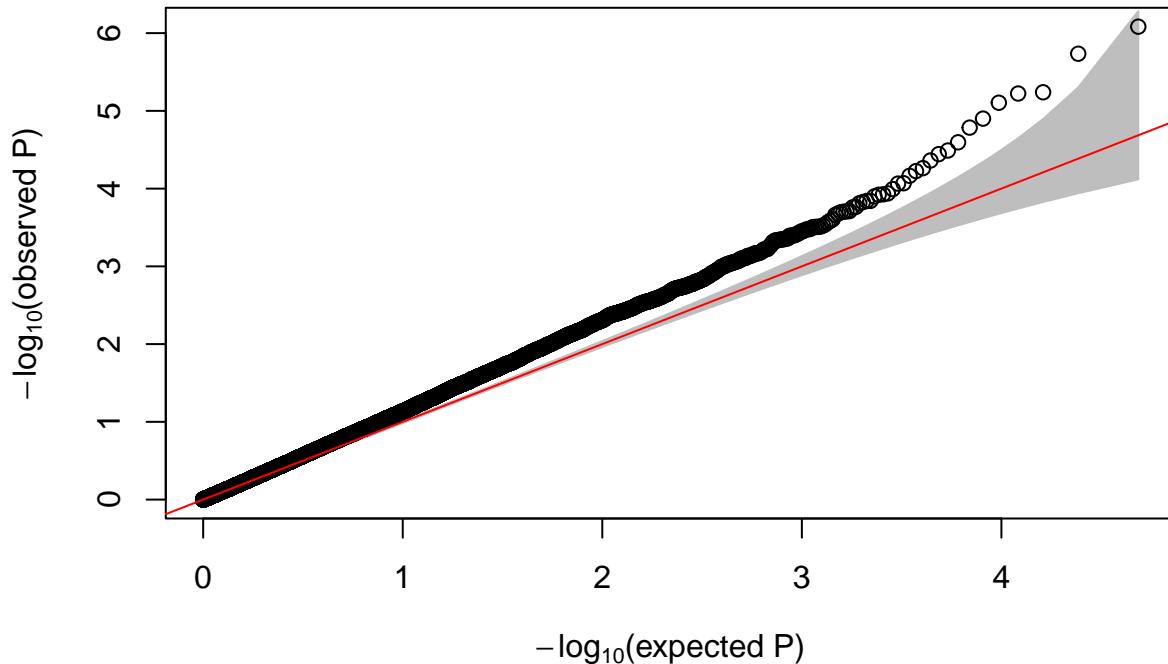
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Idn.original)

```



```
summary(summa.fit.idn0)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           601          0     89      0      0      0            0
## NotSig        22631        48525 48368 48525 48524 48525        48525
## Up            25293          0    68      0      1      0            0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0            0            0            0            0            0
## NotSig        48525        48525        48525        48525        48525        48525
## Up             0            0            0            0            0            0            0
##             Idn.original   X1       X2       X3       X4       X5       X6       X7       X8       X9       X10
## Down           1 18458 16255 13932 12369 10607 10670 7127 7268 7937 7845
## NotSig        48523 12783 19492 22225 25214 26772 28368 32682 33558 32750 32626
## Up             1 17284 12778 12368 10942 11146 9487 8716 7699 7838 8054
##             X11      X12      X13      X14      X15      X16      X17      X18      X19
## Down           8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig        33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up             6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.idn0, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	0.10041678	5.0379308	5.261247	8.262335e-07	0.04009298	5.554521
## 1554830_a_at	-0.19493497	2.6289573	-5.071015	1.840998e-06	0.04466721	4.581839
## 1555229_a_at	-0.39799402	0.6820437	-4.793267	5.765255e-06	0.07258511	3.111078
## 1562121_at	-0.17768900	0.1193435	-4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	-0.20693649	-0.3358964	-4.716413	7.857574e-06	0.07625776	2.217700
## 201645_at	-0.26341443	1.8007395	-4.598154	1.258368e-05	0.10177050	2.811715
## 219675_s_at	-0.09225380	5.0965517	-4.530517	1.642267e-05	0.11384430	2.813060
## 224785_at	0.15288095	3.6686028	4.418797	2.536641e-05	0.15386311	2.382161
## 217279_x_at	-0.21058986	0.8980683	-4.355435	3.236753e-05	0.17451492	1.784988
## 218315_s_at	0.09320256	3.2742864	4.327517	3.601303e-05	0.17475323	2.058275

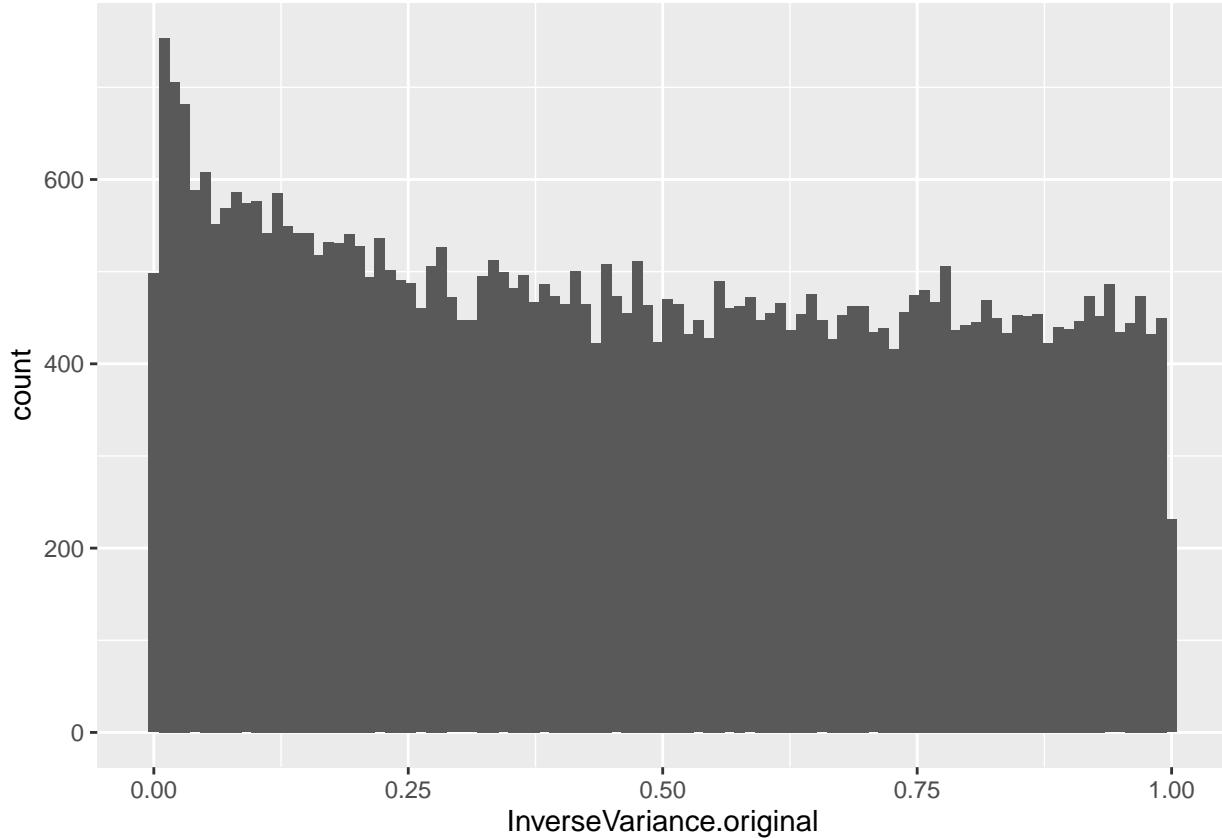
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/InverseVariance.original.rda")

summa.fit.invV <- decideTests(fit)
toptable.invV <- topTable(fit, coef = "InverseVariance.original", number = dim(counts.ok)[1])
toptable.invV <- toptable.invV[order(toptable.invV$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = InverseVariance.original)) + geom_histogram(bins = 100)

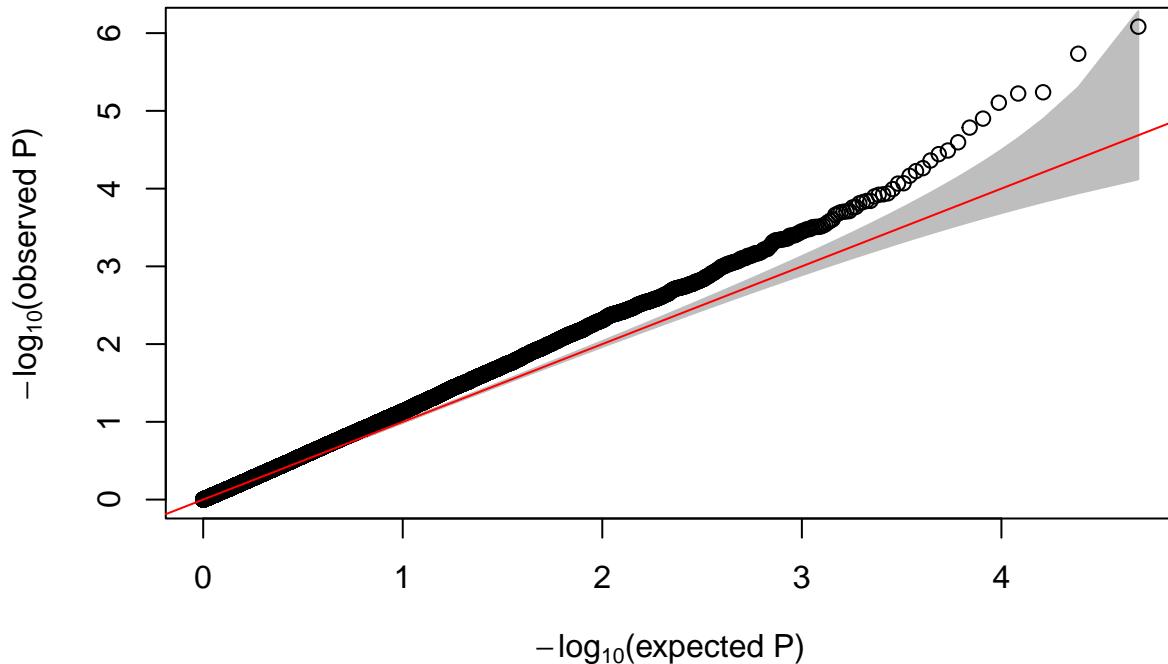
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$InverseVariance.original)

```



```
summary(summa.fit.invV)
```

```
##              (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down             601          0     89      0      0      0           0
## NotSig          22631        48525 48368 48525 48524 48525        48525
## Up              25293          0     68      0      1      0           0
##              dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down             0            0           0           0           0           0           0
## NotSig          48525        48525        48525        48525        48525        48525
## Up               0            0           0           0           0           0           0
##              InverseVariance.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down             1 18458 16255 13932 12369 10607 10670 7127 7268
## NotSig          48523 12783 19492 22225 25214 26772 28368 32682 33558
## Up               1 17284 12778 12368 10942 11146 9487 8716 7699
##              X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down            7937  7845  8259  5401  5277  5729  4520  4006  3269  2649  2552
## NotSig         32750 32626 33413 36682 36536 37362 38935 40443 41052 43512 43299
## Up              7838  8054  6853  6442  6712  5434  5070  4076  4204  2364  2674
```

```
head(toptable.invV, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	-0.10041678	5.0379308	-5.261247	8.262337e-07	0.04009299	5.554520
## 1554830_a_at	0.19493497	2.6289573	5.071015	1.840997e-06	0.04466720	4.581840
## 1555229_a_at	0.39799402	0.6820437	4.793267	5.765254e-06	0.07258511	3.111078
## 1562121_at	0.17768900	0.1193435	4.784088	5.983317e-06	0.07258511	2.725248
## 216922_x_at	0.20693649	-0.3358964	4.716413	7.857573e-06	0.07625775	2.217700
## 201645_at	0.26341444	1.8007395	4.598154	1.258368e-05	0.10177048	2.811716
## 219675_s_at	0.09225380	5.0965517	4.530517	1.642267e-05	0.11384429	2.813061
## 224785_at	-0.15288095	3.6686028	-4.418797	2.536640e-05	0.15386309	2.382161
## 217279_x_at	0.21058986	0.8980683	4.355435	3.236753e-05	0.17451493	1.784988
## 218315_s_at	-0.09320256	3.2742864	-4.327517	3.601302e-05	0.17475318	2.058275

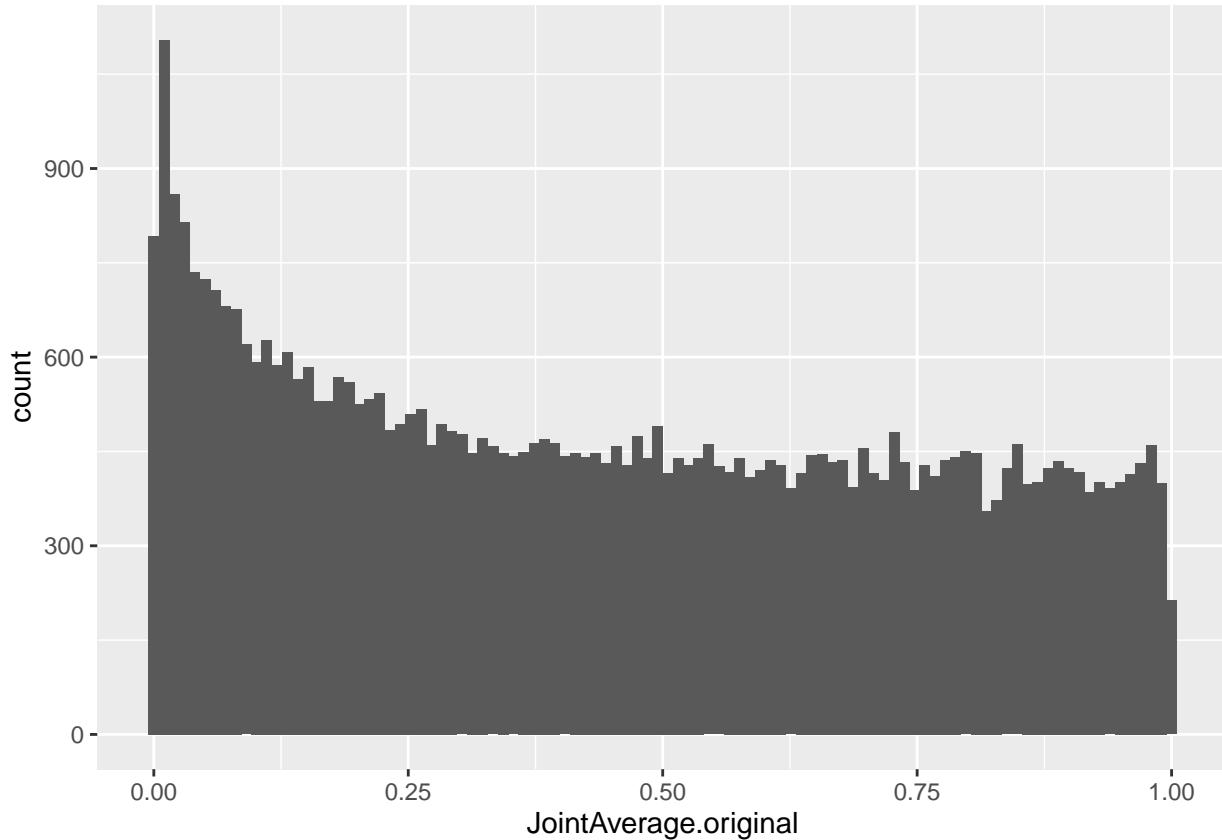
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/JointAverage.original.rda")

summa.fit.jAv <- decideTests(fit)
toptable.jAv <- topTable(fit, coef = "JointAverage.original", number = dim(counts.ok)[1])
toptable.jAv <- toptable.jAv[order(toptable.jAv$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = JointAverage.original)) + geom_histogram(bins = 100)

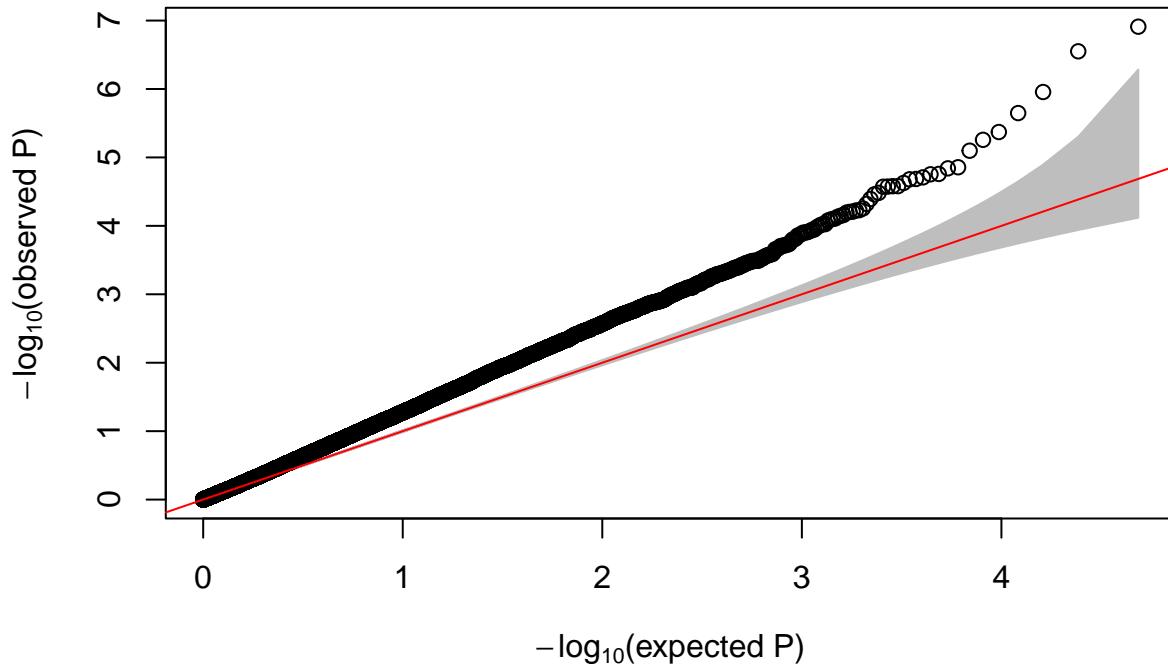
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$JointAverage.original)

```



```
summary(summa.fit.jAv)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           652          0   133     0     0      0            0
## NotSig        22384        48525 48287 48525 48523    48525        48525
## Up            25489          0   105     0     2      0            0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0            0            0            0            0
## NotSig        48525        48525        48525        48525        48525        48525
## Up             0            0            0            0            0            0
##             JointAverage.original X1     X2     X3     X4     X5     X6     X7     X8
## Down           4 18442 16220 13776 12136 10395 9204 8860 7171
## NotSig        48519 12846 19867 22227 25503 26837 28794 32469 34517
## Up            2 17237 12438 12522 10886 11293 10527 7196 6837
##             X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7878  8295  6707  6483  6533  5517  4799  3766  3870  2125  2492
## NotSig       32481 32429 33893 36673 36908 37372 39297 41135 41683 43741 43570
## Up            8166  7801  7925  5369  5084  5636  4429  3624  2972  2659  2463
```

```
head(toptable.jAv, 10)
```

```
##              logFC    AveExpr         t    P.Value adj.P.Val      B
## 212329_at    0.2195191 3.0460263 5.700501 1.228358e-07 0.005960606 7.048836
## 227973_at   -0.1597969 4.8121414 -5.511355 2.814911e-07 0.006829677 6.552754
## 230036_at   -0.2558527 5.6260651 -5.192128 1.106285e-06 0.017894160 5.298819
## 212764_at   -0.2404495 5.3623273 -5.022728 2.248735e-06 0.027279965 4.640577
## 218986_s_at -0.2717643 5.5019428 -4.867899 4.253549e-06 0.041280692 4.042695
## 212916_at    0.1069686 5.4256914  4.803493 5.527292e-06 0.044701976 3.809334
## 221687_s_at  0.2632330 1.2179241  4.712505 7.976086e-06 0.055291364 3.021021
## 239988_at   -0.3715954 2.4479933 -4.572309 1.392629e-05 0.068527057 2.875294
## 230146_s_at -0.2414716 0.3778259 -4.563086 1.444150e-05 0.068527057 2.445160
## 220238_s_at -0.1720925 3.5912361 -4.515235 1.742494e-05 0.068527057 2.738133
```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/JointEnergy.original.rda")

summa.fit.jEn <- decideTests(fit)
summary(summa.fit.jEn)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           606          0    92     0     0          0          0
## NotSig        22617        48525  48365  48525  48524        48525        48525
## Up            25302          0    68     0     1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0
##          JointEnergy.original   X1      X2      X3      X4      X5      X6      X7      X8
## Down           0 18444 16251 13895 12315 10572 10671 7151 7283
## NotSig        48525 12802 19536 22267 25315 26837 28376 32639 33532
## Up            0 17279 12738 12363 10895 11116 9478 8735 7710
##          X9      X10      X11      X12      X13      X14      X15      X16      X17      X18      X19
## Down          7926 7830 8235 5423 5281 5679 4536 3994 3259 2674 2529
## NotSig       32779 32608 33497 36606 36529 37450 38900 40469 41049 43478 43352
## Up            7820 8087 6793 6496 6715 5396 5089 4062 4217 2373 2644

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/JointEntropy.original.rda")

summa.fit.jEnt <- decideTests(fit)
summary(summa.fit.jEnt)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           605          0    91     0     0          0          0
## NotSig        22627        48525  48366  48525  48524        48525        48525
## Up            25293          0    68     0     1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0
##          JointEntropy.original   X1      X2      X3      X4      X5      X6      X7      X8
## Down           0 18452 16251 13908 12356 10576 10666 7100 7280
## NotSig        48525 12783 19543 22243 25254 26856 28373 32734 33528
## Up            0 17290 12731 12374 10915 11093 9486 8691 7717
##          X9      X10      X11      X12      X13      X14      X15      X16      X17      X18      X19
## Down          7964 7862 8261 5425 5263 5691 4529 3972 3299 2676 2545
## NotSig       32699 32584 33418 36603 36542 37423 38927 40507 40997 43468 43320
## Up            7862 8079 6846 6497 6720 5411 5069 4046 4229 2381 2660

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/MCC.original.rda")

summa.fit.mcc <- decideTests(fit)
summary(summa.fit.mcc)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           645          0   132     0     0          0          0
## NotSig        22465        48525  48286  48525  48523        48525        48525
## Up            25415          0   107     0     2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0

```

```

## NotSig      48525          48525          48525 48525          48525
## Up          0              0              0      0      0
## MCC.original X1    X2    X3    X4    X5    X6    X7    X8    X9    X10
## Down        0 18499 16154 14087 12105 10549 10609 6942 7052 8238 7862
## NotSig      48525 12696 19850 21845 25609 26686 28609 32789 33942 32311 32522
## Up          0 17330 12521 12593 10811 11290 9307 8794 7531 7976 8141
##           X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down        8107 5355 5173 5712 4534 3692 3136 2702 2511
## NotSig     33685 36732 36704 37205 38943 41050 41272 43663 43545
## Up          6733 6438 6648 5608 5048 3783 4117 2160 2469

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/MaximumProbability.original.rda")

summa.fit.maxProb <- decideTests(fit)
summary(summa.fit.maxProb)

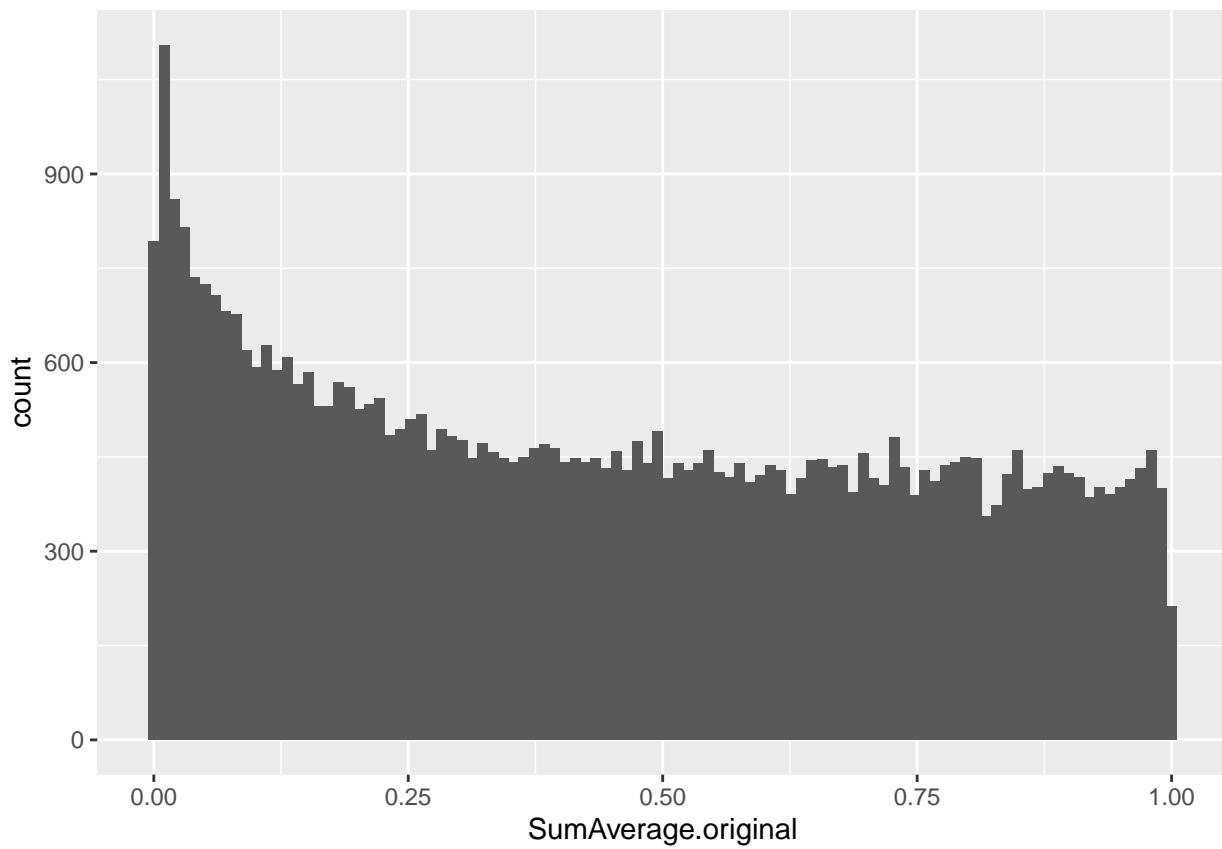
##      (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down       600          0    95    0    0      0          0
## NotSig    22656        48525 48368 48525 48524    48525        48525
## Up         25269          0    62    0    1      0          0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down        0            0          0      0      0          0
## NotSig    48525          48525          48525 48525        48525
## Up          0            0          0      0      0          0
## MaximumProbability.original X1    X2    X3    X4    X5    X6    X7
## Down        0 18481 16250 13886 12271 10591 10688 7243
## NotSig      48525 12765 19554 22271 25361 26848 28380 32495
## Up          0 17279 12721 12368 10893 11086 9457 8787
##           X8    X9   X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down       7279 7970 7856 8144 5464 5268 5632 4610 4109 3118 2668 2560
## NotSig    33524 32748 32576 33657 36510 36538 37530 38803 40275 41287 43493 43314
## Up         7722 7807 8093 6724 6551 6719 5363 5112 4141 4120 2364 2651

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SumAverage.original.rda")

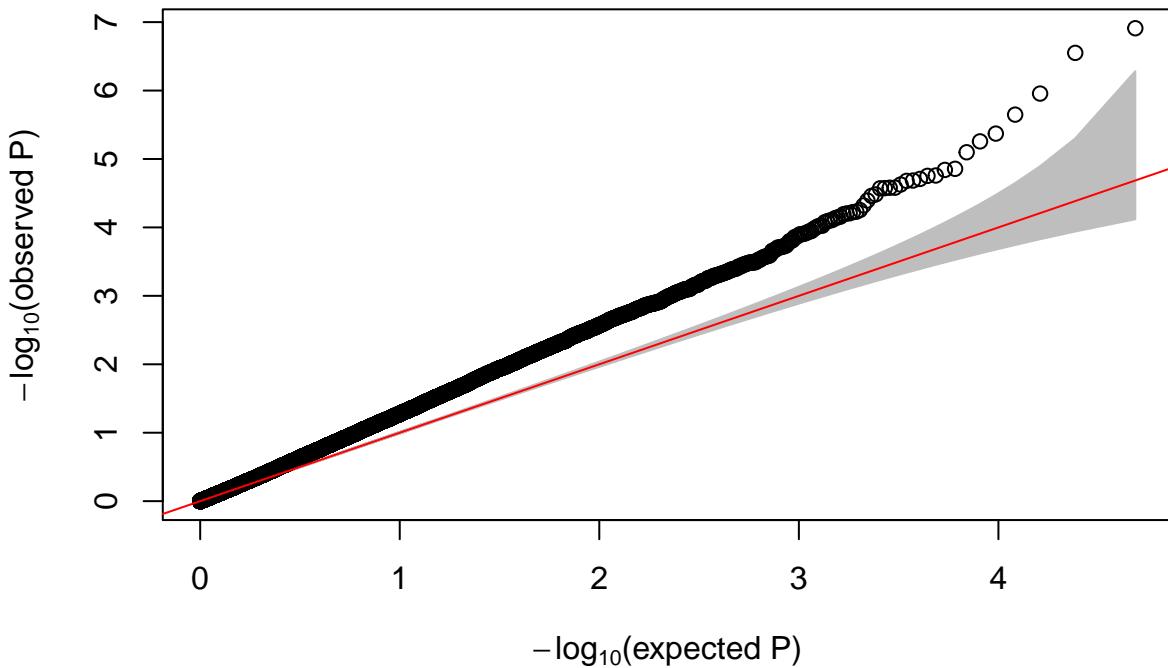
summa.fit.sumAv <- decideTests(fit)
toptable.sumAv <- topTable(fit, coef = "SumAverage.original", number = dim(counts.ok)[1])
toptable.sumAv <- toptable.sumAv[order(toptable.sumAv$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = SumAverage.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$SumAverage.original)
```



```
summary(summa.fit.sumAv)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      652      0 133 0 0 0 0
## NotSig   22384 48525 48287 48525 48523 48525 48525
## Up       25489 0 105 0 2 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## SumAverage.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      4 18442 16220 13776 12136 10395 9204 8860 7171
## NotSig   48519 12846 19867 22227 25503 26837 28794 32469 34517
## Up       2 17237 12438 12522 10886 11293 10527 7196 6837
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    7878 8295 6707 6483 6533 5517 4799 3766 3870 2125 2492
## NotSig  32481 32429 33893 36673 36908 37372 39297 41135 41683 43741 43570
## Up     8166 7801 7925 5369 5084 5636 4429 3624 2972 2659 2463
head(toptable.sumAv, 10)

##          logFC AveExpr      t P.Value adj.P.Val      B
## 212329_at  0.2195191 3.0460263 5.700501 1.228358e-07 0.005960606 7.048836
## 227973_at -0.1597969 4.8121414 -5.511355 2.814911e-07 0.006829677 6.552754
## 230036_at -0.2558527 5.6260651 -5.192128 1.106285e-06 0.017894160 5.298819
## 212764_at -0.2404495 5.3623273 -5.022728 2.248735e-06 0.027279965 4.640577
## 218986_s_at -0.2717643 5.5019428 -4.867899 4.253549e-06 0.041280692 4.042695
## 212916_at  0.1069686 5.4256914  4.803493 5.527292e-06 0.044701976 3.809334
## 221687_s_at 0.2632330 1.2179241  4.712505 7.976086e-06 0.055291364 3.021021
## 239988_at -0.3715954 2.4479933 -4.572309 1.392629e-05 0.068527057 2.875294
## 230146_s_at -0.2414716 0.3778259 -4.563086 1.444150e-05 0.068527057 2.445160
## 220238_s_at -0.1720925 3.5912361 -4.515235 1.742494e-05 0.068527057 2.738133

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SumEntropy.original.rda")

summa.fit.sumEnt <- decideTests(fit)
summary(summa.fit.sumEnt)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      603 0 95 0 0 0 0
## NotSig   22634 48525 48361 48525 48524 48525 48525
## Up       25288 0 69 0 1 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## SumEntropy.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      0 18455 16250 13898 12344 10570 10671 7095 7270
## NotSig   48525 12775 19550 22247 25269 26877 28369 32736 33530
## Up       0 17295 12725 12380 10912 11078 9485 8694 7725
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    7983 7862 8252 5432 5263 5695 4528 3978 3286 2674 2542
## NotSig  32670 32582 33425 36595 36539 37418 38924 40512 41011 43478 43337
## Up     7872 8081 6848 6498 6723 5412 5073 4035 4228 2373 2646

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SumSquares.original.rda")

summa.fit.sumSq <- decideTests(fit)
summary(summa.fit.sumSq)

```

```

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           606          0    97     0     0       0          0
## NotSig        22627        48525 48362 48525 48524     48525        48525
## Up            25292          0   66     0     1       0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0          0          0          0       0          0
## NotSig        48525        48525          0          0       48525 48525        48525
## Up            0          0          0          0       0          0          0
##          SumSquares.original   X1      X2      X3      X4      X5      X6      X7      X8
## Down           0 18451 16240 13889 12290 10563 10681 7204 7283
## NotSig        48525 12792 19549 22283 25346 26860 28369 32570 33537
## Up            0 17282 12736 12353 10889 11102 9475 8751 7705
##          X9      X10      X11      X12      X13      X14      X15      X16      X17      X18      X19
## Down         7933  7850  8215  5430  5275  5670  4558  4020  3208  2689  2555
## NotSig      32781 32558 33523 36585 36541 37465 38848 40432 41127 43450 43315
## Up           7811  8117  6787  6510  6709  5390  5119  4073  4190  2386  2655

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/GrayLevelNonUniformity.original")

summa.fit.g1NU <- decideTests(fit)
summary(summa.fit.g1NU)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           598          0    82     0     0       0          0
## NotSig        22663        48525 48384 48525 48524     48525        48525
## Up            25264          0   59     0     1       0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0          0          0          0       0          0
## NotSig        48525        48525          0          0       48525 48525        48525
## Up            0          0          0          0       0          0          0
##          GrayLevelNonUniformity.original   X1      X2      X3      X4      X5      X6
## Down           0 18511 16224 14022 12376 10561 10664
## NotSig        48525 12729 19691 21981 25167 26857 28431
## Up            0 17285 12610 12522 10982 11107 9430
##          X7      X8      X9      X10      X11      X12      X13      X14      X15      X16      X17      X18
## Down         7195  7270  8089  7751  8110  5477  5291  5590  4621  3976  3154  2605
## NotSig      32396 33464 32458 32916 33540 36514 36484 37539 38792 40545 41234 43602
## Up           8934  7791  7978  7858  6875  6534  6750  5396  5112  4004  4137  2318
##          X19
## Down         2596
## NotSig      43231
## Up           2698

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/GrayLevelNonUniformityNormalized")

summa.fit.g1NUn <- decideTests(fit)
summary(summa.fit.g1NUn)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           603          0    98     0     0       0          0
## NotSig        22751        48525 48359 48525 48523     48525        48525
## Up            25171          0   68     0     2       0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0          0          0          0       0          0
## NotSig        48525        48525          0          0       48525 48525        48525

```

```

## Up          0          0          0          0          0
##      GrayLevelNonUniformityNormalized.original   X1   X2   X3   X4   X5
## Down          0 18505 16202 14055 12387 10462
## NotSig        48525 12723 19734 21897 25154 27032
## Up          0 17297 12589 12573 10984 11031
##      X6   X7   X8   X9   X10  X11  X12  X13  X14  X15  X16  X17
## Down 10665 6795 7288 8207 7849 8284 5529 5335 5619 4575 4094 3086
## NotSig 28427 33097 33386 32216 32757 33272 36432 36494 37195 38904 40334 41322
## Up    9433 8633 7851 8102 7919 6969 6564 6696 5711 5046 4097 4117
##      X18  X19
## Down 2661 2586
## NotSig 43501 43221
## Up    2363 2718

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/GrayLevelVariance.original.rda")

summa.fit.glVar <- decideTests(fit)
summary(summa.fit.glVar)

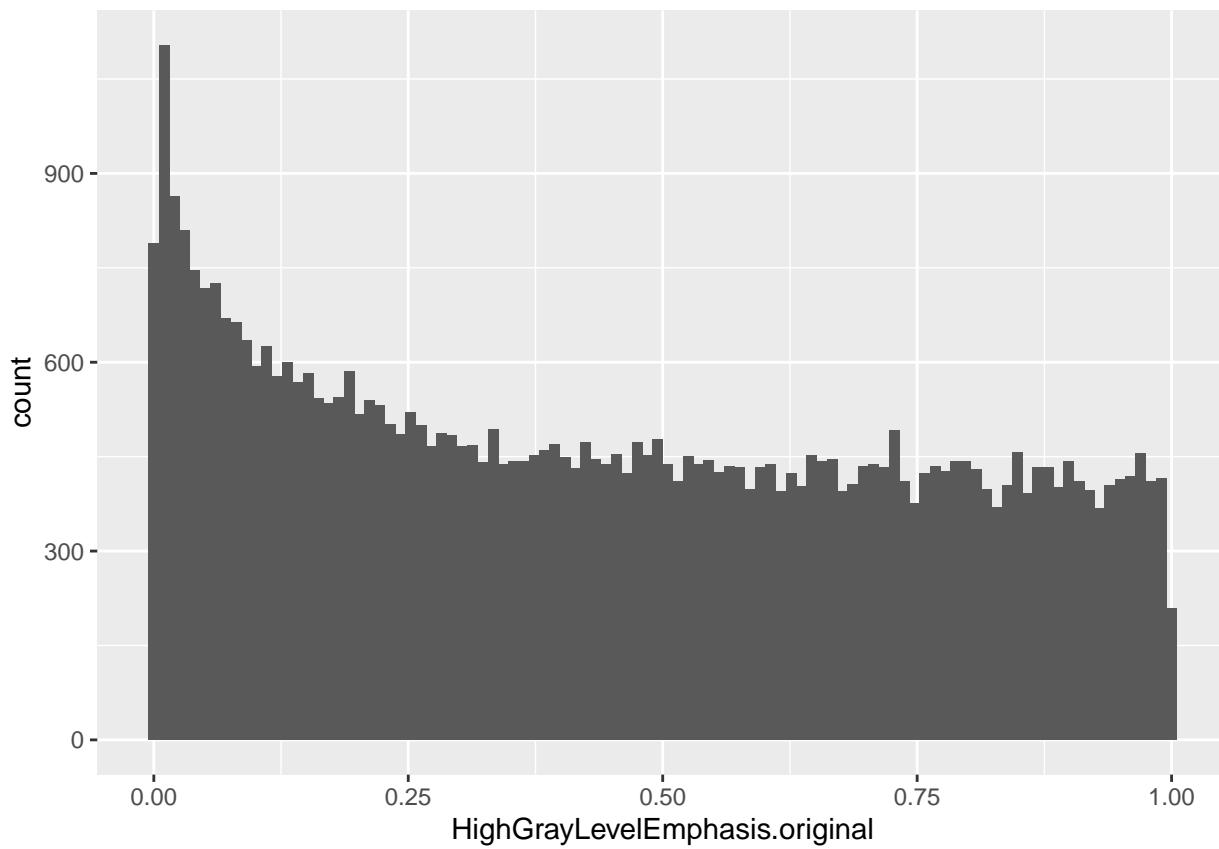
##      (Intercept) GroupSevere  SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down          603          0   98    0    0      0          0          0
## NotSig        22751        48525 48359 48525 48523    48525        48525
## Up           25171          0   68    0    2      0          0          0
##      dusty_exposeY history_asthmaY CoughNo chronic cough     BMI Cr_wheezengY
## Down          0            0          0          0      0          0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up           0            0          0          0      0          0          0
##      GrayLevelVariance.original   X1   X2   X3   X4   X5   X6   X7
## Down          0 18505 16202 14055 12387 10462 10665 6795
## NotSig        48525 12723 19734 21897 25154 27032 28427 33097
## Up          0 17297 12589 12573 10984 11031  9433 8633
##      X8   X9   X10  X11  X12  X13  X14  X15  X16  X17  X18  X19
## Down 7288 8207 7849 8284 5529 5335 5619 4575 4094 3086 2661 2586
## NotSig 33386 32216 32757 33272 36432 36494 37195 38904 40334 41322 43501 43221
## Up    7851 8102 7919 6969 6564 6696 5711 5046 4097 4117 2363 2718

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/HighGrayLevelEmphasis.original.rda")

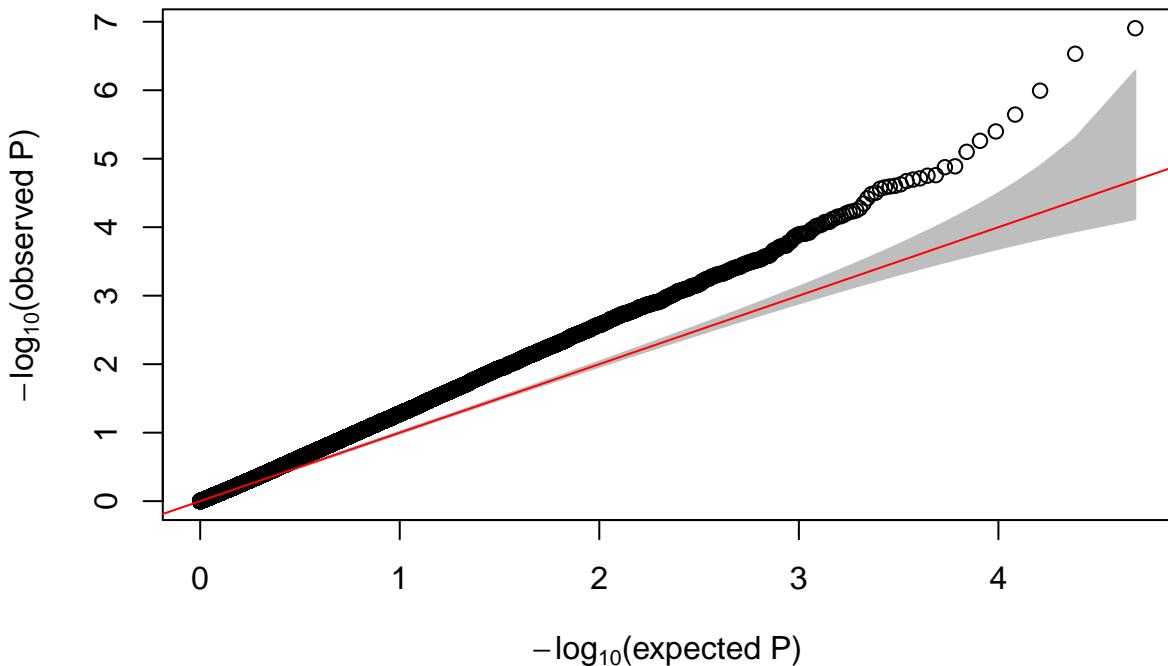
summa.fit.hglEm <- decideTests(fit)
toptable.hglEm <- topTable(fit, coef = "HighGrayLevelEmphasis.original", number = dim(counts.ok)[1])
toptable.hglEm <- toptable.hglEm[order(toptable.hglEm$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = HighGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$HighGrayLevelEmphasis.original)
```



```
summary(summa.fit.hg1Em)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      654      0 134      0 0      0      0
## NotSig   22384    48525 48286 48525 48523    48525    48525
## Up       25487      0 105      0 2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0 0      0      0
## NotSig   48525      48525      48525 48525    48525    48525
## Up       0      0      0      0 0      0      0
##      HighGrayLevelEmphasis.original X1 X2 X3 X4 X5 X6 X7
## Down      4 18444 16217 13780 12132 10396 9210 8864
## NotSig   48519 12844 19869 22210 25503 26832 28789 32481
## Up       2 17237 12439 12535 10890 11297 10526 7180
##      X8 X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    7172 7879 8292 6709 6491 6531 5520 4800 3768 3865 2127 2490
## NotSig  34515 32460 32440 33894 36661 36913 37365 39294 41127 41695 43732 43575
## Up     6838 8186 7793 7922 5373 5081 5640 4431 3630 2965 2666 2460
head(toptable.hg1Em, 10)

```

```

##          logFC AveExpr      t P.Value adj.P.Val      B
## 212329_at  0.2196732 3.0460263 5.697704 1.243631e-07 0.006034721 7.040103
## 227973_at -0.1595674 4.8121414 -5.501652 2.936198e-07 0.007123949 6.514425
## 230036_at -0.2571485 5.6260651 -5.212540 1.014825e-06 0.016414800 5.379352
## 212764_at -0.2406094 5.3623273 -5.020708 2.267672e-06 0.027509696 4.632637
## 218986_s_at -0.2728846 5.5019428 -4.883333 3.993645e-06 0.038758321 4.101052
## 212916_at  0.1071366 5.4256914  4.805750 5.476957e-06 0.044294886 3.817662
## 221687_s_at 0.2637242 1.2179241  4.713958 7.929777e-06 0.054970347 3.027325
## 239988_at -0.3733070 2.4479933 -4.591606 1.290532e-05 0.070061359 2.943295
## 230146_s_at -0.2424403 0.3778259 -4.583726 1.331315e-05 0.070061359 2.514680
## 203238_s_at -0.3927748 2.0908241 -4.515877 1.738117e-05 0.070061359 2.648608

```

```
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LongRunEmphasis.original.rda")
```

```
summa.fit.lrEm <- decideTests(fit)
summary(summa.fit.lrEm)
```

```

##      (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      581      0 92 0 0      0      0
## NotSig   22790    48525 48369 48525 48523    48525    48525
## Up       25154      0 64 0 2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0 0      0      0
## NotSig   48525      48525      48525 48525    48525    48525
## Up       0      0      0      0 0      0      0
##      LongRunEmphasis.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      0 18517 16207 14031 12419 10458 10671 6821 7314
## NotSig   48525 12703 19714 21925 25097 27068 28419 33115 33396
## Up       0 17305 12604 12569 11009 10999 9435 8589 7815
##      X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down    8196 7824 8265 5534 5334 5637 4634 4168 3022 2653 2693
## NotSig  32281 32864 33270 36421 36502 37191 38770 40203 41475 43538 43280
## Up     8048 7837 6990 6570 6689 5697 5121 4154 4028 2334 2552

```

```
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LongRunHighGrayLevelEmphasis.rda")
```

```
summa.fit.lrHem <- decideTests(fit)
summary(summa.fit.lrHem)
```

```

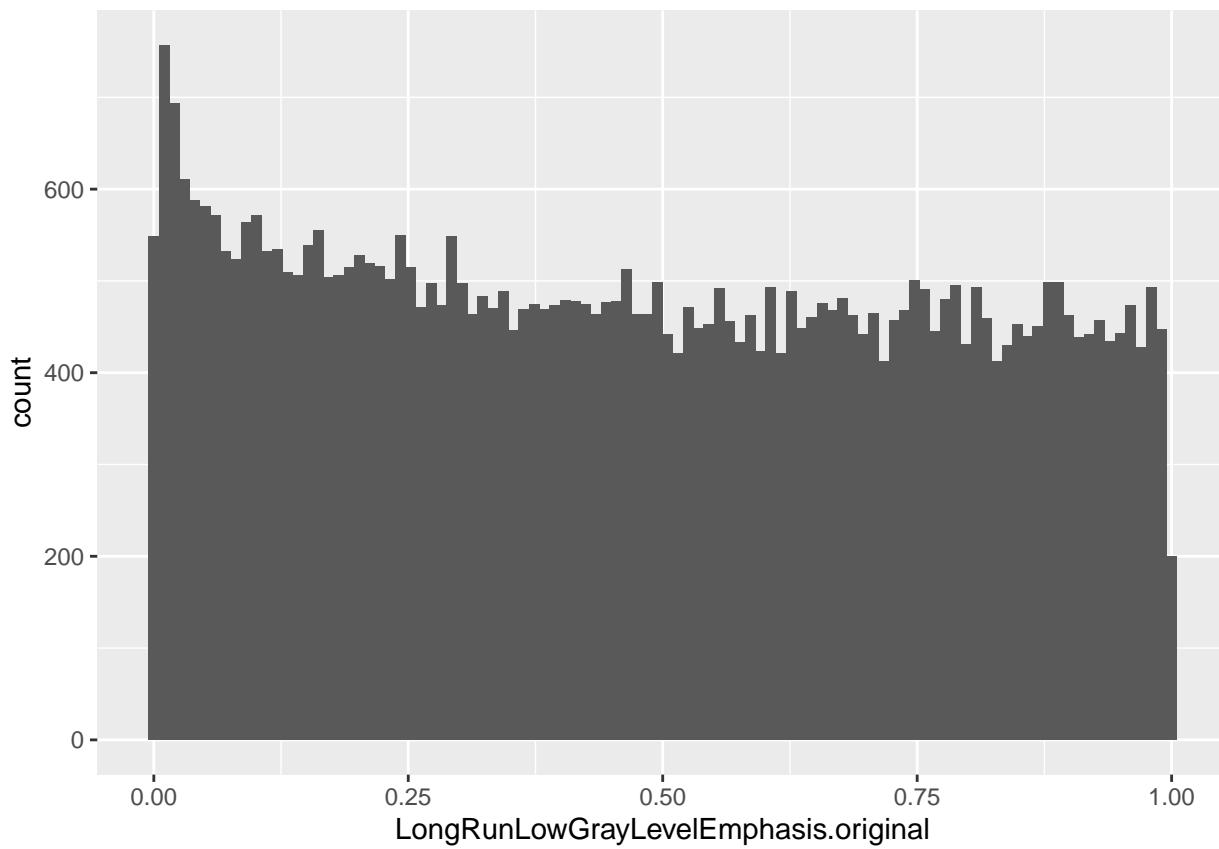
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down            592           0     89     0     0           0           0
## NotSig         22768        48525 48381 48525 48523       48525       48525
## Up             25165           0    55     0     2           0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down            0           0           0           0           0           0
## NotSig         48525           48525           48525       48525       48525
## Up             0           0           0           0           0           0
##          LongRunHighGrayLevelEmphasis.original   X1     X2     X3     X4     X5
## Down           0 18563 16146 14048 12379 10535
## NotSig        48525 12693 19824 21925 25187 26897
## Up             0 17269 12555 12552 10959 11093
##          X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down      10734 6943 7269 8163 7874 8222 5524 5355 5622 4605 4306 2847
## NotSig    28304 33004 33440 32366 32631 33395 36477 36426 37299 38809 39942 41747
## Up        9487 8578 7816 7996 8020 6908 6524 6744 5604 5111 4277 3931
##          X18    X19
## Down      2568 2550
## NotSig   43671 43268
## Up        2286 2707

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LongRunLowGrayLevelEmphasis.RData")

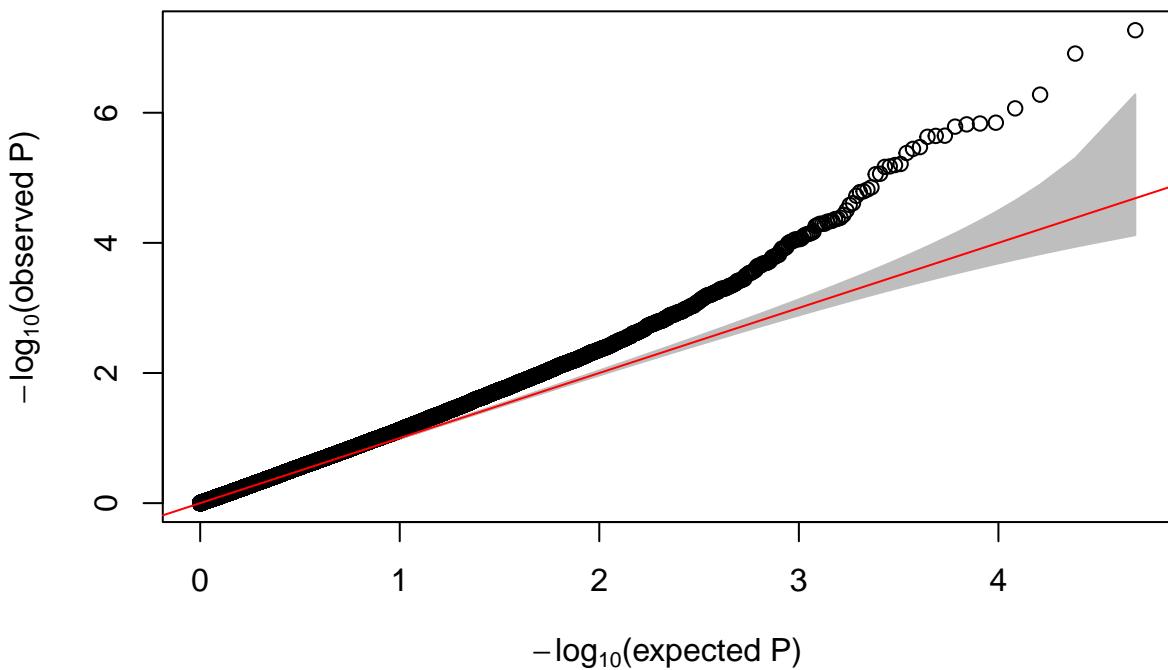
summa.fit.lrLem <- decideTests(fit)
toptable.lrLEM <- topTable(fit, coef = "LongRunLowGrayLevelEmphasis.original", number = dim(counts.ok)[1])
toptable.lrLEM <- toptable.lrLEM[order(toptable.lrLEM$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LongRunLowGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$LongRunLowGrayLevelEmphasis.original)
```



```
summary(summa.fit.lrLem)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      568      0   100      0      0      0      0
## NotSig   22783  48525 48361 48525 48521  48525  48525
## Up       25174      0    64      0     4      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525 48525 48525  48525
## Up       0      0      0      0      0      0      0
##      LongRunLowGrayLevelEmphasis.original   X1     X2     X3     X4     X5     X6
## Down      2 18390 16115 13941 12445 10167 10533
## NotSig   48498 12762 19893 22047 25114 27314 28677
## Up       25 17373 12517 12537 10966 11044  9315
##      X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down   6799 7247 8236 7789 7962 5539 5335 5658 4621 4103 2892 2638
## NotSig 33070 33610 32104 32866 33768 36473 36518 37105 38742 40143 41775 43510
## Up     8656 7668 8185 7870 6795 6513 6672 5762 5162 4279 3858 2377
##      X19
## Down   1962
## NotSig 44676
## Up     1887

head(toptable.lrLEm, 10)

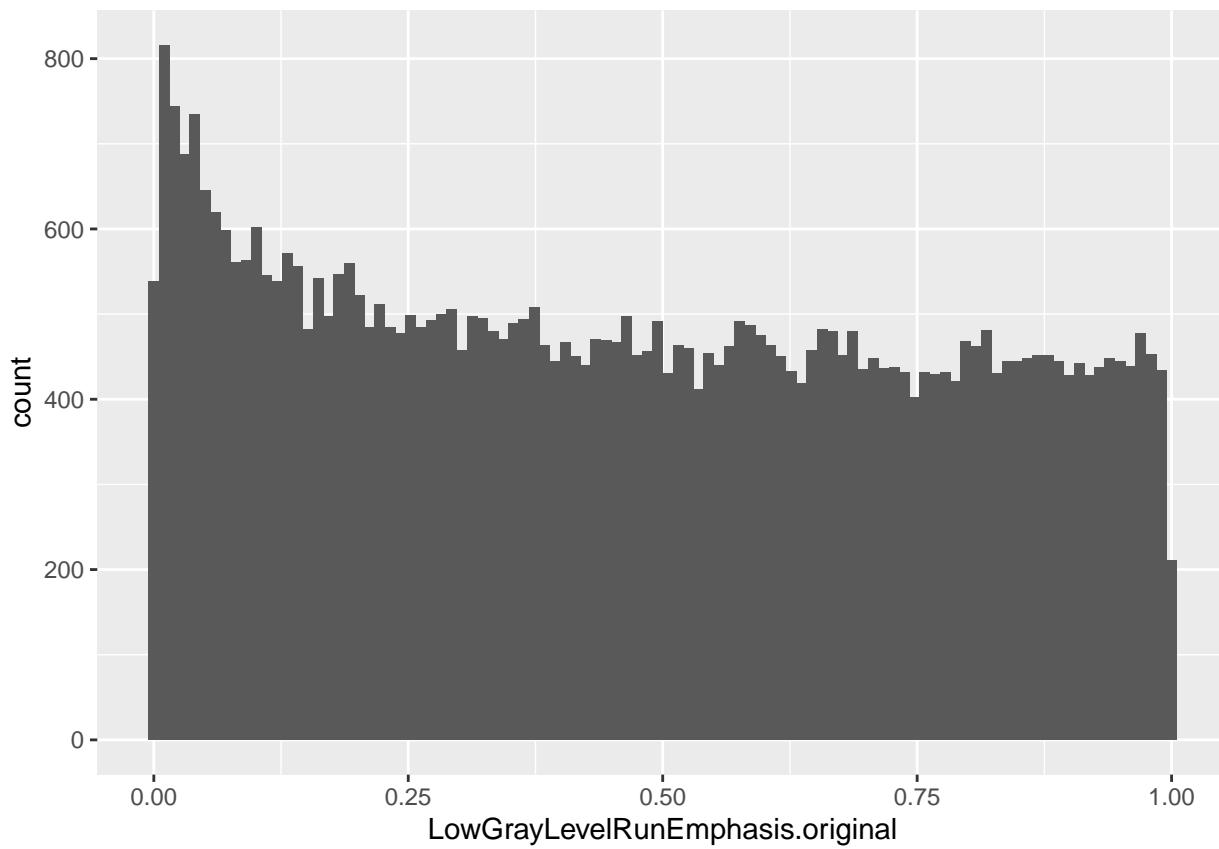
##          logFC AveExpr      t    P.Value adj.P.Val      B
## 221816_s_at 0.12774320 6.663139 5.885750 5.396119e-08 0.002618467 8.119250
## 203610_s_at 0.11783840 5.433915 5.700220 1.231877e-07 0.002988842 7.355332
## 208436_s_at 0.16661079 5.092808 5.366532 5.270703e-07 0.008525361 5.992282
## 203567_s_at 0.10588114 5.983397 5.252799 8.566394e-07 0.009918120 5.521922
## 202145_at   0.29135696 3.641079 5.132813 1.421808e-06 0.009918120 5.025263
## 221622_s_at 0.07202188 6.095018 5.125906 1.463620e-06 0.009918120 5.021955
## 214059_at   0.43303799 3.679703 5.118620 1.509025e-06 0.009918120 4.985502
## 228617_at   0.27153207 5.754949 5.099453 1.635136e-06 0.009918120 4.906834
## 204747_at   0.30693328 5.588170 5.022798 2.250488e-06 0.010336031 4.615017
## 212203_x_at 0.09147248 8.127608 5.020738 2.269808e-06 0.010336031 4.379757

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LowGrayLevelRunEmphasis.original")

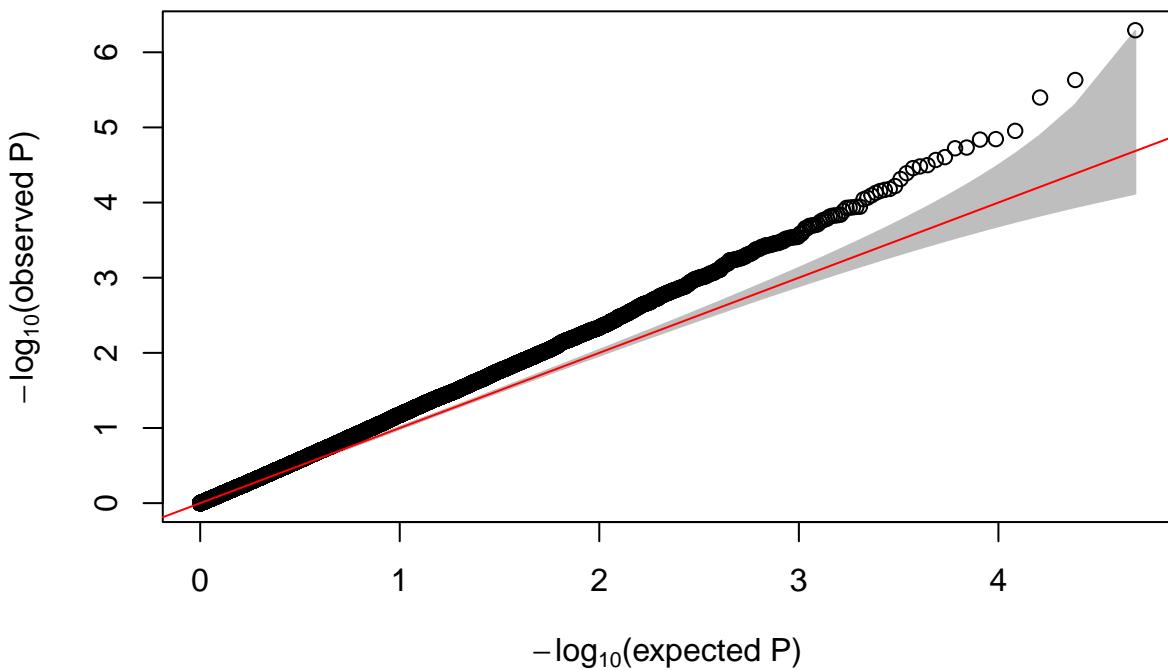
summa.fit.lowGLRem <- decideTests(fit)
toptable.lowGLRem <- topTable(fit, coef = "LowGrayLevelRunEmphasis.original", number = dim(counts.ok)[1])
toptable.lowGLRem <- toptable.lowGLRem[order(toptable.lowGLRem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LowGrayLevelRunEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$LowGrayLevelRunEmphasis.original)
```



```
summary(summa.fit.lowGLRem)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      617      0 115 0 0 0 0
## NotSig   22650 48525 48320 48525 48523 48525 48525
## Up       25258 0 90 0 2 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## LowGrayLevelRunEmphasis.original X1 X2 X3 X4 X5 X6
## Down      0 18492 16048 14100 12264 10448 10566
## NotSig   48524 12709 20084 21850 25403 26787 28695
## Up       1 17324 12393 12575 10858 11290 9264
## X7 X8 X9 X10 X11 X12 X13 X14 X15 X16 X17 X18
## Down   6759 7088 8231 7875 8035 5359 5188 5670 4507 3752 3050 2731
## NotSig 33150 33979 32335 32389 33822 36827 36626 37193 38966 40870 41364 43596
## Up    8616 7458 7959 8261 6668 6339 6711 5662 5052 3903 4111 2198
## X19
## Down   2259
## NotSig 44086
## Up    2180

head(toptable.lowGLRem, 10)

##          logFC AveExpr      t  P.Value adj.P.Val      B
## 239988_at  0.29153851 2.4479933 5.374462 5.090753e-07 0.02470288 5.838132
## 230036_at  0.17733877 5.6260651 5.013367 2.339017e-06 0.05675041 4.586602
## 241514_at -0.40961125 -0.7748055 -4.883115 3.999111e-06 0.06468562 2.382877
## 218986_s_at 0.18204571 5.5019428 4.629470 1.111286e-05 0.11497359 3.132002
## 226130_at -0.15498912 4.2551221 -4.565501 1.431036e-05 0.11497359 2.938669
## 238453_at -0.23061480 1.0245559 -4.561747 1.452339e-05 0.11497359 2.583608
## 228077_at -0.14854086 3.5670907 -4.499613 1.852879e-05 0.11497359 2.691687
## 233127_at -0.31237659 1.0540609 -4.493787 1.895494e-05 0.11497359 2.331430
## 1563051_at -0.16786385 3.5601254 -4.424154 2.484116e-05 0.13010649 2.419399
## 212579_at   0.09259941 6.9622936 4.401279 2.713437e-05 0.13010649 2.161734

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/RunEntropy.original.rda")

summa.fit.runEnt <- decideTests(fit)
summary(summa.fit.runEnt)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      603 0 85 0 0 0 0
## NotSig   22674 48525 48380 48525 48524 48525 48525
## Up       25248 0 60 0 1 0 0
## dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down      0 0 0 0 0 0 0
## NotSig   48525 48525 48525 48525 48525 48525 48525
## Up       0 0 0 0 0 0 0
## RunEntropy.original X1 X2 X3 X4 X5 X6 X7 X8
## Down      0 18513 16216 14024 12400 10519 10650 6764 7257
## NotSig   48525 12704 19669 21959 25158 26997 28432 33165 33497
## Up       0 17308 12640 12542 10967 11009 9443 8596 7771
## X9 X10 X11 X12 X13 X14 X15 X16 X17 X18 X19
## Down   8157 7842 8292 5448 5351 5648 4547 4021 3229 2625 2589
## NotSig 32342 32781 33231 36568 36424 37295 38928 40434 41108 43566 43224
## Up    8026 7902 7002 6509 6750 5582 5050 4070 4188 2334 2712

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/RunLengthNonUniformity.original.rda")

summa.fit.rlNU <- decideTests(fit)
summary(summa.fit.rlNU)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           597          0     76      0      0          0          0
## NotSig        22681        48525 48393 48525 48524        48525        48525
## Up            25247          0     56      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezeNgy
## Down           0             0          0          0          0          0
## NotSig        48525        48525          0          0        48525 48525        48525
## Up             0             0          0          0          0          0
##          RunLengthNonUniformity.original   X1     X2     X3     X4     X5     X6
## Down           0 18527 16212 14023 12387 10574 10679
## NotSig        48525 12707 19703 21983 25148 26820 28405
## Up             0 17291 12610 12519 10990 11131 9441
##          X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down         7178 7286 8111 7753 8163 5466 5320 5580 4639 4000 3144 2625
## NotSig      32431 33447 32429 32889 33470 36529 36457 37521 38759 40506 41248 43570
## Up           8916 7792 7985 7883 6892 6530 6748 5424 5127 4019 4133 2330
##          X19
## Down         2618
## NotSig      43188
## Up           2719

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/RunLengthNonUniformityNormalized.rda")

summa.fit.rlNUn <- decideTests(fit)
summary(summa.fit.rlNUn)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           609          0     80      0      0          0          0
## NotSig        22646        48525 48384 48525 48524        48525        48525
## Up            25270          0     61      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezeNgy
## Down           0             0          0          0          0          0
## NotSig        48525        48525          0          0        48525 48525        48525
## Up             0             0          0          0          0          0
##          RunLengthNonUniformityNormalized.original   X1     X2     X3     X4     X5
## Down           0 18510 16205 14021 12406 10509
## NotSig        48525 12706 19685 21953 25151 27011
## Up             0 17309 12635 12551 10968 11005
##          X6     X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17
## Down         10670 6789 7258 8166 7845 8325 5406 5339 5661 4556 3952 3289
## NotSig      28415 33085 33490 32327 32763 33205 36639 36453 37301 38902 40526 41026
## Up           9440 8651 7777 8032 7917 6995 6480 6733 5563 5067 4047 4210
##          X18     X19
## Down         2652 2589
## NotSig      43517 43233
## Up           2356 2703

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/RunPercentage.original.rda")

summa.fit.rPer <- decideTests(fit)

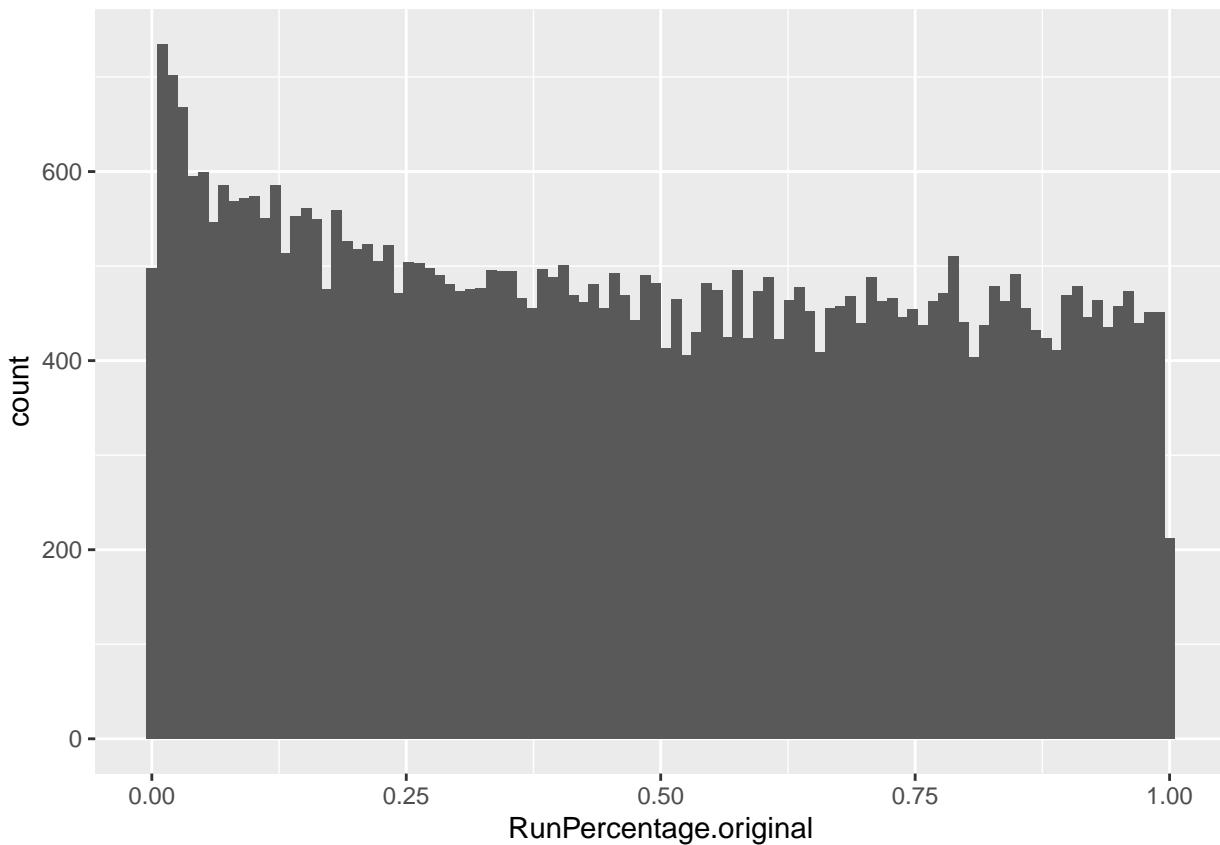
```

```

toptable.rPer <- topTable(fit, coef = "RunPercentage.original", number = dim(counts.ok)[1])
toptable.rPer <- toptable.rPer[order(toptable.rPer$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = RunPercentage.original)) + geom_histogram(bins = 100)

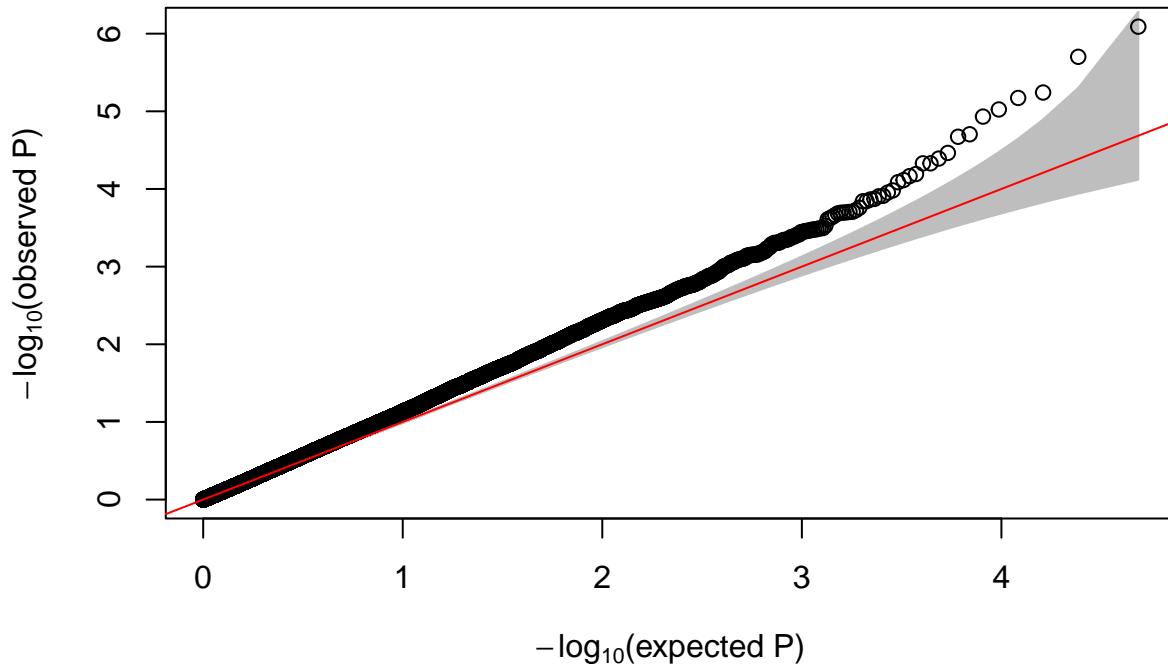
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$RunPercentage.original)

```



```
summary(summa.fit.rPer)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           603          0     89      0      0        0            0
## NotSig        22623        48525  48369  48525  48524      48525        48525
## Up            25299          0     67      0      1        0            0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0             0        0        0        0        0            0
## NotSig        48525        48525        0        0        0        0        48525
## Up             0             0        0        0        0        0            0
##          RunPercentage.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           1 18465 16258 13930 12364 10610 10673 7118 7269
## NotSig        48523 12775 19495 22226 25217 26768 28360 32699 33562
## Up            1 17285 12772 12369 10944 11147 9492 8708 7694
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7936  7846  8248  5398  5294  5708  4529  4009  3254  2653  2545
## NotSig       32745 32624 33434 36685 36501 37397 38919 40442 41078 43509 43308
## Up            7844  8055  6843  6442  6730  5420  5077  4074  4193  2363  2672
```

```
head(toptable.rPer, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	-0.10110173	5.0379308	-5.265039	8.130249e-07	0.03945204	5.564559
## 1554830_a_at	0.19610034	2.6289573	5.052871	1.985626e-06	0.04817625	4.497213
## 1555229_a_at	0.40029739	0.6820437	4.794857	5.728299e-06	0.08165790	3.084803
## 1562121_at	0.17767386	0.1193435	4.754906	6.731202e-06	0.08165790	2.598570
## 216922_x_at	0.20640961	-0.3358964	4.669918	9.463463e-06	0.09184291	2.040448
## 201645_at	0.26581933	1.8007395	4.616600	1.169779e-05	0.09460586	2.854891
## 219675_s_at	0.09199390	5.0965517	4.483312	1.974977e-05	0.12892525	2.645362
## 224785_at	-0.15500844	3.6686028	-4.464435	2.125506e-05	0.12892525	2.531718
## 217279_x_at	0.21105056	0.8980683	4.340107	3.432266e-05	0.18505633	1.716275
## 218315_s_at	-0.09311102	3.2742864	-4.295988	4.060615e-05	0.18918227	1.946197

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/RunVariance.original.rda")

summa.fit.rVar <- decideTests(fit)
summary(summa.fit.rVar)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           597          0     90      0      0          0          0
## NotSig        22719        48525 48376 48525 48523        48525        48525
## Up            25209          0     59      0      2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0          0
##          RunVariance.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           0 18539 16216 14027 12415 10484 10707 6676 7274
## NotSig        48525 12690 19670 21926 25112 27043 28369 33399 33494
## Up             0 17296 12639 12572 10998 10998 9449 8450 7757
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          8181 7831 8254 5557 5347 5621 4607 4136 3075 2654 2579
## NotSig       32310 32816 33289 36392 36450 37284 38804 40255 41342 43528 43246
## Up            8034 7878 6982 6576 6728 5620 5114 4134 4108 2343 2700

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ShortRunEmphasis.original.rda"

summa.fit.shREM <- decideTests(fit)
summary(summa.fit.shREM)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           596          0     85      0      0          0          0
## NotSig        22721        48525 48381 48525 48523        48525        48525
## Up            25208          0     59      0      2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0          0
##          ShortRunEmphasis.original   X1     X2     X3     X4     X5     X6     X7
## Down           0 18516 16182 14030 12391 10490 10656 6849
## NotSig        48525 12693 19766 21927 25175 27015 28431 33012
## Up             0 17316 12577 12568 10959 11020 9438 8664
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7284 8158 7848 8263 5486 5341 5612 4581 4098 3089 2630 2590
## NotSig       33433 32319 32799 33296 36526 36456 37247 38874 40320 41350 43551 43223
## Up            7808 8048 7878 6966 6513 6728 5666 5070 4107 4086 2344 2712

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ShortRunHighGrayLevelEmphasis.rda"

summa.fit.shRH <- decideTests(fit)
summary(summa.fit.shRH)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           591          0     87      0      0          0          0
## NotSig        22637        48525 48372 48525 48525        48525        48525
## Up            25297          0     66      0      0          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0

```

```

## NotSig      48525          48525          48525 48525          48525
## Up          0              0              0      0      0
##           ShortRunHighGrayLevelEmphasis.original   X1    X2    X3    X4    X5
## Down          0 18496 16153 13832 12408 10440
## NotSig      48525 12686 19739 22339 25198 27145
## Up          0 17343 12633 12354 10919 10940
##           X6    X7    X8    X9    X10   X11   X12   X13   X14   X15   X16   X17
## Down 10586 6958 7214 7853 7914 8531 5505 5323 5719 4500 3838 3364
## NotSig 28571 32905 33576 32965 32571 33046 36489 36482 37175 39083 40792 40933
## Up    9368 8662 7735 7707 8040 6948 6531 6720 5631 4942 3895 4228
##           X18   X19
## Down 2608 2442
## NotSig 43611 43412
## Up    2306 2671

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ShortRunLowGrayLevelEmphasis.R")

summa.fit.shRL <- decideTests(fit)
summary(summa.fit.shRL)

##           (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      591          0 100 0 0 0 0
## NotSig    22684        48525 48357 48525 48523 48525 48525
## Up       25250          0 68 0 2 0 0
##           dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down          0          0 0 0 0 0 0
## NotSig     48525        48525 48525 48525 48525 48525 48525
## Up          0          0 0 0 0 0 0
##           ShortRunLowGrayLevelEmphasis.original   X1    X2    X3    X4    X5
## Down          0 18556 16189 13836 12316 10583
## NotSig      48525 12642 19815 22190 25333 26815
## Up          0 17327 12521 12499 10876 11127
##           X6    X7    X8    X9    X10   X11   X12   X13   X14   X15   X16   X17
## Down 10804 6875 7267 8210 7924 8342 5316 5399 5757 4821 4036 3208
## NotSig 28118 32899 33562 32224 32623 33093 36808 36355 37049 38412 40352 41077
## Up    9603 8751 7696 8091 7978 7090 6401 6771 5719 5292 4137 4240
##           X18   X19   X20
## Down 2791 2801 2281
## NotSig 43258 43075 43977
## Up    2476 2649 2267

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/HighGrayLevelZoneEmphasis.original.R")

summa.fit.hglZEM <- decideTests(fit)
summary(summa.fit.hglZEM)

##           (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      608          0 142 0 0 0 0
## NotSig    22700        48525 48256 48525 48523 48525 48525
## Up       25217          0 127 0 2 0 0
##           dusty_exposeY history_asthmaY CoughNo chronic cough BMI Cr_wheezengY
## Down          0          0 0 0 0 0 0
## NotSig     48525        48525 48525 48525 48525 48525 48525
## Up          0          0 0 0 0 0 0
##           HighGrayLevelZoneEmphasis.original   X1    X2    X3    X4    X5    X6

```

```

## Down          0 18644 16012 13595 11473 9819 9163
## NotSig       48525 12577 20315 22542 24151 27897 29036
## Up           0 17304 12198 12388 12901 10809 10326
## X7      X8     X9    X10   X11   X12   X13   X14   X15   X16   X17   X18
## Down     8992  6977  7396  8761  6706  6444  6406  5835  4957  4120  3683  3125
## NotSig  32503 34494 33387 31601 33500 36563 36704 37124 39149 40211 41896 43069
## Up       7030  7054  7742  8163  8319  5518  5415  5566  4419  4194  2946  2331
## X19     X20
## Down     2079  2845
## NotSig  43741 43198
## Up       2705  2482

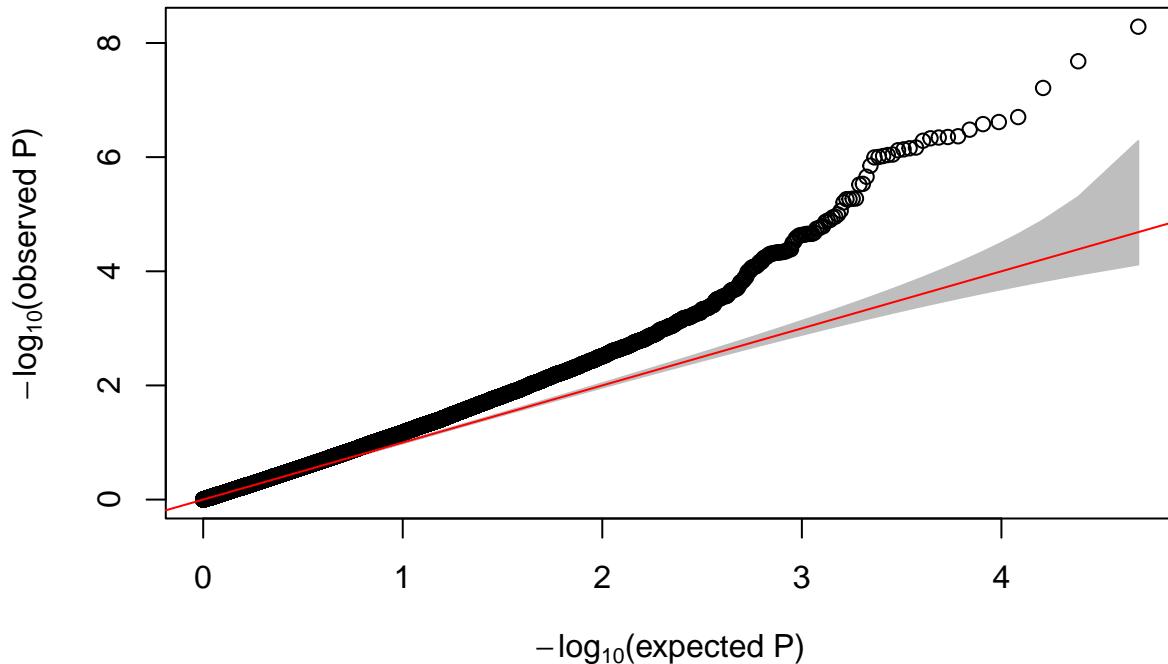
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeAreaEmphasis.original.rda")

summa.fit.larAEm <- decideTests(fit)
toptable.larAEm <- topTable(fit, coef = "LargeAreaEmphasis.original", number = dim(counts.ok)[1])
toptable.larAEm <- toptable.larAEm[order(toptable.larAEm$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LargeAreaEmphasis.original)) + geom_histogram(bins = 100)

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$LargeAreaEmphasis.original)

```



```
summary(summa.fit.larAEm)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           590          0   110     0     1      0            0
## NotSig        22743        48525 48325 48525 48519    48525        48525
## Up            25192          0   90     0     5      0            0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0      0       0            0
## NotSig        48525        48525        48525    48525        48525        48525
## Up             0            0          0          0      0       0            0
##          LargeAreaEmphasis.original X1     X2     X3     X4     X5     X6     X7
## Down           8 18446 16006 14101 12365 10183  9282  8518
## NotSig        48438 12711 20082 21886 25190 27176 28732 33378
## Up            79 17368 12437 12538 10970 11166 10511  6629
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         7523 7977 8279 6584 6497 6640 5644 5029 3962 4215 2287 1933
## NotSig      33787 32366 32322 34228 36455 36604 37307 38998 40816 41076 43571 44454
## Up          7215 8182 7924 7713 5573 5281 5574 4498 3747 3234 2667 2138
head(toptable.larAEm, 10)
```

```
##          logFC AveExpr      t    P.Value    adj.P.Val      B
## 230036_at  0.20563742 5.626065 6.399638 5.178948e-09 0.0002513085 10.358990
## 222986_s_at 0.05655418 7.893641 6.095749 2.090387e-08 0.0005071800  8.847290
## 239988_at  0.28344604 2.447993 5.856891 6.137996e-08 0.0009928209  7.910719
## 204747_at  0.27452096 5.588170 5.591531 1.986236e-07 0.0020620811  6.850120
## 228617_at  0.24109252 5.754949 5.545631 2.427412e-07 0.0020620811  6.645829
## 218986_s_at 0.19645239 5.501943 5.526582 2.637527e-07 0.0020620811  6.608164
## 206133_at  0.23002381 5.082622 5.475041 3.299511e-07 0.0020620811  6.404180
## 203568_s_at 0.11150882 4.180112 5.413383 4.307413e-07 0.0020620811  6.181011
## 221816_s_at 0.10094490 6.663139 5.406529 4.436560e-07 0.0020620811  6.034845
## 214059_at  0.37567108 3.679703 5.401473 4.534260e-07 0.0020620811  6.132976
```

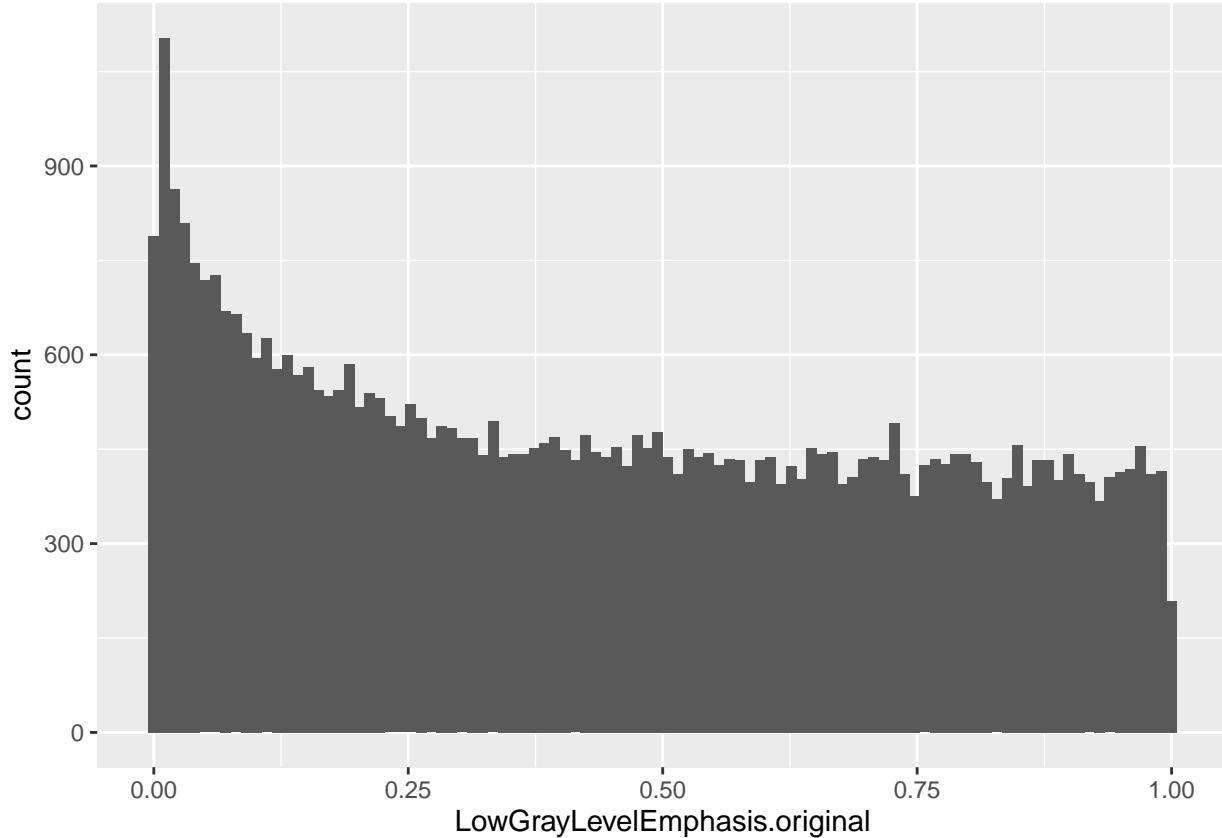
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LowGrayLevelEmphasis.original")

summa.fit.lowGLem <- decideTests(fit)
toptable.lowGLem <- topTable(fit, coef = "LowGrayLevelEmphasis.original", number = dim(counts.ok)[1])
toptable.lowGLem <- toptable.lowGLem[order(toptable.lowGLem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LowGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

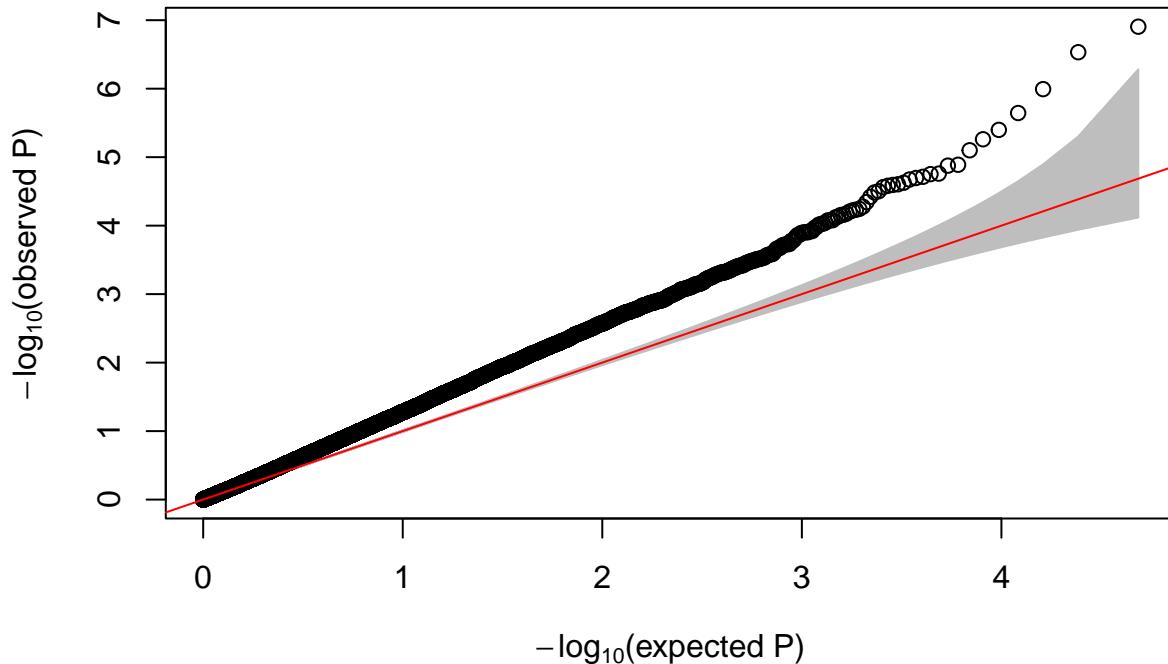
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$LowGrayLevelEmphasis.original)

```



```
summary(summa.fit.lowGLem)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down       654           0   134     0     0      0           0
## NotSig    22384        48525 48286 48525 48523    48525        48525
## Up        25487           0  105     0     2      0           0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down          0             0           0           0           0           0
## NotSig     48525           48525           48525 48525 48525        48525
## Up           0             0           0           0           0           0
##          LowGrayLevelEmphasis.original X1     X2     X3     X4     X5     X6     X7
## Down            2 18444 16217 13780 12132 10396  9210  8864
## NotSig        48519 12844 19869 22210 25503 26832 28789 32481
## Up             4 17237 12439 12535 10890 11297 10526  7180
##          X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down       7172  7879  8292  6709  6491  6531  5520  4800  3768  3865  2127  2490
## NotSig    34515 32460 32440 33894 36661 36913 37365 39294 41127 41695 43732 43575
## Up        6838  8186  7793  7922  5373  5081  5640  4431  3630  2965  2666  2460
```

```
head(toptable.lowGLem, 10)
```

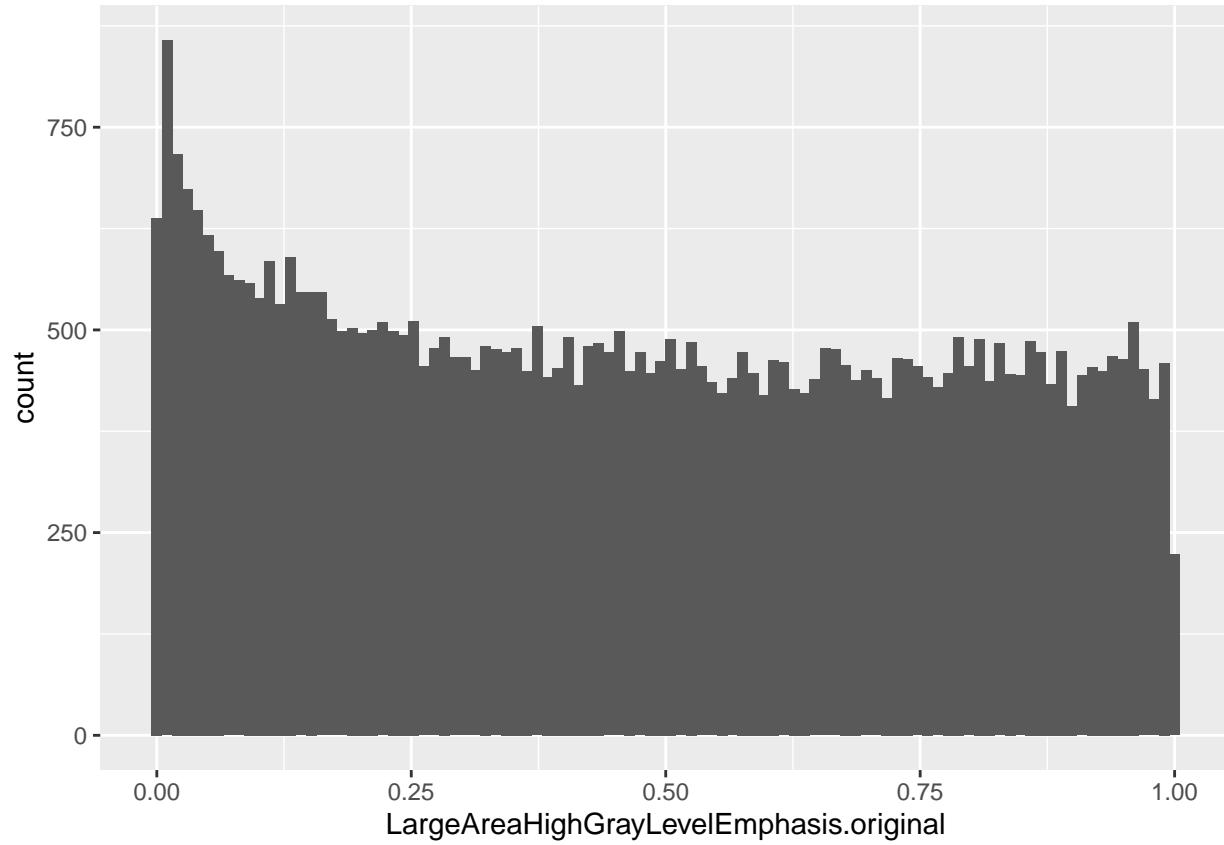
	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 212329_at	-0.2196732	3.0460263	-5.697704	1.243631e-07	0.006034721	7.040103
## 227973_at	0.1595674	4.8121414	5.501652	2.936197e-07	0.007123948	6.514425
## 230036_at	0.2571485	5.6260651	5.212541	1.014825e-06	0.016414796	5.379352
## 212764_at	0.2406094	5.3623273	5.020708	2.267672e-06	0.027509698	4.632637
## 218986_s_at	0.2728846	5.5019428	4.883333	3.993644e-06	0.038758314	4.101052
## 212916_at	-0.1071366	5.4256914	-4.805750	5.476957e-06	0.044294886	3.817662
## 221687_s_at	-0.2637242	1.2179241	-4.713958	7.929778e-06	0.054970353	3.027325
## 239988_at	0.3733070	2.4479933	4.591606	1.290531e-05	0.070061351	2.943295
## 230146_s_at	0.2424403	0.3778259	4.583726	1.331315e-05	0.070061351	2.514679
## 203238_s_at	0.3927748	2.0908241	4.515877	1.738118e-05	0.070061351	2.648608

```

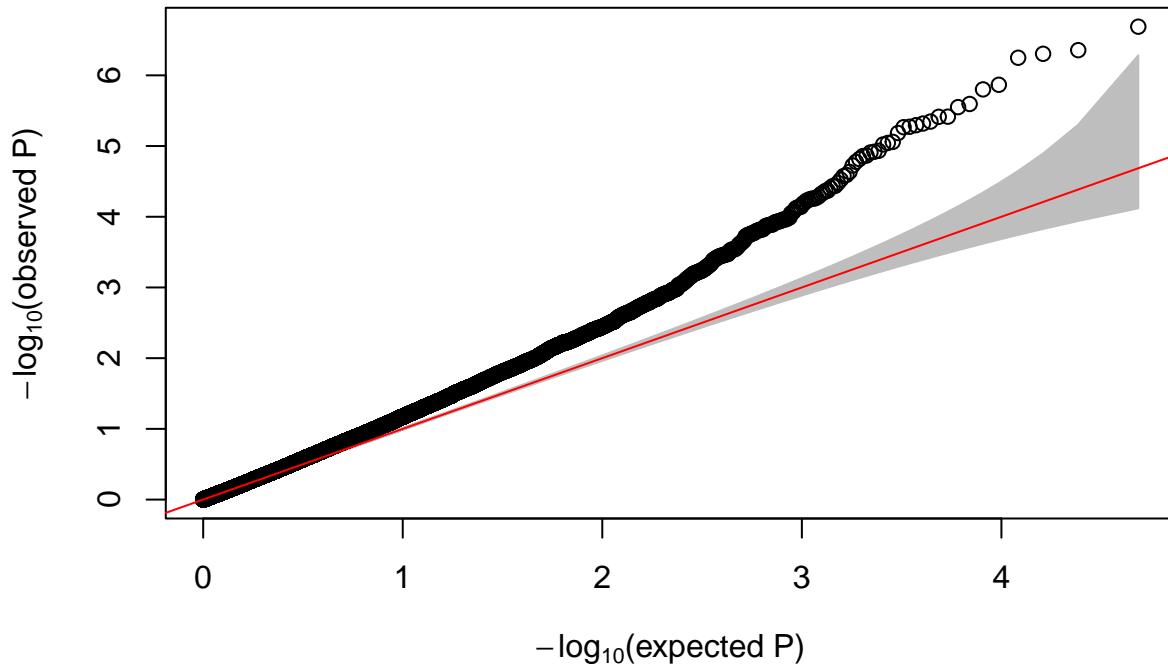
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeAreaHighGrayLevelEmphasi")

summa.fit.larAHigh <- decideTests(fit)
toptable.larAHigh <- topTable(fit, coef = "LargeAreaHighGrayLevelEmphasis.original",
  number = dim(counts.ok)[1])
toptable.larAHigh <- toptable.larAHigh[order(toptable.larAHigh$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LargeAreaHighGrayLevelEmphasis.original)) + geom_histogram(bins = 100)


# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$LargeAreaHighGrayLevelEmphasis.original)

```



```
summary(summa.fit.larAHig)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down      585          0   116     0     0       0           0
## NotSig   22900        48525 48297 48525 48523     48525       48525
## Up       25040          0   112     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough    BMI Cr_wheezengY
## Down      0            0           0           0       0       0           0
## NotSig   48525        48525        48525     48525 48525       48525
## Up       0            0           0           0       0       0           0
##          LargeAreaHighGrayLevelEmphasis.original X1     X2     X3     X4     X5
## Down          4 18385 16108 14044 12308 10219
## NotSig        48494 12787 19892 21911 25242 27280
## Up          27 17353 12525 12570 10975 11026
##          X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down     9342 8617 7556 7960 8253 6650 6423 6527 5593 5090 3600 4625
## NotSig   28651 33140 33623 32373 32414 34112 36668 36678 37388 38814 41539 40124
## Up       10532 6768 7346 8192 7858 7763 5434 5320 5544 4621 3386 3776
##          X18    X19
## Down     2342 2129
## NotSig   43503 44105
## Up       2680 2291
```

```
head(toptable.larAHig, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 230036_at	0.20920585	5.6260651	5.584157	2.051083e-07	0.006841793	6.874963
## 1563431_x_at	-0.08343605	7.6428042	-5.408125	4.405553e-07	0.006841793	6.041527
## 222816_s_at	0.18314213	4.6986392	5.380549	4.960758e-07	0.006841793	6.044920
## 229354_at	0.54715261	0.6668949	5.350664	5.639809e-07	0.006841793	5.540182
## 239887_at	0.41407150	0.1790370	5.143335	1.359882e-06	0.012788765	4.617850
## 228617_at	0.27290624	5.7549490	5.107373	1.581300e-06	0.012788765	4.930849
## 236156_at	0.36210130	3.3538067	4.993351	2.541791e-06	0.017080917	4.510562

```

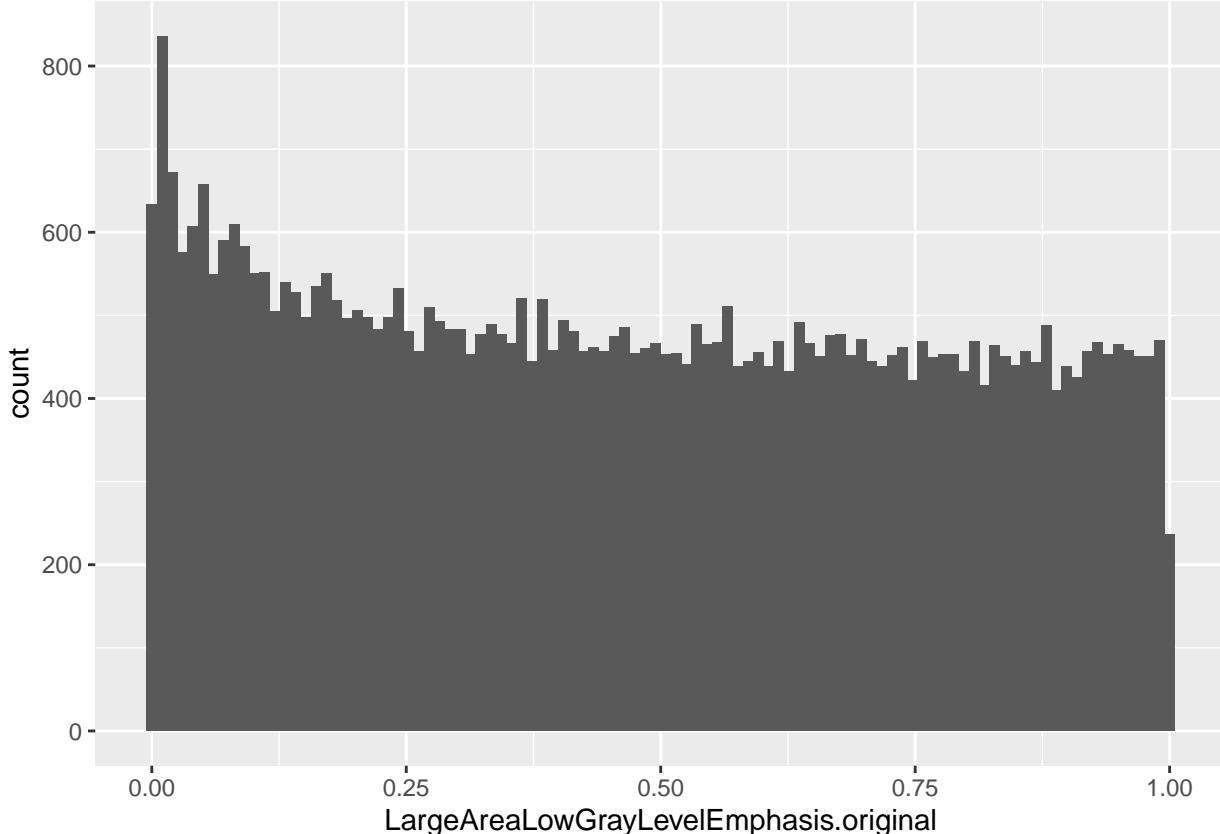
## 206133_at      0.25297810 5.0826216  4.968556 2.816019e-06 0.017080917 4.422292
## 214059_at      0.42034549 3.6797030  4.892809 3.844441e-06 0.017516030 4.136214
## 242057_at      0.36945631 1.9120105  4.891825 3.859954e-06 0.017516030 3.978593

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeAreaLowGrayLevelEmphasis.RData")

summa.fit.larALow <- decideTests(fit)
toptable.larALow <- topTable(fit, coef = "LargeAreaLowGrayLevelEmphasis.original",
                               number = dim(counts.ok)[1])
toptable.larALow <- toptable.larALow[order(toptable.larALow$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LargeAreaLowGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

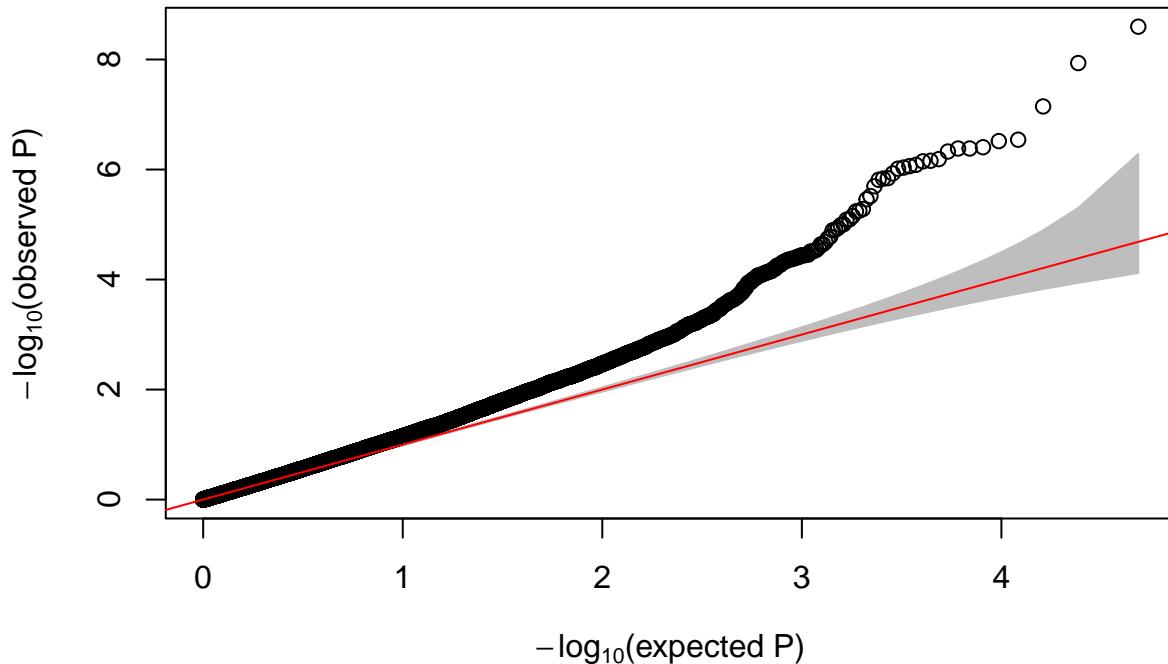
```



```

# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$LargeAreaLowGrayLevelEmphasis.original)

```



```
summary(summa.fit.larALow)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down      585          0   106     0     1       0           0
## NotSig   22765        48525 48338 48525 48520     48525       48525
## Up       25175          0   81     0     4       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough     BMI Cr_wheezengY
## Down      0            0           0           0       0       0           0
## NotSig   48525        48525        48525     48525 48525       48525
## Up        0            0           0           0       0       0           0
##          LargeAreaLowGrayLevelEmphasis.original X1     X2     X3     X4     X5
## Down          4 18466 16019 14080 12388 10166
## NotSig        48451 12698 20063 21902 25155 27205
## Up           70 17361 12443 12543 10982 11154
##          X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down     10546 6649 7208 8206 7886 7779 5599 5257 5613 4529 3912 2957
## NotSig   28695 33407 33735 32316 32420 34182 36433 36550 37241 38919 40514 41590
## Up       9284 8469 7582 8003 8219 6564 6493 6718 5671 5077 4099 3978
##          X18    X19
## Down     2679 2090
## NotSig   43570 44537
## Up       2276 1898
```

```
head(toptable.larALow)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 222986_s_at	0.05851532	7.893641	6.553491	2.531362e-09	0.0001228344	10.913376
## 230036_at	0.19976717	5.626065	6.224828	1.159703e-08	0.0002813728	9.590333
## 239988_at	0.27602778	2.447993	5.823270	7.133678e-08	0.0011538725	7.760237
## 208436_s_at	0.13612935	5.092808	5.507022	2.872284e-07	0.0025188102	6.548899
## 204747_at	0.26873749	5.588170	5.493822	3.041811e-07	0.0025188102	6.451316
## 218986_s_at	0.19093654	5.501943	5.434486	3.933100e-07	0.0025188102	6.234535

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LowGrayLevelZoneEmphasis.orig"

summa.fit.lowGLZem <- decideTests(fit)
summary(summa.fit.lowGLZem)

##      (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down       608          0   142     0     0        0           0
## NotSig    22700        48525 48256 48525 48523     48525        48525
## Up        25217          0   127     0     2        0           0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down          0             0           0           0           0           0
## NotSig     48525          48525         48525        48525        48525
## Up          0             0           0           0           0           0
##      LowGrayLevelZoneEmphasis.original X1     X2     X3     X4     X5     X6
## Down                  0 18644 16012 13595 11473 9819 9163
## NotSig                48525 12577 20315 22542 24151 27897 29036
## Up                    0 17304 12198 12388 12901 10809 10326
##      X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down     8992 6977 7396 8761 6706 6444 6406 5835 4957 4120 3683 3125
## NotSig   32503 34494 33387 31601 33500 36563 36704 37124 39149 40211 41896 43069
## Up       7030 7054 7742 8163 8319 5518 5415 5566 4419 4194 2946 2331
##      X19    X20
## Down     2079 2845
## NotSig   43741 43198
## Up       2705 2482

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SizeZoneNonUniformity.origina

summa.fit.sizZNU <- decideTests(fit)
summary(summa.fit.sizZNU)

##      (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down       580          0   87     0     0        0           0
## NotSig    22880        48525 48377 48525 48523     48525        48525
## Up        25065          0   61     0     2        0           0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down          0             0           0           0           0           0
## NotSig     48525          48525         48525        48525        48525
## Up          0             0           0           0           0           0
##      SizeZoneNonUniformity.original X1     X2     X3     X4     X5     X6     X7
## Down                  0 18526 16146 13766 12029 10493 10492 7187
## NotSig                48525 12724 19881 22350 25789 26918 28775 32451
## Up                    0 17275 12498 12409 10707 11114 9258 8887
##      X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down     7333 8086 7822 8121 5570 5081 5620 4631 4255 2945 2642 2585
## NotSig   33380 32501 32736 33533 36303 37054 37278 38783 40011 41590 43526 43228
## Up       7812 7938 7967 6871 6652 6390 5627 5111 4259 3990 2357 2712

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SizeZoneNonUniformityNormaliz

summa.fit.sizZNU <- decideTests(fit)
summary(summa.fit.sizZNU)

##      (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down       592          0   112     0     0        0           0

```

```

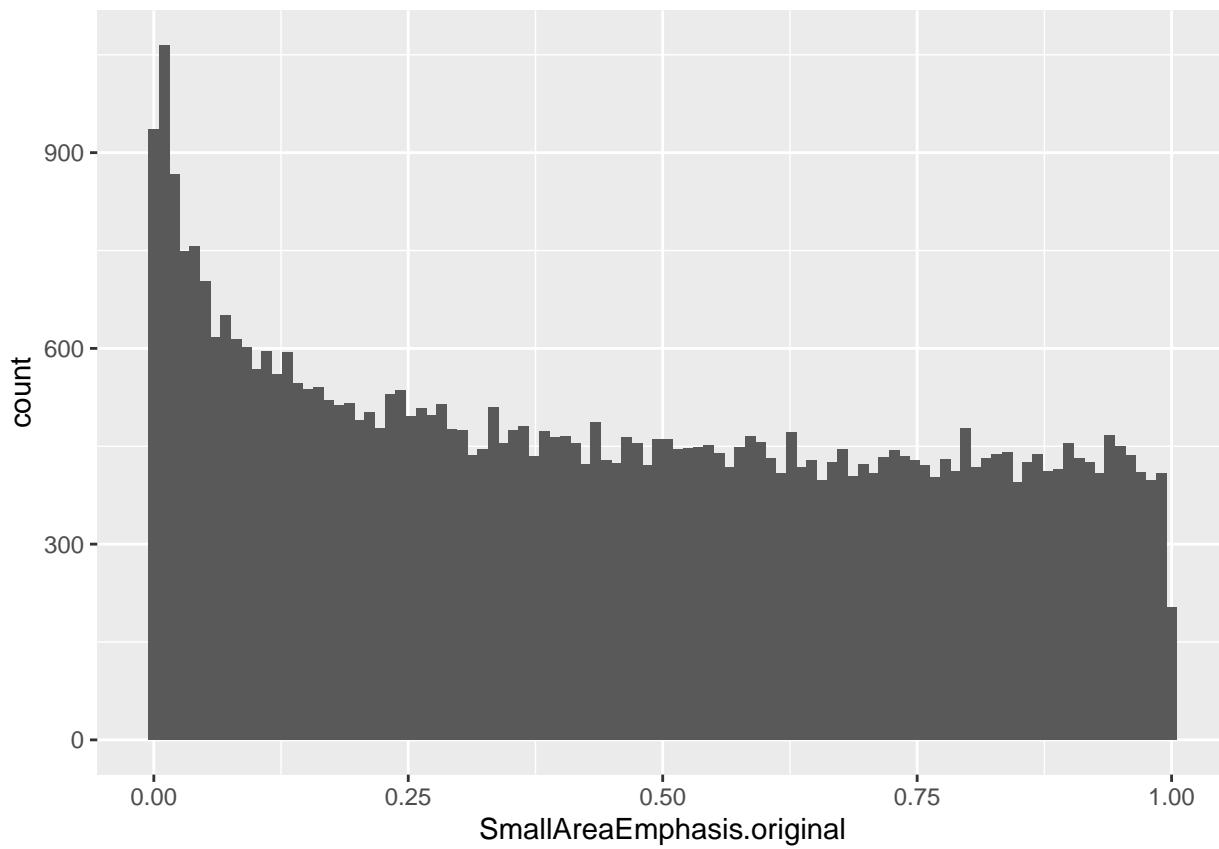
## NotSig      22659      48525 48335 48525 48523      48525      48525
## Up         25274          0    78     0     2          0          0
##       dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down          0          0          0          0          0          0
## NotSig      48525      48525          48525 48525      48525
## Up          0          0          0          0          0          0
##       SizeZoneNonUniformityNormalized.original   X1     X2     X3     X4     X5
## Down          0 18421 16241 14068 12344 10436
## NotSig      48525 12781 19701 21868 25181 26973
## Up          0 17323 12583 12589 11000 11116
##       X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down  10685 6995 7327 8181 7874 8155 5558 5318 5627 4533 4249 2900
## NotSig 28448 32710 33317 32307 32635 33504 36359 36539 37180 38935 40013 41752
## Up     9392 8820 7881 8037 8016 6866 6608 6668 5718 5057 4263 3873
##       X18    X19
## Down  2607 2659
## NotSig 43578 43361
## Up     2340 2505

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SmallAreaEmphasis.original.rda")

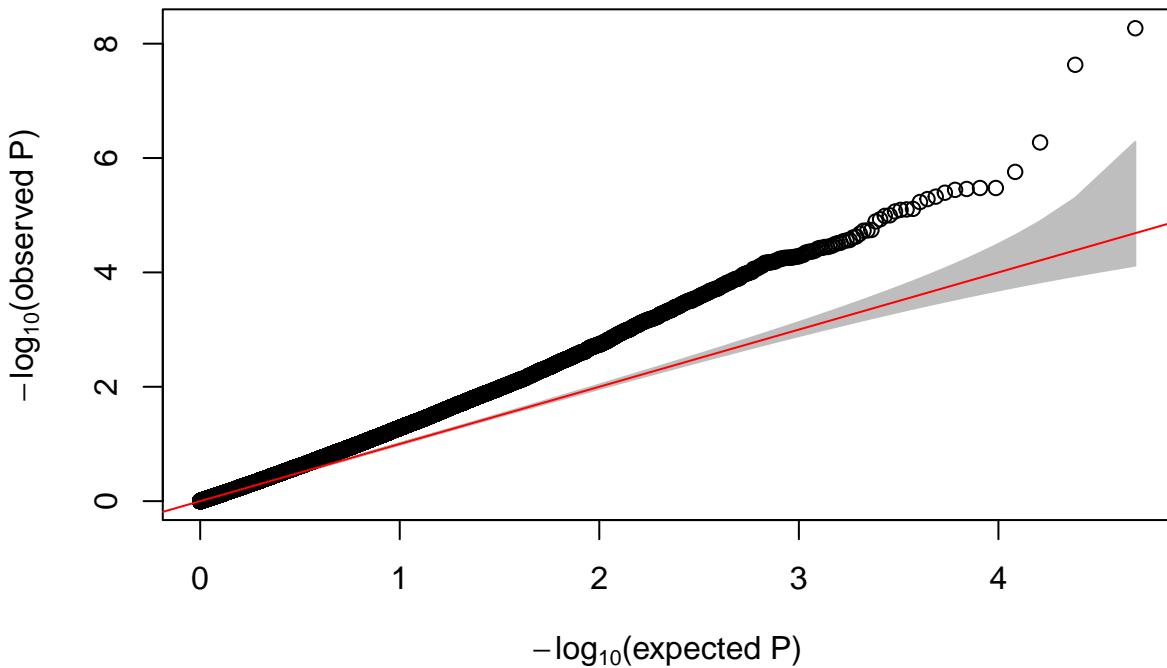
summa.fit.smAem <- decideTests(fit)
toptable.smAem <- topTable(fit, coef = "SmallAreaEmphasis.original", number = dim(counts.ok)[1])
toptable.smAem <- toptable.smAem[order(toptable.smAem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = SmallAreaEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$SmallAreaEmphasis.original)
```



```
summary(summa.fit.smAem)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      587      0   130      0     1      0      0
## NotSig   22819  48525 48268 48525 48519  48525 48525
## Up       25119      0   127      0     5      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0     0      0      0
## NotSig   48525      48525      48525 48525 48525 48525
## Up       0      0      0      0     0      0      0
##      SmallAreaEmphasis.original X1     X2     X3     X4     X5     X6     X7
## Down      46 18604 15859 14156 12467 10314 9073 8490
## NotSig   48449 12570 20467 21813 25014 26859 29144 33356
## Up       30 17351 12199 12556 11044 11352 10308 6679
##      X8     X9    X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down    7437 7862 8549 6503 6432 6665 5790 4931 3740 4020 2344 1878
## NotSig 33910 32589 31958 34338 36525 36634 37195 39056 41241 41466 43325 44553
## Up      7178 8074 8018 7684 5568 5226 5540 4538 3544 3039 2856 2094
head(toptable.smAem, 10)

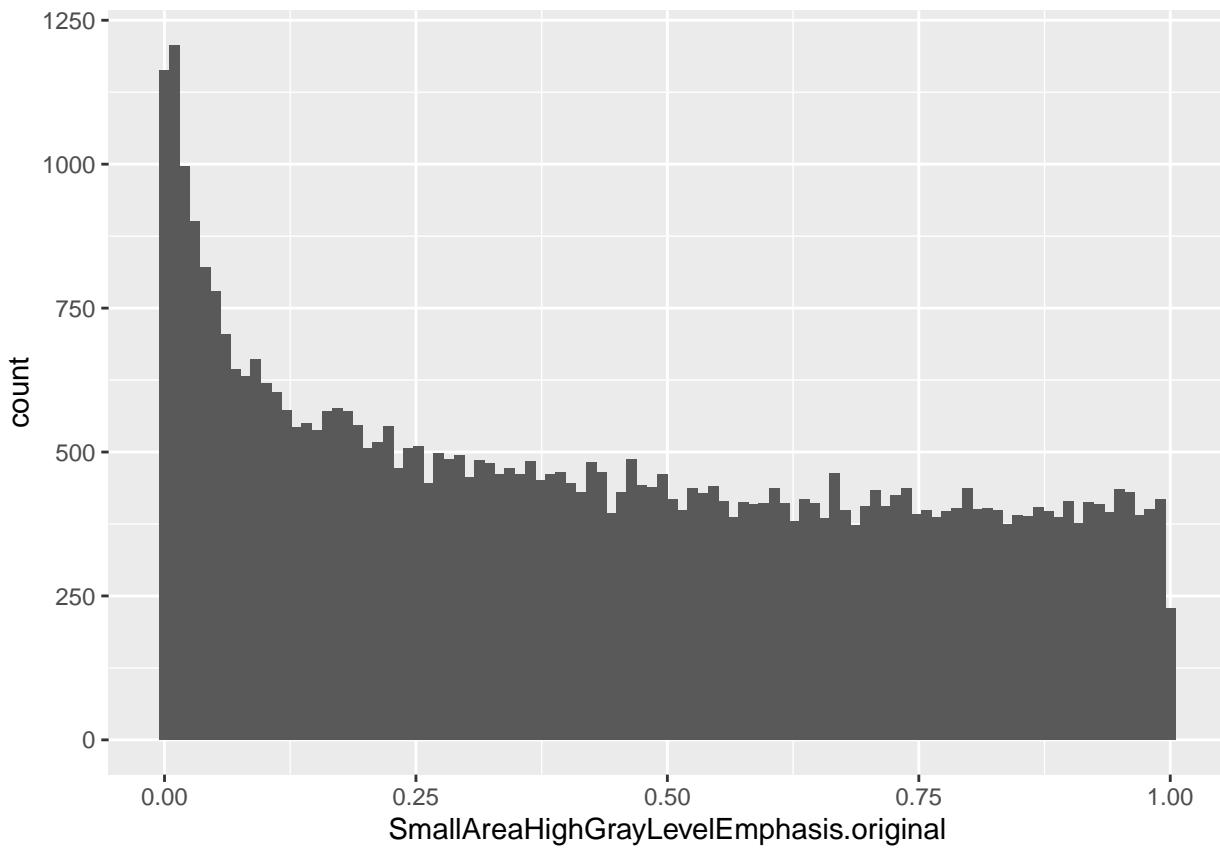
##          logFC AveExpr      t    P.Value adj.P.Val      B
## 230036_at -0.23389097 5.626065 -6.391864 5.374149e-09 0.0002607806 10.327115
## 239988_at -0.33778162 2.447993 -6.071003 2.341064e-08 0.0005680006 8.675677
## 218986_s_at -0.21989277 5.501943 -5.363555 5.340094e-07 0.0086376012 5.964775
## 222986_s_at -0.05427099 7.893641 -5.083631 1.747382e-06 0.0211979237 4.603441
## 1555764_s_at -0.17061490 4.881008 -4.927222 3.340242e-06 0.0217824165 4.266649
## 218408_at -0.18505000 4.198970 -4.927101 3.341900e-06 0.0217824165 4.275307
## 230363_s_at -0.16087086 1.889961 -4.917311 3.478964e-06 0.0217824165 4.123673
## 204747_at -0.29617099 5.588170 -4.909052 3.598831e-06 0.0217824165 4.153794
## 208087_s_at -0.30002166 2.591420 -4.880801 4.040015e-06 0.0217824165 4.059002
## 226603_at -0.18394563 6.059371 -4.842147 4.729805e-06 0.0229513790 3.868261

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SmallAreaHighGrayLevelEmphasi

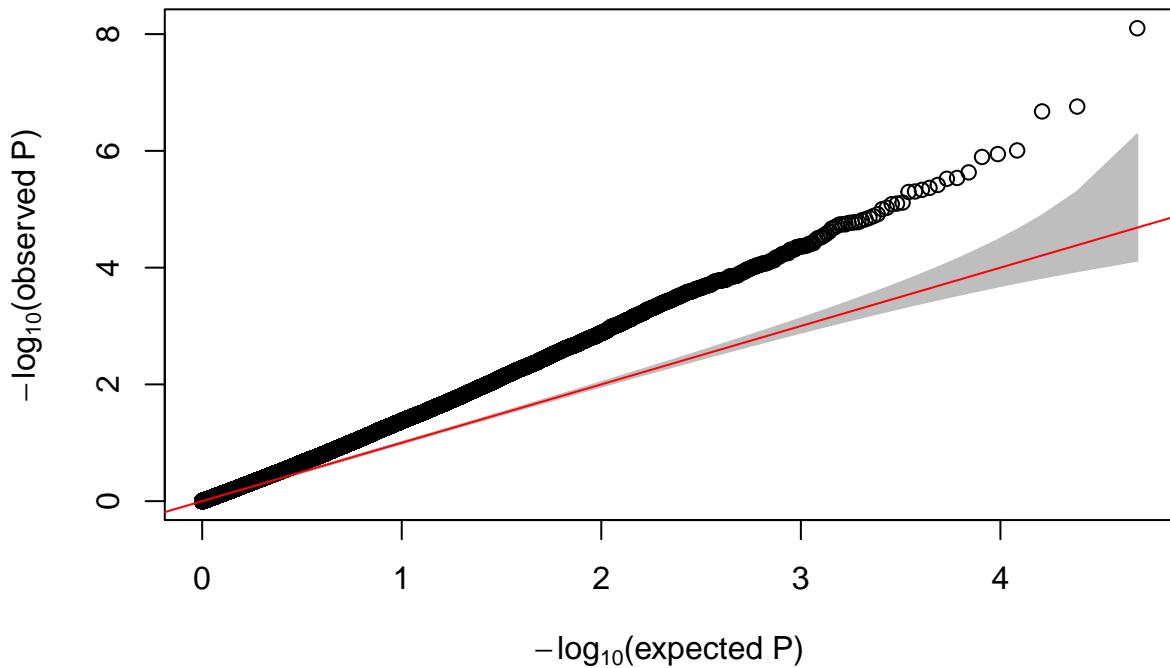
summa.fit.smAHem <- decideTests(fit)
toptable.smAHem <- topTable(fit, coef = "SmallAreaHighGrayLevelEmphasis.original",
  number = dim(counts.ok)[1])
toptable.smAHem <- toptable.idmn0[order(toptable.smAHem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = SmallAreaHighGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$SmallAreaHighGrayLevelEmphasis.original)
```



```
summary(summa.fit.smAHem)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      576      0     81      0      1      0      0
## NotSig   22720    48525  48398  48525  48519    48525    48525
## Up       25229      0     46      0      5      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##      SmallAreaHighGrayLevelEmphasis.original   X1     X2     X3     X4     X5
## Down          22 18603 15869 13559 12700 11267
## NotSig        48463 12613 20631 22649 24504 27064
## Up          40 17309 12025 12317 11321 10194
##      X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down    8815  8356  6915  7063  8856  6639  6551  6379  5734  4975  4692  2806
## NotSig  29822 33452 34627 34102 31607 33811 36452 36952 37402 38954 39289 41851
## Up      9888  6717  6983  7360  8062  8075  5522  5194  5389  4596  4544  3868
##      X18    X19
## Down    2803  2162
## NotSig 43105 44252
## Up      2617  2111
head(toptable.smAlem)

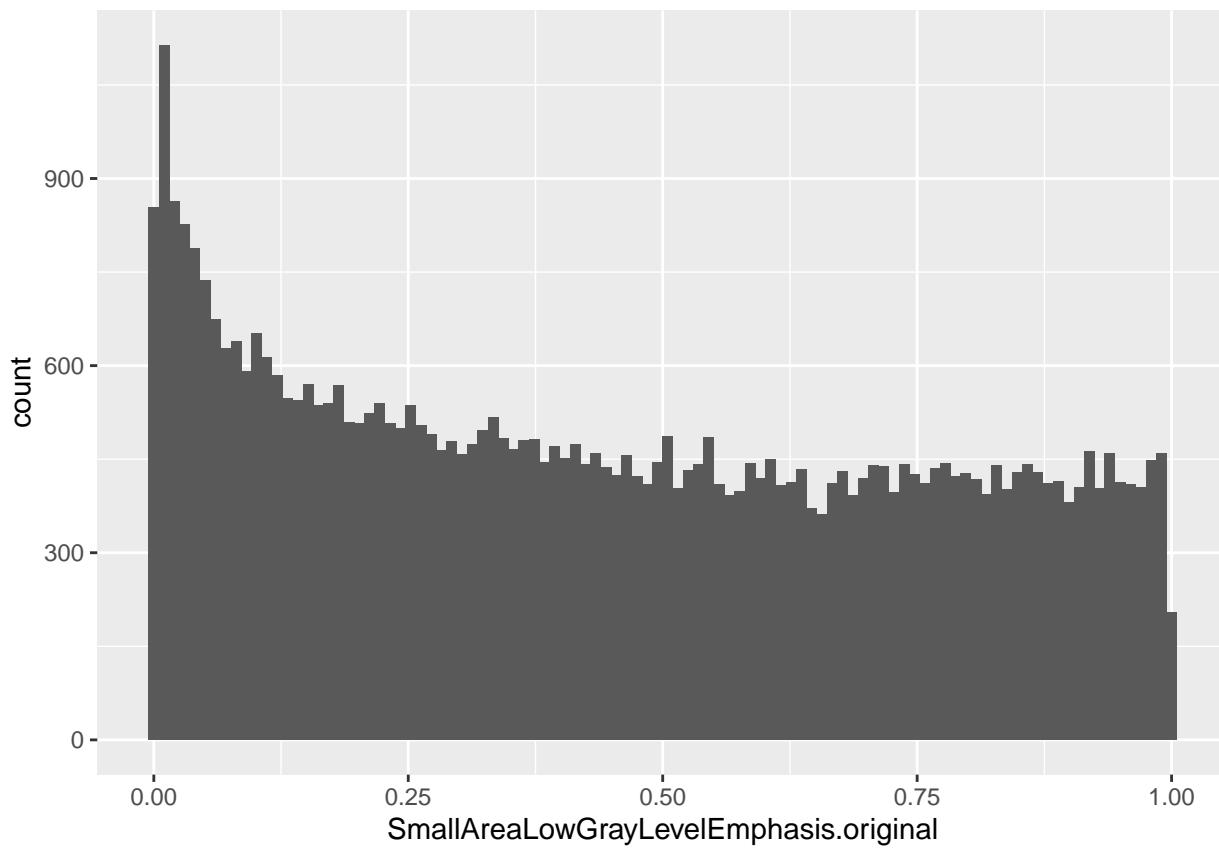
##           logFC     AveExpr       t     P.Value adj.P.Val       B
## 203893_at    0.1004168  5.0379308  5.261247 8.262337e-07 0.04009299 5.554520
## 1554830_a_at -0.1949350  2.6289573 -5.071015 1.840997e-06 0.04466720 4.581840
## 1555229_a_at -0.3979940  0.6820437 -4.793267 5.765254e-06 0.07258511 3.111078
## 216922_x_at  -0.2069365 -0.3358964 -4.716413 7.857573e-06 0.07625775 2.217700
## 201645_at     -0.2634144  1.8007395 -4.598154 1.258368e-05 0.10177048 2.811716
## 1562121_at   -0.1776890  0.1193435 -4.784088 5.983317e-06 0.07258511 2.725248

load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/SmallAreaLowGrayLevelEmphasis

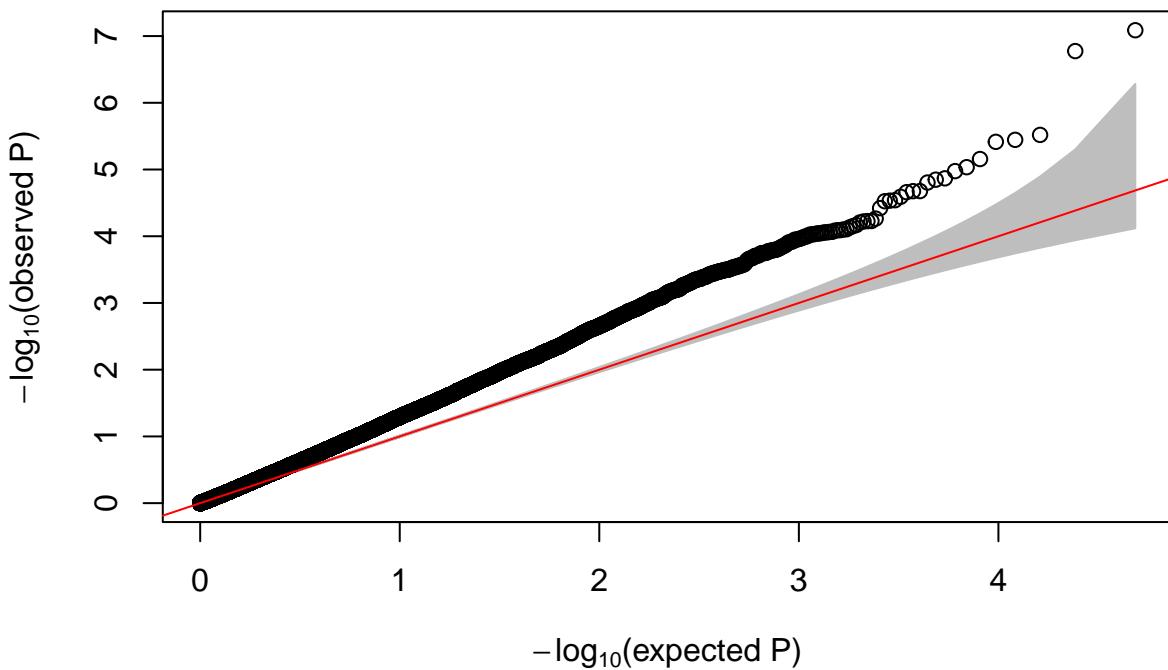
summa.fit.smALem <- decideTests(fit)
toptable.smALem <- topTable(fit, coef = "SmallAreaLowGrayLevelEmphasis.original",
  number = dim(counts.ok)[1])
toptable.smALem <- toptable.smALem[order(toptable.smALem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = SmallAreaLowGrayLevelEmphasis.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$SmallAreaLowGrayLevelEmphasis.original)
```



```
summary(summa.fit.smALem)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      627      0   135      0      0      0      0
## NotSig   22638    48525 48272 48525 48523    48525    48525
## Up       25260      0   118      0      2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525    48525    48525    48525
## Up       0      0      0      0      0      0      0
##      SmallAreaLowGrayLevelEmphasis.original   X1     X2     X3     X4     X5
## Down      3 18570 16046 13967 11052 10097
## NotSig   48520 12683 20018 21935 25002 27398
## Up       2 17272 12461 12623 12471 11030
##      X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17
## Down   9289 8759 7258 7916 8179 6646 6443 6594 5605 4835 3663 3579
## NotSig 28773 32828 34231 32442 32618 34114 36664 36708 37562 39237 41243 42168
## Up    10463 6938 7036 8167 7728 7765 5418 5223 5358 4453 3619 2778
##      X18    X19
## Down   2205 2637
## NotSig 43524 43821
## Up    2796 2067

head(toptable.smALem, 10)

##          logFC    AveExpr        t    P.Value adj.P.Val      B
## 212329_at  0.2089765 3.0460263 5.792749 8.177133e-08 0.003967954 7.442436
## 230036_at -0.2543247 5.6260651 -5.630095 1.678353e-07 0.004072103 7.066311
## 227973_at -0.1211576 4.8121414 -4.951176 3.026886e-06 0.037343973 4.365688
## 238453_at  0.3190908 1.0245559  4.909722 3.589034e-06 0.037343973 3.646829
## 231956_at -0.2904725 3.1575164 -4.892719 3.847911e-06 0.037343973 4.062413
## 222732_at  0.1378213 4.6077523  4.746493 6.965847e-06 0.056336291 3.596343
## 218986_s_at -0.2429174 5.5019428 -4.676379 9.226060e-06 0.063956368 3.318632
## 230363_s_at -0.2120024 1.8899609 -4.642312 1.056679e-05 0.064094199 3.055009
## 1554252_a_at  0.2852936 0.8997812  4.579325 1.355966e-05 0.068889218 2.446105
## 212764_at   -0.2040041 5.3623273 -4.567677 1.419664e-05 0.068889218 2.923277

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ZoneEntropy.original.rda")

summa.fit.zoneEn <- decideTests(fit)
summary(summa.fit.zoneEn)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      596      0   112      0      0      0      0
## NotSig   22682    48525 48338 48525 48523    48525    48525
## Up       25247      0    75      0      2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525    48525    48525    48525
## Up       0      0      0      0      0      0      0
##      ZoneEntropy.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down      0 18479 16203 14076 12457 10402 10675 7010 7273
## NotSig   48525 12724 19734 21874 25055 27085 28404 32655 33407
## Up       0 17322 12588 12575 11013 11038 9446 8860 7845
##      X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down   8140 7813 8257 5563 5272 5602 4626 4234 2916 2589 2680
## NotSig 32370 32852 33312 36364 36624 37230 38745 40079 41684 43566 43316
## Up    8015 7860 6956 6598 6629 5693 5154 4212 3925 2370 2529

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ZonePercentage.original.rda")

summa.fit.zonePer <- decideTests(fit)
summary(summa.fit.zonePer)

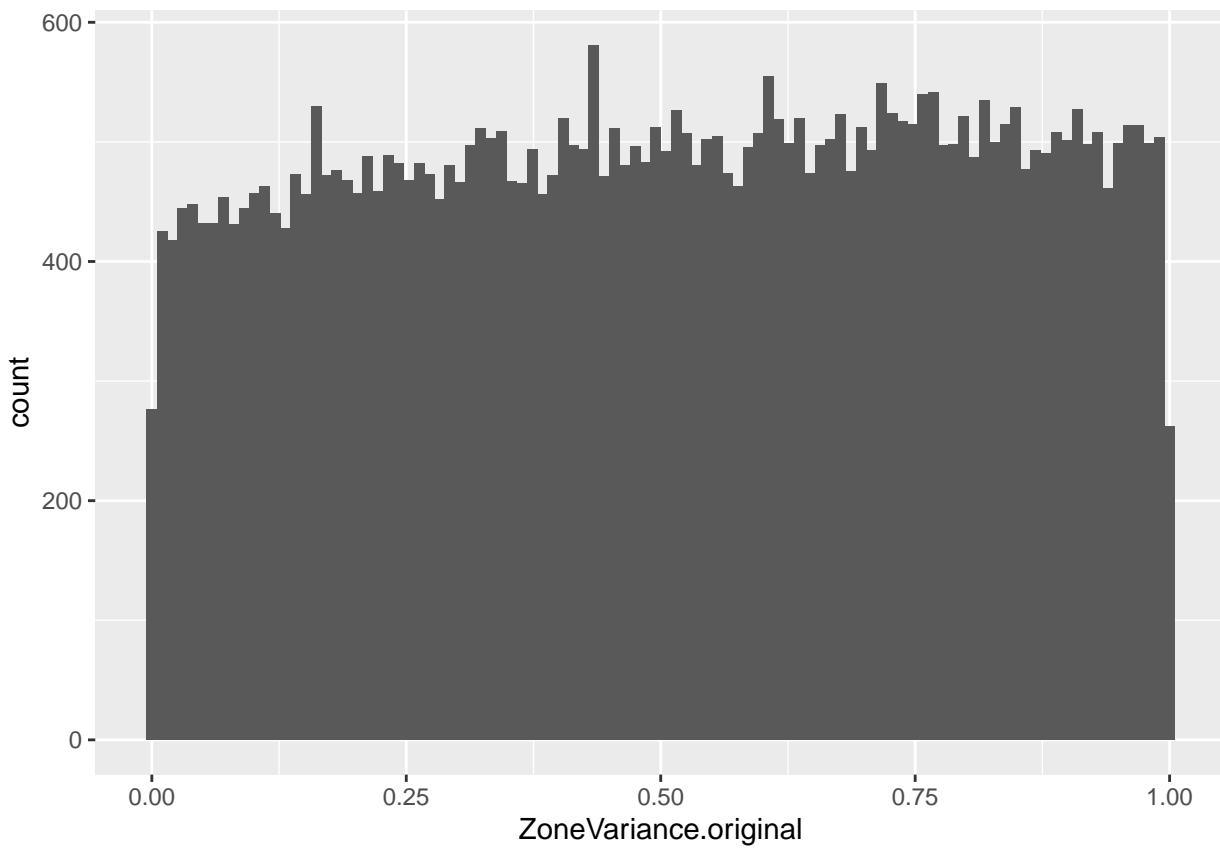
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           583          0    99     0     0          0          0
## NotSig        22794        48525 48360 48525 48523        48525        48525
## Up            25148          0    66     0     2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0            0          0          0          0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0            0          0          0          0          0
##          ZonePercentage.original   X1      X2      X3      X4      X5      X6      X7      X8
## Down           0 18537 16022 13766 12166 10462 10593 7117 7229
## NotSig        48525 12737 20223 22335 25555 26980 28585 32631 33514
## Up             0 17251 12280 12424 10804 11083 9347 8777 7782
##          X9      X10      X11      X12      X13      X14      X15      X16      X17      X18      X19
## Down          8081 7798 8193 5553 5118 5619 4674 4142 2979 2614 2638
## NotSig        32515 32750 33431 36399 36911 37223 38705 40183 41531 43558 43394
## Up            7929 7977 6901 6573 6496 5683 5146 4200 4015 2353 2493

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/ZoneVariance.original.rda")

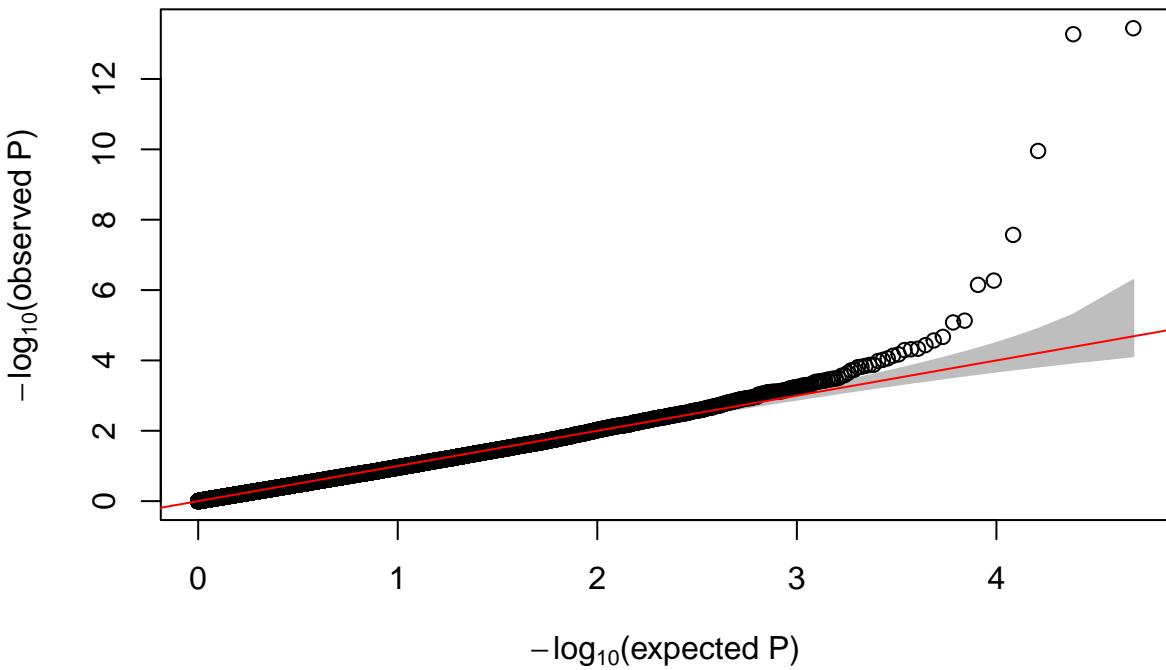
summa.fit.zoneVar <- decideTests(fit)
toptable.zoneVar <- topTable(fit, coef = "ZoneVariance.original", number = dim(counts.ok)[1])
toptable.zoneVar <- toptable.zoneVar[order(toptable.zoneVar$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = ZoneVariance.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$ZoneVariance.original)
```



```
summary(summa.fit.zoneVar)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      601      0     92      0      0      0      0
## NotSig   23058    48525  48377  48525  48523   48525    48525
## Up       24866      0     56      0      2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525    48525      0      0      0      0      0
## Up       0      0      0      0      0      0      0
##      ZoneVariance.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down      2 18540 16207 14053 12381 10504 10708 7190 7285
## NotSig   48519 12722 19692 21936 25201 26951 28349 32477 33444
## Up       4 17263 12626 12536 10943 11070 9468 8858 7796
##      X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    8119 7860 8285 5549 5228 5604 4676 4231 2847 2679 2594
## NotSig  32447 32674 33328 36352 36749 37242 38734 40129 41842 43446 43250
## Up      7959 7991 6912 6624 6548 5679 5115 4165 3836 2400 2681
head(toptable.zoneVar, 10)

##          logFC     AveExpr        t     P.Value   adj.P.Val
## 1563431_x_at -0.12432417 7.6428042 -8.840757 3.608635e-14 1.294321e-09
## 202707_at      0.34377252 0.6160692  8.762647 5.334655e-14 1.294321e-09
## 224373_s_at   -0.09173196 8.7260074 -7.211806 1.109891e-10 1.795249e-06
## 205528_s_at   0.35063443 -0.4655939  6.039538 2.698394e-08 3.273490e-04
## 214839_at      0.26838589 -0.3360599  5.361933 5.375122e-07 5.216556e-03
## 205749_at      0.39494033 -0.7929581  5.296588 7.108909e-07 5.749330e-03
## 229354_at      0.42040518  0.6668949  4.731441 7.398254e-06 5.045322e-02
## 214355_x_at   0.12967369  3.3885361  4.702228 8.317893e-06 5.045322e-02
## 241877_at     -0.24826623  3.2108169 -4.462134 2.144741e-05 1.156373e-01
## 233493_at      0.29651078 -0.8714817  4.401795 2.708830e-05 1.314460e-01
##          B
## 1563431_x_at 21.656163
## 202707_at     18.277906
## 224373_s_at  14.032629
## 205528_s_at  7.206709
## 214839_at     4.777424
## 205749_at     4.377613
## 229354_at     3.353227
## 214355_x_at  3.361073
## 241877_at     2.427462
## 233493_at     1.404218

load("/Users/carlacasanovasuzarez/Desktop/Radiomic features models (indiv)/DependenceEntropy.original.rda")

summa.fit.depEn <- decideTests(fit)
summary(summa.fit.depEn)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      601      0     96      0      0      0      0
## NotSig   22636    48525  48359  48525  48524   48525    48525
## Up       25288      0     70      0      1      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525    48525      0      0      0      0      0
## Up       0      0      0      0      0      0      0
##      DependenceEntropy.original   X1     X2     X3     X4     X5     X6     X7

```

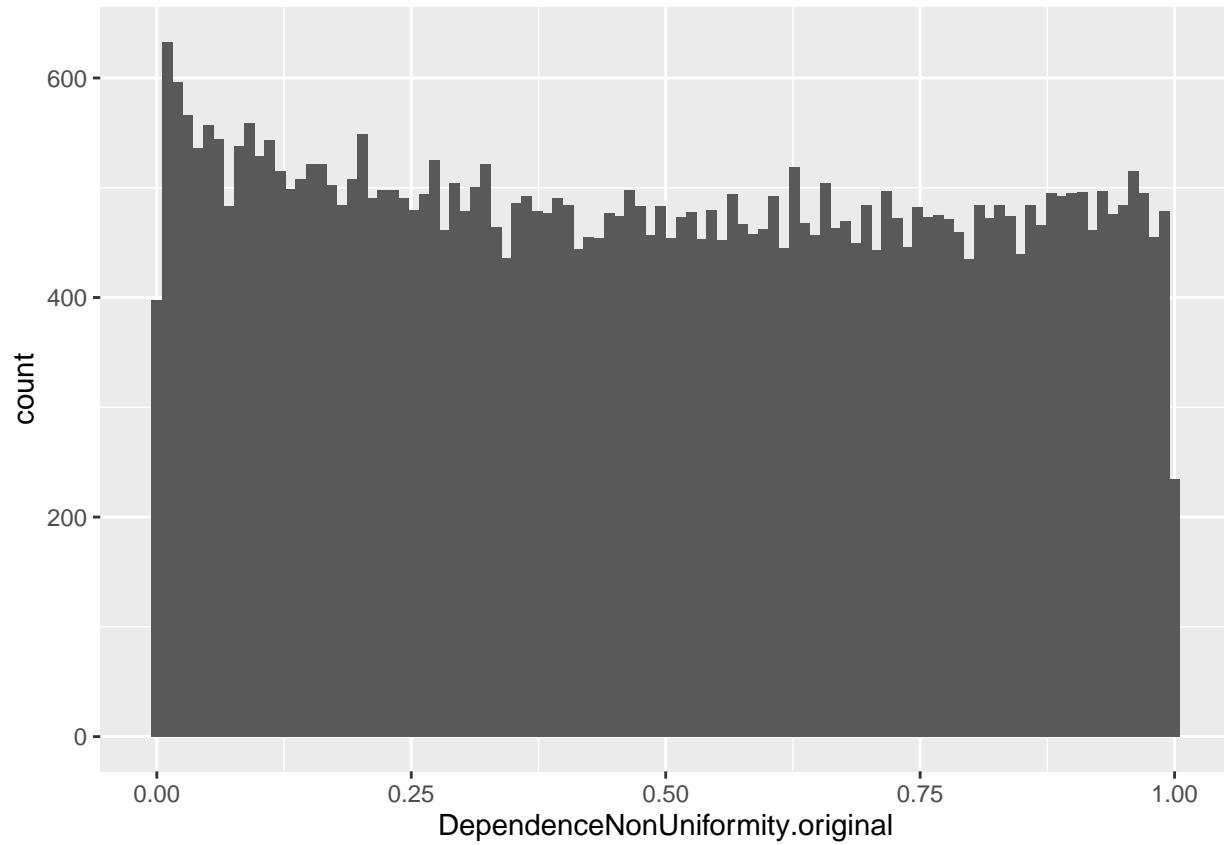
```

## Down          0 18474 16244 13936 12383 10538 10667 6971
## NotSig       48525 12751 19564 22146 25210 26935 28379 32901
## Up           0 17300 12717 12443 10932 11052 9479 8653
## X8      X9   X10   X11   X12   X13   X14   X15   X16   X17   X18   X19
## Down    7273  8058  7849  8267  5444  5305  5649  4526  3964  3328  2653  2576
## NotSig  33483 32524 32679 33347 36596 36470 37450 38929 40490 40954 43502 43250
## Up      7769  7943  7997  6911  6485  6750  5426  5070  4071  4243  2370  2699

load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/DependenceNonUniformity.original")

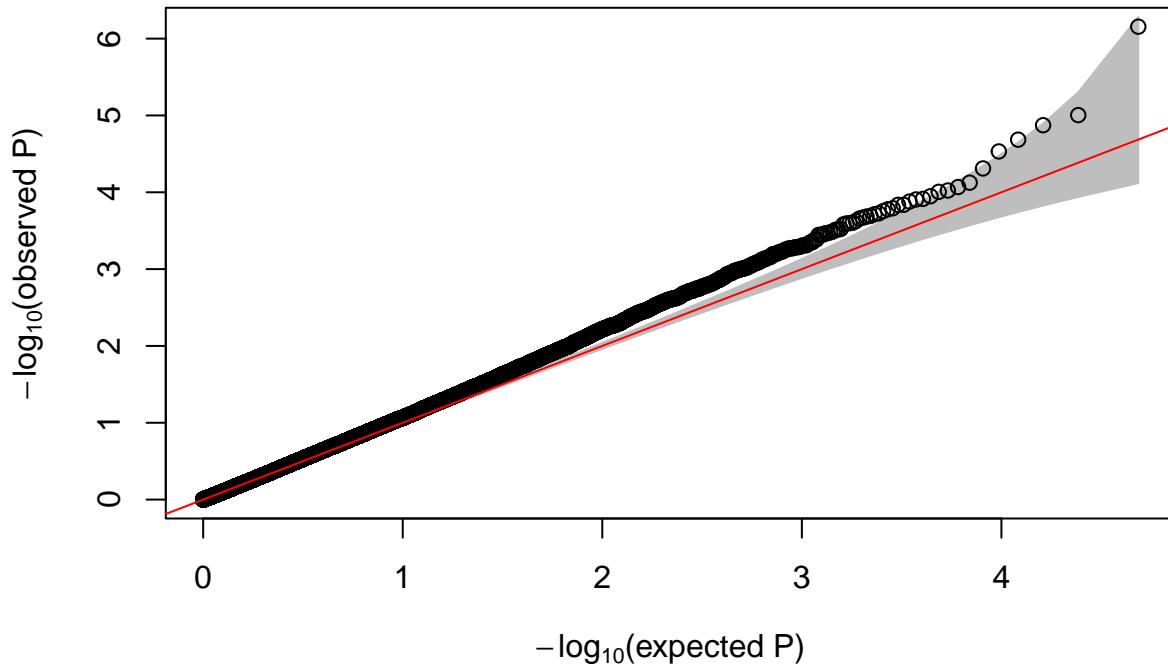
summa.fit.depNU <- decideTests(fit)
toptable.depNU <- topTable(fit, coef = "DependenceNonUniformity.original", number = dim(counts.ok)[1])
toptable.depNU <- toptable.depNU[order(toptable.depNU$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = DependenceNonUniformity.original)) + geom_histogram(bins = 100)



```

QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom\$DependenceNonUniformity.original)



```
summary(summa.fit.depNU)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down            598          0     98      0      0        0           0
## NotSig         22702        48525 48360 48525 48523        48525        48525
## Up             25225          0    67      0      2        0           0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down            0            0           0           0           0           0           0
## NotSig         48525        48525        48525        48525        48525        48525
## Up              0            0           0           0           0           0           0
##             DependenceNonUniformity.original   X1     X2     X3     X4     X5     X6
## Down           1 18539 16252 13982 12418 10526 10683
## NotSig        48524 12703 19615 22020 25099 26987 28405
## Up             0 17283 12658 12523 11008 11012  9437
##             X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down          6823  7277  8141  7736  8288  5504  5380  5570  4667  4131  3112  2660
## NotSig       33216 33426 32396 33041 33261 36464 36395 37431 38691 40255 41289 43499
## Up            8486  7822  7988  7748  6976  6557  6750  5524  5167  4139  4124  2366
##             X19
## Down          2601
## NotSig       43191
## Up            2733
```

```
head(toptable.depNU, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 215368_at	-0.42495040	-0.3006190	-5.300458	6.992227e-07	0.03392978	3.7069385
## 207528_s_at	0.32831671	3.4589663	4.658653	9.898575e-06	0.21672819	3.2093833
## 214769_at	0.31016556	3.2341450	4.582273	1.339896e-05	0.21672819	2.8692370
## 211560_s_at	0.25959781	-0.5812311	4.471790	2.065678e-05	0.25059261	1.2033406
## 206742_at	0.39414196	-0.1501561	4.380450	2.940696e-05	0.28539451	1.2522073
## 241067_at	-0.30422796	0.1543272	-4.246603	4.895558e-05	0.39592828	1.0167009
## 212038_s_at	-0.05622987	6.9334155	-4.132557	7.500896e-05	0.42313263	1.3190044

```

## 244699_at     0.15777630 2.3802461 4.097417 8.542553e-05 0.42313263 1.2230700
## 205148_s_at   0.28695961 1.4321409 4.068936 9.487257e-05 0.42313263 0.9707889
## 216864_at    -0.35973298 -1.6516964 -4.058288 9.865535e-05 0.42313263 -0.5211694

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/DependenceNonUniformityNormalized")

summa.fit.depNUn <- decideTests(fit)
summary(summa.fit.depNUn)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down           604          0  92   0   0      0          0
## NotSig        22659        48525 48371 48525 48524    48525        48525
## Up            25262          0  62   0   1      0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down           0             0          0          0      0      0
## NotSig        48525          48525          48525        48525        48525
## Up             0             0          0          0      0      0
##          DependenceNonUniformityNormalized.original X1   X2   X3   X4   X5
## Down           0 18512 16236 14005 12417 10499
## NotSig        48525 12709 19626 21992 25108 27030
## Up             0 17304 12663 12528 11000 10996
##          X6   X7   X8   X9   X10  X11  X12  X13  X14  X15  X16  X17
## Down          10683 6730 7266 8149 7838 8283 5439 5349 5591 4577 4034 3244
## NotSig       28386 33280 33475 32360 32815 33257 36588 36426 37416 38849 40391 41061
## Up            9456 8515 7784 8016 7872 6985 6498 6750 5518 5099 4100 4220
##          X18  X19
## Down          2660 2577
## NotSig       43486 43238
## Up            2379 2710

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/DependenceVariance.original")

summa.fit.depVar <- decideTests(fit)
summary(summa.fit.depVar)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down           603          0  87   0   0      0          0
## NotSig        22651        48525 48377 48525 48524    48525        48525
## Up            25271          0  61   0   1      0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down           0             0          0          0      0      0
## NotSig        48525          48525          48525        48525        48525
## Up             0             0          0          0      0      0
##          DependenceVariance.original X1   X2   X3   X4   X5   X6   X7
## Down           0 18525 16218 14007 12397 10525 10670 6770
## NotSig        48525 12693 19658 21984 25145 26993 28385 33182
## Up             0 17307 12649 12534 10983 11007 9470 8573
##          X8   X9   X10  X11  X12  X13  X14  X15  X16  X17  X18  X19
## Down          7223 8173 7847 8262 5464 5326 5650 4583 4004 3254 2628 2598
## NotSig       33566 32309 32788 33261 36541 36455 37326 38844 40459 41040 43530 43186
## Up            7736 8043 7890 7002 6520 6744 5549 5098 4062 4231 2367 2741

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/HighGrayLevelRunEmphasis.original")

summa.fit.hglRem <- decideTests(fit)
topTable.hglRem <- topTable(fit, coef = "HighGrayLevelRunEmphasis.original", number = dim(counts.ok)[1])

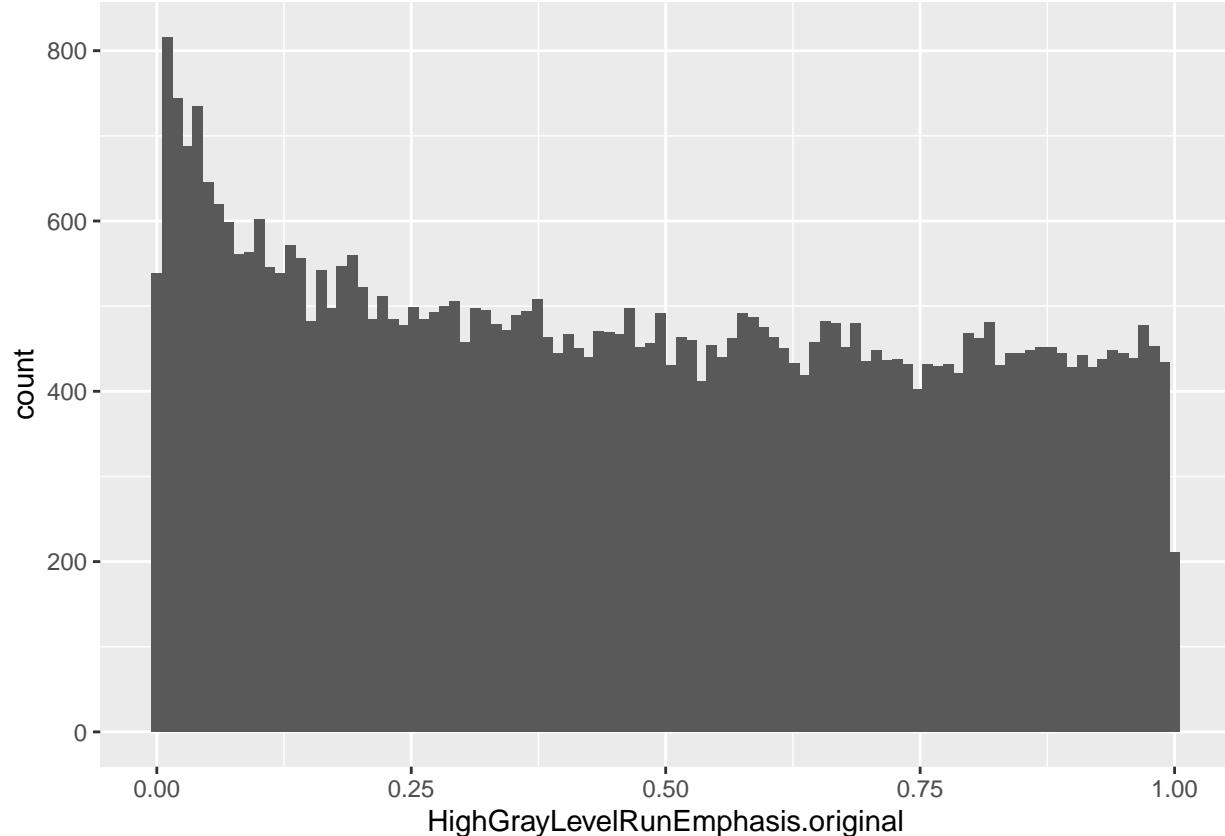
```

```

toptable.hglRem <- toptable.hglRem[order(toptable.hglRem$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = HighGrayLevelRunEmphasis.original)) + geom_histogram(bins = 100)

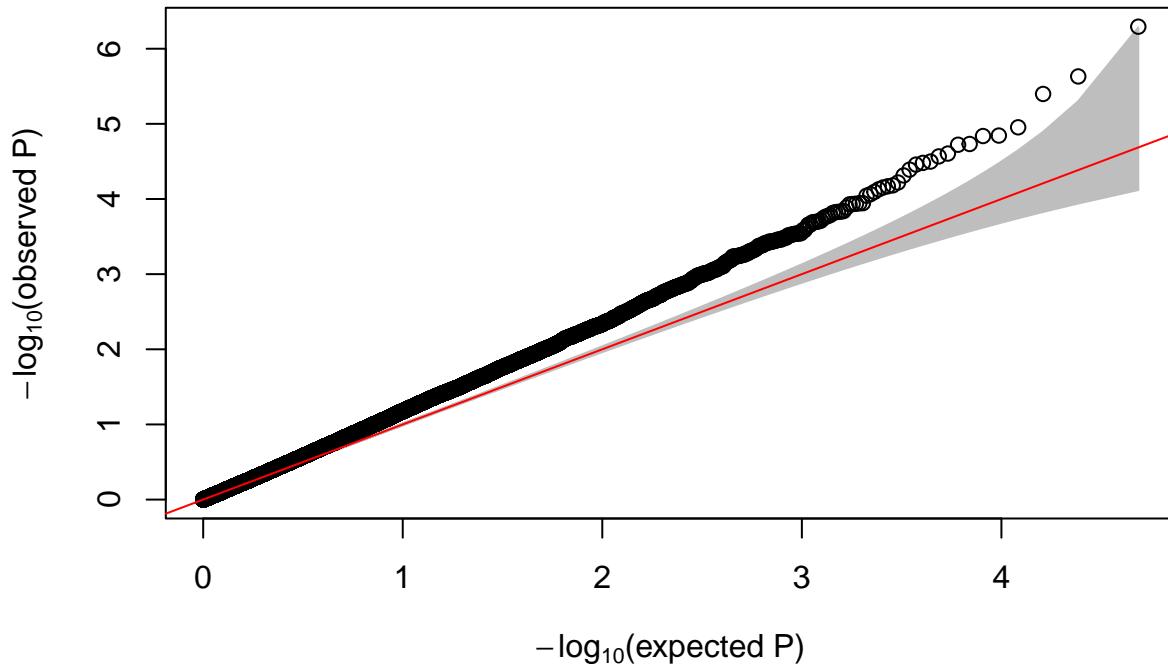
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$HighGrayLevelRunEmphasis.original)

```



```
summary(summa.fit.hglRem)
```

```
##             (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           617          0   115      0     0       0          0
## NotSig        22650        48525 48320 48525 48523     48525        48525
## Up            25258          0   90      0     2       0          0
##             dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0       0       0          0
## NotSig        48525        48525        48525        48525        48525        48525
## Up             0            0          0          0       0       0          0
##             HighGrayLevelRunEmphasis.original X1      X2      X3      X4      X5      X6
## Down           1 18492 16048 14100 12264 10448 10566
## NotSig        48524 12709 20084 21850 25403 26787 28695
## Up             0 17324 12393 12575 10858 11290  9264
##             X7      X8      X9      X10     X11     X12     X13     X14     X15     X16     X17     X18
## Down          6759 7088 8231 7875 8035 5359 5188 5670 4507 3752 3050 2731
## NotSig        33150 33979 32335 32389 33822 36827 36626 37193 38966 40870 41364 43596
## Up            8616 7458 7959 8261 6668 6339 6711 5662 5052 3903 4111 2198
##             X19
## Down         2259
## NotSig       44086
## Up           2180
```

```
head(toptable.hglRem, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 239988_at	-0.29153851	2.4479933	-5.374462	5.090765e-07	0.02470294	5.838130
## 230036_at	-0.17733875	5.6260651	-5.013366	2.339024e-06	0.05675057	4.586600
## 241514_at	0.40961126	-0.7748055	4.883115	3.999113e-06	0.06468565	2.382877
## 218986_s_at	-0.18204570	5.5019428	-4.629469	1.111286e-05	0.11497386	3.132002
## 226130_at	0.15498911	4.2551221	4.565500	1.431038e-05	0.11497386	2.938668
## 238453_at	0.23061485	1.0245559	4.561747	1.452336e-05	0.11497386	2.583610
## 228077_at	0.14854086	3.5670907	4.499613	1.852879e-05	0.11497386	2.691687

```

## 233127_at      0.31237657  1.0540609  4.493786 1.895499e-05 0.11497386 2.331428
## 1563051_at     0.16786384  3.5601254  4.424154 2.484120e-05 0.13010647 2.419398
## 212579_at     -0.09259944  6.9622936 -4.401280 2.713426e-05 0.13010647 2.161738

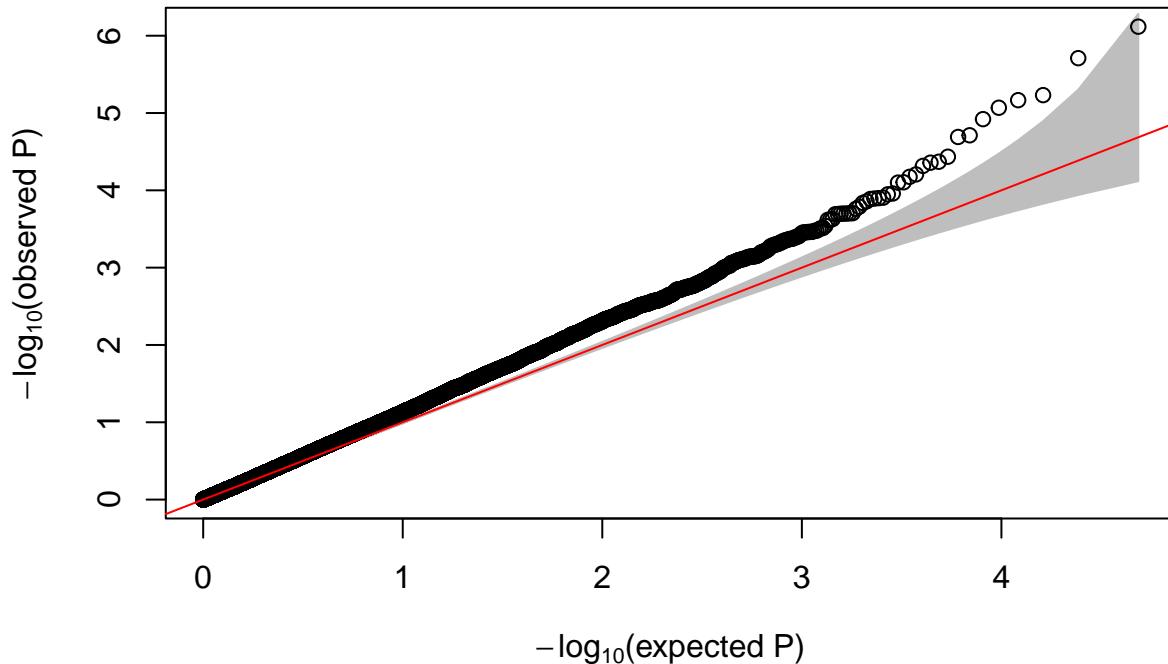
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeDependenceEmphasis.original")

summa.fit.larDepEm <- decideTests(fit)
toptable.larDepEm <- topTable(fit, coef = "LargeDependenceEmphasis.original", number = dim(counts.ok)[1])
toptable.larDepEm <- toptable.larDepEm[order(toptable.larDepEm$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LargeDependenceEmphasis.original)) + geom_histogram(bins = 100)

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$LargeDependenceEmphasis.original)

```



```
summary(summa.fit.larDepEm)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           602          0     90      0      0          0          0
## NotSig        22623        48525 48368 48525 48524        48525        48525
## Up            25300          0     67      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0             0          0          0          0          0          0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0             0          0          0          0          0          0
##          LargeDependenceEmphasis.original   X1     X2     X3     X4     X5     X6
## Down           1 18464 16257 13936 12358 10610 10673
## NotSig        48523 12776 19500 22220 25225 26773 28362
## Up             1 17285 12768 12369 10942 11142  9490
##          X7     X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down         7123  7269  7933  7844  8248  5397  5294  5708  4526  4006  3252  2655
## NotSig       32693 33562 32753 32632 33438 36684 36504 37398 38917 40448 41087 43506
## Up            8709  7694  7839  8049  6839  6444  6727  5419  5082  4071  4186  2364
##          X19
## Down        2551
## NotSig      43301
## Up          2673
```

```
head(toptable.larDepEm)
```

```
##          logFC     AveExpr      t    P.Value adj.P.Val      B
## 203893_at    0.1010219 5.0379308 5.279648 7.640199e-07 0.03707406 5.623121
## 1554830_a_at -0.1956586 2.6289573 -5.057077 1.951147e-06 0.04733971 4.517832
## 1555229_a_at -0.3988574 0.6820437 -4.788864 5.868924e-06 0.08270166 3.075136
## 1562121_at   -0.1770310 0.1193435 -4.751753 6.817242e-06 0.08270166 2.602550
## 216922_x_at  -0.2066764 -0.3358964 -4.695589 8.541167e-06 0.08289203 2.127148
## 201645_at    -0.2647713 1.8007395 -4.610326 1.199216e-05 0.09698663 2.839749
```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeDependenceHighGrayLevelEmphasis.original")

summa.fit.larDepHigh <- decideTests(fit)
summary(summa.fit.larDepHigh)

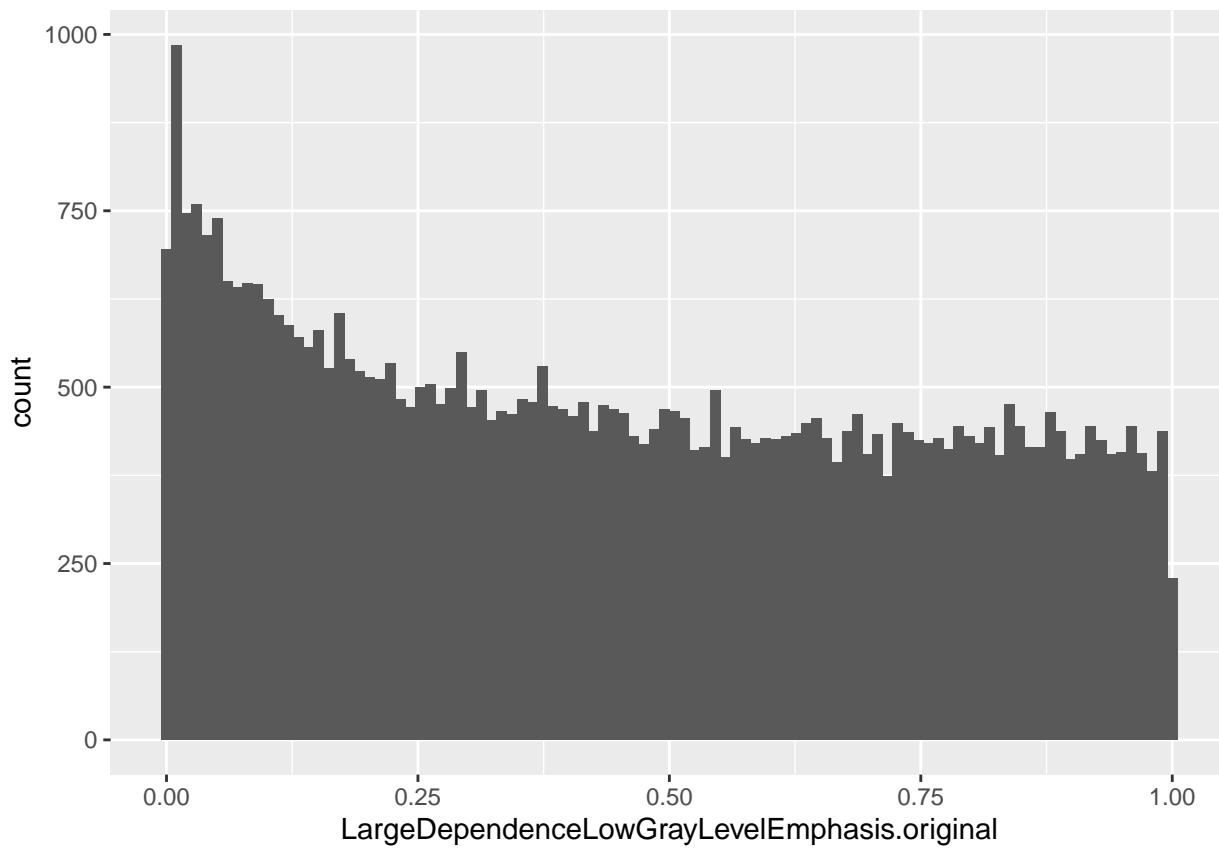
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           657          0   139     0     0          0          0
## NotSig        22393        48525 48264 48525 48523        48525        48525
## Up            25475          0   122     0     2          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic cough      BMI Cr_wheezengY
## Down           0             0          0          0          0          0
## NotSig        48525        48525          0        48525 48525        48525
## Up             0             0          0          0          0          0
##          LargeDependenceHighGrayLevelEmphasis.original X1     X2     X3     X4
## Down           0 18494 16196 13741 12101
## NotSig        48525 12772 19694 22359 25620
## Up             0 17259 12635 12425 10804
##          X5     X6     X7     X8     X9     X10    X11    X12    X13    X14    X15    X16
## Down       10460 9225 8758 7298 7838 8470 6718 6489 6477 5509 4789 3874
## NotSig     26720 28774 32559 34287 32679 32159 33777 36669 37078 37169 39238 40855
## Up        11345 10526 7208 6940 8008 7896 8030 5367 4970 5847 4498 3796
##          X17    X18    X19
## Down       3798 2149 2494
## NotSig    41840 43667 43491
## Up         2887 2709 2540

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/LargeDependenceLowGrayLevelEmphasis.original")

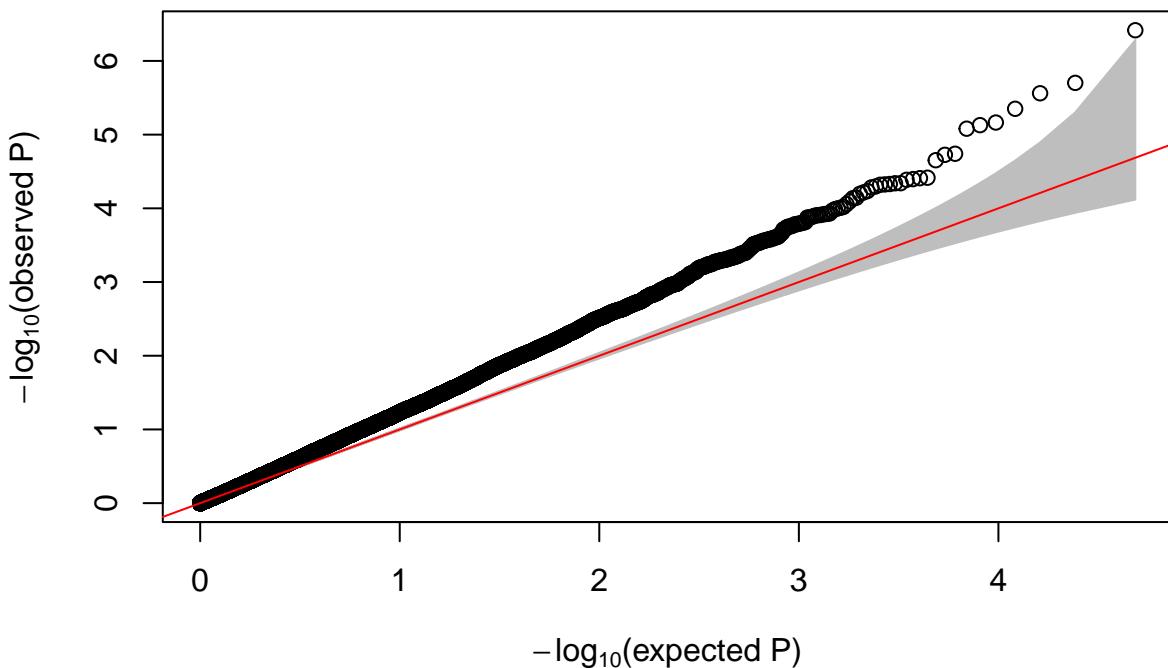
summa.fit.larDepLow <- decideTests(fit)
toptable.larDepLow <- topTable(fit, coef = "LargeDependenceLowGrayLevelEmphasis.original",
                                 number = dim(counts.ok)[1])
toptable.larDepLow <- toptable.larDepLow[order(toptable.larDepLow$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = LargeDependenceLowGrayLevelEmphasis.original)) +
  geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$LargeDependenceLowGrayLevelEmphasis.original)
```



```
summary(summa.fit.larDepLow)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      656      0   119      0     1      0      0
## NotSig  22450  48525 48317 48525 48522  48525  48525
## Up       25419      0    89      0     2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig  48525      48525      48525 48525 48525  48525
## Up       0      0      0      0      0      0      0
##      LargeDependenceLowGrayLevelEmphasis.original   X1   X2   X3   X4
## Down      1 18376 16277 13909 12246
## NotSig  48522 12899 19838 22027 25399
## Up       2 17250 12410 12589 10880
##      X5   X6   X7   X8   X9   X10  X11  X12  X13  X14  X15  X16
## Down  10437 9280 8971 7232 7943 8083 6771 6465 6701 5552 4907 3792
## NotSig 26803 28706 32431 34391 32306 32779 33915 36711 36532 37377 39226 41103
## Up    11285 10539 7123 6902 8276 7663 7839 5349 5292 5596 4392 3630
##      X17  X18  X19
## Down  4017 2128 2568
## NotSig 41454 43698 43592
## Up    3054 2699 2365
head(toptable.larDepLow, 10)

```

```

##      logFC    AveExpr        t    P.Value adj.P.Val      B
## 212329_at -0.2326719 3.0460263 -5.440190 3.832987e-07 0.01859957 5.879025
## 230146_s_at 0.2876540 0.3778259 5.052795 1.984712e-06 0.04441945 3.749684
## 227973_at  0.1521623 4.8121414 4.974488 2.746179e-06 0.04441945 4.428084
## 230036_at  0.2711817 5.6260651 4.856236 4.461261e-06 0.05412067 4.008626
## 203238_s_at 0.4520526 2.0908241 4.750411 6.849849e-06 0.05756046 3.325836
## 202174_s_at 0.1354318 5.7516296 4.730062 7.434079e-06 0.05756046 3.537436
## 212764_at  0.2522699 5.3623273 4.702490 8.303416e-06 0.05756046 3.437421
## 241358_at  0.5291955 -0.3638065 4.504586 1.816711e-05 0.10128191 1.685112
## 230846_at  0.3068441 1.0762390 4.496023 1.878490e-05 0.10128191 2.253641
## 212916_at  -0.1105720 5.4256914 -4.452653 2.223889e-05 0.10791420 2.538019

```

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SmallDependenceEmphasis.original"

summa.fit.smDepEm <- decideTests(fit)
summary(summa.fit.smDepEm)

```

```

##      (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      588      0   89     0     0      0      0
## NotSig  22737  48525 48317 48525 48523  48525  48525
## Up       25200      0    65     0     2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig  48525      48525      48525 48525 48525  48525
## Up       0      0      0      0      0      0      0
##      SmallDependenceEmphasis.original   X1   X2   X3   X4   X5   X6
## Down      0 18573 16132 13989 12352 10443 10702
## NotSig  48525 12682 19885 22024 25230 27073 28390
## Up       0 17270 12508 12512 10943 11009  9433
##      X7   X8   X9   X10  X11  X12  X13  X14  X15  X16  X17  X18
## Down  6753 7246 8154 7790 8207 5452 5285 5593 4606 4085 3114 2671
## NotSig 33228 33463 32364 32909 33385 36578 36566 37311 38831 40338 41280 43445
## Up    8544 7816 8007 7826 6933 6495 6674 5621 5088 4102 4131 2409

```

```

##          X19
## Down    2602
## NotSig 43188
## Up     2735
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SmallDependenceHighGrayLevelEmphasis.RData")
summa.fit.smDepHigh <- decideTests(fit)
summary(summa.fit.smDepHigh)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      599           0    79   0    1       0           0
## NotSig   22752        48525 48392 48525 48520     48525        48525
## Up       25174           0   54   0    4       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0             0           0           0       0       0           0
## NotSig   48525           48525           48525     48525     48525        48525
## Up       0             0           0           0       0       0           0
##          SmallDependenceHighGrayLevelEmphasis.original X1   X2   X3   X4
## Down      0 18449 16234 13880 12405
## NotSig   48525 12766 19722 22178 25190
## Up       0 17310 12569 12467 10930
##          X5   X6   X7   X8   X9   X10  X11  X12  X13  X14  X15  X16
## Down    10304 9294 8503 7561 7976 7999 6886 6348 6857 5537 5019 4328
## NotSig  27330 28691 33423 33764 32361 32671 33345 36889 36254 37435 39081 40043
## Up      10891 10540 6599 7200 8188 7855 8294 5288 5414 5553 4425 4154
##          X17  X18  X19
## Down    4185 2478 2277
## NotSig  41221 43393 44175
## Up      3119 2654 2073
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/SmallDependenceLowGrayLevelEmphasis.RData")
summa.fit.smDepLow <- decideTests(fit)
summary(summa.fit.smDepLow)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      592           0    79   0    0       0           0
## NotSig   22740        48525 48395 48525 48523     48525        48525
## Up       25193           0   51   0    2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0             0           0           0       0       0           0
## NotSig   48525           48525           48525     48525     48525        48525
## Up       0             0           0           0       0       0           0
##          SmallDependenceLowGrayLevelEmphasis.original X1   X2   X3   X4
## Down      0 18544 16054 13843 12265
## NotSig   48525 12737 20071 22274 25425
## Up       0 17244 12400 12408 10835
##          X5   X6   X7   X8   X9   X10  X11  X12  X13  X14  X15  X16
## Down    10512 10726 6818 7241 8048 7818 8233 5440 5246 5601 4607 4308
## NotSig  26945 28325 33129 33483 32565 32778 33381 36594 36650 37287 38832 39902
## Up      11068 9474 8578 7801 7912 7929 6911 6491 6629 5637 5086 4315
##          X17  X18  X19
## Down    2929 2685 2591
## NotSig  41594 43428 43230

```

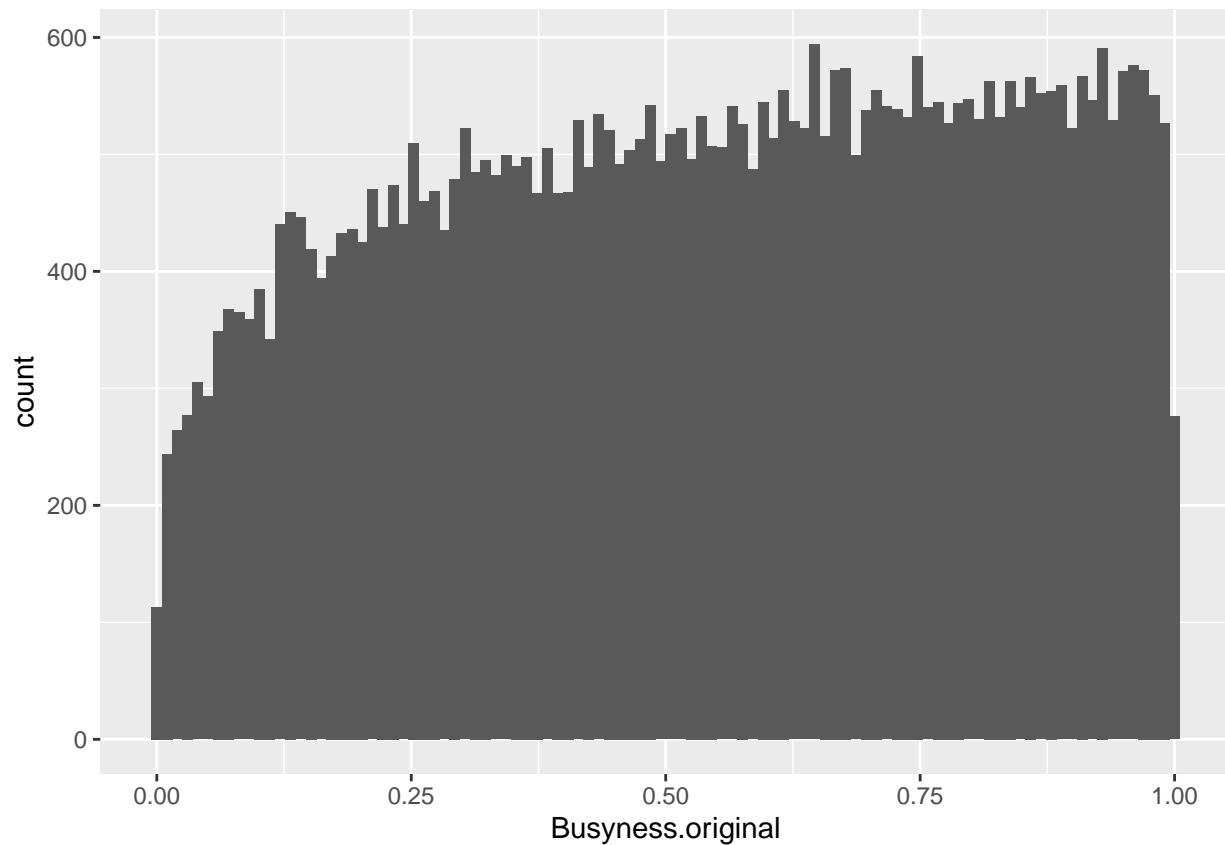
```

## Up      4002  2412  2704
load("/Users/carlacasanova.suarez/Desktop/Radiomic features models (indiv)/Busyness.original.rda")

summa.fit.busy <- decideTests(fit)
toptable.busy <- topTable(fit, coef = "Busyness.original", number = dim(counts.ok)[1])
toptable.busy <- toptable.busy[order(toptable.busy$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Busyness.original)) + geom_histogram(bins = 100)

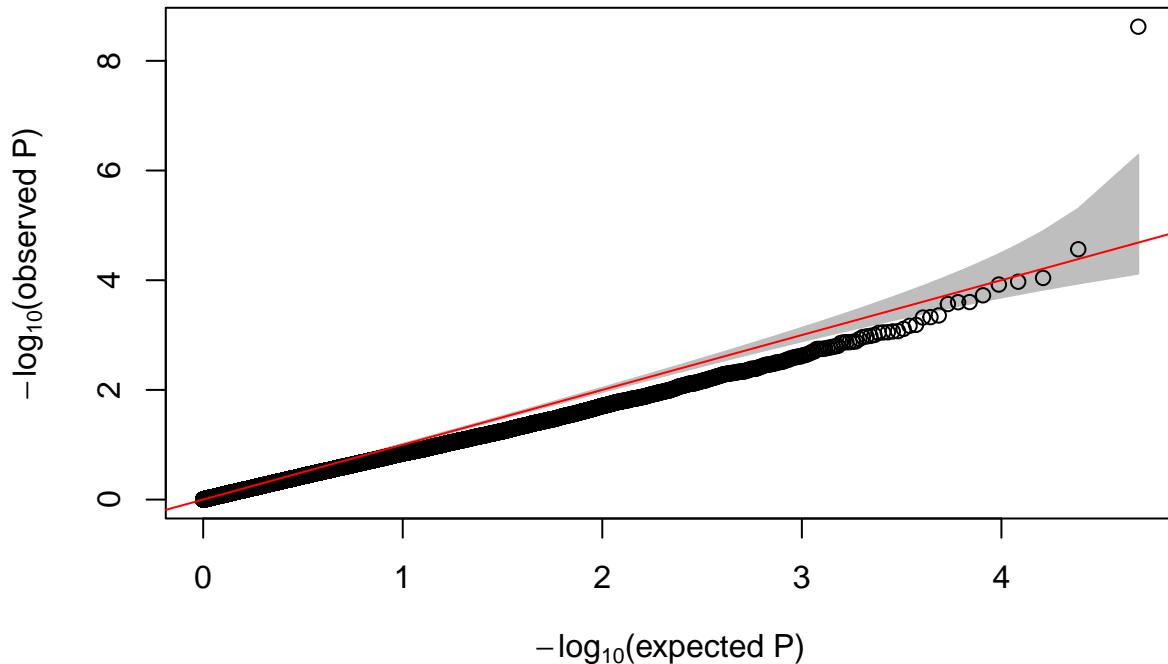
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Busyness.original)

```



```
summary(summa.fit.busy)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down      596          0     95   0   0   0       0
## NotSig    22703        48525 48373 48525 48523 48525       48525
## Up       25226          0     57   0   2   0       0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough    BMI Cr_wheezengY
## Down      0            0           0       0       0       0       0
## NotSig    48525        48525        48525 48525 48525       48525
## Up        0            0           0       0       0       0       0
##          Busyness.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18496 16099 13909 12205 10506 10623 7149 7252 8034
## NotSig    48524 12784 19896 22131 25521 26951 28483 32467 33491 32612
## Up        1 17245 12530 12485 10799 11068 9419 8909 7782 7879
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down     7829 8287 5527 5221 5432 4646 4175 2923 2627 2591
## NotSig   32716 33349 36370 36727 37593 38807 40206 41588 43569 43220
## Up       7980 6889 6628 6577 5500 5072 4144 4014 2329 2714
```

```
head(toptable.busy, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val
## 232577_at	0.9176569	0.3902588	6.566481	2.382831e-09	0.0001156269
## 238763_at	0.7837212	0.3957949	4.399967	2.728206e-05	0.6619310945
## 218540_at	-0.3353031	2.5303325	-4.080717	9.085652e-05	0.9999897388
## 230026_at	0.8767203	2.3909989	4.037362	1.065232e-04	0.9999897388
## 217923_at	-0.2912297	5.0552122	-4.004682	1.200098e-04	0.9999897388
## 238181_at	-1.1875417	-1.0498092	-3.879328	1.885132e-04	0.9999897388
## 210841_s_at	0.5759793	1.5357202	3.799436	2.501878e-04	0.9999897388
## 202191_s_at	0.4772884	4.4615809	3.797542	2.518610e-04	0.9999897388
## 210842_at	0.6952086	1.8397401	3.775651	2.719850e-04	0.9999897388
## 226428_at	-0.2965105	3.3969470	-3.637380	4.390586e-04	0.9999897388
	B				

```

## 232577_at    0.5404565
## 238763_at   -2.2885126
## 218540_at   -1.8934568
## 230026_at   -1.4005356
## 217923_at   -0.8634380
## 238181_at   -3.9065611
## 210841_s_at -2.1718226
## 202191_s_at -1.2259012
## 210842_at   -1.9560649
## 226428_at   -2.1891575

load("/Users/carlacasanovasuzarez/Desktop/Radiomic features models (indiv)/Coarseness.original.rda")

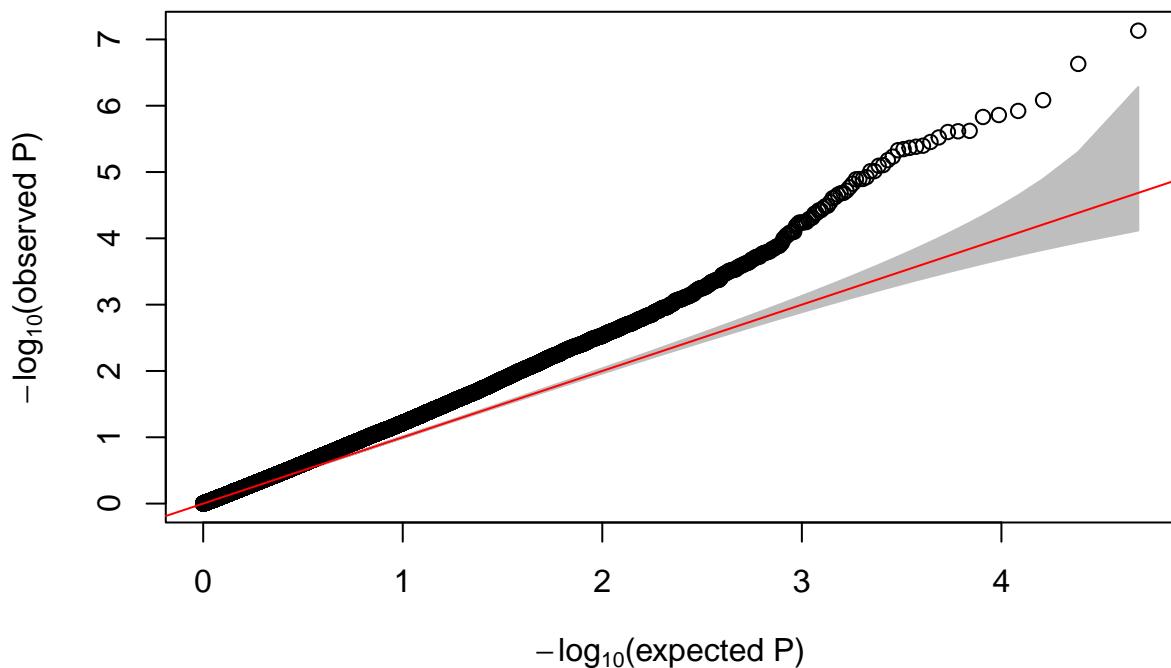
summa.fit.coar <- decideTests(fit)
toptable.coar <- topTable(fit, coef = "Coarseness.original", number = dim(counts.ok)[1])
toptable.coar <- toptable.coar[order(toptable.coar$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Coarseness.original)) + geom_histogram(bins = 100)

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Coarseness.original)

```

A histogram titled 'Coarseness.original' showing the distribution of p-values. The x-axis is labeled 'Coarseness.original' and ranges from 0.00 to 1.00 with major ticks every 0.25. The y-axis is labeled 'Count' and ranges from 0 to 1000 with major ticks at 0, 250, 500, 750, and 1000. The distribution is highly skewed to the right, with the highest frequency of approximately 900 counts occurring at the lowest p-values near 0.00. As the p-value increases, the count drops sharply, with most other bins containing fewer than 500 counts, and a long tail extending up to 1.00.



```
summary(summa.fit.coar)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           606          0   122     0     1       0             0
## NotSig        22673        48525 48307 48525 48520      48525         48525
## Up            25246          0   96     0     4       0             0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough     BMI Cr_wheezengY
## Down           0           0           0           0       0       0             0
## NotSig        48525        48525        48525      48525 48525         48525
## Up             0           0           0           0       0       0             0
##          Coarseness.original X1     X2     X3     X4     X5     X6     X7     X8
## Down           3 18392 16051 14162 12286 10342 10471 6678 7087
## NotSig        48483 12815 20128 21778 25305 26889 28835 33228 33972
## Up            39 17318 12346 12585 10934 11294 9219 8619 7466
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          8243 7903 7758 5556 5256 5688 4444 3714 3188 2757 2381
## NotSig        32375 32272 34198 36425 36552 37116 39087 40905 41210 43544 43983
## Up            7907 8350 6569 6544 6717 5721 4994 3906 4127 2224 2161
```

```
head(toptable.coar, 10)
```

```
##          logFC AveExpr      t    P.Value adj.P.Val      B
## 230036_at  0.20501321 5.626065 5.815328 7.383980e-08 0.003583076 7.834249
## 239988_at  0.30128756 2.447993 5.553819 2.340761e-07 0.005679271 6.624939
## 218986_s_at 0.20531863 5.501943 5.261416 8.252085e-07 0.011953777 5.547686
## 214059_at  0.41147689 3.679703 5.173247 1.198576e-06 0.011953777 5.219442
## 221816_s_at 0.10713753 6.663139 5.139561 1.381107e-06 0.011953777 4.988945
## 204439_at  0.35754484 5.068404 5.123399 1.478056e-06 0.011953777 5.000675
## 204747_at  0.27510314 5.588170 5.007778 2.393581e-06 0.013434957 4.522903
## 228617_at  0.25440943 5.754949 5.004232 2.429005e-06 0.013434957 4.500641
## 222986_s_at 0.05173578 7.893641 4.998069 2.491800e-06 0.013434957 4.257048
## 206133_at  0.24167375 5.082622 4.952401 3.009000e-06 0.014209066 4.346784
```

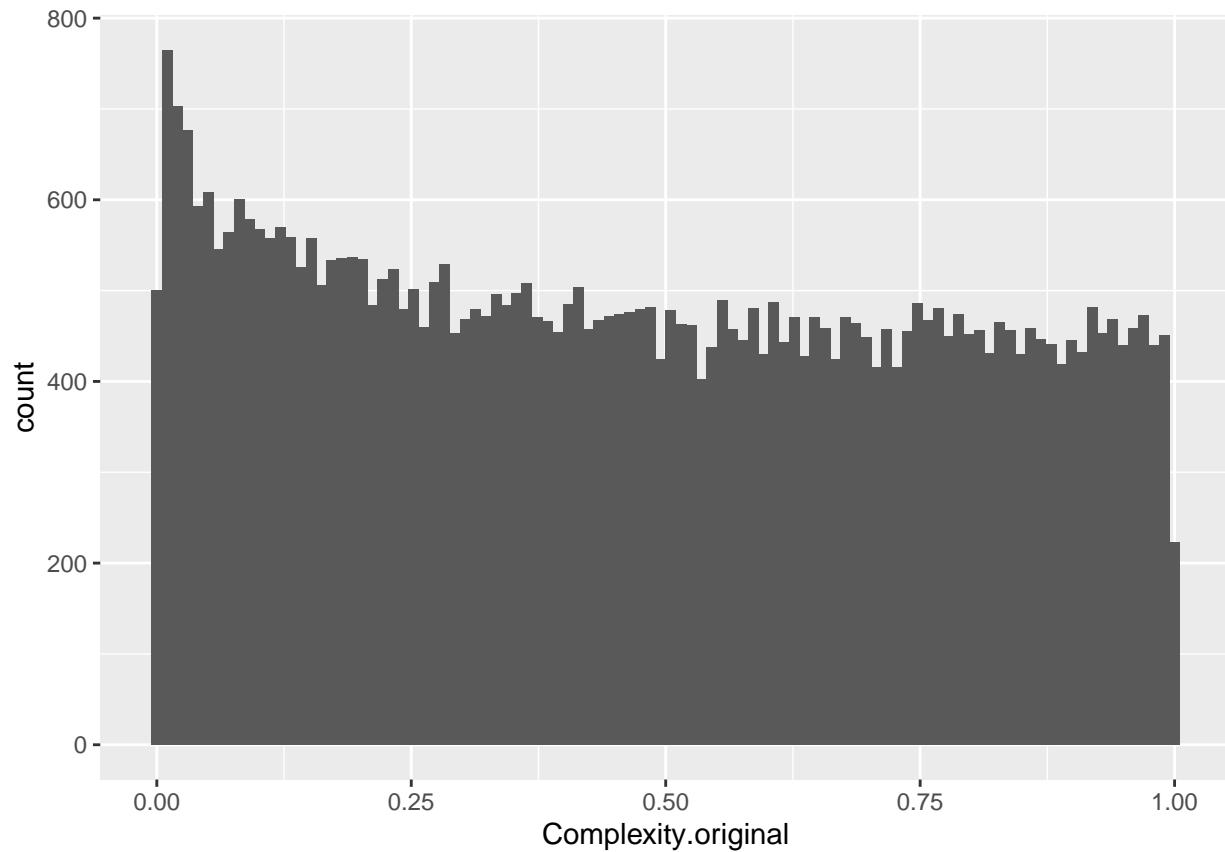
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Complexity.original.rda")

summa.fit.comp <- decideTests(fit)
toptable.comp <- topTable(fit, coef = "Complexity.original", number = dim(counts.ok)[1])
toptable.comp <- toptable.comp[order(toptable.comp$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Complexity.original)) + geom_histogram(bins = 100)

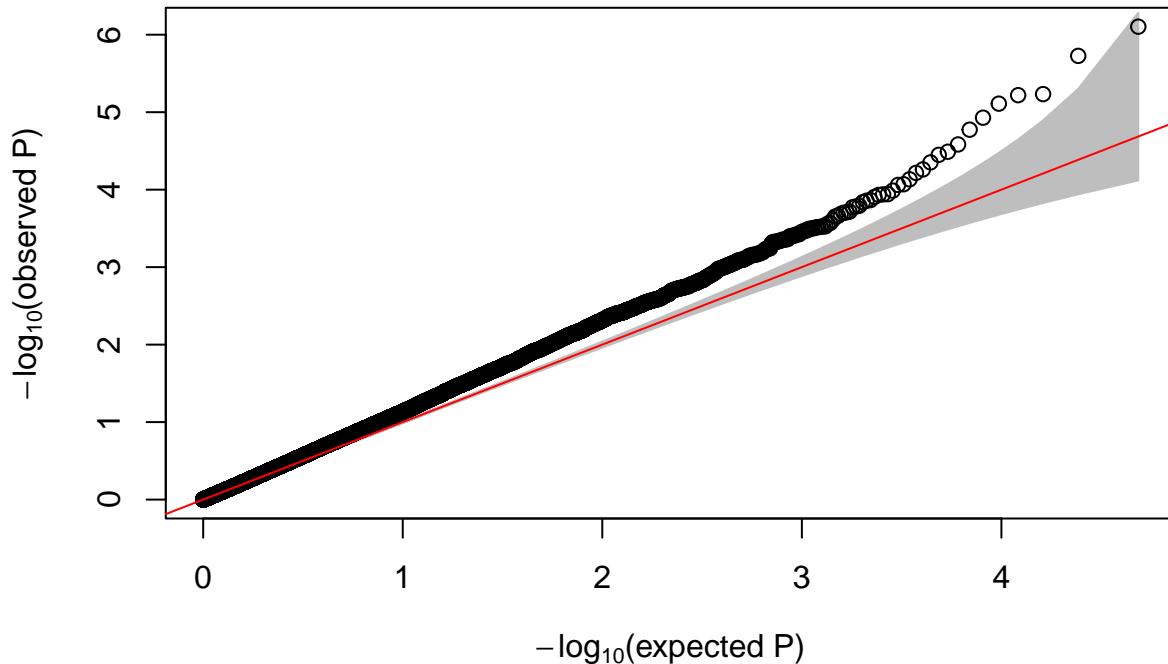
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Complexity.original)

```



```
summary(summa.fit.comp)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           602          0     89      0      0          0          0
## NotSig        22629        48525 48368 48525 48524        48525        48525
## Up            25294          0     68      0      1          0          0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0          0          0          0
## NotSig        48525        48525          0          0        48525 48525        48525
## Up             0            0          0          0          0          0          0
##          Complexity.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down           1 18453 16252 13936 12365 10621 10673 7125 7273
## NotSig        48523 12788 19494 22217 25221 26755 28372 32680 33552
## Up             1 17284 12779 12372 10939 11149 9480 8720 7700
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down         7928 7843 8264 5402 5280 5733 4518 4010 3268 2648 2555
## NotSig       32762 32621 33408 36673 36535 37358 38937 40437 41054 43509 43302
## Up            7835 8061 6853 6450 6710 5434 5070 4078 4203 2368 2668
```

```
head(toptable.comp, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 203893_at	-0.10050961	5.0379308	-5.272424	7.878688e-07	0.03823133	5.598422
## 1554830_a_at	0.19450868	2.6289573	5.066498	1.876000e-06	0.04551646	4.566115
## 1555229_a_at	0.39726757	0.6820437	4.789937	5.843420e-06	0.07319211	3.101878
## 1562121_at	0.17741058	0.1193435	4.782027	6.033352e-06	0.07319211	2.721147
## 216922_x_at	0.20685436	-0.3358964	4.719360	7.765207e-06	0.07536134	2.227633
## 201645_at	0.26393274	1.8007395	4.614905	1.177649e-05	0.09524232	2.868120
## 219675_s_at	0.09202201	5.0965517	4.524326	1.682589e-05	0.11663945	2.790847
## 224785_at	-0.15243003	3.6686028	-4.411605	2.608065e-05	0.15819547	2.358060
## 217279_x_at	0.21032113	0.8980683	4.355177	3.239944e-05	0.17238384	1.785049
## 218315_s_at	-0.09323833	3.2742864	-4.331093	3.552475e-05	0.17238384	2.070468

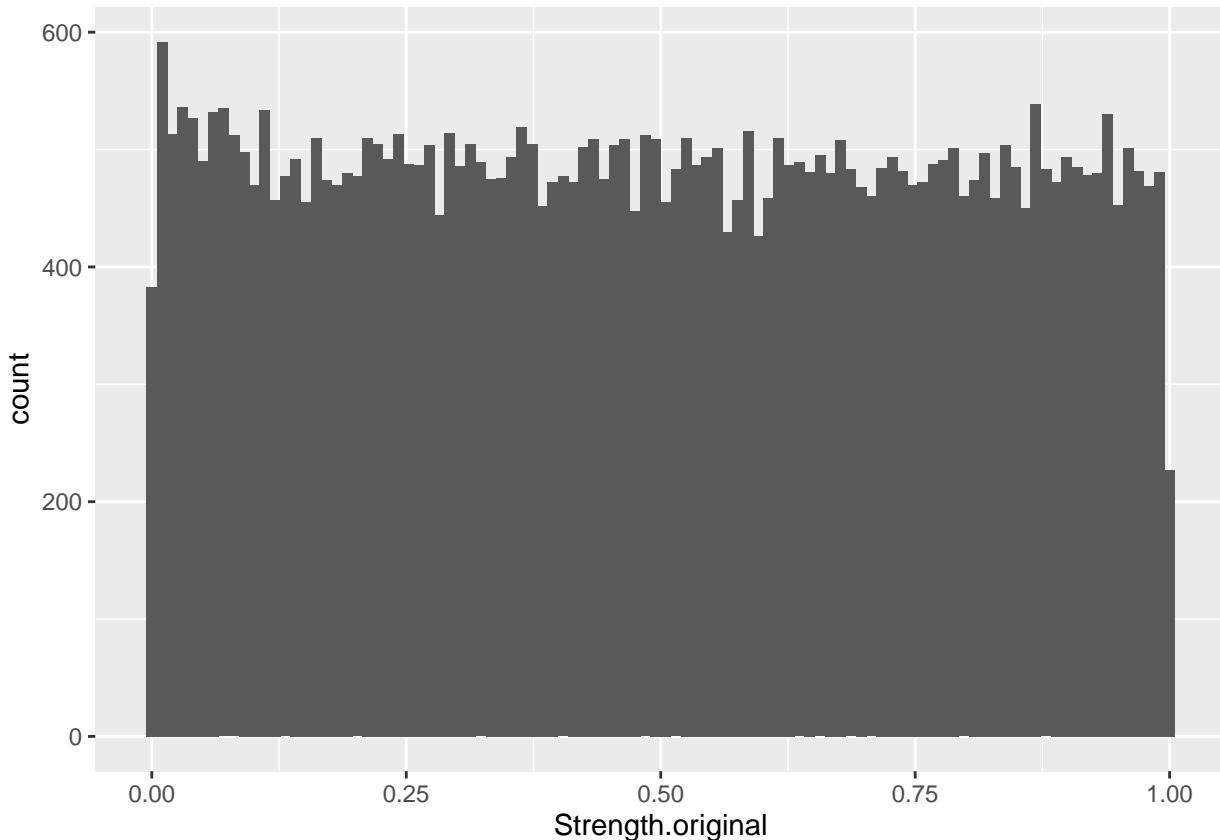
```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Strength.original.rda")

summa.fit.strength <- decideTests(fit)
toptable.strength <- topTable(fit, coef = "Strength.original", number = dim(counts.ok)[1])
toptable.strength <- toptable.strength[order(toptable.strength$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = Strength.original)) + geom_histogram(bins = 100)

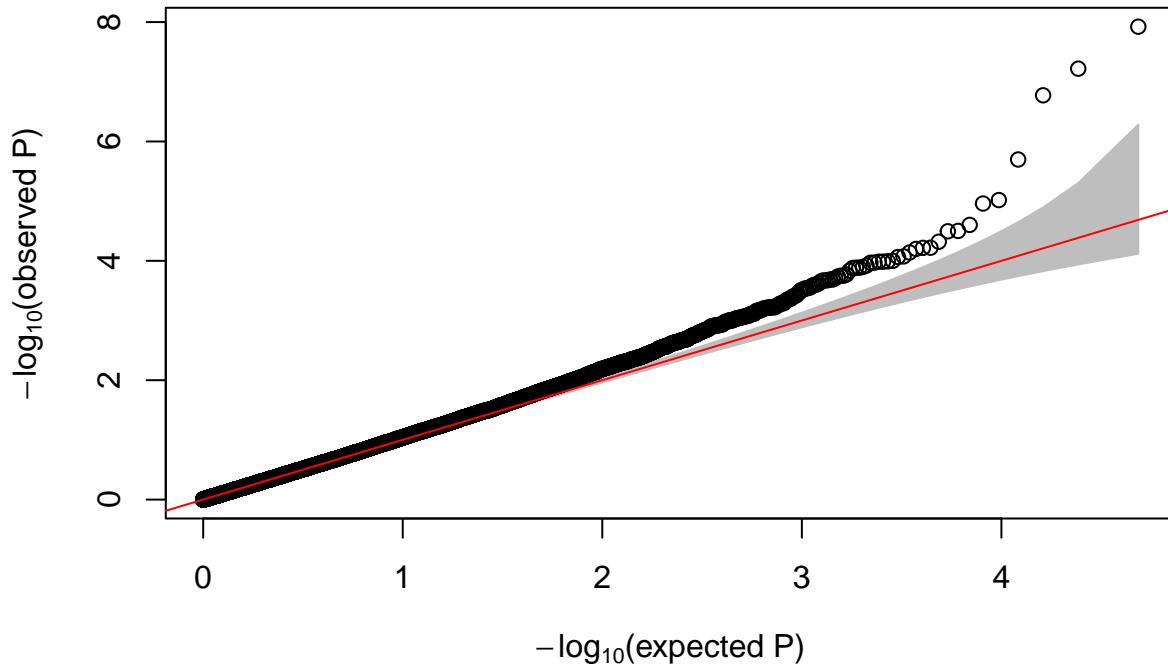
```



```

# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$Strength.original)

```



```
summary(summa.fit.strength)
```

```
##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down           603          0    94     0     0      0          0
## NotSig        22973        48525 48371 48525 48523    48525        48525
## Up            24949          0   60     0     2      0          0
##          dusty_exposeY history_asthmaY CoughNo chronic_cough      BMI Cr_wheezengY
## Down           0            0          0          0      0      0          0
## NotSig        48525        48525        48525    48525 48525        48525
## Up             0            0          0          0      0      0          0
##          Strength.original   X1      X2      X3      X4      X5      X6      X7      X8      X9
## Down           0 18551 16212 14053 12422 10398 10727 7263 7300 8095
## NotSig        48521 12705 19646 21933 25134 27152 28328 32403 33449 32513
## Up             4 17269 12667 12539 10969 10975 9470 8859 7776 7917
##          X10     X11     X12     X13     X14     X15     X16     X17     X18     X19
## Down          7893  8273  5523  5254  5597  4706  4189  2930  2694  2513
## NotSig       32505 33429 36406 36711 37246 38669 40175 41727 43434 43394
## Up            8127  6823  6596  6560  5682  5150  4161  3868  2397  2618
```

```
head(toptable.strength, 10)
```

	logFC	AveExpr	t	P.Value	adj.P.Val	B
## 1557124_at	0.23097028	1.1177454	6.218611	1.193466e-08	0.0005791295	9.423889
## 210299_s_at	0.17385089	2.8765271	5.860849	6.032529e-08	0.0014636423	8.019843
## 215704_at	0.32925757	0.7895572	5.629074	1.685273e-07	0.0027259287	6.987630
## 215109_at	0.12211612	2.9937086	5.050635	2.004632e-06	0.0243186924	4.747304
## 225601_at	0.15841982	1.3044442	4.666745	9.585570e-06	0.0886396168	3.294559
## 234455_at	-0.28398360	-1.6105994	-4.633064	1.096008e-05	0.0886396168	1.512755
## 214505_s_at	0.15118216	2.0527430	4.422875	2.497340e-05	0.1723586820	2.430373
## 201540_at	0.12429598	4.4346419	4.362381	3.152178e-05	0.1723586820	2.078193
## 234952_s_at	0.07680998	2.9083361	4.358716	3.196761e-05	0.1723586820	2.209159
## 1559612_at	0.16889162	1.3911415	4.252768	4.783372e-05	0.2321131328	1.841648

```

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Imc1.original.rda")
summa.fit.imc1 <- decideTests(fit)
summary(summa.fit.imc1)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down      596           0     94    0    0       0           0
## NotSig   22658         48525  48370  48525 48523     48525       48525
## Up       25271           0     61    0    2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0           0           0       0       0
## NotSig        48525         48525         48525     48525 48525       48525
## Up            0             0           0           0       0       0
##          Imc1.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18548 16176 13844 12308 10571 10850 7040 7021 8230
## NotSig        48525 12721 19849 22210 25260 26945 28093 32637 34231 32247
## Up            0 17256 12500 12471 10957 11009 9582 8848 7273 8048
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19    X20
## Down        7956  8389  5436  5429  5784  4815  4335  3022  2774  2612  2231
## NotSig     32500 33111 36518 36214 36989 38366 39906 41338 43272 43114 44117
## Up         8069  7025  6571  6882  5752  5344  4284  4165  2479  2799  2177

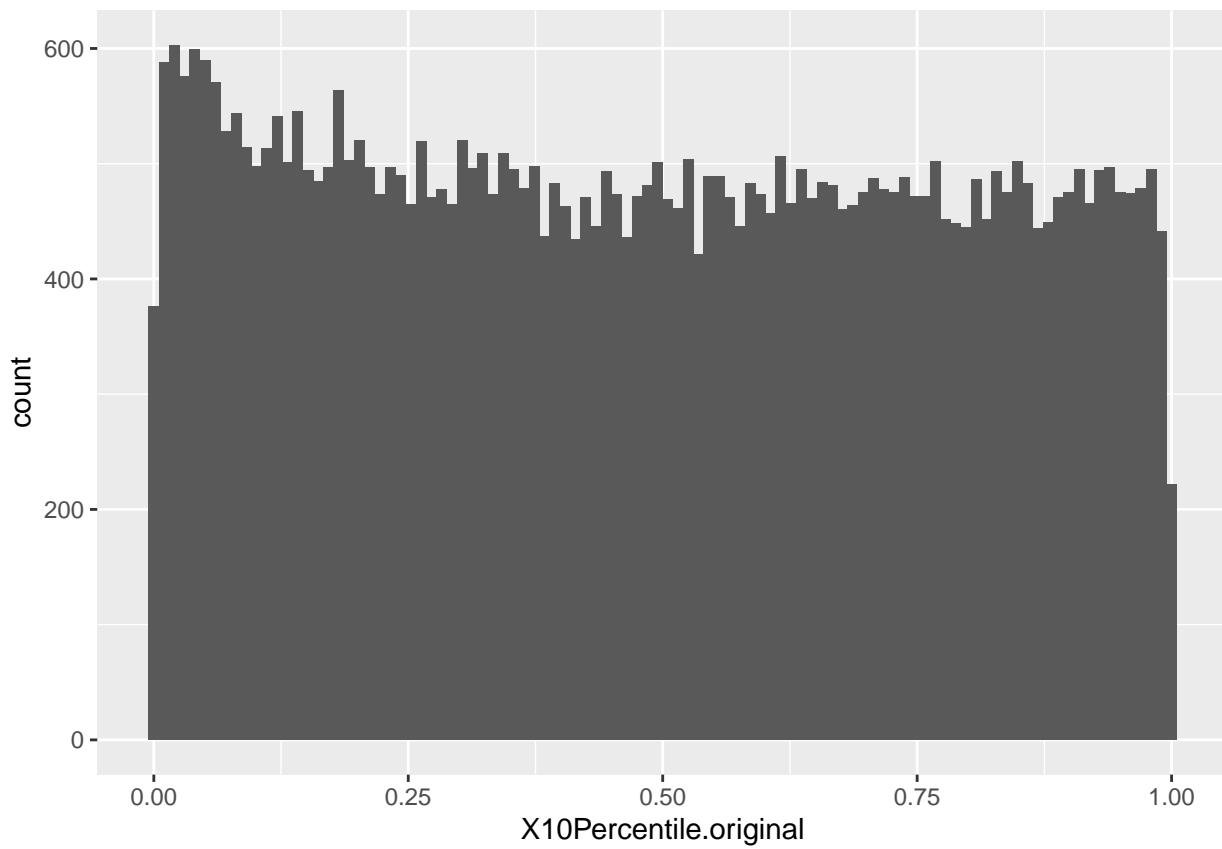
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Imc2.original.rda")
summa.fit.imc2 <- decideTests(fit)
summary(summa.fit.imc2)

##          (Intercept) GroupSevere  SexM    Age Dwalk FEV1PSPC fume_exposeY
## Down       601           0     92    0    0       0           0
## NotSig   22684         48525  48372  48525 48523     48525       48525
## Up       25240           0     61    0    2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0             0           0           0       0       0
## NotSig        48525         48525         48525     48525 48525       48525
## Up            0             0           0           0       0       0
##          Imc2.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18515 16160 13869 12361 10488 10678 7038 7171 8091
## NotSig        48525 12714 19812 22196 25190 27075 28427 32785 33736 32483
## Up            0 17296 12553 12460 10974 10962 9420 8702 7618 7951
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down        7872  8229  5533  5294  5643  4645  4095  3080  2630  2678
## NotSig     32621 33389 36384 36477 37298 38772 40354 41353 43536 43327
## Up         8032  6907  6608  6754  5584  5108  4076  4092  2359  2520

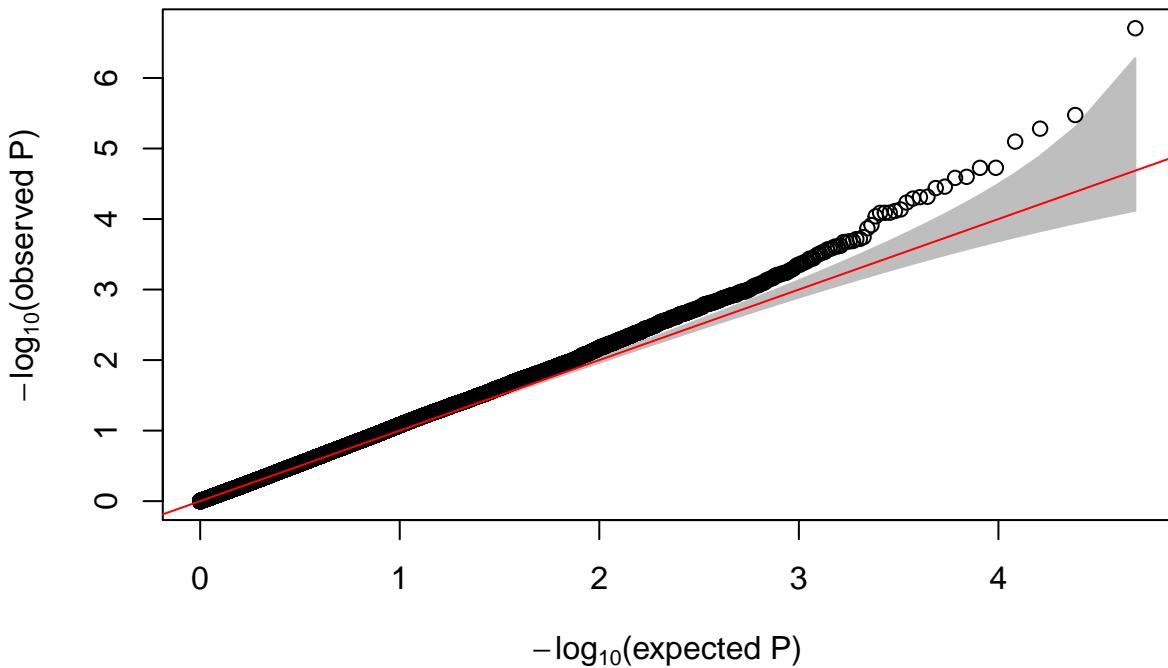
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/X10Percentile.original.rda")
summa.fit.X10 <- decideTests(fit)
toptable.X10 <- topTable(fit, coef = "X10Percentile.original", number = dim(counts.ok)[1])
toptable.X10 <- toptable.X10[order(toptable.X10$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = X10Percentile.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$X10Percentile.original)
```



```
summary(summa.fit.X10)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      591      0   98      0   0      0      0
## NotSig   22727    48525 48362 48525 48523    48525    48525
## Up       25207      0   65      0   2      0      0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525    48525      0      0      0      0      0
## Up       0      0      0      0      0      0      0
##          X10Percentile.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down      0 18567 16135 14054 12413 10356 10713 7173 7247
## NotSig   48524 12694 19844 21934 25112 27338 28370 32406 33503
## Up       1 17264 12546 12537 11000 10831 9442 8946 7775
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    8164 7840 8281 5505 5300 5596 4698 4301 2845 2722 2591
## NotSig  32375 32685 33314 36443 36525 37220 38683 39935 41749 43332 43210
## Up      7986 8000 6930 6577 6700 5709 5144 4289 3931 2471 2724
head(toptable.X10, 10)

##          logFC AveExpr      t      P.Value adj.P.Val      B
## 225418_at  1.8679623 3.3494210 5.593235 1.972251e-07 0.00957035 5.969165
## 1570578_at  1.2890057 1.4967816 4.926212 3.353578e-06 0.08136618 3.175678
## 232079_s_at  2.0221278 2.6051990 4.817120 5.235331e-06 0.08468148 3.085408
## 232078_at   1.7369539 0.8111837 4.712473 7.984488e-06 0.09686182 2.012978
## 217446_x_at -0.4377652 4.1435225 -4.496340 1.877505e-05 0.15212013 2.385669
## 1564028_s_at  1.6186633 0.2894055 4.495873 1.880929e-05 0.15212013 1.267321
## 202231_at   0.3063878 6.7005036 4.420212 2.523273e-05 0.15841033 2.420150
## 205734_s_at  -0.8839158 2.0935103 -4.411301 2.611608e-05 0.15841033 1.437815
## 203149_at   0.9965351 4.0875738 4.336939 3.474648e-05 0.17672114 1.879047
## 202367_at   0.5145628 2.8798338 4.324626 3.641858e-05 0.17672114 1.500392

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/X90Percentile.original.rda")
summa.fit.X90 <- decideTests(fit)
summary(summa.fit.X90)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      566      0   96      0   0      0      0
## NotSig   22801    48525 48369 48525 48523    48525    48525
## Up       25158      0   60      0   2      0      0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525    48525      0      0      0      0      0
## Up       0      0      0      0      0      0      0
##          X90Percentile.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down      0 18554 16213 13877 12334 10334 10718 7184 7259
## NotSig   48525 12686 19695 22170 25208 27320 28340 32390 33490
## Up       0 17285 12617 12478 10983 10871 9467 8951 7776
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    8139 7819 8287 5562 5339 5611 4689 4277 2973 2692 2600
## NotSig  32421 32785 33323 36311 36456 37254 38697 39987 41506 43427 43201
## Up      7965 7921 6915 6652 6730 5660 5139 4261 4046 2406 2724

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Entropy.original.rda")
summa.fit.ent <- decideTests(fit)
summary(summa.fit.ent)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY

```

```

## Down      605      0     93      0      0      0      0
## NotSig   22617    48525  48364  48525  48524    48525    48525
## Up       25303      0     68      0      1      0      0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##          Entropy.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18453 16242 13878 12329 10569 10661 7119 7269 7952
## NotSig   48525 12780 19563 22275 25304 26884 28393 32706 33533 32734
## Up       0 17292 12720 12372 10892 11072 9471 8700 7723 7839
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7859  8259  5446  5268  5713  4534  3988  3273  2659  2536
## NotSig  32582 33430 36568 36540 37380 38919 40510 41039 43500 43347
## Up      8084  6836  6511  6717  5432  5072  4027  4213  2366  2642

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Energy.original.rda")
summa.fit.ency <- decideTests(fit)
summary(summa.fit.ency)

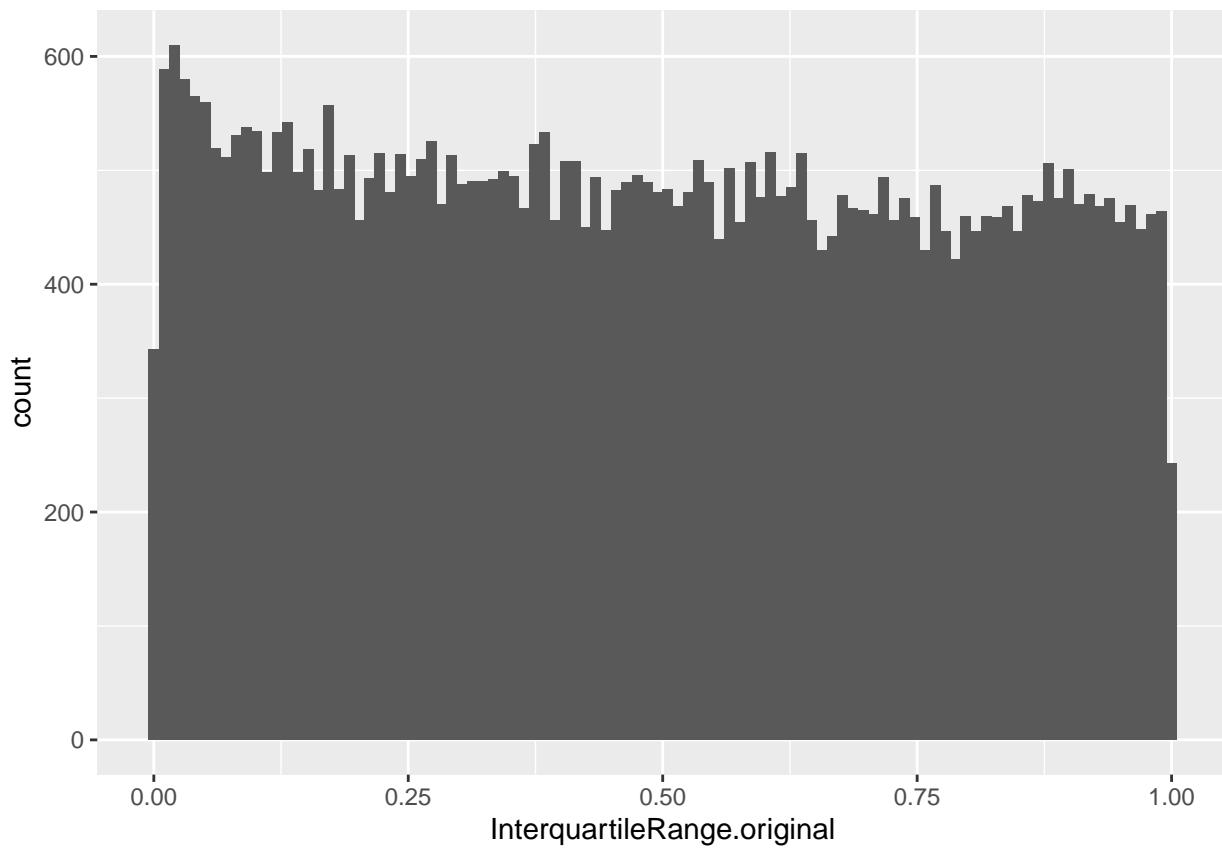
##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      573      0     94      0      0      0      0
## NotSig   22882    48525  48365  48525  48523    48525    48525
## Up       25070      0     66      0      2      0      0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##          Energy.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18574 16147 14064 12374 10380 10553 7149 7284 8024
## NotSig   48525 12669 19782 21911 25142 27199 28702 32542 33419 32579
## Up       0 17282 12596 12550 11009 10946 9270 8834 7822 7922
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7887  8237  5602  5351  5626  4653  4267  2722  2709  2606
## NotSig  32561 33456 36222 36452 37166 38678 40039 42047 43353 43155
## Up      8077  6832  6701  6722  5733  5194  4219  3756  2463  2764

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/InterquartileRange.original.rda")

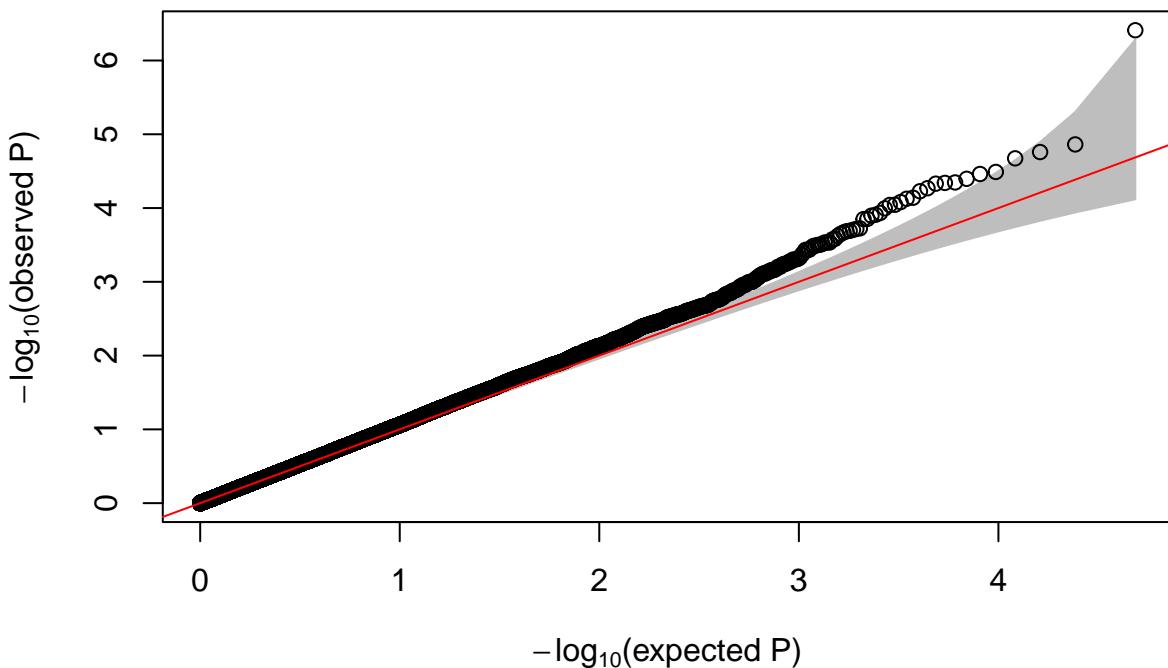
summa.fit.intq <- decideTests(fit)
toptable.intq <- topTable(fit, coef = "InterquartileRange.original", number = dim(counts.ok)[1])
toptable.intq <- toptable.intq[order(toptable.intq$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = InterquartileRange.original)) + geom_histogram(bins = 100)

```



```
# QQplot plot for p-values computed by limma
GWASTools:::qqPlot(p.val.voom$InterquartileRange.original)
```



```
summary(summa.fit.intq)
```

	(Intercept)	GroupSevere	SexM	Age	Dwalk	FEV1PSPC	fume_exposeY
--	-------------	-------------	------	-----	-------	----------	--------------

```

## Down      559      0     80      0      0      0      0
## NotSig   22801    48525  48404  48525  48523   48525    48525
## Up       25165      0     41      0      2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##      InterquartileRange.original X1     X2     X3     X4     X5     X6     X7
## Down      0 18511 16113 13885 12342 10540 10624 7045
## NotSig   48524 12842 19925 22083 25161 26771 28519 32599
## Up       1 17172 12487 12557 11022 11214 9382 8881
##      X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7334  8215  7798  8119  5627  5327  5631  4674  4501  2825  2635  2507
## NotSig  33394 32237 32775 33592 36251 36495 37184 38737 39538 41821 43440 43351
## Up      7797  8073  7952  6814  6647  6703  5710  5114  4486  3879  2450  2667
head(toptable.intq, 10)

##          logFC     AveExpr        t    P.Value adj.P.Val        B
## 202814_s_at  0.3732773  5.2711632  5.437160 3.889115e-07 0.01887193 5.7703167
## 202815_s_at  0.3568653  4.4813489  4.576102 1.373196e-05 0.22674183 2.5691282
## 207720_at   -0.5690804  0.6048606 -4.515522 1.742030e-05 0.22674183 0.5659996
## 226426_at   0.2681267  5.3109313  4.465243 2.119344e-05 0.22674183 2.3920929
## 212769_at   -0.2963126  4.9146649 -4.355103 3.241599e-05 0.22674183 1.9381902
## 215897_at   0.4786812  1.0450237  4.338541 3.453621e-05 0.22674183 0.6025368
## 1552915_at  0.9694990 -0.6807490  4.299066 4.014250e-05 0.22674183 -0.7399409
## 218660_at   -0.2880625  6.2337504 -4.269144 4.496611e-05 0.22674183 1.8535282
## 1557126_a_at -0.5475201  2.4320863 -4.265234 4.563611e-05 0.22674183 0.9581359
## 208686_s_at  0.2552648  5.0900203  4.258987 4.672681e-05 0.22674183 1.6876191

load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Kurtosis.original.rda")
summa.fit.kur <- decideTests(fit)
summary(summa.fit.kur)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      535      0     93      0     1      0      0
## NotSig   22827    48525  48380  48525  48522   48525    48525
## Up       25163      0     52      0     2      0      0
##      dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525  48525    48525    48525
## Up       0      0      0      0      0      0      0
##      Kurtosis.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18481 16179 13838 12296 10389 10611 6938 7297 8126
## NotSig   48525 12904 19857 22149 25212 27112 28540 32791 33508 32452
## Up       0 17140 12489 12538 11017 11024 9374 8796 7720 7947
##      X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7745  8301  5512  5388  5585  4609  4178  3148  2644  2598
## NotSig  32943 33322 36361 36388 37292 38891 40107 41182 43510 43190
## Up      7837  6902  6652  6749  5648  5025  4240  4195  2371  2737
load("/Users/carlacasanovasuarez/Desktop/Radiomic features models (indiv)/Maximum.original.rda")
summa.fit.max <- decideTests(fit)
summary(summa.fit.max)

##          (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY

```

```

## Down      594      0     89      0      0      0      0
## NotSig   22698    48525  48383  48525  48523   48525   48525
## Up       25233      0     53      0      2      0      0
## dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525   48525   48525   48525
## Up       0      0      0      0      0      0      0
## Maximum.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18516 16129 14056 12400 10458 10709 7185 7218 8107
## NotSig   48525 12769 19948 21911 25126 27049 28316 32403 33566 32471
## Up       0 17240 12448 12558 10999 11018 9500 8937 7741 7947
## X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7820  8319  5575  5230  5558  4600  4307  2879  2609  2626
## NotSig  32738 33272 36304 36712 37416 38842 39904 41681 43569 43163
## Up      7967  6934  6646  6583  5551  5083  4314  3965  2347  2736

load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/MeanAbsoluteDeviation.original")
summa.fit.meanAb <- decideTests(fit)
summary(summa.fit.meanAb)

## (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      568      0    104      0      0      0      0
## NotSig   22792    48525  48354  48525  48523   48525   48525
## Up       25165      0     67      0     2      0      0
## dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525   48525   48525   48525
## Up       0      0      0      0      0      0      0
## MeanAbsoluteDeviation.original   X1     X2     X3     X4     X5     X6     X7
## Down      0 18561 16096 13762 12246 10533 10478 7122
## NotSig   48525 12815 19946 22277 25320 26829 28877 32463
## Up       0 17149 12483 12486 10959 11163 9170 8940
## X8     X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7336  8201  7844  8199  5491  5370  5590  4659  4093  3044  2644  2770
## NotSig  33413 32259 32766 33394 36481 36407 37226 38761 40279 41482 43508 43175
## Up      7776  8065  7915  6932  6553  6748  5709  5105  4153  3999  2373  2580

load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/Mean.original.rda")
summa.fit.mean <- decideTests(fit)
summary(summa.fit.mean)

## (Intercept) GroupSevere SexM Age Dwalk FEV1PSPC fume_exposeY
## Down      581      0     96      0      0      0      0
## NotSig   22780    48525  48363  48525  48523   48525   48525
## Up       25164      0     66      0     2      0      0
## dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down      0      0      0      0      0      0      0
## NotSig   48525      48525      48525   48525   48525   48525
## Up       0      0      0      0      0      0      0
## Mean.original   X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down      0 18564 16167 14001 12370 10304 10744 7181 7254 8138
## NotSig   48525 12683 19791 22009 25158 27426 28285 32411 33498 32413
## Up       0 17278 12567 12515 10997 10795 9496 8933 7773 7974
## X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down    7839  8305  5516  5346  5608  4691  4271  2931  2702  2592

```

```

## NotSig 32730 33294 36393 36443 37227 38692 39998 41590 43368 43197
## Up      7956  6926  6616  6736  5690  5142  4256  4004  2455  2736
load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Median.original.rda")
summa.fit.med <- decideTests(fit)
summary(summa.fit.med)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           586          0    96     0     0       0           0
## NotSig        22756        48525 48363 48525 48523    48525       48525
## Up            25183          0    66     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down           0             0           0           0       0       0
## NotSig        48525          48525          48525 48525       48525       48525
## Up             0             0           0           0       0       0
##          Median.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18562 16155 14026 12378 10307 10730 7178 7252 8134
## NotSig        48525 12685 19807 21979 25152 27451 28313 32422 33474 32411
## Up             0 17278 12563 12520 10995 10767 9482 8925 7799 7980
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7846  8280  5515  5329  5596  4690  4256  2913  2706  2589
## NotSig        32725 33317 36408 36451 37253 38689 40020 41628 43369 43185
## Up            7954  6928  6602  6745  5676  5146  4249  3984  2450  2736

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Minimum.original.rda")
summa.fit.min <- decideTests(fit)
summary(summa.fit.min)

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/Range.original.rda")
summa.fit.range <- decideTests(fit)
summary(summa.fit.range)

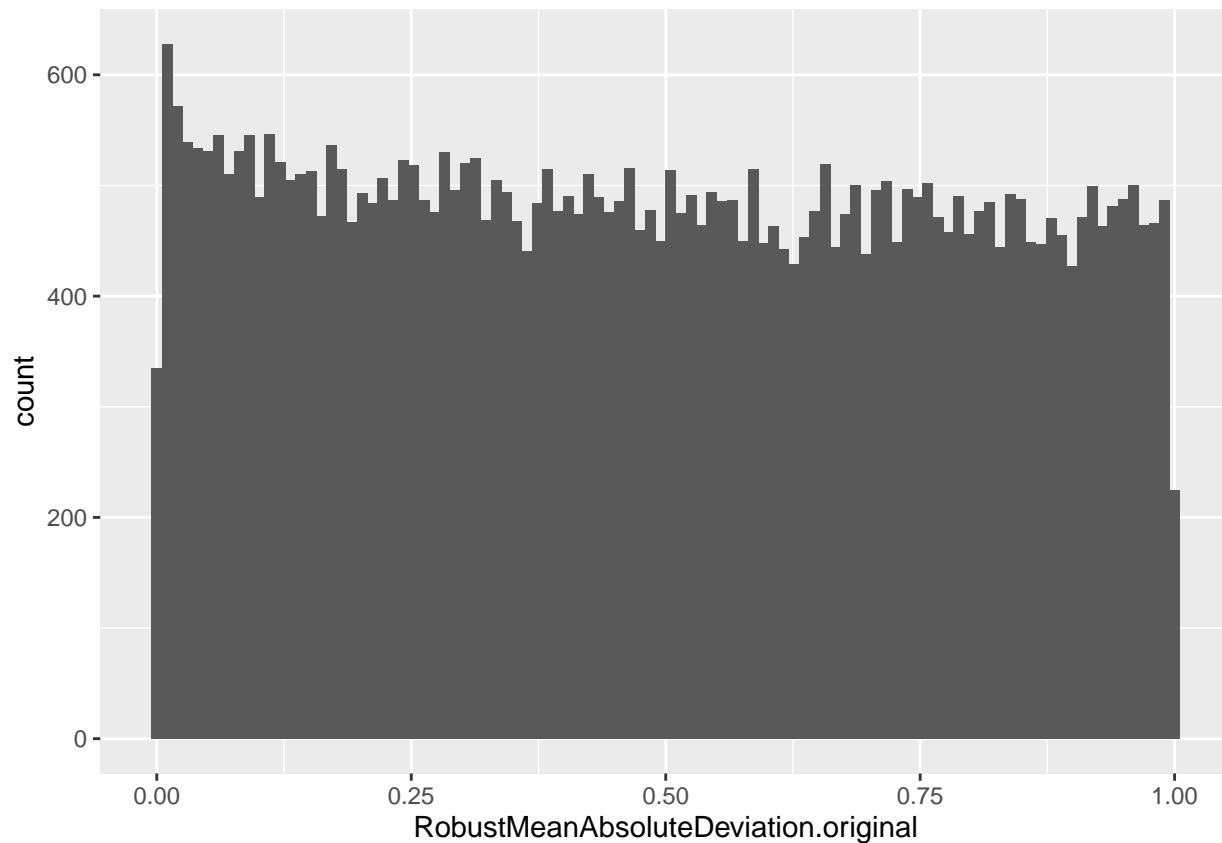
##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           594          0    89     0     0       0           0
## NotSig        22698        48525 48383 48525 48523    48525       48525
## Up            25233          0    53     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough   BMI Cr_wheezengY
## Down           0             0           0           0       0       0
## NotSig        48525          48525          48525 48525       48525       48525
## Up             0             0           0           0       0       0
##          Range.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18516 16129 14056 12400 10458 10709 7185 7218 8107
## NotSig        48525 12769 19948 21911 25126 27049 28316 32403 33566 32471
## Up             0 17240 12448 12558 10999 11018 9500 8937 7741 7947
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7820  8319  5575  5230  5558  4600  4307  2879  2609  2626
## NotSig        32738 33272 36304 36712 37416 38842 39904 41681 43569 43163
## Up            7967  6934  6646  6583  5551  5083  4314  3965  2347  2736

load("/Users/carlacasanova/Downloads/Radiomic features models (indiv)/RobustMeanAbsoluteDeviation.o

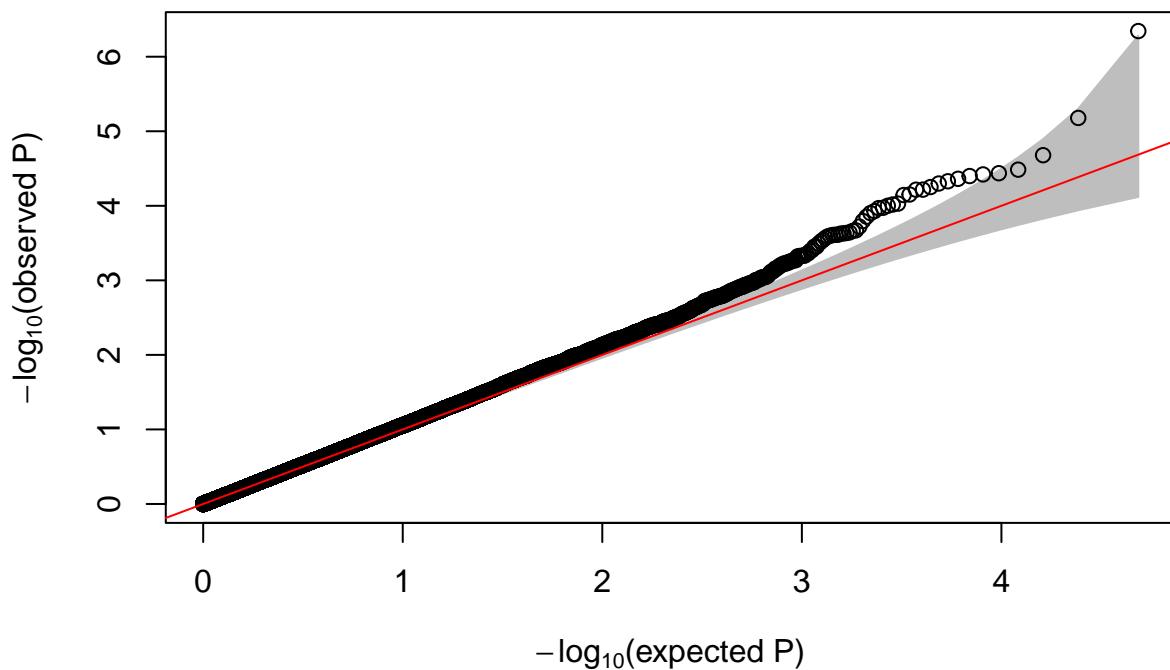
summa.fit.robustM <- decideTests(fit)
toptable.robustM <- topTable(fit, coef = "RobustMeanAbsoluteDeviation.original",
                                number = dim(counts.ok)[1])
toptable.robustM <- toptable.robustM[order(toptable.robustM$P.Value), ]
p.val.voom <- as.data.frame(fit$p.value)

```

```
# P-value distribution of results computed by limma
ggplot(data = p.val.voom, aes(x = RobustMeanAbsoluteDeviation.original)) + geom_histogram(bins = 100)
```



```
# QQplot plot for p-values computed by limma
GWASTools::qqPlot(p.val.voom$RobustMeanAbsoluteDeviation.original)
```



```

summary(summa.fit.robustM)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down      566           0    99     0     0       0           0
## NotSig    22696        48525 48361 48525 48523     48525       48525
## Up       25263           0   65     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0           0           0           0       0       0           0
## NotSig   48525        48525           0           0       48525 48525       48525
## Up       0           0           0           0       0       0           0
##          RobustMeanAbsoluteDeviation.original   X1     X2     X3     X4     X5     X6
## Down      0 18524 16210 13858 12205 10647 10700
## NotSig   48524 12753 19744 22125 25456 26600 28351
## Up       1 17248 12571 12542 10864 11278 9474
##          X7     X8     X9    X10    X11    X12    X13    X14    X15    X16    X17    X18
## Down    7078 7330 8322 7918 8235 5505 5431 5744 4807 4318 2976 2801
## NotSig  32530 33465 32004 32540 33328 36427 36254 37017 38427 39856 41458 43145
## Up      8917 7730 8199 8067 6962 6593 6840 5764 5291 4351 4091 2579
##          X19    X20
## Down    2858 2168
## NotSig  43005 44198
## Up      2662 2159

head(toptable.robustM, 10)

##          logFC     AveExpr       t    P.Value adj.P.Val         B
## 202814_s_at  0.3866122 5.2711632 5.405595 4.528322e-07 0.02197368 5.6158215
## 207720_at   -0.6189316 0.6048606 -4.761404 6.628514e-06 0.16082433 1.0151831
## 230825_at    0.6573018 1.0470995 4.470464 2.094525e-05 0.22706849 0.8956456
## 202815_s_at  0.3562382 4.4813489 4.354616 3.273064e-05 0.22706849 1.8481946
## 231264_at    0.9482917 1.0264606 4.325574 3.656647e-05 0.22706849 0.4529331
## 212769_at   -0.3040292 4.9146649 -4.315810 3.795082e-05 0.22706849 1.7962493
## 1552915_at   1.0046610 -0.6807490 4.302613 3.990243e-05 0.22706849 -0.8322306
## 213132_s_at -0.4582360 1.4077957 -4.280209 4.343885e-05 0.22706849 0.5001447
## 201969_at    0.2865061 3.3327030 4.259980 4.688979e-05 0.22706849 1.2723018
## 215897_at    0.4901017 1.0450237 4.241656 5.024250e-05 0.22706849 0.2949648

load("/Users/carlacasanovasanchez/Desktop/Radiomic features models (indiv)/RootMeanSquared.original.rda")
summa.fit.root <- decideTests(fit)
summary(summa.fit.root)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down      566           0    92     0     0       0           0
## NotSig    22821        48525 48374 48525 48523     48525       48525
## Up       25138           0   59     0     2       0           0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down      0           0           0           0       0       0           0
## NotSig   48525        48525           0           0       48525 48525       48525
## Up       0           0           0           0       0       0           0
##          RootMeanSquared.original   X1     X2     X3     X4     X5     X6     X7     X8
## Down      0 18511 16132 14056 12435 10415 10407 6961 7356
## NotSig   48525 12703 19905 21934 25090 27025 28964 32767 33479
## Up       0 17311 12488 12535 11000 11085 9154 8797 7690
##          X9     X10    X11    X12    X13    X14    X15    X16    X17    X18    X19    X20
## Down    8155 8020 8298 5546 5499 5723 4714 4256 2952 2864 2450 2343

```

```

## NotSig 32290 32243 33308 36381 36177 37044 38582 39960 41534 43151 43470 43937
## Up      8080  8262  6919  6598  6849  5758  5229  4309  4039  2510  2605  2245
load("/Users/carlacasanova.suarez/Desktop/Radiomic features models (indiv)/Skewness.original.rda")
summa.fit.skw <- decideTests(fit)
summary(summa.fit.skw)

##          (Intercept) GroupSevere SexM   Age Dwalk FEV1PSPC fume_exposeY
## Down           534          0    83     0     1        0            0
## NotSig         22820        48525 48396 48525 48522       48525        48525
## Up            25171          0    46     0     2        0            0
##          dusty_exposeY history_asthmaY CoughNo chronic cough    BMI Cr_wheezengY
## Down           0            0          0          0        0        0            0
## NotSig        48525          48525          48525        48525        48525        48525
## Up             0            0          0          0        0        0            0
##          Skewness.original X1     X2     X3     X4     X5     X6     X7     X8     X9
## Down           0 18496 16185 13823 12325 10409 10610 7047 7325 8122
## NotSig        48525 12874 19833 22165 25164 27065 28537 32618 33454 32467
## Up             0 17155 12507 12537 11036 11051 9378 8860 7746 7936
##          X10    X11    X12    X13    X14    X15    X16    X17    X18    X19
## Down          7757 8299 5525 5396 5596 4613 4161 3181 2628 2609
## NotSig       32893 33307 36349 36376 37286 38878 40115 41107 43526 43136
## Up            7875 6919 6651 6753 5643 5034 4249 4237 2371 2780

```

Features with positive DE

Load RadAR object in order to retrieve rowdata later:

```

load("/Users/carlacasanova.suarez/Documents/Master Bioinformatics UAB/Prácticas Radiomics/Radiomic features.RData")
rdr_L1_final

## class: SummarizedExperiment
## dim: 101 1773
## metadata(1): extractor
## assays(2): values adjusted_min_int_center
## rownames(101): Elongation.original Flatness.original ...
## Complexity.original Strength.original
## rowData names(4): feature_name image_type feature_description
## feature_type
## colnames(1773): 23140000005 23140000006 ... 26658003992 26658003997
## colData names(201): filename sample_id ... change.fv1 D_SUBJID

```

Load annotation data of genes stored in annotation.sputum.ok object to check which ones have annotations:

```

load("/Users/carlacasanova.suarez/Documents/Master Bioinformatics UAB/Prácticas Radiomics/Radiomic features.RData")

```

Create a vector with feature names of features positively associated with genes DE:

```

pos_rf <- c("Sphericity.original", "Variance.original", "Autocorrelation.original",
           "ClusterShade.original", "Contrast.original", "DifferenceAverage.original", "Id.original",
           "Idm.original", "Idmn.original", "Idn.original", "InverseVariance.original",
           "JointAverage.original", "SumAverage.original", "HighGrayLevelEmphasis.original",
           "LongRunLowGrayLevelEmphasis.original", "LowGrayLevelRunEmphasis.original", "RunPercentage.original",
           "LargeAreaEmphasis.original", "LowGrayLevelEmphasis.original", "LargeAreaHighGrayLevelEmphasis.original",
           "LargeAreaLowGrayLevelEmphasis.original", "SmallAreaEmphasis.original", "SmallAreaHighGrayLevelEmphasis.original",
           "SmallAreaLowGrayLevelEmphasis.original", "ZoneVariance.original", "DependenceNonUniformity.original")

```

```
"HighGrayLevelRunEmphasis.original", "LargeDependenceEmphasis.original", "LargeDependenceLowGrayLevel
"Busyness.original", "Coarseness.original", "Complexity.original", "Strength.original",
"X10Percentile.original", "InterquartileRange.original")
```

Not all the features are equally robust. We're just interested in *first order, shape* and *glcm*:

```
# Create a data frame with feature types
feature_names <- substr(pos_rf, 1, nchar(pos_rf) - 9)

# Check row data of rdr object which as feature name and feature type
ids <- rowData(rdr_L1_final)$feature_name %in% feature_names
out <- cbind(feature_names, feature.type = rowData(rdr_L1_final)[ids, ]$feature_type)
out <- as.data.frame(out)

out
```

	feature_names	feature.type
## 1	Sphericity	first_order_shape
## 2	Variance	first_order_statistics
## 3	Autocorrelation	first_order_statistics
## 4	ClusterShade	grey_level_co-occurrence_matrix
## 5	Contrast	grey_level_co-occurrence_matrix
## 6	DifferenceAverage	grey_level_co-occurrence_matrix
## 7	Id	grey_level_co-occurrence_matrix
## 8	Idm	grey_level_co-occurrence_matrix
## 9	Idmn	grey_level_co-occurrence_matrix
## 10	Idn	grey_level_co-occurrence_matrix
## 11	InverseVariance	grey_level_co-occurrence_matrix
## 12	JointAverage	grey_level_co-occurrence_matrix
## 13	SumAverage	grey_level_co-occurrence_matrix
## 14	HighGrayLevelEmphasis	grey_level_co-occurrence_matrix
## 15	LongRunLowGrayLevelEmphasis	grey_level_run_length_matrix
## 16	LowGrayLevelRunEmphasis	grey_level_run_length_matrix
## 17	RunPercentage	grey_level_run_length_matrix
## 18	LargeAreaEmphasis	grey_level_run_length_matrix
## 19	LowGrayLevelEmphasis	first_order_statistics
## 20	LargeAreaHighGrayLevelEmphasis	grey_level_size_zone_matrix
## 21	LargeAreaLowGrayLevelEmphasis	grey_level_size_zone_matrix
## 22	SmallAreaEmphasis	grey_level_size_zone_matrix
## 23	SmallAreaHighGrayLevelEmphasis	grey_level_size_zone_matrix
## 24	SmallAreaLowGrayLevelEmphasis	grey_level_size_zone_matrix
## 25	ZoneVariance	grey_level_size_zone_matrix
## 26	DependenceNonUniformity	grey_level_size_zone_matrix
## 27	HighGrayLevelRunEmphasis	grey_level_dependence_matrix
## 28	LargeDependenceEmphasis	grey_level_dependence_matrix
## 29	LargeDependenceLowGrayLevelEmphasis	grey_level_dependence_matrix
## 30	Busyness	grey_level_dependence_matrix
## 31	Coarseness	neighbouring_grey_tone_difference_matrix
## 32	Complexity	neighbouring_grey_tone_difference_matrix
## 33	Strength	neighbouring_grey_tone_difference_matrix
## 34	X10Percentile	first_order_statistics
## 35	InterquartileRange	first_order_shape

First order enrichment analysis

Check features are *first order*:

```
first.order.DE <- out[out$feature.type == "first_order_statistics", ]  
  
# In this case, the only features correlated are LowGrayLevelEmphasis and  
# Autocorrelation  
first.order.DE  
  
## feature_names feature.type  
## 2 Variance first_order_statistics  
## 3 Autocorrelation first_order_statistics  
## 19 LowGrayLevelEmphasis first_order_statistics  
## 34 X10Percentile first_order_statistics
```

Store names of genes DE ($p.\text{adj} < 0.01$ if possible):

```
# Create bools for genes with the most restrictive p.value  
dd.fo.Auto <- toptable.autoc$adj.P.Val < 0.01 & !is.na(toptable.autoc$adj.P.Val)  
dd.fo.Variance <- toptable.variance$adj.P.Val < 0.04 & !is.na(toptable.variance$adj.P.Val)  
dd.fo.X10 <- toptable.X10$adj.P.Val < 0.01 & !is.na(toptable.X10$adj.P.Val)  
  
deGenes.fo <- c(rownames(toptable.variance[dd.fo.Variance, ]), rownames(toptable.X10[dd.fo.X10,  
]), rownames(toptable.autoc[dd.fo.Auto, ]))  
  
deGenes.fo  
  
## [1] "202814_s_at" "230825_at" "1561431_at" "225418_at" "212329_at"  
## [6] "227973_at"  
length(deGenes.fo)  
  
## [1] 6  
table(duplicated(deGenes.fo))  
  
##  
## FALSE  
## 6
```

Check if there are annotations available:

```
# Check info  
annotation.sputum.ok[deGenes.fo, ]
```

```
## # A tibble: 6 x 9  
##   PROBEID    ENSEMBL ENTREZID SYMBOL GENENAME GO     EVIDENCE ONTOLOGY GENETYPE  
##   <chr>      <chr>   <chr>   <chr>   <chr>   <chr>   <chr>   <chr>  
## 1 202814_s_at "ENSG00~" "10614"  "HEXI~" "HEXIM ~" "GO:~" "IBA|IC~" "BP|CC|~" "protei~  
## 2 230825_at   ""       ""       ""       ""       ""       ""       ""       ""  
## 3 1561431_at  ""       ""       ""       ""       ""       ""       ""       ""  
## 4 225418_at   "ENSG00~" "5819"   "NECT~" "nectin~" "GO:~" "HDA|IB~" "BP|CC|~" "protei~  
## 5 212329_at   "ENSG00~" "22937"  "SCAP"   "SREBF ~" "GO:~" "IDA|IE~" "BP|CC|~" "protei~  
## 6 227973_at   "ENSG00~" "205327" "C2or~" "chromo~" "GO:~" "IDA|IE~" "BP|CC"   "protei~
```

Create gene universe:

```
geneUniverse.fo <- rownames(toptable.autoc[!is.na(toptable.autoc$P.Value), ])  
length(geneUniverse.fo)
```

```

## [1] 48525

Change annotation to ENTREZ:
# Retrieve ENTREZ names
deGenes.fo.entrez <- unlist(mget(deGenes.fo, envir = hgu133plus2ENTREZID, ifnotfound = NA))
geneUniverse.fo.entrez <- unlist(mget(geneUniverse.fo, envir = hgu133plus2ENTREZID,
                                         ifnotfound = NA))

GO enrichment:
ans.go.fo <- enrichGO(gene = deGenes.fo.entrez, ont = "BP", universe = geneUniverse.fo.entrez,
                       OrgDb = "org.Hs.eg.db", readable = TRUE, pvalueCutoff = 0.05)

# See results
tab.go.fo <- as.data.frame(ans.go.fo@result)
# tab.go.fo<- subset(tab.go.fo, Count>5)
tab.go.fo[1:5, 1:6]

##           ID                               Description
## GO:0045089 GO:0045089 positive regulation of innate immune response
## GO:0050792 GO:0050792 regulation of viral process
## GO:0002833 GO:0002833 positive regulation of response to biotic stimulus
## GO:0045088 GO:0045088 regulation of innate immune response
## GO:0031349 GO:0031349 positive regulation of defense response
##          GeneRatio    BgRatio      pvalue   p.adjust
## GO:0045089      2/4 127/15058 0.0004187940 0.03059353
## GO:0050792      2/4 148/15058 0.0005683204 0.03059353
## GO:0002833      2/4 160/15058 0.0006638456 0.03059353
## GO:0045088      2/4 213/15058 0.0011727686 0.03059353
## GO:0031349      2/4 254/15058 0.0016628762 0.03059353

ans.kegg.fo <- enrichKEGG(gene = deGenes.fo.entrez, universe = geneUniverse.fo.entrez,
                           organism = "hsa", pvalueCutoff = 0.05)

# See results
tab.kegg.fo <- as.data.frame(ans.kegg.fo@result)
# tab.kegg.fo<- subset(tab.kegg.fo, Count>5)
tab.kegg.fo[1:5, 1:6]

##           ID                               Description GeneRatio BgRatio
## hsa04520 hsa04520 Adherens junction      1/1 68/6910
## hsa04514 hsa04514 Cell adhesion molecules 1/1 144/6910
## hsa05168 hsa05168 Herpes simplex virus 1 infection 1/1 435/6910
## NA          <NA>                                <NA>      <NA>      <NA>
## NA.1        <NA>                                <NA>      <NA>      <NA>
##          pvalue   p.adjust
## hsa04520 0.00984081 0.02952243
## hsa04514 0.02083936 0.03125904
## hsa05168 0.06295224 0.06295224
## NA          NA       NA
## NA.1        NA       NA

DisGeNet analysis. Get API:
library(disgenet2r)

# Get API
```

```

disgenet_api_key <- get_disgenet_api_key(email = "carlacasanovasuarez@gmail.com",
                                         password = "mypassword1234", verbose = TRUE)

Sys.setenv(DISGENET_API_KEY = disgenet_api_key)

res_enrich.fo <- disease_enrichment(entities = deGenes.fo.entrez, vocabulary = "ENTREZ",
                                       database = "CURATED")

res.table.disgenet.fo <- res_enrich.fo@qresult
res.table.disgenet.fo

```

	ID	Description	source	Ratio	BgRatio
##	C0019348	Herpes Simplex Infections	CURATED	1/3	2/9703
##	23 C0403824	Teratozoospermia	CURATED	1/3	3/9703
##	24 C0403825	Globozoospermia	CURATED	1/3	4/9703
##	38 C1861537	OROFACIAL CLEFT 1	CURATED	1/3	2/9703
##	17 C0079774	Peripheral T-Cell Lymphoma	CURATED	1/3	10/9703
##	18 C0234985	Mental deterioration	CURATED	1/3	9/9703
##	35 C1270972	Mild cognitive disorder	CURATED	1/3	9/9703
##	21 C0338656	Impaired cognition	CURATED	1/3	14/9703
##	15 C0036421	Systemic Scleroderma	CURATED	1/3	19/9703
##	19 C0242339	Dyslipidemias	CURATED	1/3	24/9703
##	27 C0598784	Dyslipoproteinemias	CURATED	1/3	24/9703
##	10 C0026769	Multiple Sclerosis	CURATED	1/3	45/9703
##	31 C0751324	Multiple Sclerosis, Acute Fulminating	CURATED	1/3	45/9703
##	2 C0004153	Atherosclerosis	CURATED	1/3	59/9703
##	9 C0023893	Liver Cirrhosis, Experimental	CURATED	2/3	774/9703
##	16 C0079744	Diffuse Large B-Cell Lymphoma	CURATED	1/3	55/9703
##	37 C1563937	Atherogenesis	CURATED	1/3	59/9703
##	1 C0002395	Alzheimer's Disease	CURATED	1/3	101/9703
##	6 C0011265	Presenile dementia	CURATED	1/3	99/9703
##	13 C0030567	Parkinson Disease	CURATED	1/3	85/9703
##	20 C0276496	Familial Alzheimer Disease (FAD)	CURATED	1/3	100/9703
##	25 C0494463	Alzheimer Disease, Late Onset	CURATED	1/3	99/9703
##	26 C0546126	Acute Confusional Senile Dementia	CURATED	1/3	99/9703
##	29 C0750900	Alzheimer's Disease, Focal Onset	CURATED	1/3	99/9703
##	30 C0750901	Alzheimer Disease, Early Onset	CURATED	1/3	99/9703
##	3 C0005684	Malignant neoplasm of urinary bladder	CURATED	1/3	141/9703
##	4 C0005695	Bladder Neoplasm	CURATED	1/3	140/9703
##	11 C0026998	Acute Myeloid Leukemia, M1	CURATED	1/3	125/9703
##	32 C0919267	ovarian neoplasm	CURATED	1/3	134/9703
##	33 C1140680	Malignant neoplasm of ovary	CURATED	1/3	137/9703
##	39 C1879321	Acute Myeloid Leukemia (AML-M2)	CURATED	1/3	125/9703
##	8 C0023467	Leukemia, Myelocytic, Acute	CURATED	1/3	173/9703
##	12 C0027627	Neoplasm Metastasis	CURATED	1/3	217/9703
##	28 C0678222	Breast Carcinoma	CURATED	1/3	538/9703
##	34 C1257931	Mammary Neoplasms, Human	CURATED	1/3	525/9703
##	36 C1458155	Mammary Neoplasms	CURATED	1/3	527/9703
##	40 C2239176	Liver carcinoma	CURATED	1/3	507/9703
##	41 C4704874	Mammary Carcinoma, Human	CURATED	1/3	525/9703
##	14 C0033578	Prostatic Neoplasms	CURATED	1/3	616/9703
##	22 C0376358	Malignant neoplasm of prostate	CURATED	1/3	616/9703
##	5 C0006142	Malignant neoplasm of breast	CURATED	1/3	1074/9703
##	pvalue	FDR disease_class			

```

## 7 0.0006183654 0.01267388      C01;C17
## 23 0.0009274525 0.01267388     C12
## 24 0.0012364759 0.01267388     C12
## 38 0.0006183654 0.01267388     C05;C07;C16
## 17 0.0030892780 0.01809434     C04;C15;C20
## 18 0.0027806369 0.01809434     F03
## 35 0.0027806369 0.01809434     F03
## 21 0.0043232056 0.02215643     F03
## 15 0.0058641826 0.02671461     C17
## 19 0.0074035689 0.02759512     C18
## 27 0.0074035689 0.02759512     C18
## 10 0.0138516385 0.04368594     C10;C20
## 31 0.0138516385 0.04368594     C10;C20
## 2 0.0181348002 0.04373687     C14
## 9 0.0180623456 0.04373687     C06;C23
## 16 0.0169123079 0.04373687     C04;C15;C20
## 37 0.0181348002 0.04373687     C14
## 1 0.0309098368 0.05069213     C10;F03
## 6 0.0303040293 0.05069213     C10;F03
## 13 0.0260563057 0.05069213     C10
## 20 0.0306069646 0.05069213     C10;F03
## 25 0.0303040293 0.05069213     C10;F03
## 26 0.0303040293 0.05069213     C10;F03
## 29 0.0303040293 0.05069213     C10;F03
## 30 0.0303040293 0.05069213     C10;F03
## 3 0.0429730606 0.05683534     C04;C12;C13
## 4 0.0426727069 0.05683534     C04;C12;C13
## 11 0.0381598578 0.05683534     C04
## 32 0.0408692651 0.05683534     C04;C13;C19
## 33 0.0417712688 0.05683534     C04;C13;C19
## 39 0.0381598578 0.05683534     C04
## 8 0.0525512405 0.06733128     C04
## 12 0.0656165835 0.08152363     C04;C23
## 28 0.1573183336 0.16973820     C04;C17
## 34 0.1537265805 0.16973820     C04;C17
## 36 0.1542798209 0.16973820     C04;C17
## 40 0.1487365557 0.16973820     C04;C06
## 41 0.1537265805 0.16973820     C04;C17
## 14 0.1786556376 0.18312203     C04;C12
## 22 0.1786556376 0.18312203     C04;C12
## 5 0.2967173894 0.29671739     C04;C17
##
## 7
## 23
## 24
## 38 Musculoskeletal Diseases;Stomatognathic Diseases;Congenital, Hereditary, and Neonatal Diseases and
## 17
## 18
## 35
## 21
## 15
## 19
## 27
## 10
                                         dis
                                         Infections;Skin and Connective Tissue Diseases
                                         Male Urogenital System Diseases
                                         Male Urogenital System Diseases
                                         Neoplasms;Hemic and Lymphatic Diseases;Immune System Diseases
                                         Male Urogenital System Diseases
                                         Male Urogenital System Diseases
                                         Skin and Connective Tissue Diseases
                                         Nutritional and Metabolic Diseases
                                         Nutritional and Metabolic Diseases
                                         Nervous System Diseases;Immune System Diseases

```

```

## 31 Nervous System Diseases;Immune S
## 2 Cardiova
## 9 Digestive System Diseases;Pathological Conditions, Sig
## 16 Neoplasms;Hemic and Lymphatic Diseases;Immune S
## 37 Cardiova
## 1 Nervous System Diseases;Me
## 6 Nervous System Diseases;Me
## 13 Nervous S
## 20 Nervous System Diseases;Me
## 25 Nervous System Diseases;Me
## 26 Nervous System Diseases;Me
## 29 Nervous System Diseases;Me
## 30 Nervous System Diseases;Me

## 3 Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy
## 4 Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy
## 11
## 32 Neoplasms;Female Urogenital Diseases and Pregnancy Complications;Endocrine S
## 33 Neoplasms;Female Urogenital Diseases and Pregnancy Complications;Endocrine S
## 39
## 8
## 12 Neoplasms;Pathological Conditions, Sig
## 28 Neoplasms;Skin and Connective T
## 34 Neoplasms;Skin and Connective T
## 36 Neoplasms;Skin and Connective T
## 40 Neoplasms;Digestive S
## 41 Neoplasms;Skin and Connective T
## 14 Neoplasms;Male Urog
## 22 Neoplasms;Male Urog
## 5 Neoplasms;Skin and Connective T

## disease_semantic_type shared_geneid shared_symbol Count gg
## 7 Disease or Syndrome 5819 NECTIN2 1 0.2
## 23 Disease or Syndrome 5819 NECTIN2 1 0.2
## 24 Finding 5819 NECTIN2 1 0.2
## 38 Disease or Syndrome 5819 NECTIN2 1 0.2
## 17 Neoplastic Process 5819 NECTIN2 1 0.2
## 18 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 35 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 21 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 15 Disease or Syndrome 5819 NECTIN2 1 0.2
## 19 Disease or Syndrome 5819 NECTIN2 1 0.2
## 27 Pathologic Function 5819 NECTIN2 1 0.2
## 10 Disease or Syndrome 5819 NECTIN2 1 0.2
## 31 Disease or Syndrome 5819 NECTIN2 1 0.2
## 2 Disease or Syndrome 5819 NECTIN2 1 0.2
## 9 Experimental Model of Disease 5819;10614 NECTIN2;HEXIM1 2 0.4
## 16 Neoplastic Process 5819 NECTIN2 1 0.2
## 37 Pathologic Function 5819 NECTIN2 1 0.2
## 1 Disease or Syndrome 5819 NECTIN2 1 0.2
## 6 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 13 Disease or Syndrome 5819 NECTIN2 1 0.2
## 20 Disease or Syndrome 5819 NECTIN2 1 0.2
## 25 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 26 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2
## 29 Mental or Behavioral Dysfunction 5819 NECTIN2 1 0.2

```

```

## 30          Disease or Syndrome      5819      NECTIN2    1 0.2
## 3          Neoplastic Process      5819      NECTIN2    1 0.2
## 4          Neoplastic Process      5819      NECTIN2    1 0.2
## 11         Neoplastic Process      5819      NECTIN2    1 0.2
## 32         Neoplastic Process      5819      NECTIN2    1 0.2
## 33         Neoplastic Process      5819      NECTIN2    1 0.2
## 39         Neoplastic Process      5819      NECTIN2    1 0.2
## 8          Neoplastic Process      5819      NECTIN2    1 0.2
## 12         Neoplastic Process      5819      NECTIN2    1 0.2
## 28         Neoplastic Process      5819      NECTIN2    1 0.2
## 34         Neoplastic Process      5819      NECTIN2    1 0.2
## 36         Neoplastic Process      5819      NECTIN2    1 0.2
## 40         Neoplastic Process     22937      SCAP      1 0.2
## 41         Neoplastic Process      5819      NECTIN2    1 0.2
## 14         Neoplastic Process      5819      NECTIN2    1 0.2
## 22         Neoplastic Process      5819      NECTIN2    1 0.2
## 5          Neoplastic Process      5819      NECTIN2    1 0.2

```

```

# save(res.table.disgenet.fo, file =
# '/Users/carlacasanova-suarez/Desktop/DisGenet_fo_features.rda')

```

MSigDb enrichment analysis (group C7 immunologic signature):

```

# Load terms for genes coded by ENTREZ of the gene set C7
c3.tf <- read.gmt("/Users/carlacasanova-suarez/Downloads/c7.all.v7.5.1.entrez.gmt.txt")

# Enrichment
ans.tf.fo <- enricher(deGenes.fo.entrez, TERM2GENE = c3.tf)
tab.tf.fo <- as.data.frame(ans.tf.fo@result)
# tab.tf.fo<- subset(tab.tf.fo, Count>5)
tab.tf.fo[1:5, 1:5]

##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS VS_WT_ACT_CD8_TCELL_DN
##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS VS_WT_ACT_CD8_TCELL_DN
##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS VS_WT_ACT_CD8_TCELL_DN
##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS VS_WT_ACT_CD8_TCELL_DN
##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE AGE_18_55YO_VACCINATED VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS VS_WT_ACT_CD8_TCELL_DN
## 
```

```

## GSE34217_MIR17_92_OVEREXPRESS_VS_WT_ACT_CD8_TCELL_DN
##
## GSE42724_MEMORY_VS_B1_BCELL_DN
## GSE29618_PRE_VS_DAY7_POST_TIV_FLU_VACCINE_MONOCYTE_DN
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE_AGE_18_55YO_VACCINATED_VS_CONTROL_TREATED_IN_VITRO_W
## MATSUMIYA_PBMC_MODIFIED_VACCINIA_ANKARA_VACCINE_AGE_18_55YO_VACCINATED_VS_CONTROL_TREATED_IN_VITRO_W
## GSE34217_MIR17_92_OVEREXPRESS_VS_WT_ACT_CD8_TCELL_DN

```

Shape

```
shape.DE <- out[out$feature.type == "first_order_shape", ]
```

In this case, these features are not correlated

```
shape.DE
```

```

##           feature_names      feature.type
## 1             Sphericity first_order_shape
## 35 InterquartileRange first_order_shape

```

Store names of genes DE (p.adj < 0.01 if possible):

```

# Create bools for genes with the most restrictive p.value
dd.shape.s <- toptable.sphericity$adj.P.Val < 0.01 & !is.na(toptable.sphericity$adj.P.Val)
dd.shape.intq <- toptable.intq$adj.P.Val < 0.02 & !is.na(toptable.intq$adj.P.Val)

```

```
deGenes.shape <- c(rownames(toptable.sphericity[dd.shape.s, ]), rownames(toptable.intq[dd.shape.intq, ]))
```

```
deGenes.shape
```

```

## [1] "1555057_at"   "233228_at"    "221916_at"    "1561614_at"   "1560222_at"
## [6] "1557566_at"   "239013_at"    "202814_s_at"

```

```
length(deGenes.shape)
```

```
## [1] 8
```

```
table(duplicated(deGenes.shape))
```

```

##
## FALSE
##     8

```

Check if there are annotations available:

```

# Check info
annotation.sputum.ok[deGenes.shape, ]

```

```

## # A tibble: 8 x 9
##   PROBEID    ENSEMBL ENTREZID SYMBOL GENENAME GO      EVIDENCE ONTOLOGY GENETYPE
##   <chr>      <chr>   <chr>   <chr>   <chr>   <chr>   <chr>   <chr>
## 1 1555057_at "ENSG00~" "4724"   "NDUF~"  "NADH:u~" "GO:~"  "IBA|ID~" "BP|CC|~" "protei~
## 2 233228_at   ""       ""       ""       ""       ""       ""       ""       ""
## 3 221916_at   "ENSG00~" "4747"   "NEFL"   "neurof~" "GO:~"  "IDA|IE~" "BP|CC|~" "protei~
## 4 1561614_at  "ENSG00~" "6546"   "SLC8~"  "solute~" "GO:~"  "IBA|IC~" "BP|CC|~" "protei~
## 5 1560222_at   ""       "100287~" "LINC~"  "long i~"  ""       ""       ""       "ncRNA"
## 6 1557566_at   ""       "100507~" "LOC1~"  "unchar~" ""       ""       ""       "ncRNA"
## 7 239013_at    "ENSG00~" "9117"   "SEC22~" "SEC22 ~" "GO:~"  "IEA|IP~" "BP|CC|~" "protei~

```

```

## 8 202814_s_at "ENSG00~ "10614" "HEXI~ "HEXIM ~ "GO:~ "IBA|IC~ "BP|CC|~ "protei~
Gene universe shape:
geneUniverse.sh <- rownames(toptable.sphericity[!is.na(toptable.sphericity$P.Value),
    ])
length(geneUniverse.sh)

## [1] 48525

Change annotation to ENTREZ:
# Retrieve ENTREZ names
deGenes.sh.entrez <- unlist(mget(deGenes.shape, envir = hgu133plus2ENTREZID, ifnotfound = NA))
geneUniverse.sh.entrez <- unlist(mget(geneUniverse.sh, envir = hgu133plus2ENTREZID,
    ifnotfound = NA))

GO enrichment:
ans.go.sh <- enrichGO(gene = deGenes.sh.entrez, ont = "BP", universe = geneUniverse.sh.entrez,
    OrgDb = "org.Hs.eg.db", readable = TRUE, pvalueCutoff = 0.05)

# See results
tab.go.sh <- as.data.frame(ans.go.sh@result)
# tab.go.sh<- subset(tab.go.sh, Count>5)
tab.go.sh[1:5, 1:6]

##           ID
## GO:0051591 GO:0051591
## GO:0071901 GO:0071901
## GO:0046683 GO:0046683
## GO:0014074 GO:0014074
## GO:0006469 GO:0006469
##                               Description
## GO:0051591                     response to cAMP
## GO:0071901 negative regulation of protein serine/threonine kinase activity
## GO:0046683                     response to organophosphorus
## GO:0014074                     response to purine-containing compound
## GO:0006469 negative regulation of protein kinase activity
##       GeneRatio   BgRatio      pvalue   p.adjust
## GO:0051591      2/5 83/15058 0.0002969660 0.04324596
## GO:0071901      2/5 107/15058 0.0004933050 0.04324596
## GO:0046683      2/5 114/15058 0.0005597626 0.04324596
## GO:0014074      2/5 120/15058 0.0006200137 0.04324596
## GO:0006469      2/5 192/15058 0.0015770028 0.04461063

KEGG enrichment:
ans.kegg.sh <- enrichKEGG(gene = deGenes.sh.entrez, organism = "hsa", universe = geneUniverse.sh.entrez
    pvalueCutoff = 0.05)

# See results
tab.kegg.sh <- as.data.frame(ans.kegg.sh@result)
# tab.kegg.sh <- subset(tab.kegg.sh, Count>5)
tab.kegg.sh[1:5, 1:6]

##           ID
## hsa05014 hsa05014
## hsa05022 hsa05022
##                               Description
## hsa05014                     Amyotrophic lateral sclerosis
## hsa05022 Pathways of neurodegeneration - multiple diseases

```

```

## hsa04961 hsa04961 Endocrine and other factor-regulated calcium reabsorption
## hsa04978 hsa04978                                         Mineral absorption
## hsa05412 hsa05412           Arrhythmogenic right ventricular cardiomyopathy
##     GeneRatio BgRatio      pvalue   p.adjust
## hsa05014      2/3 341/6910 0.007047181 0.09460395
## hsa05022      2/3 439/6910 0.011573203 0.09460395
## hsa04961      1/3 51/6910 0.021981963 0.09460395
## hsa04978      1/3 56/6910 0.024119551 0.09460395
## hsa05412      1/3 74/6910 0.031789076 0.09460395

```

Disgenet:

```

res_enrich.sh <- disease_enrichment(entities = deGenes.sh.entrez, vocabulary = "ENTREZ",
                                       database = "CURATED")

res.table.disgenet.sh <- res_enrich.sh@qresult
res.table.disgenet.sh

```

	ID	Description	source
##	C0025160	Megacolon	CURATED
## 5	C1843164	Charcot-Marie-Tooth disease, demyelinating, Type 1F	CURATED
## 43	C1843225	CHARCOT-MARIE-TOOTH DISEASE, AXONAL, TYPE 2E (disorder)	CURATED
## 44	C4693509	CHARCOT-MARIE-TOOTH DISEASE, DOMINANT INTERMEDIATE G	CURATED
## 56	C4749824	Charcot-Marie-Tooth disease type 2B5	CURATED
## 57	C0206157	Myopathies, Nemaline	CURATED
## 13	C0751267	Encephalopathy, Subacute Necrotizing, Infantile	CURATED
## 31	C0751268	Encephalopathy, Subacute Necrotizing, Juvenile	CURATED
## 32	C0022333	Jacksonian Seizure	CURATED
## 2	C0023264	Leigh Disease	CURATED
## 3	C0027055	Myocardial Reperfusion Injury	CURATED
## 6	C0038220	Status Epilepticus	CURATED
## 9	C0149958	Complex partial seizures	CURATED
## 11	C0234533	Generalized seizures	CURATED
## 14	C0234535	Clonic Seizures	CURATED
## 15	C0270823	Petit mal status	CURATED
## 16	C0270824	Visual seizure	CURATED
## 17	C0270844	Tonic Seizures	CURATED
## 18	C0270846	Epileptic drop attack	CURATED
## 19	C0311335	Grand Mal Status Epilepticus	CURATED
## 20	C0393734	Complex Partial Status Epilepticus	CURATED
## 21	C0422850	Seizures, Somatosensory	CURATED
## 22	C0422852	Seizures, Auditory	CURATED
## 23	C0422853	Olfactory seizure	CURATED
## 24	C0422854	Gustatory seizure	CURATED
## 25	C0422855	Vertiginous seizure	CURATED
## 26	C0494475	Tonic - clonic seizures	CURATED
## 27	C0751056	Non-epileptic convulsion	CURATED
## 28	C0751110	Single Seizure	CURATED
## 29	C0751123	Atonic Absence Seizures	CURATED
## 30	C0751494	Convulsive Seizures	CURATED
## 33	C0751495	Seizures, Focal	CURATED
## 34	C0751496	Seizures, Sensory	CURATED
## 35	C0751522	Status Epilepticus, Subclinical	CURATED
## 36	C0751523	Non-Convulsive Status Epilepticus	CURATED
## 37	C0751524	Simple Partial Status Epilepticus	CURATED

```

## 39 C0751651 Mitochondrial Diseases CURATED
## 41 C1838951 LEIGH SYNDROME DUE TO MITOCHONDRIAL COMPLEX I DEFICIENCY CURATED
## 42 C1838979 MITOCHONDRIAL COMPLEX I DEFICIENCY CURATED
## 45 C1850597 Leigh Syndrome Due To Mitochondrial Complex II Deficiency CURATED
## 46 C1850598 Leigh Syndrome due to Mitochondrial Complex III Deficiency CURATED
## 47 C1850599 Leigh Syndrome due to Mitochondrial Complex IV Deficiency CURATED
## 48 C1850600 Leigh Syndrome due to Mitochondrial Complex V Deficiency CURATED
## 49 C2931891 Necrotizing encephalopathy, infantile subacute, of Leigh CURATED
## 50 C3495874 Nonepileptic Seizures CURATED
## 51 C4048158 Convulsions CURATED
## 52 C4316903 Absence Seizures CURATED
## 53 C4317109 Epileptic Seizures CURATED
## 54 C4317123 Myoclonic Seizures CURATED
## 55 C4505436 Generalized Absence Seizures CURATED
## 12 C0151744 Myocardial Ischemia CURATED
## 8 C0036572 Seizures CURATED
## 40 C1269683 Major Depressive Disorder CURATED
## 10 C0041696 Unipolar Depression CURATED
## 1 C0005586 Bipolar Disorder CURATED
## 4 C0023893 Liver Cirrhosis, Experimental CURATED
## 7 C0036341 Schizophrenia CURATED

##      Ratio   BgRatio      pvalue        FDR disease_class
## 5     1/4    1/9703  0.0004122861  0.004700062      C06
## 43    1/4    1/9703  0.0004122861  0.004700062  C10;C16
## 44    1/4    1/9703  0.0004122861  0.004700062  C10;C16
## 56    1/4    1/9703  0.0004122861  0.004700062      <NA>
## 57    1/4    1/9703  0.0004122861  0.004700062  C10;C16
## 13    1/4    8/9703  0.0032947205  0.026405160  C05;C10
## 31    1/4    9/9703  0.0037059874  0.026405160  C10;C16;C18
## 32    1/4    9/9703  0.0037059874  0.026405160  C10;C16;C18
## 2     1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 3     1/4   47/9703  0.0192400484  0.048107604  C10;C16;C18
## 6     1/4   85/9703  0.0345917438  0.048107604  C14;C23
## 9     1/4   68/9703  0.0277463314  0.048107604  C10;C23
## 11    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 14    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 15    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 16    1/4   67/9703  0.0273425296  0.048107604  C10;C23
## 17    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 18    1/4   102/9703  0.0414009447  0.048107604  C10;C23
## 19    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 20    1/4   67/9703  0.0273425296  0.048107604  C10;C23
## 21    1/4   67/9703  0.0273425296  0.048107604  C10;C23
## 22    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 23    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 24    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 25    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 26    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 27    1/4   104/9703  0.0421996525  0.048107604  C10;C23
## 28    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 29    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 30    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 33    1/4   101/9703  0.0410014036  0.048107604  C10;C23
## 34    1/4   104/9703  0.0421996525  0.048107604  C10;C23

```

```

## 35 1/4 101/9703 0.0410014036 0.048107604 C10;C23
## 36 1/4 67/9703 0.0273425296 0.048107604 C10;C23
## 37 1/4 67/9703 0.0273425296 0.048107604 C10;C23
## 38 1/4 67/9703 0.0273425296 0.048107604 C10;C23
## 39 1/4 49/9703 0.0200525663 0.048107604 C18
## 41 1/4 37/9703 0.0151698771 0.048107604 C10;C16;C18
## 42 1/4 30/9703 0.0123132288 0.048107604 C18
## 45 1/4 36/9703 0.0147621643 0.048107604 C10;C16;C18
## 46 1/4 36/9703 0.0147621643 0.048107604 C10;C16;C18
## 47 1/4 36/9703 0.0147621643 0.048107604 C10;C16;C18
## 48 1/4 36/9703 0.0147621643 0.048107604 C10;C16;C18
## 49 1/4 36/9703 0.0147621643 0.048107604 C10;C16;C18
## 50 1/4 101/9703 0.0410014036 0.048107604 C10;C23
## 51 1/4 102/9703 0.0414009447 0.048107604 C10;C23
## 52 1/4 102/9703 0.0414009447 0.048107604 C10;C23
## 53 1/4 101/9703 0.0410014036 0.048107604 C10;C23
## 54 1/4 104/9703 0.0421996525 0.048107604 C10;C23
## 55 1/4 101/9703 0.0410014036 0.048107604 C10;C23
## 12 1/4 176/9703 0.0706222646 0.078930766 C14
## 8 1/4 218/9703 0.0869071859 0.095263646 C10;C23
## 40 1/4 243/9703 0.0964984140 0.103781313 F03
## 10 1/4 259/9703 0.1025970161 0.108296850 F03
## 1 1/4 477/9703 0.1826528979 0.189294821 F03
## 4 1/4 774/9703 0.2829517913 0.288004502 C06;C23
## 7 1/4 883/9703 0.3173385310 0.317338531 F03
##
## 5
## 43 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutrition and Metabolism
## 44 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutrition and Metabolism
## 56
## 57 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Pathological Conditions and Mechanisms
## 13 Musculoskeletal Diseases
## 31 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutrition and Metabolism
## 32 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutrition and Metabolism
## 2 Nervous System Diseases;Pathological Conditions and Mechanisms
## 3 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutrition and Metabolism
## 6 Cardiovascular Diseases;Pathological Conditions and Mechanisms
## 9 Nervous System Diseases;Pathological Conditions and Mechanisms
## 11 Nervous System Diseases;Pathological Conditions and Mechanisms
## 14 Nervous System Diseases;Pathological Conditions and Mechanisms
## 15 Nervous System Diseases;Pathological Conditions and Mechanisms
## 16 Nervous System Diseases;Pathological Conditions and Mechanisms
## 17 Nervous System Diseases;Pathological Conditions and Mechanisms
## 18 Nervous System Diseases;Pathological Conditions and Mechanisms
## 19 Nervous System Diseases;Pathological Conditions and Mechanisms
## 20 Nervous System Diseases;Pathological Conditions and Mechanisms
## 21 Nervous System Diseases;Pathological Conditions and Mechanisms
## 22 Nervous System Diseases;Pathological Conditions and Mechanisms
## 23 Nervous System Diseases;Pathological Conditions and Mechanisms
## 24 Nervous System Diseases;Pathological Conditions and Mechanisms
## 25 Nervous System Diseases;Pathological Conditions and Mechanisms
## 26 Nervous System Diseases;Pathological Conditions and Mechanisms
## 27 Nervous System Diseases;Pathological Conditions and Mechanisms
## 28 Nervous System Diseases;Pathological Conditions and Mechanisms

```

```

## 29 Nervous System Diseases;Pathological Condi
## 30 Nervous System Diseases;Pathological Condi
## 33 Nervous System Diseases;Pathological Condi
## 34 Nervous System Diseases;Pathological Condi
## 35 Nervous System Diseases;Pathological Condi
## 36 Nervous System Diseases;Pathological Condi
## 37 Nervous System Diseases;Pathological Condi
## 38 Nervous System Diseases;Pathological Condi
## 39 Nervous System Diseases;Pathological Condi
## 41 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 42 Nutritiona
## 45 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 46 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 47 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 48 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 49 Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritiona
## 50 Nervous System Diseases;Pathological Condi
## 51 Nervous System Diseases;Pathological Condi
## 52 Nervous System Diseases;Pathological Condi
## 53 Nervous System Diseases;Pathological Condi
## 54 Nervous System Diseases;Pathological Condi
## 55 Nervous System Diseases;Pathological Condi
## 12 Nervous System Diseases;Pathological Condi
## 8 Nervous System Diseases;Pathological Condi
## 40
## 10
## 1
## 4 Digestive System Diseases;Pathological Condi
## 7

##          disease_semantic_type shared_geneid shared_symbol Count    gg
## 5            Pathologic Function      6546     SLC8A1    1 0.125
## 43           Disease or Syndrome     4747      NEFL    1 0.125
## 44           Disease or Syndrome     4747      NEFL    1 0.125
## 56           Disease or Syndrome     4747      NEFL    1 0.125
## 57           Disease or Syndrome     4747      NEFL    1 0.125
## 13           Disease or Syndrome     4747      NEFL    1 0.125
## 31           Disease or Syndrome     4724     NDUFS4    1 0.125
## 32           Disease or Syndrome     4724     NDUFS4    1 0.125
## 2            Disease or Syndrome     6546     SLC8A1    1 0.125
## 3            Disease or Syndrome     4724     NDUFS4    1 0.125
## 6            Pathologic Function      6546     SLC8A1    1 0.125
## 9            Disease or Syndrome     6546     SLC8A1    1 0.125
## 11           Disease or Syndrome     6546     SLC8A1    1 0.125
## 14           Disease or Syndrome     6546     SLC8A1    1 0.125
## 15           Disease or Syndrome     6546     SLC8A1    1 0.125
## 16           Disease or Syndrome     6546     SLC8A1    1 0.125
## 17           Disease or Syndrome     6546     SLC8A1    1 0.125
## 18           Disease or Syndrome     6546     SLC8A1    1 0.125
## 19           Disease or Syndrome     6546     SLC8A1    1 0.125
## 20           Disease or Syndrome     6546     SLC8A1    1 0.125
## 21           Disease or Syndrome     6546     SLC8A1    1 0.125
## 22           Pathologic Function      6546     SLC8A1    1 0.125
## 23           Pathologic Function      6546     SLC8A1    1 0.125
## 24           Disease or Syndrome     6546     SLC8A1    1 0.125

```

```

## 25           Sign or Symptom      6546     SLC8A1    1 0.125
## 26           Disease or Syndrome 6546     SLC8A1    1 0.125
## 27           Disease or Syndrome 6546     SLC8A1    1 0.125
## 28           Sign or Symptom      6546     SLC8A1    1 0.125
## 29           Disease or Syndrome 6546     SLC8A1    1 0.125
## 30           Disease or Syndrome 6546     SLC8A1    1 0.125
## 33           Sign or Symptom      6546     SLC8A1    1 0.125
## 34           Disease or Syndrome 6546     SLC8A1    1 0.125
## 35           Sign or Symptom      6546     SLC8A1    1 0.125
## 36           Disease or Syndrome 6546     SLC8A1    1 0.125
## 37           Disease or Syndrome 6546     SLC8A1    1 0.125
## 38           Disease or Syndrome 6546     SLC8A1    1 0.125
## 39           Disease or Syndrome 4724     NDUFS4    1 0.125
## 41           Disease or Syndrome 4724     NDUFS4    1 0.125
## 42           Disease or Syndrome 4724     NDUFS4    1 0.125
## 45           Disease or Syndrome 4724     NDUFS4    1 0.125
## 46           Disease or Syndrome 4724     NDUFS4    1 0.125
## 47           Disease or Syndrome 4724     NDUFS4    1 0.125
## 48           Disease or Syndrome 4724     NDUFS4    1 0.125
## 49           Disease or Syndrome 4724     NDUFS4    1 0.125
## 50           Disease or Syndrome 6546     SLC8A1    1 0.125
## 51           Sign or Symptom      6546     SLC8A1    1 0.125
## 52           Disease or Syndrome 6546     SLC8A1    1 0.125
## 53           Disease or Syndrome 6546     SLC8A1    1 0.125
## 54           Sign or Symptom      6546     SLC8A1    1 0.125
## 55           Disease or Syndrome 6546     SLC8A1    1 0.125
## 12           Disease or Syndrome 6546     SLC8A1    1 0.125
## 8            Sign or Symptom      6546     SLC8A1    1 0.125
## 40 Mental or Behavioral Dysfunction 4747     NEFL    1 0.125
## 10 Mental or Behavioral Dysfunction 4747     NEFL    1 0.125
## 1  Mental or Behavioral Dysfunction 4747     NEFL    1 0.125
## 4   Experimental Model of Disease 10614    HEXIM1   1 0.125
## 7  Mental or Behavioral Dysfunction 4747     NEFL    1 0.125

# save(res.table.disgenet.sh, file =
# '/Users/carlacasanovasuarez/Desktop/DisGenet_shape_features.rda')

```

MSigDb enrichment analysis (group C7 immunologic signature):

```
# Load terms for genes coded by ENTREZ of the gene set C7
c3.tf <- read.gmt("/Users/carlacasanovasuarez/Downloads/c7.all.v7.5.1.entrez.gmt.txt")
```

```
# Enrichment
ans.tf.sh <- enricher(deGenes.sh.entrez, TERM2GENE = c3.tf)
tab.tf.sh <- as.data.frame(ans.tf.sh@result)
# tab.tf.sh <- subset(tab.tf.sh, Count>5)
tab.tf.sh[1:5, 1:5]
```

```
##
## GSE28726_NAIVE_VS_ACTIVATED_VA24NEG_NKTCELL_DN          GSE28726_NAIVE_VS_ACTIVATI
## GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_TCELL_40H_TSST_ACT_DN GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_
## GSE37416_OH_VS_12H_F_TULARENSIS_LVS_NEUTROPHIL_UP        GSE37416_OH_VS_12H_F_TULAREN
## GSE2770_IL12_VS_IL4_TREATED_ACT_CD4_TCELL_48H_DN          GSE2770_IL12_VS_IL4_TREATED_
## SCHERER_PBMC_APSP_WETVAX_AGE_18_40YO_5_TO_7DY_UP          SCHERER_PBMC_APSP_WETVAX_AGE
```

```

## GSE28726_NAIVE_VS_ACTIVATED_VA24NEG_NKTCELL_DN GSE28726_NAIVE_VS_ACTIVATI
## GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_TCELL_40H_TSST_ACT_DN GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_T
## GSE37416_OH_VS_12H_F_TULARENSIS_LVS_NEUTROPHIL_UP GSE37416_OH_VS_12H_F_TULAREN
## GSE2770_IL12_VS_IL4_TREATED_ACT_CD4_TCELL_48H_DN GSE2770_IL12_VS_IL4_TREATED_A
## SCHERER_PBMC_APSP_WETVAX AGE_18_40YO_5_TO_7DY_UP SCHERER_PBMC_APSP_WETVAX_AGE_18_40YO_5_TO_7DY_UP

##                                     GeneRatio
## GSE28726_NAIVE_VS_ACTIVATED_VA24NEG_NKTCELL_DN      2/6
## GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_TCELL_40H_TSST_ACT_DN 2/6
## GSE37416_OH_VS_12H_F_TULARENSIS_LVS_NEUTROPHIL_UP    2/6
## GSE2770_IL12_VS_IL4_TREATED_ACT_CD4_TCELL_48H_DN      2/6
## SCHERER_PBMC_APSP_WETVAX AGE_18_40YO_5_TO_7DY_UP        1/6
##                                     BgRatio
## GSE28726_NAIVE_VS_ACTIVATED_VA24NEG_NKTCELL_DN      197/21355
## GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_TCELL_40H_TSST_ACT_DN 197/21355
## GSE37416_OH_VS_12H_F_TULARENSIS_LVS_NEUTROPHIL_UP    197/21355
## GSE2770_IL12_VS_IL4_TREATED_ACT_CD4_TCELL_48H_DN      199/21355
## SCHERER_PBMC_APSP_WETVAX AGE_18_40YO_5_TO_7DY_UP        24/21355
##                                     pvalue
## GSE28726_NAIVE_VS_ACTIVATED_VA24NEG_NKTCELL_DN      0.001239475
## GSE36476_YOUNG_VS_OLD_DONOR_MEMORY_CD4_TCELL_40H_TSST_ACT_DN 0.001239475
## GSE37416_OH_VS_12H_F_TULARENSIS_LVS_NEUTROPHIL_UP    0.001239475
## GSE2770_IL12_VS_IL4_TREATED_ACT_CD4_TCELL_48H_DN      0.001264518
## SCHERER_PBMC_APSP_WETVAX AGE_18_40YO_5_TO_7DY_UP        0.006725019

```

glcm

```

glcm.DE <- out[out$feature.type == "grey_level_co-occurrence_matrix", ]

# In this case, these features tighly correlated: id, idm, idmn, idn. Fueatures
# correlated with first order are also found, such as JointAverage and
# SumAverage (they are also correlated between them)
glcm.DE

```

```

##           feature_names          feature.type
## 4       ClusterShade grey_level_co-occurrence_matrix
## 5       Contrast   grey_level_co-occurrence_matrix
## 6 DifferenceAverage grey_level_co-occurrence_matrix
## 7             Id   grey_level_co-occurrence_matrix
## 8            Idm   grey_level_co-occurrence_matrix
## 9            Idmn  grey_level_co-occurrence_matrix
## 10           Idn   grey_level_co-occurrence_matrix
## 11     InverseVariance grey_level_co-occurrence_matrix
## 12       JointAverage grey_level_co-occurrence_matrix
## 13       SumAverage  grey_level_co-occurrence_matrix
## 14 HighGrayLevelEmphasis grey_level_co-occurrence_matrix

```

Store names of genes DE (p.adj < 0.01 if possible):

```

# Create bools for genes with the most restrictive p.value
dd.glcm.clusS <- toptable.sphericity$adj.P.Val < 0.01 & !is.na(toptable.sphericity$adj.P.Val)
dd.glcm.sum <- toptable.sumAv$adj.P.Val < 0.01 & !is.na(toptable.sumAv$adj.P.Val)
dd.glcm.id <- toptable.id0$adj.P.Val < 0.05 & !is.na(toptable.id0$adj.P.Val)
dd.glcm.idm <- toptable.idm0$adj.P.Val < 0.05 & !is.na(toptable.idm0$adj.P.Val)
dd.glcm.hg1Em <- toptable.hg1Em$adj.P.Val < 0.01 & !is.na(toptable.hg1Em$adj.P.Val)

```

```

deGenes.glcM <- c(rownames(toptable.idM[dd.glcM.idM, ]), rownames(toptable.id0[dd.glcM.id,
]), rownames(toptable.clustSh[dd.glcM.clusS, ]), rownames(toptable.sumAv[dd.glcM.sum,
]), rownames(toptable.hg1Em[dd.glcM.hg1Em, ]))

deGenes.glcM

## [1] "203893_at"      "1554830_a_at"    "203893_at"      "1554830_a_at"    "214027_x_at"
## [6] "239081_at"      "204233_s_at"    "213564_x_at"    "201030_x_at"    "233092_s_at"
## [11] "230774_at"       "212329_at"     "227973_at"      "212329_at"      "227973_at"

length(deGenes.glcM)

## [1] 15

table(duplicated(deGenes.glcM))

##
## FALSE  TRUE
## 11      4

deGenes.glcM <- unique(deGenes.glcM)

```

Check if there are annotations available:

```

# Check info
annotation.sputum.ok[deGenes.glcM, ]

```

```

## # A tibble: 11 x 9
##   PROBEID    ENSEMBL ENTREZID SYMBOL GENENAME GO      EVIDENCE ONTOLOGY GENETYPE
##   <chr>      <chr>    <chr>    <chr>    <chr>    <chr>    <chr>    <chr>
## 1 203893_at "ENSG0~" "102157~" "AK6"     "adenyl~" "GO:~"   "HDA|IB~" "BP|CC|~" "protei~"
## 2 1554830_a_~ "ENSG0~" "55240"   "STEA~"   "STEAP3~" "GO:~"   "IBA|ID~" "BP|CC|~" "protei~"
## 3 214027_x_at "ENSG0~" "1674|5~" "DES|~"   "desmin~" "GO:~"   "HDA|IB~" "BP|CC|~" "protei~"
## 4 239081_at   ""        ""        ""        ""        ""        ""        ""        ""
## 5 204233_s_at "ENSG0~" "1119"    "CHKA"   "cholin~" "GO:~"   "IBA|ID~" "BP|CC|~" "protei~"
## 6 213564_x_at "ENSG0~" "3945"    "LDHB"   "lactat~" "GO:~"   "HDA|IB~" "BP|CC|~" "protei~"
## 7 201030_x_at "ENSG0~" "3945"    "LDHB"   "lactat~" "GO:~"   "HDA|IB~" "BP|CC|~" "protei~"
## 8 233092_s_at   ""        ""        ""        ""        ""        ""        ""        ""
## 9 230774_at   "ENSG0~" "145482"  "PTGR~"  "prosta~" "GO:~"   "IBA|ID~" "BP|CC|~" "protei~"
## 10 212329_at  "ENSG0~" "22937"   "SCAP"   "SREBF ~" "GO:~"   "IDA|IE~" "BP|CC|~" "protei~"
## 11 227973_at  "ENSG0~" "205327"  "C2or~"  "chromo~" "GO:~"   "IDA|IE~" "BP|CC"   "protei~"

```

Gene universe shape:

```

geneUniverse.glcM <- rownames(toptable.sumAv[!is.na(toptable.sumAv$P.Value), ])
length(geneUniverse.glcM)

```

```

## [1] 48525

```

Change annotation to ENTREZ:

```

# Retrieve ENTREZ names
deGenes.glcM.entrez <- unlist(mget(deGenes.glcM, envir = hgu133plus2ENTREZID, ifnotfound = NA))
geneUniverse.glcM.entrez <- unlist(mget(geneUniverse.glcM, envir = hgu133plus2ENTREZID,
                                         ifnotfound = NA))

```

GO enrichment:

```

ans.go.glcM <- enrichGO(gene = deGenes.glcM.entrez, ont = "BP", universe = geneUniverse.glcM.entrez,
                           OrgDb = "org.Hs.eg.db", readable = TRUE, pvalueCutoff = 0.05)

```

```

# See results
tab.go.glcml <- as.data.frame(ans.go.glcml@result)
# tab.go.glcml <- subset(tab.go.glcml, Count>5)
tab.go.glcml[1:5, 1:6]

##           ID                               Description
## GO:0006646 GO:0006646      phosphatidylethanolamine biosynthetic process
## GO:0046940 GO:0046940      nucleoside monophosphate phosphorylation
## GO:1902931 GO:1902931 negative regulation of alcohol biosynthetic process
## GO:0006089 GO:0006089      lactate metabolic process
## GO:0006825 GO:0006825      copper ion transport
##       GeneRatio   BgRatio      pvalue   p.adjust
## GO:0006646     1/7 10/15058 0.004640363 0.06320076
## GO:0046940     1/7 11/15058 0.005103383 0.06320076
## GO:1902931     1/7 13/15058 0.006028868 0.06320076
## GO:0006089     1/7 15/15058 0.006953615 0.06320076
## GO:0006825     1/7 15/15058 0.006953615 0.06320076

KEGG enrichment:
ans.kegg.glcml <- enrichKEGG(gene = deGenes.glcml.entrez, universe = geneUniverse.glcml.entrez,
                                organism = "hsa", pvalueCutoff = 0.05)

# See results
tab.kegg.glcml <- as.data.frame(ans.kegg.glcml@result)
# tab.kegg.glcml <- subset(tab.kegg.glcml, Count>5)
tab.kegg.glcml[1:5, 1:6]

##           ID                               Description GeneRatio BgRatio
## hsa00640 hsa00640      Propanoate metabolism     1/4 31/6910
## hsa04216 hsa04216      Ferroptosis             1/4 40/6910
## hsa00270 hsa00270 Cysteine and methionine metabolism 1/4 45/6910
## hsa00620 hsa00620      Pyruvate metabolism     1/4 46/6910
## hsa00010 hsa00010 Glycolysis / Gluconeogenesis 1/4 62/6910
##       pvalue   p.adjust
## hsa00640 0.01782845 0.06665618
## hsa04216 0.02295951 0.06665618
## hsa00270 0.02580139 0.06665618
## hsa00620 0.02636903 0.06665618
## hsa00010 0.03541745 0.06665618

Disgenet:
res_enrich.glcml <- disease_enrichment(entities = deGenes.glcml.entrez, vocabulary = "ENTREZ",
                                           database = "CURATED")

res.table.disgenet.glcml <- res_enrich.glcml@qresult
res.table.disgenet.glcml

##           ID                               Description source Ratio
## 1  C0002884      Hypochromic anemia CURATED 1/4
## 25 C3279904 Lactate Dehydrogenase B Deficiency CURATED 1/4
## 26 C3808920 ANEMIA, HYPOCHROMIC MICROCYTIC, WITH IRON OVERLOAD 2 CURATED 1/4
## 24 C2673913 Anemia, Hypochromic Microcytic, With Iron Overload CURATED 1/4
## 3  C0007124 Noninfiltrating Intraductal Carcinoma CURATED 1/4
## 21 C1332347 Atypical Ductal Breast Hyperplasia CURATED 1/4

```

```

## 9 C0038219 Status Dysraphicus CURATED 1/4
## 10 C0080178 Spina Bifida CURATED 1/4
## 11 C0266508 Rachischisis CURATED 1/4
## 6 C0025521 Inborn Errors of Metabolism CURATED 1/4
## 15 C0948089 Acute Coronary Syndrome CURATED 1/4
## 4 C0007134 Renal Cell Carcinoma CURATED 1/4
## 17 C1266042 Chromophobe Renal Cell Carcinoma CURATED 1/4
## 18 C1266043 Sarcomatoid Renal Cell Carcinoma CURATED 1/4
## 19 C1266044 Collecting Duct Carcinoma of the Kidney CURATED 1/4
## 20 C1306837 Papillary Renal Cell Carcinoma CURATED 1/4
## 12 C0279702 Conventional (Clear Cell) Renal Cell Carcinoma CURATED 1/4
## 7 C0027626 Neoplasm Invasiveness CURATED 1/4
## 14 C0678222 Breast Carcinoma CURATED 1/4
## 16 C1257931 Mammary Neoplasms, Human CURATED 1/4
## 22 C1458155 Mammary Neoplasms CURATED 1/4
## 23 C2239176 Liver carcinoma CURATED 1/4
## 27 C4704874 Mammary Carcinoma, Human CURATED 1/4
## 8 C0033578 Prostatic Neoplasms CURATED 1/4
## 13 C0376358 Malignant neoplasm of prostate CURATED 1/4
## 5 C0023893 Liver Cirrhosis, Experimental CURATED 1/4
## 2 C0006142 Malignant neoplasm of breast CURATED 1/4

##      BgRatio      pvalue      FDR disease_class
## 1    1/9703 0.0004122861 0.003710575      C15
## 25   1/9703 0.0004122861 0.003710575      C16;C18
## 26   1/9703 0.0004122861 0.003710575      <NA>
## 24   2/9703 0.0008244448 0.005565002      C15
## 3    5/9703 0.0020601559 0.009270702      C04
## 21   5/9703 0.0020601559 0.009270702      C04
## 9    12/9703 0.0049390244 0.014817073      C10;C16
## 10   12/9703 0.0049390244 0.014817073      C10;C16
## 11   12/9703 0.0049390244 0.014817073      C10;C16
## 6    17/9703 0.0069915423 0.018877164      C16;C18
## 15   33/9703 0.0135382665 0.033230291      C14
## 4    128/9703 0.0517452655 0.087320136     C04;C12;C13
## 17   128/9703 0.0517452655 0.087320136     C04;C12;C13
## 18   128/9703 0.0517452655 0.087320136     C04;C12;C13
## 19   128/9703 0.0517452655 0.087320136     C04;C12;C13
## 20   128/9703 0.0517452655 0.087320136     C04;C12;C13
## 12   148/9703 0.0596452881 0.094730752     C04;C12;C13
## 7    184/9703 0.0737408156 0.110611223     C04;C23
## 14   538/9703 0.2040615790 0.239550549     C04;C17
## 16   525/9703 0.1995347613 0.239550549     C04;C17
## 22   527/9703 0.2002324484 0.239550549     C04;C17
## 23   507/9703 0.1932350159 0.239550549     C04;C06
## 27   525/9703 0.1995347613 0.239550549     C04;C17
## 8    616/9703 0.2308206162 0.249286266     C04;C12
## 13   616/9703 0.2308206162 0.249286266     C04;C12
## 5    774/9703 0.2829517913 0.293834553     C06;C23
## 2    1074/9703 0.3745940287 0.374594029     C04;C17

##                                     disease_class_name
## 1                                     Hemic and Lymphatic Diseases
## 25 Congenital, Hereditary, and Neonatal Diseases and Abnormalities; Nutritional and Metabolic Diseases
## 26
## 24                                     Hemic and Lymphatic Diseases

```

```

## 3
## 21
## 9      Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities
## 10     Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities
## 11     Nervous System Diseases;Congenital, Hereditary, and Neonatal Diseases and Abnormalities
## 6   Congenital, Hereditary, and Neonatal Diseases and Abnormalities;Nutritional and Metabolic Diseases
## 15           Cardiovascular Diseases
## 4       Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 17     Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 18     Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 19     Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 20     Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 12     Neoplasms;Male Urogenital Diseases;Female Urogenital Diseases and Pregnancy Complications
## 7       Neoplasms;Pathological Conditions, Signs and Symptoms
## 14     Neoplasms;Skin and Connective Tissue Diseases
## 16     Neoplasms;Skin and Connective Tissue Diseases
## 22     Neoplasms;Skin and Connective Tissue Diseases
## 23           Neoplasms;Digestive System Diseases
## 27     Neoplasms;Skin and Connective Tissue Diseases
## 8       Neoplasms;Male Urogenital Diseases
## 13     Neoplasms;Male Urogenital Diseases
## 5       Digestive System Diseases;Pathological Conditions, Signs and Symptoms
## 2       Neoplasms;Skin and Connective Tissue Diseases
## disease_semantic_type shared_geneid shared_symbol Count
## 1       Disease or Syndrome      55240    STEAP3    1
## 25      Disease or Syndrome      3945     LDHB      1
## 26      Disease or Syndrome      55240    STEAP3    1
## 24      Disease or Syndrome      55240    STEAP3    1
## 3       Neoplastic Process      3945     LDHB      1
## 21      Neoplastic Process      3945     LDHB      1
## 9       Congenital Abnormality   1119     CHKA      1
## 10      Congenital Abnormality   1119     CHKA      1
## 11      Congenital Abnormality   1119     CHKA      1
## 6   Congenital Abnormality;Disease or Syndrome   3945     LDHB      1
## 15      Disease or Syndrome      3945     LDHB      1
## 4       Neoplastic Process      3945     LDHB      1
## 17      Neoplastic Process      3945     LDHB      1
## 18      Neoplastic Process      3945     LDHB      1
## 19      Neoplastic Process      3945     LDHB      1
## 20      Neoplastic Process      3945     LDHB      1
## 12      Neoplastic Process      3945     LDHB      1
## 7       Pathologic Function     3945     LDHB      1
## 14      Neoplastic Process      3945     LDHB      1
## 16      Neoplastic Process      3945     LDHB      1
## 22      Neoplastic Process      3945     LDHB      1
## 23      Neoplastic Process      22937    SCAP      1
## 27      Neoplastic Process      3945     LDHB      1
## 8       Neoplastic Process      3945     LDHB      1
## 13      Neoplastic Process      3945     LDHB      1
## 5       Experimental Model of Disease   3945     LDHB      1
## 2       Neoplastic Process      3945     LDHB      1
## gg
## 1  0.125
## 25 0.125

```

```

## 26 0.125
## 24 0.125
## 3 0.125
## 21 0.125
## 9 0.125
## 10 0.125
## 11 0.125
## 6 0.125
## 15 0.125
## 4 0.125
## 17 0.125
## 18 0.125
## 19 0.125
## 20 0.125
## 12 0.125
## 7 0.125
## 14 0.125
## 16 0.125
## 22 0.125
## 23 0.125
## 27 0.125
## 8 0.125
## 13 0.125
## 5 0.125
## 2 0.125

# save(res.table.disgenet.glcm, file =
# '/Users/carlacasanova-suarez/Desktop/DisGenet_glcm_features.rda')
# write.csv(res.table.disgenet.glcm, './Disgenet_enrichment_glcm.csv')

```

MSigDb enrichment analysis (group C7 immunologic signature):

```

# Load terms for genes coded by ENTREZ of the gene set C7
c3.tf <- readgmt("/Users/carlacasanova-suarez/Downloads/c7.all.v7.5.1.entrez.gmt.txt")

# Enrichment
ans.tf.glcm <- enricher(deGenes.glcm.entrez, TERM2GENE = c3.tf)
tab.tf.glcm <- as.data.frame(ans.tf.glcm@result)
# tab.tf.glcm <- subset(tab.tf.glcm, Count>5)
tab.tf.glcm[1:5, 1:5]

##
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP      GSE25088_ROSIGLITAZONE_
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP            GSE27859_CD11C_IN
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN                      GSE17974
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN GSE19401_RETINOIC_ACID_VS_
## 
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP      GSE25088_ROSIGLITAZONE_
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP            GSE27859_CD11C_IN
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN                      GSE17974
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN GSE19401_RETINOIC_ACID_VS_
## 
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP      GSE25088_ROSIGLITAZONE_
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP            GSE27859_CD11C_IN
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN                      GSE17974
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN GSE19401_RETINOIC_ACID_VS_
## 
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP      GSE25088_ROSIGLITAZONE_
## GeneRatio
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP      3/6

```

```

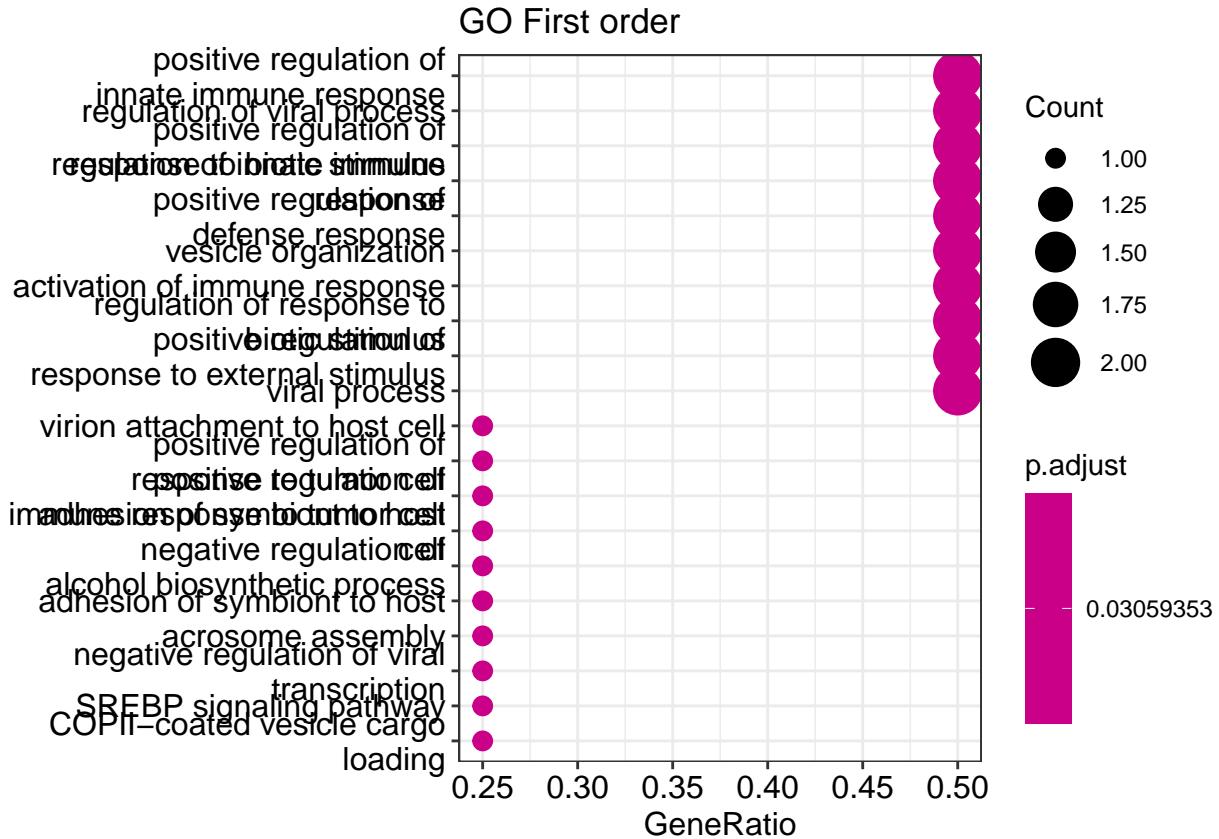
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP 2/6
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN 2/6
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN 2/6
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN 2/6
##
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP BgRatio 199/21355
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP 178/21355
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN 191/21355
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN 199/21355
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN 199/21355
##
## pvalue
## GSE25088_ROSIGLITAZONE_VS_IL4_AND_ROSIGLITAZONE_STIM_MACROPHAGE_DAY10_UP 1.561636e-05
## GSE27859_CD11C_INT_F480_HI_MACROPHAGE_VS_CD11C_ING_F480_INT_DC_UP 1.013779e-03
## GSE17974_CTRL_VS_ACT_IL4_AND_ANTI_IL12_0.5H_CD4_TCELL_DN 1.165814e-03
## GSE17322_CD103_POS_VS_CD11B_HIGH_LUNG_DC_DN 1.264518e-03
## GSE19401_RETINOIC_ACID_VS_RETINOIC_ACID_AND_PAM2CSK4_STIM_FOLLICULAR_DC_DN 1.264518e-03

```

Summary

First order:

```
# GO
dotplot(ans.go.fo, showCategory = 20) + ggtitle("GO First order")
```



```
# KEGG
x2 <- pairwise_termsim(ans.kegg.fo)
emapplot(x2)
```

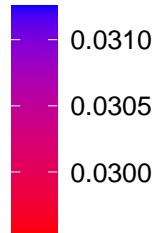
Adherens junction

hesion molecules

number of genes



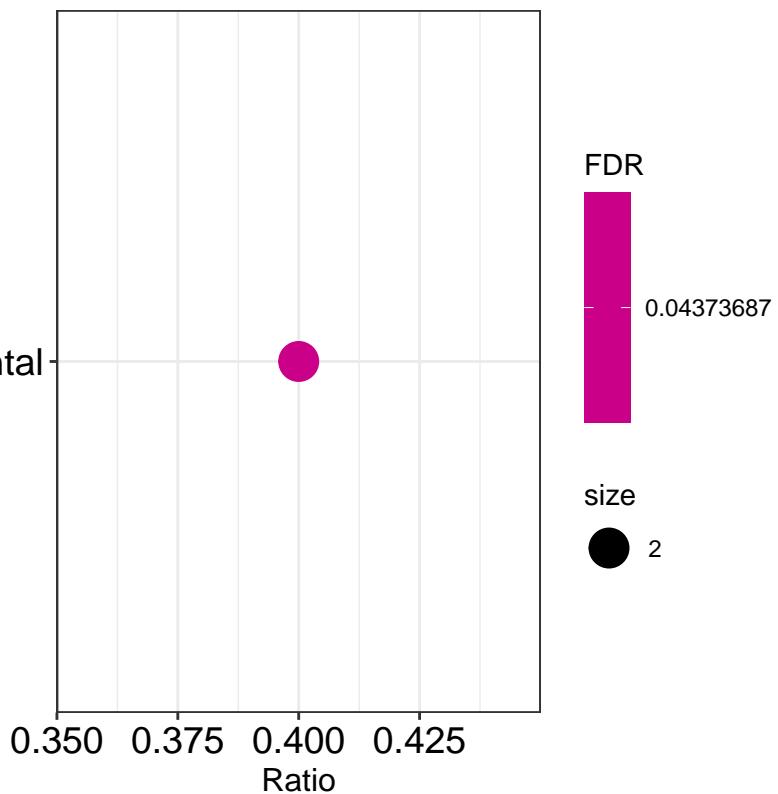
p.adjust



```
# Disgenet plot() function only displays diseases from ratios > 0.4.  
plot(res_enrich.fo, class = "Enrichment", cutoff = 0.05)
```

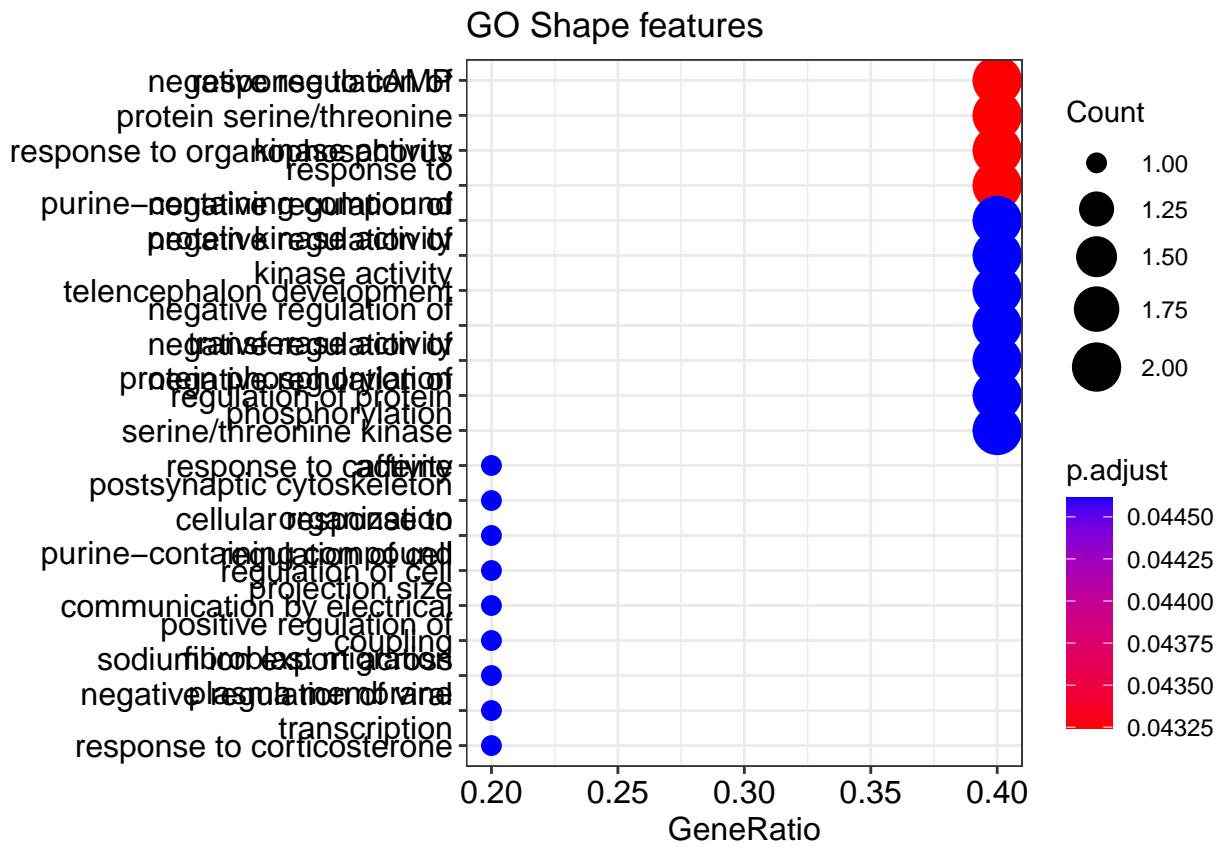
DisGeNET enrichment

Liver Cirrhosis, Experimental



Shape:

```
# GO  
dotplot(ans.go.sh, showCategory = 20) + ggtitle("GO Shape features")
```



```
# KEGG WARNING <- p.value not significant x3 <- pairwise_termsim(ans.kegg.sh)
# emapplot(x3)
```

GlcM:

```
# GO WARNING <- p.value not significant dotplot(ans.go.glcM, showCategory=20) +
# ggttitle('GO GLCM features')

# KEGG WARNING <- p.value not significant x4 <- pairwise_termsim(ans.kegg.glcM)
# emapplot(x4)
```