

Analysis 3/2

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Data manipulation

```
# Serum Overlap
new = t(serum.overlap)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
serum.overlap = new %>% as.data.frame()
serum.overlap = rownames_to_column(serum.overlap)
colnames(serum.overlap)[1] = "Patient ID"

# Serum geNorm
new = t(serum.geNorm)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
serum.geNorm = new %>% as.data.frame()
serum.geNorm = rownames_to_column(serum.geNorm)
colnames(serum.geNorm)[1] = "Patient ID"

# Serum GeneGlobe
new = t(serum.geneglobe)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
serum.geneglobe = new %>% as.data.frame()
serum.geneglobe = rownames_to_column(serum.geneglobe)
colnames(serum.geneglobe)[1] = "Patient ID"

# Serum NormFinder
new = t(serum.NormFinder)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
serum.NormFinder = new %>% as.data.frame()
serum.NormFinder = rownames_to_column(serum.NormFinder)
```

```

colnames(serum.NormFinder)[1] = "Patient ID"

# EV Overlap
new = t(EV.overlap)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
EV.overlap = new %>% as.data.frame()
EV.overlap = rownames_to_column(EV.overlap)
colnames(EV.overlap)[1] = "Patient ID"

# EV geNorm
new = t(EV.geNorm)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
EV.geNorm = new %>% as.data.frame()
EV.geNorm = rownames_to_column(EV.geNorm)
colnames(EV.geNorm)[1] = "Patient ID"

# EV GeneGlobe
new = t(EV.geneglobe)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
EV.geneglobe = new %>% as.data.frame()
EV.geneglobe = rownames_to_column(EV.geneglobe)
colnames(EV.geneglobe)[1] = "Patient ID"

# EV NormFinder
new = t(EV.NormFinder)
name_tmp <- new[1,]
new <- new[-1,]
new <- apply(new,1,as.numeric) %>% t()
colnames(new) <- (name_tmp)
EV.NormFinder = new %>% as.data.frame()
EV.NormFinder = rownames_to_column(EV.NormFinder)
colnames(EV.NormFinder)[1] = "Patient ID"

```

Data format has been changed from wide to long.

Normality test

Before the normality test, we need to remove microRNAs that has identical values among all patients.

```

# serum overlap
for (i in 2:62) {
  if(sum(!duplicated(serum.overlap[,i]))==1){
    print(i)
  }
}

```

```
}  
}
```

```
## [1] 39  
## [1] 41  
## [1] 42  
## [1] 57
```

```
serum.overlap.new = serum.overlap[,-c(39, 41, 42, 57)]
```

```
# serum geneglobe  
for (i in 2:62) {  
  if(sd(serum.geneglobe[,i]) == 0){  
    print(i)  
  }  
}
```

```
## [1] 39  
## [1] 41  
## [1] 42  
## [1] 57
```

```
serum.geneglobe.new = serum.geneglobe[,-c(39, 41, 42, 57)]
```

```
# serum geNorm  
for (i in 2:62) {  
  if(sd(serum.geNorm[,i]) == 0){  
    print(i)  
  }  
}
```

```
## [1] 39  
## [1] 41  
## [1] 42  
## [1] 57
```

```
serum.geNorm.new = serum.geNorm[,-c(39, 41, 42, 57)]
```

```
# serum NormFinder  
for (i in 2:62) {  
  if(sd(serum.NormFinder[,i]) == 0){  
    print(i)  
  }  
}
```

```
## [1] 39  
## [1] 41  
## [1] 42  
## [1] 57
```

```

serum.NormFinder.new = serum.NormFinder[,-c(39, 41, 42, 57)]

# EV overlap
for (i in 2:62) {
  if(sd(EV.overlap[,i]) == 0){
    print(i)
  }
}

# EV geneglobe
for (i in 2:62) {
  if(sum(!duplicated(EV.geneglobe[,i])) == 0){
    print(i)
  }
}

# EV geNorm
for (i in 2:62) {
  if(sd(EV.geNorm[,i]) == 0){
    print(i)
  }
}

# EV NormFinder
for (i in 2:62) {
  if(sd(EV.NormFinder[,i]) == 0){
    print(i)
  }
}

```

hsa-miR-518e-5p, hsa-miR-708-5p, hsa-miR-9-3p and hsa-miR-218-5p have been removed from serum datasets due to identical values. No microRNAs have been removed from EV datasets.

```

# serum overlap
normality.test.serum.overlap = data.frame(
  microRNA = colnames(serum.overlap.new[-1]),
  p.value = numeric(57),
  method = "Overlap"
)

for (i in 1:57) {
  test = shapiro.test(serum.overlap.new[,i+1])
  normality.test.serum.overlap$p.value[i] = test$p.value
}

# serum geNorm
normality.test.serum.geNorm = data.frame(
  microRNA = colnames(serum.geNorm.new[-1]),
  p.value = numeric(57),
  method = "geNorm"
)

for (i in 1:57) {

```

```

test = shapiro.test(serum.geNorm.new[,i+1])
normality.test.serum.geNorm$p.value[i] = test$p.value
}

# serum geNorm NormFinder
normality.test.serum.NormFinder = data.frame(
  microRNA = colnames(serum.NormFinder.new[-1]),
  p.value = numeric(57),
  method = "NormFinder"
)

for (i in 1:57) {
  test = shapiro.test(serum.NormFinder.new[,i+1])
  normality.test.serum.NormFinder$p.value[i] = test$p.value
}

# EV Overlap
normality.test.EV.overlap = data.frame(
  microRNA = colnames(EV.overlap[-1]),
  p.value = numeric(61),
  method = "Overlap"
)

for (i in 1:61) {
  test = shapiro.test(EV.overlap[,i+1])
  normality.test.EV.overlap$p.value[i] = test$p.value
}

# EV geNorm
normality.test.EV.geNorm = data.frame(
  microRNA = colnames(EV.geNorm[-1]),
  p.value = numeric(61),
  method = "geNorm"
)

for (i in 1:61) {
  test = shapiro.test(EV.geNorm[,i+1])
  normality.test.EV.geNorm$p.value[i] = test$p.value
}

# EV NormFinder
normality.test.EV.NormFinder = data.frame(
  microRNA = colnames(EV.NormFinder[-1]),
  p.value = numeric(61),
  method = "NormFinder"
)

for (i in 1:61) {
  test = shapiro.test(EV.NormFinder[,i+1])
  normality.test.EV.NormFinder$p.value[i] = test$p.value
}

normality.test.serum = data.frame(

```

```

microRNA = colnames(serum.geneglobe.new[-1]),
p.value = numeric(57),
method = "Gene Globe"
)

for (i in 1:57) {
  test = shapiro.test(serum.geneglobe.new[,i+1])
  normality.test.serum$p.value[i] = test$p.value
}

# checking distribution for EV
normality.test.EV = data.frame(
  microRNA = colnames(EV.geneglobe[-1]),
  p.value = numeric(61),
  method = "Gene Globe"
)

for (i in 1:61) {
  test = shapiro.test(EV.geneglobe[,i+1])
  normality.test.EV$p.value[i] = test$p.value
}

normality.result.serum = rbind(normality.test.serum, normality.test.serum.overlap, normality.test.serum)
normality.result.EV = rbind(normality.test.EV, normality.test.EV.overlap, normality.test.EV.geNorm, normality.test.EV.normFinder)

# Show microRNAs that have normal distribution:
normality.result.serum %>% filter(p.value >= 0.05)

##           microRNA      p.value      method
## 1 hsa-miR-103a-3p 0.13273658      Overlap
## 2  hsa-miR-24-3p 0.05672167      Overlap
## 3  hsa-let-7b-5p 0.40986900      Overlap
## 4 hsa-miR-103a-3p 0.12596183      geNorm
## 5  hsa-let-7i-5p 0.10083898      geNorm
## 6  hsa-miR-27a-3p 0.13419952 NormFinder

normality.result.EV %>% filter(p.value >= 0.05)

##           microRNA      p.value      method
## 1  hsa-miR-27a-3p 0.14754033      Overlap
## 2 hsa-miR-199a-3p 0.16866880      Overlap
## 3  hsa-miR-27b-3p 0.17270638      Overlap
## 4  hsa-miR-24-3p 0.68463055 NormFinder
## 5  hsa-miR-30c-5p 0.05263450 NormFinder
## 6  hsa-miR-27a-3p 0.12170718 NormFinder
## 7  hsa-miR-23a-3p 0.07160567 NormFinder
## 8 hsa-miR-199a-3p 0.59334601 NormFinder

```

Univariate GLM

Since it keeps giving error message when a variable contains mostly 0, we have to remove variables that keep running into errors.

```

EV.geneglobe.new = EV.geneglobe[,-c(39,41,42,57)]
EV.geNorm.new = EV.geNorm[,-c(39,41,42,57)]
EV.overlap.new = EV.overlap[,-c(39,41,42,57)]
EV.NormFinder.new = EV.NormFinder[,-c(39,41,42,57)]

# datafile combine
# left join for grade groups
serum.grade.original = left_join(serum.geneglobe.new, biopsy.grade, by = "Patient ID")
EV.grade.original = left_join(EV.geneglobe.new, biopsy.grade, by = "Patient ID")

# left join for adverse pathology
serum.all.original = left_join(serum.grade.original, adverse.pathology, by = "Patient ID")
EV.all.original = left_join(EV.grade.original, adverse.pathology, by = "Patient ID")

```

```

grade.serum.result = data.frame(
  microRNA = colnames(serum.geneglobe.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$'Biopsy Grade Group'~serum.all.original[,i+1])
  result = summary(model)
  grade.serum.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.serum.result$standard.deviation[i] = result$coefficients[2,2]
  grade.serum.result$p.value[i] = result$coefficients[2,4]
}

```

```

grade.EV.result = data.frame(
  microRNA = colnames(EV.geneglobe.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.all.original$'Biopsy Grade Group'~EV.all.original[,i+1])
  result = summary(model)
  grade.EV.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.EV.result$standard.deviation = result$coefficients[2,2]
  grade.EV.result$p.value[i] = result$coefficients[2,4]
}

```

Display result

```

grade.serum.geneglobe.result = grade.serum.result[order(grade.serum.result$p.value),];grade.serum.geneglobe.result

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 27	hsa-miR-214-3p	0.2088843522	0.07219239	0.004230744
## 30	hsa-miR-301a-3p	0.0592836631	0.02910616	0.042980506
## 54	hsa-miR-125b-5p	0.0765165009	0.03789180	0.044779707
## 57	hsa-miR-374a-5p	0.0441249056	0.02195201	0.045761440
## 16	hsa-miR-1246	-0.0683729976	0.03439914	0.048209396

## 22	hsa-miR-194-5p	0.0483824502	0.02581976	0.062401734
## 1	hsa-let-7a-5p	0.0638777478	0.03528954	0.071773139
## 26	hsa-miR-210-3p	0.0441742066	0.02524821	0.081713968
## 2	hsa-miR-100-5p	0.1464006399	0.08381238	0.082205359
## 36	hsa-miR-363-3p	0.0181003833	0.01038153	0.082772217
## 21	hsa-miR-193a-3p	0.9993547285	0.58901014	0.091307426
## 12	hsa-miR-451a	0.0172512734	0.01050553	0.102130149
## 4	hsa-miR-106a-5p	0.0251481107	0.01568157	0.110356275
## 29	hsa-miR-16-5p	0.0226760824	0.01414093	0.110377192
## 43	hsa-let-7b-5p	0.0334015704	0.02120423	0.116775718
## 37	hsa-miR-375	0.0432073787	0.02832580	0.128738343
## 19	hsa-miR-18b-5p	0.0279811632	0.01919293	0.146431803
## 20	hsa-miR-19b-3p	0.0246593811	0.01730435	0.155696780
## 49	hsa-miR-31-5p	-0.1520497179	0.10823627	0.161625897
## 14	hsa-miR-93-5p	0.0217233082	0.01564001	0.166382788
## 13	hsa-miR-874-3p	-0.0648333392	0.04842123	0.182101061
## 46	hsa-miR-122-5p	0.0218035936	0.01686692	0.197604363
## 56	hsa-miR-148a-3p	0.0302715955	0.02638440	0.252609364
## 17	hsa-miR-141-3p	0.0976555665	0.08580574	0.256433230
## 15	hsa-let-7i-5p	0.0294697914	0.02592115	0.256933071
## 35	hsa-miR-345-5p	-0.0287685152	0.02616233	0.272814686
## 5	hsa-miR-107	0.0199847534	0.01909049	0.296428998
## 3	hsa-miR-103a-3p	0.0202971510	0.01940959	0.296942632
## 10	hsa-miR-26b-5p	0.0296344829	0.02972044	0.319911013
## 50	hsa-miR-34a-5p	0.0398978623	0.04396361	0.365218557
## 11	hsa-miR-30c-5p	0.0314648470	0.03515063	0.371781243
## 48	hsa-miR-29a-3p	-0.0311120228	0.03718019	0.403704233
## 8	hsa-miR-223-3p	-0.0142123152	0.01776312	0.424596192
## 55	hsa-miR-143-3p	-0.0335351898	0.04205168	0.426115940
## 34	hsa-miR-335-5p	-0.0360296790	0.04600928	0.434492481
## 6	hsa-miR-130b-3p	-0.0341178509	0.04388010	0.437763599
## 52	hsa-miR-25-3p	0.0119505959	0.01634446	0.465526252
## 23	hsa-miR-200a-3p	0.1044814719	0.17212869	0.544538425
## 24	hsa-miR-200b-3p	0.0617196166	0.10496333	0.557184826
## 38	hsa-miR-574-3p	0.0147129783	0.02531167	0.561707976
## 40	hsa-miR-23a-3p	-0.0116371072	0.02719556	0.669178670
## 31	hsa-miR-320a	-0.0137600713	0.03241144	0.671623472
## 45	hsa-miR-199a-5p	-0.0064979710	0.01885663	0.730756275
## 33	hsa-miR-330-3p	-0.0151164267	0.04867047	0.756436245
## 44	hsa-miR-30a-5p	-0.0143582683	0.04852889	0.767634384
## 25	hsa-miR-204-5p	-0.0194449019	0.07674311	0.800236251
## 47	hsa-miR-221-3p	-0.0033848896	0.01465982	0.817630618
## 39	hsa-miR-191-5p	0.0035225207	0.01838162	0.848223348
## 9	hsa-miR-24-3p	-0.0045771153	0.02675594	0.864341499
## 18	hsa-miR-146b-3p	-0.0544263556	0.34417627	0.874509084
## 32	hsa-miR-27a-3p	-0.0035164799	0.02473883	0.887108523
## 41	hsa-miR-199a-3p	-0.0025373621	0.02312206	0.912726877
## 28	hsa-miR-222-3p	-0.0017564163	0.02962067	0.952774481
## 7	hsa-miR-146a-5p	-0.0008349978	0.01445775	0.954001686
## 53	hsa-miR-155-5p	0.0031071164	0.05400068	0.954173421
## 42	hsa-miR-21-5p	0.0013589251	0.04241463	0.974472687
## 51	hsa-miR-27b-3p	-0.0005684387	0.02378620	0.980957810


```
grade.EV.geneglobe.result = grade.EV.result[order(grade.EV.result$p.value),];grade.EV.geneglobe.result
```

##	microRNA	coefficient.estimate	standard.deviation	p.value
## 49	hsa-miR-31-5p	-0.131808289	0.03759133	0.04520534
## 17	hsa-miR-141-3p	-0.120785988	0.03759133	0.08577299
## 10	hsa-miR-26b-5p	-0.067564280	0.03759133	0.11648496
## 1	hsa-let-7a-5p	-0.058118043	0.03759133	0.13254292
## 5	hsa-miR-107	-0.053798725	0.03759133	0.13448416
## 34	hsa-miR-335-5p	-0.047381797	0.03759133	0.14074698
## 3	hsa-miR-103a-3p	-0.053058698	0.03759133	0.14209210
## 43	hsa-let-7b-5p	-0.080946097	0.03759133	0.15913141
## 11	hsa-miR-30c-5p	-0.055768397	0.03759133	0.17135788
## 15	hsa-let-7i-5p	-0.074196456	0.03759133	0.17196238
## 6	hsa-miR-130b-3p	-0.048664698	0.03759133	0.18587627
## 16	hsa-miR-1246	-0.072254452	0.03759133	0.20865896
## 39	hsa-miR-191-5p	-0.046137559	0.03759133	0.20876407
## 42	hsa-miR-21-5p	-0.062744315	0.03759133	0.21578046
## 47	hsa-miR-221-3p	-0.037742416	0.03759133	0.21769537
## 33	hsa-miR-330-3p	-0.058811806	0.03759133	0.23954683
## 31	hsa-miR-320a	-0.047549965	0.03759133	0.24737334
## 57	hsa-miR-374a-5p	-0.042461776	0.03759133	0.26099079
## 4	hsa-miR-106a-5p	-0.046304713	0.03759133	0.26355347
## 28	hsa-miR-222-3p	-0.051484490	0.03759133	0.30720725
## 14	hsa-miR-93-5p	-0.040922890	0.03759133	0.31103152
## 9	hsa-miR-24-3p	-0.034595548	0.03759133	0.31235522
## 25	hsa-miR-204-5p	-0.065420115	0.03759133	0.31412526
## 48	hsa-miR-29a-3p	-0.033496658	0.03759133	0.31569513
## 53	hsa-miR-155-5p	-0.057765954	0.03759133	0.33989789
## 40	hsa-miR-23a-3p	-0.031230972	0.03759133	0.34388517
## 8	hsa-miR-223-3p	-0.020224114	0.03759133	0.35116947
## 52	hsa-miR-25-3p	-0.039482119	0.03759133	0.35705321
## 12	hsa-miR-451a	-0.033929935	0.03759133	0.37128024
## 41	hsa-miR-199a-3p	-0.023833980	0.03759133	0.37712215
## 32	hsa-miR-27a-3p	-0.026295802	0.03759133	0.40058567
## 30	hsa-miR-301a-3p	-0.039746064	0.03759133	0.41139919
## 51	hsa-miR-27b-3p	-0.026236641	0.03759133	0.41635472
## 54	hsa-miR-125b-5p	-0.044962299	0.03759133	0.42032819
## 35	hsa-miR-345-5p	-0.033462475	0.03759133	0.42809990
## 29	hsa-miR-16-5p	-0.032005816	0.03759133	0.43198391
## 23	hsa-miR-200a-3p	0.046606581	0.03759133	0.44797036
## 45	hsa-miR-199a-5p	-0.016949789	0.03759133	0.46228787
## 37	hsa-miR-375	-0.023232795	0.03759133	0.46317593
## 36	hsa-miR-363-3p	-0.024075660	0.03759133	0.50409554
## 20	hsa-miR-19b-3p	-0.031559043	0.03759133	0.51813887
## 22	hsa-miR-194-5p	-0.029836713	0.03759133	0.51954857
## 7	hsa-miR-146a-5p	-0.017954055	0.03759133	0.52840661
## 13	hsa-miR-874-3p	-0.042209526	0.03759133	0.53343346
## 2	hsa-miR-100-5p	-0.028660043	0.03759133	0.53812457
## 50	hsa-miR-34a-5p	-0.025881068	0.03759133	0.55198908
## 56	hsa-miR-148a-3p	-0.026445305	0.03759133	0.59072884
## 26	hsa-miR-210-3p	-0.032454294	0.03759133	0.59476185
## 44	hsa-miR-30a-5p	-0.034728553	0.03759133	0.60183565
## 24	hsa-miR-200b-3p	0.019604887	0.03759133	0.68832026

```
## 38 hsa-miR-574-3p -0.016096336 0.03759133 0.73977417
## 21 hsa-miR-193a-3p -0.054530198 0.03759133 0.74146666
## 19 hsa-miR-18b-5p -0.009408160 0.03759133 0.81338283
## 27 hsa-miR-214-3p 0.007204922 0.03759133 0.87100940
## 55 hsa-miR-143-3p 0.003671712 0.03759133 0.88683142
## 46 hsa-miR-122-5p -0.003532389 0.03759133 0.89777248
## 18 hsa-miR-146b-3p -0.012767671 0.03759133 0.94411261
```

Serum overlap

```
grade.serum.overlap.result = data.frame(
  microRNA = colnames(serum.overlap.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$`Biopsy Grade Group`~serum.overlap.new[,i+1])
  result = summary(model)
  grade.serum.overlap.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.serum.overlap.result$standard.deviation[i] = result$coefficients[2,2]
  grade.serum.overlap.result$p.value[i] = result$coefficients[2,4]
}
```

```
grade.serum.overlap.result = grade.serum.overlap.result[order(grade.serum.overlap.result$p.value),]; gr
```

```
##          microRNA coefficient.estimates standard.deviation      p.value
## 29 hsa-miR-16-5p      0.743626833      0.16978024 1.909414e-05
## 43 hsa-let-7b-5p      1.047579667      0.26287385 9.431931e-05
## 20 hsa-miR-19b-3p      0.693975887      0.20708746 9.613771e-04
## 32 hsa-miR-27a-3p     -0.424680517      0.14103369 2.936033e-03
## 16 hsa-miR-1246      -0.150932197      0.05458298 6.218645e-03
## 12 hsa-miR-451a       0.316326391      0.11848278 8.210134e-03
## 36 hsa-miR-363-3p      0.260876738      0.09904067 9.094422e-03
## 51 hsa-miR-27b-3p     -0.343297093      0.13114534 9.526467e-03
## 4 hsa-miR-106a-5p      0.536975889      0.22683782 1.887180e-02
## 14 hsa-miR-93-5p       0.364202596      0.15545372 2.011542e-02
## 6 hsa-miR-130b-3p     -0.243783262      0.10568083 2.208556e-02
## 9 hsa-miR-24-3p       -0.386291378      0.16851432 2.292172e-02
## 40 hsa-miR-23a-3p     -0.310357929      0.14513226 3.368726e-02
## 31 hsa-miR-320a       -0.207607536      0.10193872 4.300240e-02
## 48 hsa-miR-29a-3p     -0.220530774      0.11077703 4.786165e-02
## 7 hsa-miR-146a-5p     -0.157672190      0.08296564 5.880502e-02
## 54 hsa-miR-125b-5p      0.106000523      0.05594328 5.955629e-02
## 8 hsa-miR-223-3p      -0.139717336      0.07385820 5.996922e-02
## 13 hsa-miR-874-3p     -0.154389320      0.08177488 6.046931e-02
## 47 hsa-miR-221-3p     -0.198539517      0.10709911 6.523415e-02
## 41 hsa-miR-199a-3p     -0.176324783      0.09943809 7.770799e-02
## 39 hsa-miR-191-5p     -0.234907274      0.13357260 8.015897e-02
## 45 hsa-miR-199a-5p     -0.117487214      0.06917166 9.096310e-02
## 21 hsa-miR-193a-3p     22.447094014     13.23010292 9.130743e-02
## 11 hsa-miR-30c-5p     -0.208800146      0.12446256 9.497673e-02
## 42 hsa-miR-21-5p      -0.166113319      0.10673869 1.212190e-01
## 34 hsa-miR-335-5p     -0.149094486      0.09745315 1.276114e-01
## 3 hsa-miR-103a-3p     -0.275998537      0.19347879 1.552739e-01
```

## 55	hsa-miR-143-3p	-0.089068748	0.06885157	1.972764e-01
## 25	hsa-miR-204-5p	-0.108587551	0.09738858	2.661849e-01
## 1	hsa-let-7a-5p	-0.141613036	0.12912908	2.740943e-01
## 33	hsa-miR-330-3p	-0.113389078	0.10411771	2.774372e-01
## 19	hsa-miR-18b-5p	0.111011623	0.10445214	2.891484e-01
## 38	hsa-miR-574-3p	-0.090381350	0.09267195	3.305923e-01
## 26	hsa-miR-210-3p	0.113081863	0.11865361	3.417135e-01
## 35	hsa-miR-345-5p	-0.074007270	0.08289457	3.730384e-01
## 57	hsa-miR-374a-5p	0.089171925	0.09995924	3.734152e-01
## 15	hsa-let-7i-5p	-0.247594062	0.28511418	3.862093e-01
## 17	hsa-miR-141-3p	0.084427766	0.09867325	3.932214e-01
## 18	hsa-miR-146b-3p	-0.789232157	0.94889994	4.065462e-01
## 28	hsa-miR-222-3p	-0.115076395	0.13954627	4.105496e-01
## 52	hsa-miR-25-3p	0.150170692	0.18742879	4.239535e-01
## 5	hsa-miR-107	-0.140222726	0.17906581	4.345022e-01
## 37	hsa-miR-375	-0.020451646	0.03229074	5.272190e-01
## 27	hsa-miR-214-3p	0.051137653	0.08136935	5.304140e-01
## 30	hsa-miR-301a-3p	0.075099773	0.12366967	5.443631e-01
## 44	hsa-miR-30a-5p	-0.034505080	0.06175808	5.769791e-01
## 22	hsa-miR-194-5p	0.031788453	0.06088318	6.021603e-01
## 56	hsa-miR-148a-3p	-0.040376321	0.07769921	6.038800e-01
## 10	hsa-miR-26b-5p	0.056042543	0.11852837	6.368549e-01
## 2	hsa-miR-100-5p	0.027587314	0.05976557	6.448731e-01
## 49	hsa-miR-31-5p	-0.029452385	0.06710085	6.611858e-01
## 53	hsa-miR-155-5p	-0.030416291	0.13039983	8.158015e-01
## 50	hsa-miR-34a-5p	0.009555039	0.04674385	8.382378e-01
## 46	hsa-miR-122-5p	-0.005397486	0.02984633	8.566734e-01
## 24	hsa-miR-200b-3p	-0.022806220	0.16116117	8.876073e-01
## 23	hsa-miR-200a-3p	-0.015201006	0.25856176	9.531773e-01

Serum geNorm

```

grade.serum.geNorm.result = data.frame(
  microRNA = colnames(serum.geNorm.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$'Biopsy Grade Group'~serum.geNorm.new[,i+1])
  result = summary(model)
  grade.serum.geNorm.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.serum.geNorm.result$standard.deviation[i] = result$coefficients[2,2]
  grade.serum.geNorm.result$p.value[i] = result$coefficients[2,4]
}

```

```

grade.serum.geNorm.result = grade.serum.geNorm.result[order(grade.serum.geNorm.result$p.value),]; grade

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 29	hsa-miR-16-5p	0.5802984754	0.15040996	0.0001538744
## 43	hsa-let-7b-5p	0.8712983568	0.23703261	0.0003041207
## 20	hsa-miR-19b-3p	0.5347978656	0.17976717	0.0032894048
## 32	hsa-miR-27a-3p	-0.4365656639	0.14772028	0.0034962584
## 16	hsa-miR-1246	-0.1555431780	0.05644853	0.0063990287
## 12	hsa-miR-451a	0.2941834625	0.11318103	0.0100361371

## 36	hsa-miR-363-3p	0.2444960689	0.09639200	0.0119572216
## 51	hsa-miR-27b-3p	-0.3403146688	0.13517316	0.0125954595
## 14	hsa-miR-93-5p	0.3468713245	0.14986305	0.0216454416
## 6	hsa-miR-130b-3p	-0.2346396167	0.10408620	0.0252571841
## 9	hsa-miR-24-3p	-0.3837171886	0.17575434	0.0301749748
## 4	hsa-miR-106a-5p	0.4487548733	0.20665674	0.0310646098
## 40	hsa-miR-23a-3p	-0.3183302478	0.15569959	0.0422063038
## 54	hsa-miR-125b-5p	0.1133525437	0.05605012	0.0444661195
## 8	hsa-miR-223-3p	-0.1512182343	0.08057450	0.0620012735
## 13	hsa-miR-874-3p	-0.1487332298	0.08179895	0.0705102206
## 7	hsa-miR-146a-5p	-0.1512345315	0.08350746	0.0716291683
## 31	hsa-miR-320a	-0.1702185879	0.09683322	0.0802946626
## 47	hsa-miR-221-3p	-0.1880783117	0.10700797	0.0803361164
## 48	hsa-miR-29a-3p	-0.1916207405	0.11023593	0.0836931204
## 11	hsa-miR-30c-5p	-0.2220751049	0.13042493	0.0901692463
## 21	hsa-miR-193a-3p	22.2611811842	13.12052767	0.0913074261
## 39	hsa-miR-191-5p	-0.2365140083	0.14126341	0.0956315517
## 45	hsa-miR-199a-5p	-0.1158885710	0.06933799	0.0962072370
## 41	hsa-miR-199a-3p	-0.1623817226	0.09793308	0.0988593570
## 34	hsa-miR-335-5p	-0.1496793849	0.09931343	0.1333444641
## 3	hsa-miR-103a-3p	-0.2786374791	0.19582186	0.1563115414
## 55	hsa-miR-143-3p	-0.0902226385	0.07114087	0.2061845256
## 42	hsa-miR-21-5p	-0.1172620008	0.09680013	0.2271710498
## 1	hsa-let-7a-5p	-0.1494689343	0.13314546	0.2629470736
## 25	hsa-miR-204-5p	-0.1103725900	0.10179135	0.2795296919
## 19	hsa-miR-18b-5p	0.1017068034	0.10176967	0.3188111563
## 33	hsa-miR-330-3p	-0.1050581619	0.10545093	0.3203142378
## 38	hsa-miR-574-3p	-0.0900448201	0.09242700	0.3311151635
## 26	hsa-miR-210-3p	0.1004088969	0.11813187	0.3963513929
## 57	hsa-miR-374a-5p	0.0832177413	0.09851350	0.3992635043
## 18	hsa-miR-146b-3p	-0.7499595823	0.91355558	0.4126621918
## 52	hsa-miR-25-3p	0.1377956534	0.17103970	0.4214050948
## 17	hsa-miR-141-3p	0.0713237905	0.09252853	0.4417126633
## 35	hsa-miR-345-5p	-0.0651441137	0.08475072	0.4429999761
## 5	hsa-miR-107	-0.1263532020	0.17609845	0.4738896861
## 15	hsa-let-7i-5p	-0.1797530825	0.27194945	0.5093821851
## 30	hsa-miR-301a-3p	0.0839712767	0.12816670	0.5131059100
## 27	hsa-miR-214-3p	0.0513494486	0.08194866	0.5316291516
## 10	hsa-miR-26b-5p	0.0746344552	0.12093936	0.5378520602
## 28	hsa-miR-222-3p	-0.0784046122	0.13357142	0.5578715553
## 37	hsa-miR-375	-0.0169317886	0.02992309	0.5721312030
## 22	hsa-miR-194-5p	0.0304273899	0.05631900	0.5896098896
## 2	hsa-miR-100-5p	0.0275917407	0.05801808	0.6348961785
## 44	hsa-miR-30a-5p	-0.0261752314	0.05853743	0.6552455290
## 56	hsa-miR-148a-3p	-0.0298686477	0.08050595	0.7110195587
## 49	hsa-miR-31-5p	-0.0216857932	0.06085515	0.7219514933
## 50	hsa-miR-34a-5p	0.0100554991	0.04184725	0.8103498932
## 53	hsa-miR-155-5p	-0.0259294537	0.13109569	0.8434090393
## 46	hsa-miR-122-5p	-0.0043972379	0.03009760	0.8839894124
## 24	hsa-miR-200b-3p	-0.0222444375	0.15267296	0.8843042976
## 23	hsa-miR-200a-3p	-0.0007220055	0.23628082	0.9975649313

```
# Serum NormFinder
grade.serum.NormFinder.result = data.frame(
```

```

microRNA = colnames(serum.NormFinder.new)[-1],
coefficient.estimates = numeric(57),
standard.deviation = numeric(57),
p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$'Biopsy Grade Group'~serum.NormFinder.new[,i+1])
  result = summary(model)
  grade.serum.NormFinder.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.serum.NormFinder.result$standard.deviation[i] = result$coefficients[2,2]
  grade.serum.NormFinder.result$p.value[i] = result$coefficients[2,4]
}

grade.serum.NormFinder.result = grade.serum.NormFinder.result[order(grade.serum.NormFinder.result$p.val

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 29	hsa-miR-16-5p	0.590567048	0.14596701	7.430342e-05
## 43	hsa-let-7b-5p	0.834214956	0.22208313	2.258228e-04
## 20	hsa-miR-19b-3p	0.654530575	0.19090001	7.358234e-04
## 32	hsa-miR-27a-3p	-0.473882400	0.15388654	2.363919e-03
## 16	hsa-miR-1246	-0.158413380	0.05673671	5.742489e-03
## 36	hsa-miR-363-3p	0.254852363	0.09339929	6.923359e-03
## 12	hsa-miR-451a	0.283680691	0.10612998	8.136198e-03
## 51	hsa-miR-27b-3p	-0.379496453	0.14333099	8.747198e-03
## 4	hsa-miR-106a-5p	0.512485946	0.19876771	1.064318e-02
## 14	hsa-miR-93-5p	0.375288698	0.14654148	1.117132e-02
## 6	hsa-miR-130b-3p	-0.248348938	0.10783898	2.230434e-02
## 9	hsa-miR-24-3p	-0.416053029	0.18443597	2.515936e-02
## 40	hsa-miR-23a-3p	-0.351934669	0.16098436	2.996025e-02
## 31	hsa-miR-320a	-0.222112788	0.10831135	4.159492e-02
## 48	hsa-miR-29a-3p	-0.248171820	0.12136908	4.218099e-02
## 54	hsa-miR-125b-5p	0.118164228	0.05813636	4.341479e-02
## 7	hsa-miR-146a-5p	-0.168546101	0.08801823	5.692504e-02
## 13	hsa-miR-874-3p	-0.159783856	0.08521761	6.224164e-02
## 47	hsa-miR-221-3p	-0.206136635	0.11243007	6.821232e-02
## 8	hsa-miR-223-3p	-0.136105573	0.07472108	7.001513e-02
## 41	hsa-miR-199a-3p	-0.185756151	0.10586315	8.083747e-02
## 42	hsa-miR-21-5p	-0.228476695	0.13104522	8.277617e-02
## 21	hsa-miR-193a-3p	18.718706447	11.03262688	9.130743e-02
## 45	hsa-miR-199a-5p	-0.115369752	0.06990793	1.004413e-01
## 39	hsa-miR-191-5p	-0.212134624	0.13539697	1.187437e-01
## 34	hsa-miR-335-5p	-0.151906642	0.09944123	1.281834e-01
## 11	hsa-miR-30c-5p	-0.194677462	0.13393318	1.476330e-01
## 55	hsa-miR-143-3p	-0.085745554	0.07035648	2.243751e-01
## 19	hsa-miR-18b-5p	0.124880115	0.10353837	2.291875e-01
## 25	hsa-miR-204-5p	-0.118427111	0.10263235	2.499128e-01
## 33	hsa-miR-330-3p	-0.119903007	0.10625550	2.604790e-01
## 57	hsa-miR-374a-5p	0.111864421	0.10055361	2.672583e-01
## 26	hsa-miR-210-3p	0.121305118	0.11610127	2.973603e-01
## 17	hsa-miR-141-3p	0.096684417	0.10467991	3.567918e-01
## 52	hsa-miR-25-3p	0.147956200	0.16285760	3.647019e-01
## 35	hsa-miR-345-5p	-0.077186241	0.08501930	3.650355e-01
## 38	hsa-miR-574-3p	-0.084623637	0.09564745	3.773511e-01

## 3	hsa-miR-103a-3p	-0.158911531	0.18730319	3.972141e-01
## 18	hsa-miR-146b-3p	-0.727042551	0.87767320	4.084407e-01
## 27	hsa-miR-214-3p	0.065241991	0.08401183	4.383189e-01
## 30	hsa-miR-301a-3p	0.093385119	0.12296346	4.484707e-01
## 28	hsa-miR-222-3p	-0.115855520	0.15338805	4.509472e-01
## 10	hsa-miR-26b-5p	0.089106716	0.12221325	4.667840e-01
## 1	hsa-let-7a-5p	-0.094046006	0.13259977	4.789930e-01
## 22	hsa-miR-194-5p	0.042845808	0.06613338	5.178086e-01
## 37	hsa-miR-375	-0.021499886	0.03492207	5.388198e-01
## 49	hsa-miR-31-5p	-0.040566832	0.07210221	5.743141e-01
## 44	hsa-miR-30a-5p	-0.035679499	0.06558573	5.870354e-01
## 2	hsa-miR-100-5p	0.028256440	0.06240504	6.511876e-01
## 56	hsa-miR-148a-3p	-0.032981128	0.08185162	6.874221e-01
## 15	hsa-let-7i-5p	-0.097029105	0.26996816	7.196661e-01
## 5	hsa-miR-107	-0.054915526	0.17634157	7.558074e-01
## 53	hsa-miR-155-5p	-0.028364199	0.13137354	8.292808e-01
## 50	hsa-miR-34a-5p	0.010952102	0.05239301	8.346307e-01
## 24	hsa-miR-200b-3p	-0.024546011	0.17088750	8.859299e-01
## 46	hsa-miR-122-5p	-0.002717991	0.03127446	9.308314e-01
## 23	hsa-miR-200a-3p	-0.020016689	0.28109576	9.433018e-01

```
EV.grade.overlap = left_join(EV.overlap.new, biopsy.grade, by = "Patient ID")
```

```
# EV overlap
```

```
grade.EV.overlap.result = data.frame(
  microRNA = colnames(EV.overlap.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.grade.overlap$`Biopsy Grade Group` ~ EV.overlap.new[,i+1])
  result = summary(model)
  grade.EV.overlap.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.EV.overlap.result$standard.deviation[i] = result$coefficients[2,2]
  grade.EV.overlap.result$p.value[i] = result$coefficients[2,4]
}
```

```
grade.EV.overlap.result = grade.EV.overlap.result[order(grade.EV.overlap.result$p.value),]; grade.EV.ov
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 39	hsa-miR-191-5p	-0.717032793	0.23458852	0.002779304
## 34	hsa-miR-335-5p	-0.259923420	0.08769020	0.003684884
## 5	hsa-miR-107	-0.600390109	0.21831842	0.006913914
## 6	hsa-miR-130b-3p	-0.531191045	0.19570640	0.007657084
## 47	hsa-miR-221-3p	-0.410993911	0.15745002	0.010239287
## 3	hsa-miR-103a-3p	-0.528797187	0.20497517	0.011134040
## 11	hsa-miR-30c-5p	-0.594040007	0.26657917	0.027782758
## 1	hsa-let-7a-5p	-0.329117578	0.15377456	0.034427976
## 10	hsa-miR-26b-5p	-0.422574536	0.20350144	0.040054672
## 33	hsa-miR-330-3p	-0.227634837	0.11371075	0.047631497
## 45	hsa-miR-199a-5p	-0.203789482	0.10898830	0.064028749
## 55	hsa-miR-143-3p	0.275599147	0.15084929	0.070273226
## 44	hsa-miR-30a-5p	0.250100538	0.14567934	0.088686912

## 41	hsa-miR-199a-3p	-0.325059284	0.19736974	0.102273562
## 36	hsa-miR-363-3p	0.194587541	0.11900933	0.104747052
## 56	hsa-miR-148a-3p	0.250287196	0.16229425	0.125753130
## 49	hsa-miR-31-5p	-0.137567553	0.09009953	0.129522941
## 12	hsa-miR-451a	0.156536199	0.10686791	0.145690525
## 27	hsa-miR-214-3p	0.124143630	0.08607541	0.151921944
## 9	hsa-miR-24-3p	-0.387650701	0.28376001	0.174543383
## 30	hsa-miR-301a-3p	-0.188097126	0.13927692	0.179476107
## 51	hsa-miR-27b-3p	-0.395832444	0.29464123	0.181752191
## 20	hsa-miR-19b-3p	0.216692398	0.16859763	0.201260384
## 13	hsa-miR-874-3p	0.175637248	0.14167344	0.217576285
## 40	hsa-miR-23a-3p	-0.349210179	0.28360985	0.220699403
## 19	hsa-miR-18b-5p	0.269592863	0.21999744	0.222893134
## 50	hsa-miR-34a-5p	0.085999390	0.07514392	0.254787922
## 25	hsa-miR-204-5p	-0.085373209	0.07714376	0.270723409
## 32	hsa-miR-27a-3p	-0.326651492	0.31275710	0.298460183
## 8	hsa-miR-223-3p	-0.138577473	0.13747277	0.315535380
## 29	hsa-miR-16-5p	0.131294684	0.14079099	0.352989135
## 22	hsa-miR-194-5p	0.103778973	0.11152146	0.354006577
## 23	hsa-miR-200a-3p	0.034126582	0.04054741	0.401717674
## 35	hsa-miR-345-5p	-0.161572097	0.20037235	0.421685815
## 54	hsa-miR-125b-5p	0.103438938	0.13516973	0.445675526
## 52	hsa-miR-25-3p	0.111081281	0.14726516	0.452200996
## 26	hsa-miR-210-3p	0.077597688	0.11981719	0.518501416
## 57	hsa-miR-374a-5p	-0.120949693	0.18681040	0.518622444
## 7	hsa-miR-146a-5p	-0.113838068	0.17616491	0.519425132
## 37	hsa-miR-375	-0.021972568	0.03980031	0.581962296
## 31	hsa-miR-320a	-0.061435392	0.12095500	0.612474322
## 2	hsa-miR-100-5p	-0.048998810	0.09908620	0.621883477
## 15	hsa-let-7i-5p	-0.099343071	0.24927051	0.690968347
## 48	hsa-miR-29a-3p	0.087026800	0.22164269	0.695302579
## 17	hsa-miR-141-3p	-0.033020020	0.10160669	0.745782488
## 21	hsa-miR-193a-3p	-0.207454031	0.68304041	0.761884209
## 46	hsa-miR-122-5p	0.008058367	0.03820029	0.833296076
## 4	hsa-miR-106a-5p	-0.049072712	0.24184719	0.839562477
## 28	hsa-miR-222-3p	0.088009042	0.43946166	0.841623562
## 42	hsa-miR-21-5p	-0.048644631	0.26332534	0.853761786
## 18	hsa-miR-146b-3p	-0.027175806	0.17892875	0.879544948
## 24	hsa-miR-200b-3p	0.004425680	0.03005721	0.883196730
## 16	hsa-miR-1246	-0.014635657	0.12446883	0.906599914
## 53	hsa-miR-155-5p	0.009612743	0.10537313	0.927470560
## 38	hsa-miR-574-3p	-0.014374684	0.18219092	0.937248890
## 43	hsa-let-7b-5p	0.008670638	0.19830897	0.965200482
## 14	hsa-miR-93-5p	0.003443433	0.23186403	0.988176496

```
# EV geNorm
```

```
grade.EV.geNorm.result = data.frame(
  microRNA = colnames(EV.geNorm.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.grade.overlap$`Biopsy Grade Group` ~ EV.geNorm.new[,i+1])
```

```

result = summary(model)
grade.EV.geNorm.result$coefficient.estimates[i] = result$coefficients[2,1]
grade.EV.geNorm.result$standard.deviation[i] = result$coefficients[2,2]
grade.EV.geNorm.result$p.value[i] = result$coefficients[2,4]
}

grade.EV.geNorm.result = grade.EV.geNorm.result[order(grade.EV.geNorm.result$p.value),]; grade.EV.geNorm

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 39	hsa-miR-191-5p	-0.542434155	0.17700281	0.002711548
## 6	hsa-miR-130b-3p	-0.488227764	0.16253626	0.003267009
## 34	hsa-miR-335-5p	-0.230527329	0.07742905	0.003541176
## 5	hsa-miR-107	-0.530338309	0.18018495	0.003923106
## 3	hsa-miR-103a-3p	-0.475156066	0.17069787	0.006278512
## 47	hsa-miR-221-3p	-0.338011894	0.12368549	0.007262618
## 10	hsa-miR-26b-5p	-0.487837676	0.18800012	0.010683581
## 11	hsa-miR-30c-5p	-0.478086536	0.19346642	0.014920451
## 1	hsa-let-7a-5p	-0.321066890	0.13422574	0.018364204
## 33	hsa-miR-330-3p	-0.227256667	0.10354029	0.030165407
## 41	hsa-miR-199a-3p	-0.320201668	0.15603029	0.042403117
## 45	hsa-miR-199a-5p	-0.191366603	0.09356731	0.043094604
## 9	hsa-miR-24-3p	-0.406316653	0.20424616	0.049016043
## 51	hsa-miR-27b-3p	-0.408264108	0.21472310	0.059736809
## 40	hsa-miR-23a-3p	-0.390078177	0.20602318	0.060799974
## 32	hsa-miR-27a-3p	-0.392292328	0.22213781	0.080028976
## 49	hsa-miR-31-5p	-0.154249656	0.09450943	0.105368416
## 35	hsa-miR-345-5p	-0.299549375	0.19300013	0.123369998
## 8	hsa-miR-223-3p	-0.182274582	0.12355565	0.142856404
## 30	hsa-miR-301a-3p	-0.187273144	0.13036312	0.153537465
## 36	hsa-miR-363-3p	0.199781086	0.13979863	0.155673466
## 28	hsa-miR-222-3p	-0.408796490	0.32208744	0.206906946
## 27	hsa-miR-214-3p	0.114782985	0.09121226	0.210768216
## 12	hsa-miR-451a	0.157105952	0.12556440	0.213379677
## 7	hsa-miR-146a-5p	-0.173425402	0.13926172	0.215523855
## 25	hsa-miR-204-5p	-0.091100442	0.07357477	0.218141150
## 15	hsa-let-7i-5p	-0.299504697	0.24387069	0.221884584
## 57	hsa-miR-374a-5p	-0.204529132	0.17624760	0.248242341
## 55	hsa-miR-143-3p	0.178582467	0.15559298	0.253431708
## 42	hsa-miR-21-5p	-0.266332186	0.23221178	0.253768016
## 31	hsa-miR-320a	-0.122922384	0.11214085	0.275286783
## 4	hsa-miR-106a-5p	-0.277395541	0.26011304	0.288438328
## 44	hsa-miR-30a-5p	0.163588209	0.15770782	0.301759743
## 56	hsa-miR-148a-3p	0.176915494	0.18537723	0.341889044
## 50	hsa-miR-34a-5p	0.074209549	0.08060720	0.359153362
## 14	hsa-miR-93-5p	-0.222626372	0.25406350	0.382698216
## 23	hsa-miR-200a-3p	0.034187106	0.04222979	0.419856622
## 38	hsa-miR-574-3p	-0.128159769	0.15922520	0.422526220
## 37	hsa-miR-375	-0.031672670	0.04011003	0.431346469
## 20	hsa-miR-19b-3p	0.150796067	0.19874358	0.449542941
## 2	hsa-miR-100-5p	-0.076214939	0.10148210	0.454162346
## 43	hsa-let-7b-5p	-0.164329693	0.22430727	0.465274250
## 16	hsa-miR-1246	-0.095079893	0.13002883	0.466118308
## 22	hsa-miR-194-5p	0.080630960	0.12241090	0.511399509

## 29	hsa-miR-16-5p	0.087181364	0.16392196	0.595849239
## 13	hsa-miR-874-3p	0.072723113	0.14128469	0.607722841
## 17	hsa-miR-141-3p	-0.047126409	0.10200768	0.644954614
## 48	hsa-miR-29a-3p	-0.094519000	0.22439963	0.674382368
## 19	hsa-miR-18b-5p	0.086378601	0.21571382	0.689575269
## 21	hsa-miR-193a-3p	-0.206401577	0.66877908	0.758160790
## 53	hsa-miR-155-5p	-0.030800705	0.10560787	0.771073917
## 52	hsa-miR-25-3p	0.038332729	0.16737508	0.819254393
## 54	hsa-miR-125b-5p	0.033762675	0.15015896	0.822494504
## 18	hsa-miR-146b-3p	-0.037411745	0.18119961	0.836788071
## 26	hsa-miR-210-3p	0.026205113	0.12936141	0.839823765
## 46	hsa-miR-122-5p	0.006540394	0.04584446	0.886802374
## 24	hsa-miR-200b-3p	0.003385959	0.03131064	0.914070810

EV Norm Finder

```

grade.EV.NormFinder.result = data.frame(
  microRNA = colnames(EV.NormFinder.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.grade.overlap$'Biopsy Grade Group' ~ EV.NormFinder.new[,i+1])
  result = summary(model)
  grade.EV.NormFinder.result$coefficient.estimates[i] = result$coefficients[2,1]
  grade.EV.NormFinder.result$standard.deviation[i] = result$coefficients[2,2]
  grade.EV.NormFinder.result$p.value[i] = result$coefficients[2,4]
}

```

```

grade.EV.NormFinder.result = grade.EV.NormFinder.result[order(grade.EV.NormFinder.result$p.value),]; gr

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 34	hsa-miR-335-5p	-0.284985328	0.09770089	0.004245477
## 39	hsa-miR-191-5p	-0.860794833	0.30689644	0.005904356
## 47	hsa-miR-221-3p	-0.480620320	0.20258973	0.019319312
## 55	hsa-miR-143-3p	0.316350175	0.13694505	0.022653518
## 5	hsa-miR-107	-0.551305748	0.24397259	0.025706531
## 6	hsa-miR-130b-3p	-0.466228904	0.21797174	0.034537036
## 44	hsa-miR-30a-5p	0.266198830	0.12476214	0.034977767
## 3	hsa-miR-103a-3p	-0.487225633	0.22893138	0.035431722
## 28	hsa-miR-222-3p	0.843029623	0.42260612	0.048405446
## 56	hsa-miR-148a-3p	0.256409042	0.13566743	0.061256064
## 19	hsa-miR-18b-5p	0.363446571	0.19831729	0.069419058
## 13	hsa-miR-874-3p	0.230382026	0.12949651	0.077849091
## 33	hsa-miR-330-3p	-0.212180583	0.12034155	0.080507934
## 1	hsa-let-7a-5p	-0.293038296	0.16701895	0.081981787
## 36	hsa-miR-363-3p	0.171827721	0.10014086	0.088857253
## 45	hsa-miR-199a-5p	-0.201755299	0.12364257	0.105441483
## 11	hsa-miR-30c-5p	-0.583676675	0.36387603	0.111421540
## 12	hsa-miR-451a	0.142550096	0.09037981	0.117465010
## 20	hsa-miR-19b-3p	0.217218555	0.13815033	0.118596616
## 27	hsa-miR-214-3p	0.123861042	0.07936335	0.121322648
## 49	hsa-miR-31-5p	-0.120192084	0.08468392	0.158492469
## 10	hsa-miR-26b-5p	-0.266395883	0.19428116	0.172963381

## 50	hsa-miR-34a-5p	0.086481533	0.06719915	0.200676029
## 30	hsa-miR-301a-3p	-0.176624449	0.14225760	0.216895541
## 29	hsa-miR-16-5p	0.138674033	0.11819746	0.243102881
## 22	hsa-miR-194-5p	0.110111673	0.09883885	0.267559653
## 54	hsa-miR-125b-5p	0.125354564	0.11319218	0.270390968
## 52	hsa-miR-25-3p	0.136607267	0.12496723	0.276595198
## 48	hsa-miR-29a-3p	0.206947689	0.19722659	0.296226340
## 41	hsa-miR-199a-3p	-0.242287327	0.24160794	0.318038887
## 26	hsa-miR-210-3p	0.103872919	0.10688975	0.333183886
## 25	hsa-miR-204-5p	-0.074314768	0.07854100	0.346018140
## 23	hsa-miR-200a-3p	0.033980049	0.03891130	0.384320453
## 42	hsa-miR-21-5p	0.207847847	0.25278972	0.412640641
## 38	hsa-miR-574-3p	0.133836256	0.18816827	0.478351948
## 14	hsa-miR-93-5p	0.120817990	0.19067659	0.527571128
## 43	hsa-let-7b-5p	0.092389209	0.16210463	0.569823496
## 8	hsa-miR-223-3p	-0.067469075	0.14656405	0.646135035
## 53	hsa-miR-155-5p	0.044649535	0.10003134	0.656172637
## 4	hsa-miR-106a-5p	0.083981201	0.19843438	0.672919092
## 16	hsa-miR-1246	0.044694874	0.11166082	0.689691219
## 15	hsa-let-7i-5p	0.075106084	0.22044695	0.733946349
## 32	hsa-miR-27a-3p	0.142585853	0.42238664	0.736295922
## 37	hsa-miR-375	-0.012676453	0.03780706	0.738009458
## 21	hsa-miR-193a-3p	-0.208095078	0.69136671	0.763960286
## 51	hsa-miR-27b-3p	-0.113796221	0.37815113	0.764008205
## 2	hsa-miR-100-5p	-0.025194073	0.09334418	0.787712808
## 46	hsa-miR-122-5p	0.007858272	0.03104194	0.800600294
## 7	hsa-miR-146a-5p	0.052945393	0.21871061	0.809145888
## 17	hsa-miR-141-3p	-0.020446550	0.09973354	0.837922233
## 24	hsa-miR-200b-3p	0.005100988	0.02879414	0.859696621
## 9	hsa-miR-24-3p	-0.064361807	0.39053538	0.869385072
## 57	hsa-miR-374a-5p	-0.020565398	0.17752962	0.907978012
## 31	hsa-miR-320a	0.012421892	0.12072974	0.918227875
## 18	hsa-miR-146b-3p	-0.017616214	0.17500277	0.919992167
## 35	hsa-miR-345-5p	-0.014892286	0.18468002	0.935868554
## 40	hsa-miR-23a-3p	-0.002430101	0.38492546	0.994973694

```
# Collect the results
```

```
# univariate GLM
```

```
adverse.serum.result = data.frame(
  microRNA = colnames(serum.geneglobe.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$`Adverse Pathology`~serum.all.original[,i+1], family = "binomial")
  result = summary(model)
  adverse.serum.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.serum.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.serum.result$p.value[i] = result$coefficients[2,4]
}

adverse.EV.result = data.frame(
```

```

microRNA = colnames(EV.geneglobe.new)[-1],
coefficient.estimates = numeric(57),
standard.deviation = numeric(57),
p.value = numeric(57)
)

for (i in 1:57) {
  model = glm(formula = EV.all.original$`Adverse Pathology`~EV.all.original[,i+1], family = "binomial")
  result = summary(model)
  adverse.EV.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.EV.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.EV.result$p.value[i] = result$coefficients[2,4]
}

# Display result
adverse.serum.geneglobe.result = adverse.serum.result[order(grade.serum.result$p.value),];adverse.serum

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 27	hsa-miR-214-3p	1.636269e-01	0.22779323	0.4725642
## 30	hsa-miR-301a-3p	-6.340394e-02	0.08759781	0.4691840
## 54	hsa-miR-125b-5p	-4.739856e-02	0.11386427	0.6772107
## 57	hsa-miR-374a-5p	-1.742749e-02	0.05527409	0.7525398
## 16	hsa-miR-1246	-1.595357e-01	0.17914020	0.3731633
## 22	hsa-miR-194-5p	-5.054277e-02	0.07782552	0.5160560
## 1	hsa-let-7a-5p	-5.815640e-02	0.10259354	0.5708078
## 26	hsa-miR-210-3p	-2.948754e-02	0.06978108	0.6726075
## 2	hsa-miR-100-5p	-2.793520e-01	0.28095327	0.3200766
## 36	hsa-miR-363-3p	-1.687577e-02	0.02835555	0.5517441
## 21	hsa-miR-193a-3p	-1.078924e+01	995.93424235	0.9913565
## 12	hsa-miR-451a	-1.726871e-02	0.02910727	0.5529950
## 4	hsa-miR-106a-5p	-1.780420e-02	0.04032471	0.6588360
## 29	hsa-miR-16-5p	-1.529534e-02	0.03732333	0.6819480
## 43	hsa-let-7b-5p	-1.435958e-02	0.05441147	0.7918514
## 37	hsa-miR-375	-1.438232e-01	0.10863550	0.1855343
## 19	hsa-miR-18b-5p	-1.071569e-02	0.04852882	0.8252398
## 20	hsa-miR-19b-3p	-2.807400e-02	0.04883464	0.5653733
## 49	hsa-miR-31-5p	-5.296181e-01	0.43366874	0.2219913
## 14	hsa-miR-93-5p	-1.555471e-02	0.04159123	0.7084117
## 13	hsa-miR-874-3p	-1.767166e-01	0.23828787	0.4583238
## 46	hsa-miR-122-5p	-1.098832e-01	0.08335869	0.1874375
## 56	hsa-miR-148a-3p	-6.912534e-02	0.08716665	0.4277632
## 17	hsa-miR-141-3p	1.266773e-01	0.28144529	0.6526415
## 15	hsa-let-7i-5p	-2.261428e-02	0.06731411	0.7369074
## 35	hsa-miR-345-5p	3.624916e-02	0.11010252	0.7419811
## 5	hsa-miR-107	-1.541960e-03	0.05178812	0.9762470
## 3	hsa-miR-103a-3p	-7.733975e-04	0.05335456	0.9884347
## 10	hsa-miR-26b-5p	-1.776254e-02	0.08142546	0.8273163
## 50	hsa-miR-34a-5p	-1.469316e-01	0.17858788	0.4106551
## 11	hsa-miR-30c-5p	-3.265028e-02	0.10546571	0.7568789
## 48	hsa-miR-29a-3p	-2.297746e-02	0.14106207	0.8706059
## 8	hsa-miR-223-3p	5.955460e-02	0.08444860	0.4806751
## 55	hsa-miR-143-3p	-6.882334e-02	0.17838172	0.6996296
## 34	hsa-miR-335-5p	1.186085e-01	0.18803654	0.5281884

## 6	hsa-miR-130b-3p	6.170570e-02	0.15861680	0.6972586
## 52	hsa-miR-25-3p	-1.761218e-02	0.04760089	0.7113847
## 23	hsa-miR-200a-3p	-4.871313e-01	0.60553589	0.4211295
## 24	hsa-miR-200b-3p	-4.880808e-01	0.38011447	0.1991292
## 38	hsa-miR-574-3p	1.467220e-02	0.06707455	0.8268490
## 40	hsa-miR-23a-3p	8.702211e-02	0.12146928	0.4737367
## 31	hsa-miR-320a	1.378718e-02	0.10268161	0.8931882
## 45	hsa-miR-199a-5p	7.022003e-02	0.09080523	0.4393426
## 33	hsa-miR-330-3p	1.200101e-01	0.17517456	0.4932881
## 44	hsa-miR-30a-5p	-2.130378e-01	0.20909443	0.3082697
## 25	hsa-miR-204-5p	3.993695e-02	0.22987725	0.8620764
## 47	hsa-miR-221-3p	4.867126e-02	0.07494440	0.5160594
## 39	hsa-miR-191-5p	2.752726e-02	0.05903736	0.6410234
## 9	hsa-miR-24-3p	5.030615e-02	0.09162081	0.5829580
## 18	hsa-miR-146b-3p	7.851333e+00	741.24087496	0.9915488
## 32	hsa-miR-27a-3p	5.830496e-02	0.09140945	0.5235753
## 41	hsa-miR-199a-3p	6.511924e-02	0.09791341	0.5060060
## 28	hsa-miR-222-3p	3.691656e-02	0.09162382	0.6870112
## 7	hsa-miR-146a-5p	5.050776e-02	0.07976619	0.5266047
## 53	hsa-miR-155-5p	9.906847e-02	0.23973866	0.6794343
## 42	hsa-miR-21-5p	-1.707690e-03	0.11993382	0.9886396
## 51	hsa-miR-27b-3p	5.175303e-02	0.08391350	0.5374045

```
adverse.EV.geneglobe.result = grade.EV.geneglobe.result[order(grade.EV.result$p.value),]; adverse.EV.geneglobe.result
```

##	microRNA	coefficient.estimate	standard.deviation	p.value
## 44	hsa-miR-30a-5p	-0.034728553	0.03759133	0.60183565
## 31	hsa-miR-320a	-0.047549965	0.03759133	0.24737334
## 15	hsa-let-7i-5p	-0.074196456	0.03759133	0.17196238
## 49	hsa-miR-31-5p	-0.131808289	0.03759133	0.04520534
## 5	hsa-miR-107	-0.053798725	0.03759133	0.13448416
## 54	hsa-miR-125b-5p	-0.044962299	0.03759133	0.42032819
## 10	hsa-miR-26b-5p	-0.067564280	0.03759133	0.11648496
## 7	hsa-miR-146a-5p	-0.017954055	0.03759133	0.52840661
## 6	hsa-miR-130b-3p	-0.048664698	0.03759133	0.18587627
## 47	hsa-miR-221-3p	-0.037742416	0.03759133	0.21769537
## 34	hsa-miR-335-5p	-0.047381797	0.03759133	0.14074698
## 33	hsa-miR-330-3p	-0.058811806	0.03759133	0.23954683
## 37	hsa-miR-375	-0.023232795	0.03759133	0.46317593
## 22	hsa-miR-194-5p	-0.029836713	0.03759133	0.51954857
## 56	hsa-miR-148a-3p	-0.026445305	0.03759133	0.59072884
## 51	hsa-miR-27b-3p	-0.026236641	0.03759133	0.41635472
## 32	hsa-miR-27a-3p	-0.026295802	0.03759133	0.40058567
## 18	hsa-miR-146b-3p	-0.012767671	0.03759133	0.94411261
## 1	hsa-let-7a-5p	-0.058118043	0.03759133	0.13254292
## 52	hsa-miR-25-3p	-0.039482119	0.03759133	0.35705321
## 42	hsa-miR-21-5p	-0.062744315	0.03759133	0.21578046
## 11	hsa-miR-30c-5p	-0.055768397	0.03759133	0.17135788
## 53	hsa-miR-155-5p	-0.057765954	0.03759133	0.33989789
## 26	hsa-miR-210-3p	-0.032454294	0.03759133	0.59476185
## 19	hsa-miR-18b-5p	-0.009408160	0.03759133	0.81338283
## 36	hsa-miR-363-3p	-0.024075660	0.03759133	0.50409554
## 43	hsa-let-7b-5p	-0.080946097	0.03759133	0.15913141
## 21	hsa-miR-193a-3p	-0.054530198	0.03759133	0.74146666

## 16	hsa-miR-1246	-0.072254452	0.03759133	0.20865896
## 20	hsa-miR-19b-3p	-0.031559043	0.03759133	0.51813887
## 30	hsa-miR-301a-3p	-0.039746064	0.03759133	0.41139919
## 41	hsa-miR-199a-3p	-0.023833980	0.03759133	0.37712215
## 38	hsa-miR-574-3p	-0.016096336	0.03759133	0.73977417
## 27	hsa-miR-214-3p	0.007204922	0.03759133	0.87100940
## 35	hsa-miR-345-5p	-0.033462475	0.03759133	0.42809990
## 12	hsa-miR-451a	-0.033929935	0.03759133	0.37128024
## 25	hsa-miR-204-5p	-0.065420115	0.03759133	0.31412526
## 2	hsa-miR-100-5p	-0.028660043	0.03759133	0.53812457
## 23	hsa-miR-200a-3p	0.046606581	0.03759133	0.44797036
## 29	hsa-miR-16-5p	-0.032005816	0.03759133	0.43198391
## 28	hsa-miR-222-3p	-0.051484490	0.03759133	0.30720725
## 9	hsa-miR-24-3p	-0.034595548	0.03759133	0.31235522
## 3	hsa-miR-103a-3p	-0.053058698	0.03759133	0.14209210
## 39	hsa-miR-191-5p	-0.046137559	0.03759133	0.20876407
## 17	hsa-miR-141-3p	-0.120785988	0.03759133	0.08577299
## 24	hsa-miR-200b-3p	0.019604887	0.03759133	0.68832026
## 46	hsa-miR-122-5p	-0.003532389	0.03759133	0.89777248
## 40	hsa-miR-23a-3p	-0.031230972	0.03759133	0.34388517
## 13	hsa-miR-874-3p	-0.042209526	0.03759133	0.53343346
## 48	hsa-miR-29a-3p	-0.033496658	0.03759133	0.31569513
## 45	hsa-miR-199a-5p	-0.016949789	0.03759133	0.46228787
## 14	hsa-miR-93-5p	-0.040922890	0.03759133	0.31103152
## 4	hsa-miR-106a-5p	-0.046304713	0.03759133	0.26355347
## 8	hsa-miR-223-3p	-0.020224114	0.03759133	0.35116947
## 55	hsa-miR-143-3p	0.003671712	0.03759133	0.88683142
## 50	hsa-miR-34a-5p	-0.025881068	0.03759133	0.55198908
## 57	hsa-miR-374a-5p	-0.042461776	0.03759133	0.26099079

Serum overlap

```
adverse.serum.overlap.result = data.frame(
  microRNA = colnames(serum.overlap.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$`Adverse Pathology`~serum.overlap.new[,i+1], family = "binom
  result = summary(model)
  adverse.serum.overlap.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.serum.overlap.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.serum.overlap.result$p.value[i] = result$coefficients[2,4]
}
```

```
adverse.serum.overlap.result = adverse.serum.overlap.result[order(adverse.serum.overlap.result$p.value)
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 52	hsa-miR-25-3p	2.090887e+00	8.716106e-01	0.01644542
## 29	hsa-miR-16-5p	1.615554e+00	7.202048e-01	0.02488474
## 1	hsa-let-7a-5p	-1.355481e+00	6.250389e-01	0.03011040
## 11	hsa-miR-30c-5p	-1.298537e+00	6.007532e-01	0.03065560
## 9	hsa-miR-24-3p	-1.476494e+00	6.840354e-01	0.03088860
## 16	hsa-miR-1246	-5.771685e-01	2.803802e-01	0.03954012

## 44	hsa-miR-30a-5p	-5.922105e-01	3.036124e-01	0.05111090
## 46	hsa-miR-122-5p	-2.818011e-01	1.462035e-01	0.05392251
## 3	hsa-miR-103a-3p	-1.552293e+00	8.674026e-01	0.07352016
## 15	hsa-let-7i-5p	-2.081450e+00	1.174070e+00	0.07625369
## 12	hsa-miR-451a	8.009060e-01	4.641847e-01	0.08445475
## 48	hsa-miR-29a-3p	-7.584001e-01	4.409071e-01	0.08541599
## 32	hsa-miR-27a-3p	-9.100101e-01	5.499359e-01	0.09797391
## 28	hsa-miR-222-3p	-7.823457e-01	5.019646e-01	0.11909880
## 5	hsa-miR-107	-1.146328e+00	7.527536e-01	0.12779723
## 36	hsa-miR-363-3p	5.439470e-01	3.591224e-01	0.12985948
## 24	hsa-miR-200b-3p	-1.416410e+00	9.356337e-01	0.13006357
## 38	hsa-miR-574-3p	-5.538446e-01	3.672417e-01	0.13152383
## 20	hsa-miR-19b-3p	1.258557e+00	8.363421e-01	0.13236649
## 41	hsa-miR-199a-3p	-5.775587e-01	3.846590e-01	0.13323088
## 43	hsa-let-7b-5p	1.630707e+00	1.086144e+00	0.13325913
## 37	hsa-miR-375	-3.047476e-01	2.033545e-01	0.13397672
## 25	hsa-miR-204-5p	-1.106738e+00	7.410099e-01	0.13529247
## 56	hsa-miR-148a-3p	-5.243034e-01	3.614094e-01	0.14685819
## 13	hsa-miR-874-3p	-4.823399e-01	3.556521e-01	0.17503143
## 47	hsa-miR-221-3p	-4.820942e-01	3.643203e-01	0.18574560
## 51	hsa-miR-27b-3p	-7.012481e-01	5.495133e-01	0.20191111
## 42	hsa-miR-21-5p	-8.907918e-01	7.008326e-01	0.20371162
## 2	hsa-miR-100-5p	-4.581562e-01	3.699594e-01	0.21556926
## 14	hsa-miR-93-5p	7.798238e-01	6.303820e-01	0.21606279
## 40	hsa-miR-23a-3p	-6.618113e-01	5.602210e-01	0.23746778
## 7	hsa-miR-146a-5p	-4.697652e-01	4.082905e-01	0.24991076
## 27	hsa-miR-214-3p	3.600160e-01	3.339265e-01	0.28097609
## 53	hsa-miR-155-5p	5.516746e-01	5.336870e-01	0.30127433
## 10	hsa-miR-26b-5p	-4.282928e-01	4.366710e-01	0.32668478
## 22	hsa-miR-194-5p	-1.828617e-01	2.043477e-01	0.37086415
## 49	hsa-miR-31-5p	-2.176451e-01	2.456558e-01	0.37563061
## 35	hsa-miR-345-5p	-2.693653e-01	3.048243e-01	0.37687227
## 50	hsa-miR-34a-5p	-1.327514e-01	1.688557e-01	0.43176053
## 33	hsa-miR-330-3p	2.967732e-01	4.318557e-01	0.49195383
## 4	hsa-miR-106a-5p	5.358765e-01	7.817068e-01	0.49301511
## 17	hsa-miR-141-3p	3.086088e-01	4.711420e-01	0.51245308
## 39	hsa-miR-191-5p	-3.051563e-01	4.947498e-01	0.53737382
## 31	hsa-miR-320a	-2.233326e-01	3.961509e-01	0.57292001
## 8	hsa-miR-223-3p	-1.866717e-01	3.528776e-01	0.59680649
## 55	hsa-miR-143-3p	-1.447435e-01	2.921180e-01	0.62024963
## 57	hsa-miR-374a-5p	-1.693405e-01	3.599488e-01	0.63802842
## 45	hsa-miR-199a-5p	-1.109986e-01	2.475703e-01	0.65389918
## 23	hsa-miR-200a-3p	-8.843425e-01	2.432184e+00	0.71615655
## 54	hsa-miR-125b-5p	-8.024785e-02	2.531465e-01	0.75124237
## 19	hsa-miR-18b-5p	-4.634130e-02	3.498725e-01	0.89462681
## 6	hsa-miR-130b-3p	3.820223e-02	4.631916e-01	0.93426813
## 34	hsa-miR-335-5p	-9.522012e-03	4.249347e-01	0.98212236
## 21	hsa-miR-193a-3p	-2.423435e+02	2.237026e+04	0.99135646
## 18	hsa-miR-146b-3p	1.804159e+02	1.703298e+04	0.99154885
## 26	hsa-miR-210-3p	2.179232e-03	4.961552e-01	0.99649551
## 30	hsa-miR-301a-3p	-6.276195e-04	4.620374e-01	0.99891617

Serum geNorm

```
adverse.serum.geNorm.result = data.frame(
```



```

microRNA = colnames(serum.geNorm.new)[-1],
coefficient.estimates = numeric(57),
standard.deviation = numeric(57),
p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$`Adverse Pathology`~serum.geNorm.new[,i+1], family = "binomial")
  result = summary(model)
  adverse.serum.geNorm.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.serum.geNorm.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.serum.geNorm.result$p.value[i] = result$coefficients[2,4]
}

adverse.serum.geNorm.result = adverse.serum.geNorm.result[order(adverse.serum.geNorm.result$p.value),];

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 52	hsa-miR-25-3p	2.035368e+00	8.300413e-01	0.01420137
## 11	hsa-miR-30c-5p	-1.483945e+00	6.446452e-01	0.02133767
## 29	hsa-miR-16-5p	1.530161e+00	6.695018e-01	0.02228227
## 1	hsa-let-7a-5p	-1.440205e+00	6.562058e-01	0.02818181
## 16	hsa-miR-1246	-6.471745e-01	2.991925e-01	0.03053576
## 9	hsa-miR-24-3p	-1.460955e+00	6.946247e-01	0.03544578
## 46	hsa-miR-122-5p	-2.701017e-01	1.450505e-01	0.06258600
## 44	hsa-miR-30a-5p	-5.474236e-01	3.016739e-01	0.06958225
## 12	hsa-miR-451a	8.113833e-01	4.523005e-01	0.07282862
## 3	hsa-miR-103a-3p	-1.551352e+00	8.861837e-01	0.08001504
## 43	hsa-let-7b-5p	1.839409e+00	1.055761e+00	0.08146327
## 48	hsa-miR-29a-3p	-7.339371e-01	4.462309e-01	0.10002192
## 32	hsa-miR-27a-3p	-9.113370e-01	5.588731e-01	0.10296016
## 20	hsa-miR-19b-3p	1.181016e+00	7.344461e-01	0.10782712
## 36	hsa-miR-363-3p	5.394087e-01	3.505696e-01	0.12388637
## 24	hsa-miR-200b-3p	-1.502561e+00	9.857575e-01	0.12744120
## 15	hsa-let-7i-5p	-1.684617e+00	1.110983e+00	0.12943593
## 25	hsa-miR-204-5p	-1.101408e+00	7.529801e-01	0.14354074
## 41	hsa-miR-199a-3p	-5.385647e-01	3.710264e-01	0.14662576
## 38	hsa-miR-574-3p	-5.343927e-01	3.698212e-01	0.14845705
## 56	hsa-miR-148a-3p	-5.310059e-01	3.685468e-01	0.14963835
## 37	hsa-miR-375	-2.930221e-01	2.041184e-01	0.15113066
## 28	hsa-miR-222-3p	-6.468562e-01	4.598788e-01	0.15955206
## 13	hsa-miR-874-3p	-4.976469e-01	3.578292e-01	0.16430465
## 14	hsa-miR-93-5p	8.795390e-01	6.408750e-01	0.16993789
## 5	hsa-miR-107	-1.007447e+00	7.409546e-01	0.17393741
## 47	hsa-miR-221-3p	-4.507810e-01	3.548811e-01	0.20400229
## 51	hsa-miR-27b-3p	-6.855488e-01	5.533490e-01	0.21537937
## 2	hsa-miR-100-5p	-4.594144e-01	3.726265e-01	0.21760986
## 40	hsa-miR-23a-3p	-6.990692e-01	5.843156e-01	0.23154453
## 7	hsa-miR-146a-5p	-4.217034e-01	3.826381e-01	0.27042063
## 27	hsa-miR-214-3p	3.634971e-01	3.404797e-01	0.28569973
## 42	hsa-miR-21-5p	-6.735273e-01	6.418784e-01	0.29403697
## 53	hsa-miR-155-5p	5.382820e-01	5.341752e-01	0.31360417
## 49	hsa-miR-31-5p	-2.237487e-01	2.414081e-01	0.35400524
## 22	hsa-miR-194-5p	-1.642362e-01	1.898309e-01	0.38694466
## 10	hsa-miR-26b-5p	-3.592135e-01	4.401688e-01	0.41445372

```
## 35 hsa-miR-345-5p -2.482234e-01 3.049162e-01 0.41560447
## 4 hsa-miR-106a-5p 5.924360e-01 7.352487e-01 0.42037967
## 50 hsa-miR-34a-5p -1.210904e-01 1.533169e-01 0.42964187
## 33 hsa-miR-330-3p 3.225822e-01 4.293031e-01 0.45240656
## 17 hsa-miR-141-3p 3.092796e-01 4.753316e-01 0.51526543
## 39 hsa-miR-191-5p -2.735208e-01 4.991032e-01 0.58367511
## 8 hsa-miR-223-3p -1.985746e-01 3.819684e-01 0.60315289
## 55 hsa-miR-143-3p -1.349068e-01 3.000633e-01 0.65300279
## 31 hsa-miR-320a -1.430796e-01 3.401956e-01 0.67406154
## 45 hsa-miR-199a-5p -9.825790e-02 2.429761e-01 0.68592352
## 23 hsa-miR-200a-3p -8.970598e-01 2.481205e+00 0.71769428
## 57 hsa-miR-374a-5p -1.244043e-01 3.513407e-01 0.72327556
## 6 hsa-miR-130b-3p 7.650762e-02 4.530430e-01 0.86589499
## 54 hsa-miR-125b-5p -3.488528e-02 2.459137e-01 0.88719073
## 26 hsa-miR-210-3p -3.721493e-02 4.932646e-01 0.93985971
## 19 hsa-miR-18b-5p -2.306884e-02 3.391759e-01 0.94577418
## 34 hsa-miR-335-5p -1.114564e-02 4.191056e-01 0.97878367
## 21 hsa-miR-193a-3p -2.403363e+02 2.218499e+04 0.99135646
## 18 hsa-miR-146b-3p 1.736847e+02 1.639749e+04 0.99154885
## 30 hsa-miR-301a-3p -8.313869e-04 4.626399e-01 0.99856616
```

```
# Serum NormFinder
```

```
adverse.serum.NormFinder.result = data.frame(
  microRNA = colnames(serum.NormFinder.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = serum.all.original$'Adverse Pathology'~serum.NormFinder.new[,i+1], family = "binomial")
  result = summary(model)
  adverse.serum.NormFinder.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.serum.NormFinder.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.serum.NormFinder.result$p.value[i] = result$coefficients[2,4]
}

adverse.serum.NormFinder.result = adverse.serum.NormFinder.result[order(adverse.serum.NormFinder.result$p.value),]
```

```
## microRNA coefficient.estimates standard.deviation p.value
## 52 hsa-miR-25-3p 1.715697e+00 7.634822e-01 0.02462729
## 16 hsa-miR-1246 -6.222907e-01 2.951999e-01 0.03502824
## 9 hsa-miR-24-3p -1.545426e+00 7.472620e-01 0.03862890
## 11 hsa-miR-30c-5p -1.292387e+00 6.315247e-01 0.04071166
## 29 hsa-miR-16-5p 1.231205e+00 6.091459e-01 0.04325918
## 1 hsa-let-7a-5p -1.216516e+00 6.172054e-01 0.04872314
## 44 hsa-miR-30a-5p -6.051467e-01 3.106174e-01 0.05139031
## 46 hsa-miR-122-5p -2.746607e-01 1.458501e-01 0.05967715
## 48 hsa-miR-29a-3p -8.080544e-01 4.811713e-01 0.09308408
## 32 hsa-miR-27a-3p -9.518543e-01 5.974440e-01 0.11111287
## 20 hsa-miR-19b-3p 1.265507e+00 8.031780e-01 0.11511221
## 38 hsa-miR-574-3p -5.687328e-01 3.741714e-01 0.12851617
## 12 hsa-miR-451a 6.264520e-01 4.130550e-01 0.12935989
## 25 hsa-miR-204-5p -1.141955e+00 7.563018e-01 0.13106389
## 3 hsa-miR-103a-3p -1.183146e+00 7.894916e-01 0.13397287
```


## 24	hsa-miR-200b-3p	-1.433134e+00	9.565341e-01	0.13406658
## 37	hsa-miR-375	-3.082428e-01	2.062748e-01	0.13508907
## 43	hsa-let-7b-5p	1.342989e+00	9.125044e-01	0.14108539
## 28	hsa-miR-222-3p	-7.879220e-01	5.419409e-01	0.14597708
## 41	hsa-miR-199a-3p	-5.715587e-01	4.060648e-01	0.15926278
## 13	hsa-miR-874-3p	-5.017362e-01	3.619503e-01	0.16568526
## 15	hsa-let-7i-5p	-1.454927e+00	1.058896e+00	0.16944024
## 36	hsa-miR-363-3p	4.607982e-01	3.398133e-01	0.17508854
## 42	hsa-miR-21-5p	-1.100672e+00	8.267388e-01	0.18307641
## 56	hsa-miR-148a-3p	-5.049462e-01	3.793172e-01	0.18312395
## 14	hsa-miR-93-5p	7.408525e-01	5.772347e-01	0.19933415
## 5	hsa-miR-107	-8.887061e-01	7.061864e-01	0.20822605
## 2	hsa-miR-100-5p	-4.566511e-01	3.737813e-01	0.22181866
## 47	hsa-miR-221-3p	-4.553039e-01	3.748433e-01	0.22449911
## 51	hsa-miR-27b-3p	-6.899639e-01	5.916293e-01	0.24352963
## 27	hsa-miR-214-3p	3.672705e-01	3.356021e-01	0.27379582
## 40	hsa-miR-23a-3p	-6.704923e-01	6.239140e-01	0.28252918
## 53	hsa-miR-155-5p	5.454816e-01	5.300057e-01	0.30338588
## 7	hsa-miR-146a-5p	-4.397915e-01	4.438917e-01	0.32180127
## 35	hsa-miR-345-5p	-2.972779e-01	3.182141e-01	0.35019702
## 49	hsa-miR-31-5p	-2.294292e-01	2.670740e-01	0.39031454
## 10	hsa-miR-26b-5p	-3.829496e-01	4.473645e-01	0.39199086
## 22	hsa-miR-194-5p	-1.691414e-01	2.180595e-01	0.43794602
## 4	hsa-miR-106a-5p	4.848808e-01	6.802145e-01	0.47594774
## 50	hsa-miR-34a-5p	-1.295112e-01	1.842593e-01	0.48213374
## 33	hsa-miR-330-3p	2.915648e-01	4.347805e-01	0.50247392
## 17	hsa-miR-141-3p	3.198987e-01	4.819782e-01	0.50686930
## 39	hsa-miR-191-5p	-2.589498e-01	5.086385e-01	0.61067938
## 31	hsa-miR-320a	-2.019864e-01	4.237848e-01	0.63362934
## 55	hsa-miR-143-3p	-1.404975e-01	3.053406e-01	0.64542038
## 8	hsa-miR-223-3p	-1.568953e-01	3.674242e-01	0.66936915
## 45	hsa-miR-199a-5p	-1.008332e-01	2.468949e-01	0.68297600
## 57	hsa-miR-374a-5p	-1.424758e-01	3.613358e-01	0.69335740
## 23	hsa-miR-200a-3p	-9.375991e-01	2.439185e+00	0.70068910
## 54	hsa-miR-125b-5p	-5.655832e-02	2.631378e-01	0.82981565
## 19	hsa-miR-18b-5p	-5.982260e-02	3.447331e-01	0.86223242
## 6	hsa-miR-130b-3p	7.688457e-02	4.608143e-01	0.86749198
## 30	hsa-miR-301a-3p	-3.600106e-02	4.515495e-01	0.93645373
## 26	hsa-miR-210-3p	-1.832301e-02	4.737829e-01	0.96915042
## 34	hsa-miR-335-5p	8.269202e-03	4.302186e-01	0.98466486
## 21	hsa-miR-193a-3p	-2.020910e+02	1.865464e+04	0.99135646
## 18	hsa-miR-146b-3p	1.701045e+02	1.605949e+04	0.99154885

```
EV.adverse.overlap = left_join(EV.overlap.new, adverse.pathology, by = "Patient ID")
```

```
# EV overlap
```

```
adverse.EV.overlap.result = data.frame(
  microRNA = colnames(EV.overlap.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
```

```
for (i in 1:57) {
```

```
  model = glm(formula = EV.adverse.overlap$`Adverse Pathology` ~ EV.overlap.new[,i+1], family = "binomial")
```

```

result = summary(model)
adverse.EV.overlap.result$coefficient.estimates[i] = result$coefficients[2,1]
adverse.EV.overlap.result$standard.deviation[i] = result$coefficients[2,2]
adverse.EV.overlap.result$p.value[i] = result$coefficients[2,4]
}

adverse.EV.overlap.result = adverse.EV.overlap.result[order(adverse.EV.overlap.result$p.value),]

# EV geNorm
adverse.EV.geNorm.result = data.frame(
  microRNA = colnames(EV.geNorm.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.adverse.overlap$`Adverse Pathology`~ EV.geNorm.new[,i+1], family = "binomial")
  result = summary(model)
  adverse.EV.geNorm.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.EV.geNorm.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.EV.geNorm.result$p.value[i] = result$coefficients[2,4]
}

adverse.EV.geNorm.result = adverse.EV.geNorm.result[order(adverse.EV.geNorm.result$p.value),]; adverse.EV.geNorm.result

```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 52	hsa-miR-25-3p	4.029608009	0.001708222	0.001708222
## 36	hsa-miR-363-3p	3.586235621	0.001851772	0.001851772
## 20	hsa-miR-19b-3p	3.650907665	0.004634764	0.004634764
## 29	hsa-miR-16-5p	3.093318698	0.005253864	0.005253864
## 1	hsa-let-7a-5p	-2.188200157	0.006622736	0.006622736
## 12	hsa-miR-451a	1.843081983	0.009018331	0.009018331
## 11	hsa-miR-30c-5p	-2.411058524	0.010563590	0.010563590
## 30	hsa-miR-301a-3p	-1.577191055	0.011735280	0.011735280
## 45	hsa-miR-199a-5p	-1.137577920	0.015603740	0.015603740
## 10	hsa-miR-26b-5p	-2.104481249	0.017780006	0.017780006
## 5	hsa-miR-107	-2.004130488	0.019745441	0.019745441
## 3	hsa-miR-103a-3p	-1.714675090	0.030313500	0.030313500
## 39	hsa-miR-191-5p	-1.606581872	0.030447900	0.030447900
## 51	hsa-miR-27b-3p	-1.779899048	0.034882715	0.034882715
## 14	hsa-miR-93-5p	3.016918605	0.052210482	0.052210482
## 47	hsa-miR-221-3p	-0.923245915	0.054975570	0.054975570
## 57	hsa-miR-374a-5p	-1.419951943	0.067421211	0.067421211
## 41	hsa-miR-199a-3p	-1.111175870	0.077015834	0.077015834
## 34	hsa-miR-335-5p	-0.891926420	0.078991455	0.078991455
## 32	hsa-miR-27a-3p	-1.581818841	0.079159491	0.079159491
## 17	hsa-miR-141-3p	-1.863990402	0.105306231	0.105306231
## 40	hsa-miR-23a-3p	-1.311783039	0.142253555	0.142253555
## 25	hsa-miR-204-5p	-0.358179828	0.143946350	0.143946350
## 24	hsa-miR-200b-3p	-0.677655134	0.183276971	0.183276971
## 9	hsa-miR-24-3p	-1.137994770	0.184237481	0.184237481
## 35	hsa-miR-345-5p	1.188240969	0.187488265	0.187488265
## 31	hsa-miR-320a	0.925809425	0.223183543	0.223183543

## 26	hsa-miR-210-3p	0.644086680	0.268266972	0.268266972
## 43	hsa-let-7b-5p	1.127935295	0.305613922	0.305613922
## 37	hsa-miR-375	-0.285927599	0.314488516	0.314488516
## 19	hsa-miR-18b-5p	-0.794274030	0.319659682	0.319659682
## 16	hsa-miR-1246	0.473590438	0.395355276	0.395355276
## 22	hsa-miR-194-5p	0.714149163	0.431471253	0.431471253
## 7	hsa-miR-146a-5p	-0.316136606	0.491937596	0.491937596
## 54	hsa-miR-125b-5p	-0.334243950	0.541574445	0.541574445
## 33	hsa-miR-330-3p	-0.245647768	0.548419151	0.548419151
## 8	hsa-miR-223-3p	-0.348643929	0.550895833	0.550895833
## 18	hsa-miR-146b-3p	0.446886897	0.560053735	0.560053735
## 56	hsa-miR-148a-3p	0.332403449	0.560246095	0.560246095
## 27	hsa-miR-214-3p	0.156634171	0.563679243	0.563679243
## 28	hsa-miR-222-3p	0.546129353	0.606841778	0.606841778
## 2	hsa-miR-100-5p	-0.216155689	0.613307072	0.613307072
## 46	hsa-miR-122-5p	-0.082418058	0.648189309	0.648189309
## 23	hsa-miR-200a-3p	-0.335564436	0.655534881	0.655534881
## 6	hsa-miR-130b-3p	-0.296284351	0.706022757	0.706022757
## 13	hsa-miR-874-3p	0.155416276	0.722366142	0.722366142
## 48	hsa-miR-29a-3p	0.203939639	0.845643562	0.845643562
## 55	hsa-miR-143-3p	-0.070487407	0.882943585	0.882943585
## 53	hsa-miR-155-5p	-0.062303774	0.882990960	0.882990960
## 4	hsa-miR-106a-5p	0.155802898	0.891273059	0.891273059
## 44	hsa-miR-30a-5p	0.073709664	0.894705691	0.894705691
## 49	hsa-miR-31-5p	0.052429430	0.915642751	0.915642751
## 50	hsa-miR-34a-5p	0.039915803	0.921889496	0.921889496
## 42	hsa-miR-21-5p	0.029348883	0.972259867	0.972259867
## 38	hsa-miR-574-3p	0.018129091	0.977443339	0.977443339
## 21	hsa-miR-193a-3p	57.314061877	0.992369993	0.992369993
## 15	hsa-let-7i-5p	-0.009940704	0.992872070	0.992872070

EV Norm Finder

```
adverse.EV.NormFinder.result = data.frame(
  microRNA = colnames(EV.NormFinder.new)[-1],
  coefficient.estimates = numeric(57),
  standard.deviation = numeric(57),
  p.value = numeric(57)
)
for (i in 1:57) {
  model = glm(formula = EV.adverse.overlap$`Adverse Pathology` ~ EV.NormFinder.new[,i+1], family = "binomial")
  result = summary(model)
  adverse.EV.NormFinder.result$coefficient.estimates[i] = result$coefficients[2,1]
  adverse.EV.NormFinder.result$standard.deviation[i] = result$coefficients[2,2]
  adverse.EV.NormFinder.result$p.value[i] = result$coefficients[2,4]
}
```

```
adverse.EV.NormFinder.result = adverse.EV.NormFinder.result[order(adverse.EV.NormFinder.result$p.value),]
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 52	hsa-miR-25-3p	2.973756540	0.9600825	0.001952284
## 36	hsa-miR-363-3p	2.104532228	0.7260553	0.003748521
## 20	hsa-miR-19b-3p	2.685104142	0.9495834	0.004688877
## 1	hsa-let-7a-5p	-2.967054797	1.0540266	0.004878155
## 29	hsa-miR-16-5p	1.928254354	0.7031062	0.006097722

## 11	hsa-miR-30c-5p	-4.444975533	1.7207415	0.009789580
## 12	hsa-miR-451a	1.257004145	0.5019255	0.012267181
## 28	hsa-miR-222-3p	4.582673344	1.9128998	0.016590098
## 14	hsa-miR-93-5p	2.762358418	1.1608805	0.017334389
## 31	hsa-miR-320a	2.498812003	1.0657535	0.019045276
## 45	hsa-miR-199a-5p	-1.331137033	0.5760347	0.020840445
## 30	hsa-miR-301a-3p	-1.582235530	0.6893331	0.021715166
## 5	hsa-miR-107	-2.932745704	1.3005568	0.024133800
## 39	hsa-miR-191-5p	-2.859902427	1.3010951	0.027943881
## 35	hsa-miR-345-5p	1.930134105	0.9191850	0.035743627
## 3	hsa-miR-103a-3p	-2.418746434	1.1579559	0.036725089
## 10	hsa-miR-26b-5p	-1.387150798	0.7556517	0.066401838
## 47	hsa-miR-221-3p	-1.375700343	0.7513321	0.067098297
## 51	hsa-miR-27b-3p	-2.642284140	1.4876690	0.075712530
## 34	hsa-miR-335-5p	-1.026645634	0.5802938	0.076863435
## 43	hsa-let-7b-5p	1.382958683	0.8390397	0.099298570
## 42	hsa-miR-21-5p	2.291930614	1.4185034	0.106150863
## 26	hsa-miR-210-3p	0.882428957	0.5535776	0.110925434
## 48	hsa-miR-29a-3p	1.445701416	0.9332384	0.121352064
## 24	hsa-miR-200b-3p	-0.825864189	0.5366628	0.123831524
## 25	hsa-miR-204-5p	-0.396401819	0.2596161	0.126791572
## 15	hsa-let-7i-5p	1.633494352	1.1069864	0.140045168
## 4	hsa-miR-106a-5p	1.370729752	0.9597712	0.153238926
## 41	hsa-miR-199a-3p	-1.116431706	0.8630409	0.195802819
## 22	hsa-miR-194-5p	0.679184917	0.5495256	0.216477965
## 16	hsa-miR-1246	0.532493634	0.4338214	0.219653862
## 17	hsa-miR-141-3p	-1.099949543	0.9605573	0.252161087
## 13	hsa-miR-874-3p	0.507655898	0.4654424	0.275406927
## 56	hsa-miR-148a-3p	0.513370283	0.4729683	0.277734673
## 44	hsa-miR-30a-5p	0.426598337	0.4578405	0.351459587
## 38	hsa-miR-574-3p	0.698617472	0.7853490	0.373700564
## 57	hsa-miR-374a-5p	-0.601477830	0.7544864	0.425333895
## 27	hsa-miR-214-3p	0.203392558	0.2592301	0.432686777
## 32	hsa-miR-27a-3p	-1.106371847	1.4503718	0.445571064
## 40	hsa-miR-23a-3p	-1.054313942	1.6343534	0.518865341
## 6	hsa-miR-130b-3p	0.435734080	0.8801806	0.620564306
## 2	hsa-miR-100-5p	-0.168567854	0.3411083	0.621181260
## 18	hsa-miR-146b-3p	0.322873890	0.6702222	0.629989542
## 23	hsa-miR-200a-3p	-0.283001082	0.6235264	0.649921052
## 37	hsa-miR-375	-0.112744088	0.2711921	0.677603859
## 7	hsa-miR-146a-5p	0.263407378	0.7192587	0.714200460
## 50	hsa-miR-34a-5p	0.109515666	0.2999026	0.714983944
## 33	hsa-miR-330-3p	-0.161419153	0.4603924	0.725879342
## 9	hsa-miR-24-3p	-0.483653540	1.5798065	0.759492477
## 54	hsa-miR-125b-5p	0.098559063	0.3937319	0.802339694
## 8	hsa-miR-223-3p	-0.136905864	0.6307221	0.828159941
## 53	hsa-miR-155-5p	0.071107333	0.3576623	0.842410283
## 19	hsa-miR-18b-5p	0.128816254	0.8303380	0.876713216
## 55	hsa-miR-143-3p	-0.033814120	0.3919786	0.931255593
## 46	hsa-miR-122-5p	0.005378519	0.1101892	0.961069366
## 49	hsa-miR-31-5p	-0.010092047	0.4694977	0.982850463
## 21	hsa-miR-193a-3p	55.649909738	5821.0735191	0.992372279

Variable selection

Firstly we extracted the significant variables.

```
# get the significant results
grade.serum.geneglobe.result.significant =
  grade.serum.geneglobe.result %>% filter(p.value <= 0.05)

grade.serum.geneglobe.result.significant

##           microRNA coefficient.estimates standard.deviation    p.value
## 1  hsa-miR-214-3p           0.20888435          0.07219239 0.004230744
## 2  hsa-miR-301a-3p           0.05928366          0.02910616 0.042980506
## 3  hsa-miR-125b-5p           0.07651650          0.03789180 0.044779707
## 4  hsa-miR-374a-5p           0.04412491          0.02195201 0.045761440
## 5    hsa-miR-1246          -0.06837300          0.03439914 0.048209396
```

```
grade.EV.geneglobe.result.significant =
  grade.EV.geneglobe.result %>% filter(p.value <= 0.05)

grade.EV.geneglobe.result.significant
```

```
##           microRNA coefficient.estimates standard.deviation    p.value
## 1 hsa-miR-31-5p          -0.1318083          0.03759133 0.04520534
```

```
# serum overlap
grade.serum.overlap.result.significant =
  grade.serum.overlap.result %>% filter(p.value <= 0.05)

grade.serum.overlap.result.significant
```

```
##           microRNA coefficient.estimates standard.deviation    p.value
## 1    hsa-miR-16-5p           0.7436268          0.16978024 1.909414e-05
## 2    hsa-let-7b-5p           1.0475797          0.26287385 9.431931e-05
## 3    hsa-miR-19b-3p           0.6939759          0.20708746 9.613771e-04
## 4    hsa-miR-27a-3p          -0.4246805          0.14103369 2.936033e-03
## 5    hsa-miR-1246          -0.1509322          0.05458298 6.218645e-03
## 6    hsa-miR-451a           0.3163264          0.11848278 8.210134e-03
## 7    hsa-miR-363-3p           0.2608767          0.09904067 9.094422e-03
## 8    hsa-miR-27b-3p          -0.3432971          0.13114534 9.526467e-03
## 9    hsa-miR-106a-5p          0.5369759          0.22683782 1.887180e-02
## 10   hsa-miR-93-5p           0.3642026          0.15545372 2.011542e-02
## 11   hsa-miR-130b-3p         -0.2437833          0.10568083 2.208556e-02
## 12   hsa-miR-24-3p          -0.3862914          0.16851432 2.292172e-02
## 13   hsa-miR-23a-3p         -0.3103579          0.14513226 3.368726e-02
## 14   hsa-miR-320a          -0.2076075          0.10193872 4.300240e-02
## 15   hsa-miR-29a-3p         -0.2205308          0.11077703 4.786165e-02
```

```
# serum geNorm
grade.serum.geNorm.result.significant =
  grade.serum.geNorm.result %>% filter(p.value <= 0.05)

grade.serum.geNorm.result.significant
```

##	microRNA	coefficient.estimate	standard.deviation	p.value
## 1	hsa-miR-16-5p	0.5802985	0.15040996	0.0001538744
## 2	hsa-let-7b-5p	0.8712984	0.23703261	0.0003041207
## 3	hsa-miR-19b-3p	0.5347979	0.17976717	0.0032894048
## 4	hsa-miR-27a-3p	-0.4365657	0.14772028	0.0034962584
## 5	hsa-miR-1246	-0.1555432	0.05644853	0.0063990287
## 6	hsa-miR-451a	0.2941835	0.11318103	0.0100361371
## 7	hsa-miR-363-3p	0.2444961	0.09639200	0.0119572216
## 8	hsa-miR-27b-3p	-0.3403147	0.13517316	0.0125954595
## 9	hsa-miR-93-5p	0.3468713	0.14986305	0.0216454416
## 10	hsa-miR-130b-3p	-0.2346396	0.10408620	0.0252571841
## 11	hsa-miR-24-3p	-0.3837172	0.17575434	0.0301749748
## 12	hsa-miR-106a-5p	0.4487549	0.20665674	0.0310646098
## 13	hsa-miR-23a-3p	-0.3183302	0.15569959	0.0422063038
## 14	hsa-miR-125b-5p	0.1133525	0.05605012	0.0444661195

serum Norm Finder

```
grade.serum.NormFinder.result.sigificant =
  grade.serum.NormFinder.result %>% filter(p.value <= 0.05)

grade.serum.NormFinder.result.sigificant
```

##	microRNA	coefficient.estimate	standard.deviation	p.value
## 1	hsa-miR-16-5p	0.5905670	0.14596701	7.430342e-05
## 2	hsa-let-7b-5p	0.8342150	0.22208313	2.258228e-04
## 3	hsa-miR-19b-3p	0.6545306	0.19090001	7.358234e-04
## 4	hsa-miR-27a-3p	-0.4738824	0.15388654	2.363919e-03
## 5	hsa-miR-1246	-0.1584134	0.05673671	5.742489e-03
## 6	hsa-miR-363-3p	0.2548524	0.09339929	6.923359e-03
## 7	hsa-miR-451a	0.2836807	0.10612998	8.136198e-03
## 8	hsa-miR-27b-3p	-0.3794965	0.14333099	8.747198e-03
## 9	hsa-miR-106a-5p	0.5124859	0.19876771	1.064318e-02
## 10	hsa-miR-93-5p	0.3752887	0.14654148	1.117132e-02
## 11	hsa-miR-130b-3p	-0.2483489	0.10783898	2.230434e-02
## 12	hsa-miR-24-3p	-0.4160530	0.18443597	2.515936e-02
## 13	hsa-miR-23a-3p	-0.3519347	0.16098436	2.996025e-02
## 14	hsa-miR-320a	-0.2221128	0.10831135	4.159492e-02
## 15	hsa-miR-29a-3p	-0.2481718	0.12136908	4.218099e-02
## 16	hsa-miR-125b-5p	0.1181642	0.05813636	4.341479e-02

EV overlap

```
grade.EV.overlap.result.sigificant =
  grade.EV.overlap.result %>% filter(p.value <= 0.05)

grade.EV.overlap.result.sigificant
```

##	microRNA	coefficient.estimate	standard.deviation	p.value
## 1	hsa-miR-191-5p	-0.7170328	0.2345885	0.002779304
## 2	hsa-miR-335-5p	-0.2599234	0.0876902	0.003684884
## 3	hsa-miR-107	-0.6003901	0.2183184	0.006913914
## 4	hsa-miR-130b-3p	-0.5311910	0.1957064	0.007657084
## 5	hsa-miR-221-3p	-0.4109939	0.1574500	0.010239287
## 6	hsa-miR-103a-3p	-0.5287972	0.2049752	0.011134040

```
## 7   hsa-miR-30c-5p      -0.5940400      0.2665792 0.027782758
## 8   hsa-let-7a-5p      -0.3291176      0.1537746 0.034427976
## 9   hsa-miR-26b-5p     -0.4225745      0.2035014 0.040054672
## 10  hsa-miR-330-3p     -0.2276348      0.1137107 0.047631497
```

```
# EV geNorm
```

```
grade.EV.geNorm.result.sigificant =
  grade.EV.geNorm.result %>% filter(p.value <= 0.05)

grade.EV.geNorm.result.sigificant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1   hsa-miR-191-5p      -0.5424342      0.17700281 0.002711548
## 2   hsa-miR-130b-3p     -0.4882278      0.16253626 0.003267009
## 3   hsa-miR-335-5p     -0.2305273      0.07742905 0.003541176
## 4   hsa-miR-107        -0.5303383      0.18018495 0.003923106
## 5   hsa-miR-103a-3p     -0.4751561      0.17069787 0.006278512
## 6   hsa-miR-221-3p     -0.3380119      0.12368549 0.007262618
## 7   hsa-miR-26b-5p     -0.4878377      0.18800012 0.010683581
## 8   hsa-miR-30c-5p     -0.4780865      0.19346642 0.014920451
## 9   hsa-let-7a-5p     -0.3210669      0.13422574 0.018364204
## 10  hsa-miR-330-3p     -0.2272567      0.10354029 0.030165407
## 11  hsa-miR-199a-3p     -0.3202017      0.15603029 0.042403117
## 12  hsa-miR-199a-5p     -0.1913666      0.09356731 0.043094604
## 13  hsa-miR-24-3p      -0.4063167      0.20424616 0.049016043
```

```
# EV Norm Finder
```

```
grade.EV.NormFinder.result.sigificant =
  grade.EV.NormFinder.result %>% filter(p.value <= 0.05)

grade.EV.NormFinder.result.sigificant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1   hsa-miR-335-5p     -0.2849853      0.09770089 0.004245477
## 2   hsa-miR-191-5p     -0.8607948      0.30689644 0.005904356
## 3   hsa-miR-221-3p     -0.4806203      0.20258973 0.019319312
## 4   hsa-miR-143-3p      0.3163502      0.13694505 0.022653518
## 5   hsa-miR-107        -0.5513057      0.24397259 0.025706531
## 6   hsa-miR-130b-3p     -0.4662289      0.21797174 0.034537036
## 7   hsa-miR-30a-5p      0.2661988      0.12476214 0.034977767
## 8   hsa-miR-103a-3p     -0.4872256      0.22893138 0.035431722
## 9   hsa-miR-222-3p      0.8430296      0.42260612 0.048405446
```

```
# get the significant results
```

```
adverse.serum.geneglobe.result.sigificant =
  adverse.serum.geneglobe.result %>% filter(p.value <= 0.05)

adverse.serum.geneglobe.result.sigificant
```

```
## [1] microRNA          coefficient.estimates standard.deviation
## [4] p.value
## <0 rows> (or 0-length row.names)
```



```
adverse.EV.geneglobe.result.significant =
  adverse.EV.geneglobe.result %>% filter(p.value <= 0.05)
```

```
adverse.EV.geneglobe.result.significant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1 hsa-miR-31-5p          -0.1318083          0.03759133 0.04520534
```

```
# serum overlap
```

```
adverse.serum.overlap.result.significant =
  adverse.serum.overlap.result %>% filter(p.value <= 0.05)
```

```
adverse.serum.overlap.result.significant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1 hsa-miR-25-3p          2.0908871          0.8716106 0.01644542
## 2 hsa-miR-16-5p          1.6155543          0.7202048 0.02488474
## 3 hsa-let-7a-5p         -1.3554812          0.6250389 0.03011040
## 4 hsa-miR-30c-5p         -1.2985369          0.6007532 0.03065560
## 5 hsa-miR-24-3p         -1.4764937          0.6840354 0.03088860
## 6 hsa-miR-1246          -0.5771685          0.2803802 0.03954012
```

```
# serum geNorm
```

```
adverse.serum.geNorm.result.significant =
  adverse.serum.geNorm.result %>% filter(p.value <= 0.05)
```

```
adverse.serum.geNorm.result.significant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1 hsa-miR-25-3p          2.0353684          0.8300413 0.01420137
## 2 hsa-miR-30c-5p         -1.4839446          0.6446452 0.02133767
## 3 hsa-miR-16-5p          1.5301606          0.6695018 0.02228227
## 4 hsa-let-7a-5p         -1.4402051          0.6562058 0.02818181
## 5 hsa-miR-1246          -0.6471745          0.2991925 0.03053576
## 6 hsa-miR-24-3p         -1.4609546          0.6946247 0.03544578
```

```
# serum Norm Finder
```

```
adverse.serum.NormFinder.result.significant =
  adverse.serum.NormFinder.result %>% filter(p.value <= 0.05)
```

```
adverse.serum.NormFinder.result.significant
```

```
##          microRNA coefficient.estimates standard.deviation    p.value
## 1 hsa-miR-25-3p          1.7156966          0.7634822 0.02462729
## 2 hsa-miR-1246          -0.6222907          0.2951999 0.03502824
## 3 hsa-miR-24-3p         -1.5454262          0.7472620 0.03862890
## 4 hsa-miR-30c-5p         -1.2923866          0.6315247 0.04071166
## 5 hsa-miR-16-5p          1.2312051          0.6091459 0.04325918
## 6 hsa-let-7a-5p         -1.2165157          0.6172054 0.04872314
```



```
# EV overlap
adverse.EV.overlap.result.sigificant =
  adverse.EV.overlap.result %>% filter(p.value <= 0.05)

adverse.EV.overlap.result.sigificant
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 1	hsa-miR-25-3p	3.816730	1.2055790	0.001546094
## 2	hsa-miR-363-3p	2.814177	0.9285707	0.002440242
## 3	hsa-miR-19b-3p	3.532837	1.1897376	0.002983568
## 4	hsa-let-7a-5p	-2.734409	0.9725701	0.004930663
## 5	hsa-miR-16-5p	2.539840	0.9087568	0.005192367
## 6	hsa-miR-30c-5p	-3.403659	1.2811012	0.007888087
## 7	hsa-miR-451a	1.546254	0.6032458	0.010370504
## 8	hsa-miR-301a-3p	-1.646580	0.6727733	0.014387053
## 9	hsa-miR-199a-5p	-1.256875	0.5260986	0.016892114
## 10	hsa-miR-93-5p	3.590601	1.5209104	0.018234407
## 11	hsa-miR-107	-2.612350	1.1106244	0.018665496
## 12	hsa-miR-26b-5p	-1.976253	0.8901228	0.026405015
## 13	hsa-miR-191-5p	-2.192511	0.9885581	0.026562459
## 14	hsa-miR-103a-3p	-2.182950	1.0071167	0.030194849
## 15	hsa-miR-27b-3p	-2.325135	1.1385488	0.041132484

```
# EV geNorm
adverse.EV.geNorm.result.sigificant =
  adverse.EV.geNorm.result %>% filter(p.value <= 0.05)

adverse.EV.geNorm.result.sigificant
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
## 1	hsa-miR-25-3p	4.029608	0.001708222	0.001708222
## 2	hsa-miR-363-3p	3.586236	0.001851772	0.001851772
## 3	hsa-miR-19b-3p	3.650908	0.004634764	0.004634764
## 4	hsa-miR-16-5p	3.093319	0.005253864	0.005253864
## 5	hsa-let-7a-5p	-2.188200	0.006622736	0.006622736
## 6	hsa-miR-451a	1.843082	0.009018331	0.009018331
## 7	hsa-miR-30c-5p	-2.411059	0.010563590	0.010563590
## 8	hsa-miR-301a-3p	-1.577191	0.011735280	0.011735280
## 9	hsa-miR-199a-5p	-1.137578	0.015603740	0.015603740
## 10	hsa-miR-26b-5p	-2.104481	0.017780006	0.017780006
## 11	hsa-miR-107	-2.004130	0.019745441	0.019745441
## 12	hsa-miR-103a-3p	-1.714675	0.030313500	0.030313500
## 13	hsa-miR-191-5p	-1.606582	0.030447900	0.030447900
## 14	hsa-miR-27b-3p	-1.779899	0.034882715	0.034882715

```
# EV Norm Finder
adverse.EV.NormFinder.result.sigificant =
  adverse.EV.NormFinder.result %>% filter(p.value <= 0.05)

adverse.EV.NormFinder.result.sigificant
```

##	microRNA	coefficient.estimates	standard.deviation	p.value
----	----------	-----------------------	--------------------	---------

```
## 1    hsa-miR-25-3p          2.973757          0.9600825 0.001952284
## 2    hsa-miR-363-3p        2.104532          0.7260553 0.003748521
## 3    hsa-miR-19b-3p        2.685104          0.9495834 0.004688877
## 4    hsa-let-7a-5p        -2.967055          1.0540266 0.004878155
## 5    hsa-miR-16-5p         1.928254          0.7031062 0.006097722
## 6    hsa-miR-30c-5p       -4.444976          1.7207415 0.009789580
## 7    hsa-miR-451a          1.257004          0.5019255 0.012267181
## 8    hsa-miR-222-3p        4.582673          1.9128998 0.016590098
## 9    hsa-miR-93-5p         2.762358          1.1608805 0.017334389
## 10   hsa-miR-320a          2.498812          1.0657535 0.019045276
## 11   hsa-miR-199a-5p       -1.331137          0.5760347 0.020840445
## 12   hsa-miR-301a-3p      -1.582236          0.6893331 0.021715166
## 13    hsa-miR-107          -2.932746          1.3005568 0.024133800
## 14   hsa-miR-191-5p       -2.859902          1.3010951 0.027943881
## 15   hsa-miR-345-5p         1.930134          0.9191850 0.035743627
## 16   hsa-miR-103a-3p      -2.418746          1.1579559 0.036725089
```

Then we do the backward stepwise selection.

Outcome: biopsy grade group

```
library(MASS)
```

```
##
## Attaching package: 'MASS'

## The following object is masked from 'package:dplyr':
##
##      select
```

```
# serum geneglobe
```

```
fullmodel.serum.geneglobe = glm(data = serum.all.original, formula = 'Biopsy Grade Group' ~ 'hsa-miR-1246' +
serum.grade.final = stepAIC(object = fullmodel.serum.geneglobe, direction = "backward")
```

```
## Start:  AIC=512.49
## 'Biopsy Grade Group' ~ 'hsa-miR-1246' + 'hsa-miR-214-3p' + 'hsa-miR-301a-3p' +
##      'hsa-miR-125b-5p' + 'hsa-miR-374a-5p'
##
##              Df Deviance    AIC
## - 'hsa-miR-125b-5p'  1   138.84 510.97
## - 'hsa-miR-301a-3p'  1   138.85 510.99
## - 'hsa-miR-374a-5p'  1   139.53 511.97
## <none>                138.51 512.49
## - 'hsa-miR-214-3p'   1   140.54 513.44
## - 'hsa-miR-1246'     1   143.69 517.94
##
## Step:  AIC=510.97
## 'Biopsy Grade Group' ~ 'hsa-miR-1246' + 'hsa-miR-214-3p' + 'hsa-miR-301a-3p' +
##      'hsa-miR-374a-5p'
##
##              Df Deviance    AIC
```

```
## - 'hsa-miR-301a-3p' 1 139.09 509.34
## - 'hsa-miR-374a-5p' 1 140.04 510.73
## <none> 138.84 510.97
## - 'hsa-miR-214-3p' 1 142.23 513.87
## - 'hsa-miR-1246' 1 143.69 515.94
##
## Step: AIC=509.34
## 'Biopsy Grade Group' ~ 'hsa-miR-1246' + 'hsa-miR-214-3p' + 'hsa-miR-374a-5p'
##
## Df Deviance AIC
## <none> 139.09 509.34
## - 'hsa-miR-374a-5p' 1 140.74 509.72
## - 'hsa-miR-214-3p' 1 142.27 511.93
## - 'hsa-miR-1246' 1 143.75 514.03
```

```
##
## Call:
## glm(formula = 'Biopsy Grade Group' ~ 'hsa-miR-1246' + 'hsa-miR-214-3p' +
##       'hsa-miR-374a-5p', data = serum.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.1166  -0.5446  -0.4482   0.4430   3.4868
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      1.57858    0.08033   19.652  <2e-16 ***
## 'hsa-miR-1246'   -0.09023    0.03493   -2.583   0.0105 *
## 'hsa-miR-214-3p'  0.16870    0.07906    2.134   0.0341 *
## 'hsa-miR-374a-5p' 0.03781    0.02464    1.534   0.1265
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.6989441)
##
##      Null deviance: 150.31  on 202  degrees of freedom
## Residual deviance: 139.09  on 199  degrees of freedom
## AIC: 509.34
##
## Number of Fisher Scoring iterations: 2
```

```
## Start: AIC=505.61
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-27a-3p' + serum.overlap.new$'hsa-miR-320a' +
```

```

## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-451a' +
## serum.overlap.new$'hsa-miR-363-3p' + serum.overlap.new$'hsa-miR-27b-3p' +
## serum.overlap.new$'hsa-miR-106a-5p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-24-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-29a-3p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-451a' 1 121.36 503.65
## - serum.overlap.new$'hsa-miR-363-3p' 1 121.43 503.78
## - serum.overlap.new$'hsa-miR-106a-5p' 1 121.44 503.78
## - serum.overlap.new$'hsa-miR-19b-3p' 1 121.47 503.84
## - serum.overlap.new$'hsa-miR-320a' 1 121.54 503.95
## - serum.overlap.new$'hsa-miR-27b-3p' 1 121.54 503.96
## - serum.overlap.new$'hsa-miR-1246' 1 121.66 504.15
## - serum.overlap.new$'hsa-miR-93-5p' 1 122.00 504.72
## - serum.overlap.new$'hsa-miR-24-3p' 1 122.22 505.08
## <none> 121.33 505.61
## - serum.overlap.new$'hsa-miR-29a-3p' 1 122.67 505.84
## - serum.overlap.new$'hsa-miR-27a-3p' 1 122.78 506.02
## - serum.overlap.new$'hsa-miR-16-5p' 1 124.10 508.19
## - serum.overlap.new$'hsa-miR-130b-3p' 1 124.50 508.85
## - serum.overlap.new$'hsa-miR-23a-3p' 1 125.39 510.30
## - serum.overlap.new$'hsa-let-7b-5p' 1 128.42 515.13
##
## Step: AIC=503.65
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-27a-3p' + serum.overlap.new$'hsa-miR-320a' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-363-3p' +
## serum.overlap.new$'hsa-miR-27b-3p' + serum.overlap.new$'hsa-miR-106a-5p' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-130b-3p' +
## serum.overlap.new$'hsa-miR-24-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-29a-3p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-363-3p' 1 121.44 501.79
## - serum.overlap.new$'hsa-miR-106a-5p' 1 121.49 501.87
## - serum.overlap.new$'hsa-miR-19b-3p' 1 121.54 501.95
## - serum.overlap.new$'hsa-miR-320a' 1 121.54 501.95
## - serum.overlap.new$'hsa-miR-27b-3p' 1 121.57 502.01
## - serum.overlap.new$'hsa-miR-1246' 1 121.69 502.20
## - serum.overlap.new$'hsa-miR-93-5p' 1 122.02 502.75
## - serum.overlap.new$'hsa-miR-24-3p' 1 122.38 503.36
## <none> 121.36 503.65
## - serum.overlap.new$'hsa-miR-29a-3p' 1 122.72 503.92
## - serum.overlap.new$'hsa-miR-27a-3p' 1 122.80 504.06
## - serum.overlap.new$'hsa-miR-130b-3p' 1 124.52 506.87
## - serum.overlap.new$'hsa-miR-16-5p' 1 124.63 507.05
## - serum.overlap.new$'hsa-miR-23a-3p' 1 125.40 508.30
## - serum.overlap.new$'hsa-let-7b-5p' 1 128.43 513.14
##
## Step: AIC=501.79
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-19b-3p' +

```

```

## serum.overlap.new$'hsa-miR-27a-3p' + serum.overlap.new$'hsa-miR-320a' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-27b-3p' +
## serum.overlap.new$'hsa-miR-106a-5p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-24-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-29a-3p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-106a-5p' 1 121.57 500.01
## - serum.overlap.new$'hsa-miR-320a' 1 121.58 500.03
## - serum.overlap.new$'hsa-miR-19b-3p' 1 121.65 500.14
## - serum.overlap.new$'hsa-miR-27b-3p' 1 121.66 500.15
## - serum.overlap.new$'hsa-miR-1246' 1 121.75 500.31
## - serum.overlap.new$'hsa-miR-93-5p' 1 122.16 500.99
## - serum.overlap.new$'hsa-miR-24-3p' 1 122.39 501.37
## <none> 121.44 501.79
## - serum.overlap.new$'hsa-miR-29a-3p' 1 122.79 502.03
## - serum.overlap.new$'hsa-miR-27a-3p' 1 123.03 502.42
## - serum.overlap.new$'hsa-miR-130b-3p' 1 124.52 504.87
## - serum.overlap.new$'hsa-miR-16-5p' 1 125.23 506.03
## - serum.overlap.new$'hsa-miR-23a-3p' 1 126.02 507.30
## - serum.overlap.new$'hsa-let-7b-5p' 1 128.43 511.15
##
## Step: AIC=500.01
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-27a-3p' + serum.overlap.new$'hsa-miR-320a' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-27b-3p' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-130b-3p' +
## serum.overlap.new$'hsa-miR-24-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-29a-3p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-19b-3p' 1 121.72 498.26
## - serum.overlap.new$'hsa-miR-27b-3p' 1 121.73 498.27
## - serum.overlap.new$'hsa-miR-320a' 1 121.80 498.39
## - serum.overlap.new$'hsa-miR-1246' 1 121.84 498.46
## - serum.overlap.new$'hsa-miR-93-5p' 1 122.25 499.14
## - serum.overlap.new$'hsa-miR-24-3p' 1 122.66 499.83
## <none> 121.57 500.01
## - serum.overlap.new$'hsa-miR-29a-3p' 1 122.84 500.12
## - serum.overlap.new$'hsa-miR-27a-3p' 1 123.38 501.00
## - serum.overlap.new$'hsa-miR-130b-3p' 1 124.60 503.01
## - serum.overlap.new$'hsa-miR-16-5p' 1 125.27 504.09
## - serum.overlap.new$'hsa-miR-23a-3p' 1 126.70 506.40
## - serum.overlap.new$'hsa-let-7b-5p' 1 128.47 509.21
##
## Step: AIC=498.26
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-320a' + serum.overlap.new$'hsa-miR-1246' +
## serum.overlap.new$'hsa-miR-27b-3p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-24-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-29a-3p'
##

```

```

##                                     Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-27b-3p' 1 121.88 496.52
## - serum.overlap.new$'hsa-miR-320a'    1 121.95 496.65
## - serum.overlap.new$'hsa-miR-1246'    1 122.03 496.77
## - serum.overlap.new$'hsa-miR-93-5p'   1 122.47 497.50
## - serum.overlap.new$'hsa-miR-24-3p'   1 122.86 498.16
## - serum.overlap.new$'hsa-miR-29a-3p'  1 122.90 498.21
## <none>                                121.72 498.26
## - serum.overlap.new$'hsa-miR-27a-3p'  1 123.59 499.35
## - serum.overlap.new$'hsa-miR-130b-3p' 1 124.89 501.48
## - serum.overlap.new$'hsa-miR-23a-3p'  1 126.71 504.42
## - serum.overlap.new$'hsa-miR-16-5p'   1 127.74 506.06
## - serum.overlap.new$'hsa-let-7b-5p'   1 128.50 507.25
##
## Step: AIC=496.52
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-320a' + serum.overlap.new$'hsa-miR-1246' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-130b-3p' +
## serum.overlap.new$'hsa-miR-24-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-29a-3p'
##
##                                     Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-320a'    1 122.17 495.01
## - serum.overlap.new$'hsa-miR-1246'    1 122.26 495.16
## - serum.overlap.new$'hsa-miR-93-5p'   1 122.53 495.61
## - serum.overlap.new$'hsa-miR-24-3p'   1 123.08 496.50
## <none>                                121.88 496.52
## - serum.overlap.new$'hsa-miR-29a-3p'  1 123.15 496.63
## - serum.overlap.new$'hsa-miR-27a-3p'  1 124.30 498.52
## - serum.overlap.new$'hsa-miR-130b-3p' 1 125.49 500.45
## - serum.overlap.new$'hsa-miR-23a-3p'  1 126.71 502.42
## - serum.overlap.new$'hsa-miR-16-5p'   1 127.78 504.12
## - serum.overlap.new$'hsa-let-7b-5p'   1 128.52 505.29
##
## Step: AIC=495.01
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-24-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-29a-3p'
##
##                                     Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-1246'    1 122.43 493.43
## - serum.overlap.new$'hsa-miR-93-5p'   1 122.64 493.78
## - serum.overlap.new$'hsa-miR-24-3p'   1 123.08 494.52
## - serum.overlap.new$'hsa-miR-29a-3p'  1 123.34 494.94
## <none>                                122.17 495.01
## - serum.overlap.new$'hsa-miR-27a-3p'  1 124.53 496.89
## - serum.overlap.new$'hsa-miR-130b-3p' 1 126.01 499.29
## - serum.overlap.new$'hsa-miR-23a-3p'  1 127.65 501.92
## - serum.overlap.new$'hsa-miR-16-5p'   1 127.78 502.13
## - serum.overlap.new$'hsa-let-7b-5p'   1 128.59 503.41
##

```

```
## Step: AIC=493.43
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-130b-3p' +
## serum.overlap.new$'hsa-miR-24-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-29a-3p'
```

```
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-93-5p' 1 122.93 492.26
## <none> 122.43 493.43
## - serum.overlap.new$'hsa-miR-29a-3p' 1 123.85 493.78
## - serum.overlap.new$'hsa-miR-24-3p' 1 123.90 493.87
## - serum.overlap.new$'hsa-miR-27a-3p' 1 125.60 496.63
## - serum.overlap.new$'hsa-miR-130b-3p' 1 126.22 497.63
## - serum.overlap.new$'hsa-miR-23a-3p' 1 127.67 499.95
## - serum.overlap.new$'hsa-let-7b-5p' 1 128.75 501.65
## - serum.overlap.new$'hsa-miR-16-5p' 1 129.41 502.69
##
```

```
## Step: AIC=492.26
## serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-24-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-29a-3p'
```

```
##
##
## Df Deviance AIC
## <none> 122.93 492.26
## - serum.overlap.new$'hsa-miR-29a-3p' 1 124.43 492.72
## - serum.overlap.new$'hsa-miR-24-3p' 1 124.61 493.02
## - serum.overlap.new$'hsa-miR-27a-3p' 1 126.83 496.61
## - serum.overlap.new$'hsa-miR-130b-3p' 1 127.12 497.07
## - serum.overlap.new$'hsa-miR-23a-3p' 1 128.36 499.04
## - serum.overlap.new$'hsa-let-7b-5p' 1 129.03 500.10
## - serum.overlap.new$'hsa-miR-16-5p' 1 130.92 503.05
```

```
final.model.serum.grade.overlap = glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-29a-3p' +
summary(final.model.serum.grade.overlap)
```

```
##
## Call:
## glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.overlap.new$'hsa-miR-29a-3p' +
## serum.overlap.new$'hsa-miR-24-3p' + serum.overlap.new$'hsa-miR-27a-3p' +
## serum.overlap.new$'hsa-miR-130b-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-let-7b-5p' + serum.overlap.new$'hsa-miR-16-5p')
```

```
##
## Deviance Residuals:
## Min 1Q Median 3Q Max
## -1.4881 -0.4844 -0.1563 0.2264 3.3997
##
```

```
## Coefficients:
## Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.7957 0.6017 -1.322 0.187593
## serum.overlap.new$'hsa-miR-29a-3p' -0.1824 0.1182 -1.542 0.124615
## serum.overlap.new$'hsa-miR-24-3p' 0.4873 0.2984 1.633 0.104019
## serum.overlap.new$'hsa-miR-27a-3p' -0.6328 0.2542 -2.489 0.013632 *
```

```
## serum.overlap.new$'hsa-miR-130b-3p' -0.2749      0.1066 -2.579 0.010641 *
## serum.overlap.new$'hsa-miR-23a-3p'   0.8583      0.2924  2.935 0.003731 **
## serum.overlap.new$'hsa-let-7b-5p'    1.0425      0.3350  3.112 0.002140 **
## serum.overlap.new$'hsa-miR-16-5p'    0.7983      0.2242  3.561 0.000464 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.6304016)
##
## Null deviance: 150.31  on 202  degrees of freedom
## Residual deviance: 122.93  on 195  degrees of freedom
## AIC: 492.26
##
## Number of Fisher Scoring iterations: 2
```

```
# serum geNorm
```

```
fullmodel.serum.geNorm = glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
serum.geNorm.new$'hsa-miR-27a-3p' + serum.geNorm.new$'hsa-miR-1246' +
serum.geNorm.new$'hsa-miR-451a' + serum.geNorm.new$'hsa-miR-363-3p' +
serum.geNorm.new$'hsa-miR-27b-3p' + serum.geNorm.new$'hsa-miR-93-5p' +
serum.geNorm.new$'hsa-miR-130b-3p' + serum.geNorm.new$'hsa-miR-24-3p' +
serum.geNorm.new$'hsa-miR-106a-5p' + serum.geNorm.new$'hsa-miR-23a-3p' +
serum.geNorm.new$'hsa-miR-125b-5p'
step.serum.grade.geNorm = stepAIC(object = fullmodel.serum.geNorm, direction = "backward")
```

```
## Start: AIC=504.49
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
## serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
## serum.geNorm.new$'hsa-miR-27a-3p' + serum.geNorm.new$'hsa-miR-1246' +
## serum.geNorm.new$'hsa-miR-451a' + serum.geNorm.new$'hsa-miR-363-3p' +
## serum.geNorm.new$'hsa-miR-27b-3p' + serum.geNorm.new$'hsa-miR-93-5p' +
## serum.geNorm.new$'hsa-miR-130b-3p' + serum.geNorm.new$'hsa-miR-24-3p' +
## serum.geNorm.new$'hsa-miR-106a-5p' + serum.geNorm.new$'hsa-miR-23a-3p' +
## serum.geNorm.new$'hsa-miR-125b-5p'
##
##
## Df Deviance AIC
## - serum.geNorm.new$'hsa-miR-93-5p' 1 121.86 502.50
## - serum.geNorm.new$'hsa-miR-106a-5p' 1 121.98 502.69
## - serum.geNorm.new$'hsa-miR-27a-3p' 1 122.07 502.85
## - serum.geNorm.new$'hsa-miR-27b-3p' 1 122.08 502.85
## - serum.geNorm.new$'hsa-miR-24-3p' 1 122.22 503.09
## - serum.geNorm.new$'hsa-miR-451a' 1 122.26 503.16
## - serum.geNorm.new$'hsa-miR-19b-3p' 1 122.72 503.91
## - serum.geNorm.new$'hsa-miR-363-3p' 1 123.03 504.43
## <none> 121.86 504.49
## - serum.geNorm.new$'hsa-miR-1246' 1 123.07 504.50
## - serum.geNorm.new$'hsa-let-7b-5p' 1 123.39 505.02
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 123.78 505.66
## - serum.geNorm.new$'hsa-miR-16-5p' 1 125.03 507.71
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 126.62 510.27
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 127.74 512.06
##
## Step: AIC=502.5
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
## serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
## serum.geNorm.new$'hsa-miR-27a-3p' + serum.geNorm.new$'hsa-miR-1246' +
## serum.geNorm.new$'hsa-miR-451a' + serum.geNorm.new$'hsa-miR-363-3p' +
## serum.geNorm.new$'hsa-miR-27b-3p' + serum.geNorm.new$'hsa-miR-130b-3p' +
## serum.geNorm.new$'hsa-miR-24-3p' + serum.geNorm.new$'hsa-miR-106a-5p' +
```



```

##      serum.geNorm.new$'hsa-miR-23a-3p' + serum.geNorm.new$'hsa-miR-125b-5p'
##
##
##              Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-106a-5p' 1 121.99 500.71
## - serum.geNorm.new$'hsa-miR-27a-3p' 1 122.07 500.85
## - serum.geNorm.new$'hsa-miR-27b-3p' 1 122.11 500.91
## - serum.geNorm.new$'hsa-miR-24-3p' 1 122.22 501.09
## - serum.geNorm.new$'hsa-miR-451a' 1 122.29 501.21
## - serum.geNorm.new$'hsa-miR-19b-3p' 1 122.72 501.92
## <none> 121.86 502.50
## - serum.geNorm.new$'hsa-miR-1246' 1 123.09 502.53
## - serum.geNorm.new$'hsa-miR-363-3p' 1 123.09 502.53
## - serum.geNorm.new$'hsa-let-7b-5p' 1 123.43 503.08
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 123.78 503.66
## - serum.geNorm.new$'hsa-miR-16-5p' 1 125.08 505.78
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 127.07 508.99
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 127.94 510.38
##
## Step: AIC=500.71
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
##      serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
##      serum.geNorm.new$'hsa-miR-27a-3p' + serum.geNorm.new$'hsa-miR-1246' +
##      serum.geNorm.new$'hsa-miR-451a' + serum.geNorm.new$'hsa-miR-363-3p' +
##      serum.geNorm.new$'hsa-miR-27b-3p' + serum.geNorm.new$'hsa-miR-130b-3p' +
##      serum.geNorm.new$'hsa-miR-24-3p' + serum.geNorm.new$'hsa-miR-23a-3p' +
##      serum.geNorm.new$'hsa-miR-125b-5p'
##
##              Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-27a-3p' 1 122.15 498.98
## - serum.geNorm.new$'hsa-miR-27b-3p' 1 122.18 499.02
## - serum.geNorm.new$'hsa-miR-24-3p' 1 122.34 499.28
## - serum.geNorm.new$'hsa-miR-451a' 1 122.38 499.35
## - serum.geNorm.new$'hsa-miR-19b-3p' 1 122.74 499.96
## <none> 121.99 500.71
## - serum.geNorm.new$'hsa-miR-363-3p' 1 123.28 500.84
## - serum.geNorm.new$'hsa-miR-1246' 1 123.42 501.07
## - serum.geNorm.new$'hsa-let-7b-5p' 1 123.78 501.66
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 123.78 501.66
## - serum.geNorm.new$'hsa-miR-16-5p' 1 125.55 504.54
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 127.11 507.05
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 128.09 508.61
##
## Step: AIC=498.98
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
##      serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
##      serum.geNorm.new$'hsa-miR-1246' + serum.geNorm.new$'hsa-miR-451a' +
##      serum.geNorm.new$'hsa-miR-363-3p' + serum.geNorm.new$'hsa-miR-27b-3p' +
##      serum.geNorm.new$'hsa-miR-130b-3p' + serum.geNorm.new$'hsa-miR-24-3p' +
##      serum.geNorm.new$'hsa-miR-23a-3p' + serum.geNorm.new$'hsa-miR-125b-5p'
##
##              Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-24-3p' 1 122.41 497.40
## - serum.geNorm.new$'hsa-miR-451a' 1 122.56 497.65
## - serum.geNorm.new$'hsa-miR-19b-3p' 1 122.87 498.17

```

```

## - serum.geNorm.new$'hsa-miR-27b-3p' 1 123.29 498.86
## <none> 122.15 498.98
## - serum.geNorm.new$'hsa-miR-363-3p' 1 123.59 499.35
## - serum.geNorm.new$'hsa-let-7b-5p' 1 123.81 499.72
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 123.81 499.72
## - serum.geNorm.new$'hsa-miR-1246' 1 124.08 500.15
## - serum.geNorm.new$'hsa-miR-16-5p' 1 125.61 502.65
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 128.19 506.77
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 128.45 507.18
##
## Step: AIC=497.4
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
## serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-19b-3p' +
## serum.geNorm.new$'hsa-miR-1246' + serum.geNorm.new$'hsa-miR-451a' +
## serum.geNorm.new$'hsa-miR-363-3p' + serum.geNorm.new$'hsa-miR-27b-3p' +
## serum.geNorm.new$'hsa-miR-130b-3p' + serum.geNorm.new$'hsa-miR-23a-3p' +
## serum.geNorm.new$'hsa-miR-125b-5p'
##
## Df Deviance AIC
## - serum.geNorm.new$'hsa-miR-19b-3p' 1 123.08 496.51
## - serum.geNorm.new$'hsa-miR-27b-3p' 1 123.32 496.91
## - serum.geNorm.new$'hsa-miR-451a' 1 123.35 496.96
## <none> 122.41 497.40
## - serum.geNorm.new$'hsa-miR-363-3p' 1 123.70 497.53
## - serum.geNorm.new$'hsa-let-7b-5p' 1 123.89 497.84
## - serum.geNorm.new$'hsa-miR-1246' 1 124.74 499.23
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 125.19 499.97
## - serum.geNorm.new$'hsa-miR-16-5p' 1 126.18 501.56
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 128.34 505.00
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 128.47 505.22
##
## Step: AIC=496.51
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
## serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-1246' +
## serum.geNorm.new$'hsa-miR-451a' + serum.geNorm.new$'hsa-miR-363-3p' +
## serum.geNorm.new$'hsa-miR-27b-3p' + serum.geNorm.new$'hsa-miR-130b-3p' +
## serum.geNorm.new$'hsa-miR-23a-3p' + serum.geNorm.new$'hsa-miR-125b-5p'
##
## Df Deviance AIC
## - serum.geNorm.new$'hsa-miR-451a' 1 123.71 495.56
## - serum.geNorm.new$'hsa-miR-27b-3p' 1 123.86 495.80
## - serum.geNorm.new$'hsa-miR-363-3p' 1 124.15 496.27
## <none> 123.08 496.51
## - serum.geNorm.new$'hsa-let-7b-5p' 1 124.59 496.99
## - serum.geNorm.new$'hsa-miR-1246' 1 125.21 497.99
## - serum.geNorm.new$'hsa-miR-23a-3p' 1 126.07 499.39
## - serum.geNorm.new$'hsa-miR-16-5p' 1 126.31 499.77
## - serum.geNorm.new$'hsa-miR-125b-5p' 1 128.45 503.18
## - serum.geNorm.new$'hsa-miR-130b-3p' 1 128.80 503.74
##
## Step: AIC=495.56
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
## serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-1246' +
## serum.geNorm.new$'hsa-miR-363-3p' + serum.geNorm.new$'hsa-miR-27b-3p' +

```

```

##      serum.geNorm.new$'hsa-miR-130b-3p' + serum.geNorm.new$'hsa-miR-23a-3p' +
##      serum.geNorm.new$'hsa-miR-125b-5p'
##
##                                     Df Deviance   AIC
## - serum.geNorm.new$'hsa-miR-27b-3p'   1   124.32 494.55
## - serum.geNorm.new$'hsa-miR-363-3p'   1   124.51 494.86
## <none>                                123.71 495.56
## - serum.geNorm.new$'hsa-let-7b-5p'   1   125.54 496.52
## - serum.geNorm.new$'hsa-miR-1246'     1   126.32 497.78
## - serum.geNorm.new$'hsa-miR-16-5p'    1   126.32 497.79
## - serum.geNorm.new$'hsa-miR-23a-3p'   1   127.80 500.15
## - serum.geNorm.new$'hsa-miR-125b-5p'  1   128.47 501.22
## - serum.geNorm.new$'hsa-miR-130b-3p'  1   129.09 502.19
##
## Step: AIC=494.55
## serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
##      serum.geNorm.new$'hsa-let-7b-5p' + serum.geNorm.new$'hsa-miR-1246' +
##      serum.geNorm.new$'hsa-miR-363-3p' + serum.geNorm.new$'hsa-miR-130b-3p' +
##      serum.geNorm.new$'hsa-miR-23a-3p' + serum.geNorm.new$'hsa-miR-125b-5p'
##
##                                     Df Deviance   AIC
## <none>                                124.32 494.55
## - serum.geNorm.new$'hsa-miR-363-3p'   1   125.68 494.76
## - serum.geNorm.new$'hsa-let-7b-5p'   1   126.39 495.89
## - serum.geNorm.new$'hsa-miR-16-5p'    1   126.90 496.72
## - serum.geNorm.new$'hsa-miR-1246'     1   127.06 496.98
## - serum.geNorm.new$'hsa-miR-23a-3p'   1   127.81 498.16
## - serum.geNorm.new$'hsa-miR-125b-5p'  1   128.91 499.91
## - serum.geNorm.new$'hsa-miR-130b-3p'  1   129.49 500.82

final.model.serum.grade.geNorm = glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-16-5p' +
summary(final.model.serum.grade.geNorm)

##
## Call:
## glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.geNorm.new$'hsa-miR-29a-3p' +
##      serum.geNorm.new$'hsa-miR-320a' + serum.geNorm.new$'hsa-miR-363-3p' +
##      serum.geNorm.new$'hsa-miR-125b-5p')
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.5230  -0.5357  -0.3051   0.4001   3.3450
##
## Coefficients:
##                                     Estimate Std. Error t value Pr(>|t|)
## (Intercept)                        1.55238    0.19602    7.920 1.68e-13 ***
## serum.geNorm.new$'hsa-miR-29a-3p'  -0.20265    0.11217   -1.807 0.072339 .
## serum.geNorm.new$'hsa-miR-320a'    -0.22782    0.10541   -2.161 0.031881 *
## serum.geNorm.new$'hsa-miR-363-3p'   0.23235    0.09915    2.343 0.020106 *
## serum.geNorm.new$'hsa-miR-125b-5p'  0.22892    0.06106    3.749 0.000233 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.6788982)

```

```

##
## Null deviance: 150.31 on 202 degrees of freedom
## Residual deviance: 134.42 on 198 degrees of freedom
## AIC: 504.41
##
## Number of Fisher Scoring iterations: 2

# serum NormFinder
fullmodel.serum.NormFinder = glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-miR-363-3p' +
serum.NormFinder.new$'hsa-let-7b-5p' + serum.NormFinder.new$'hsa-miR-16-5p' +
serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-23a-3p' +
serum.NormFinder.new$'hsa-miR-125b-5p' + serum.NormFinder.new$'hsa-let-7b-5p' +
serum.NormFinder.new$'hsa-miR-27b-3p' + serum.NormFinder.new$'hsa-miR-29a-3p' +
serum.NormFinder.new$'hsa-miR-21-5p' + serum.NormFinder.new$'hsa-miR-130b-3p'
step.serum.grade.NormFinder = stepAIC(object = fullmodel.serum.NormFinder, direction = "backward")

## Start: AIC=493.51
## serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-miR-363-3p' +
## serum.NormFinder.new$'hsa-let-7b-5p' + serum.NormFinder.new$'hsa-miR-16-5p' +
## serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-23a-3p' +
## serum.NormFinder.new$'hsa-miR-125b-5p' + serum.NormFinder.new$'hsa-let-7b-5p' +
## serum.NormFinder.new$'hsa-miR-27b-3p' + serum.NormFinder.new$'hsa-miR-29a-3p' +
## serum.NormFinder.new$'hsa-miR-21-5p' + serum.NormFinder.new$'hsa-miR-130b-3p'
##
##
## Df Deviance AIC
## - serum.NormFinder.new$'hsa-miR-363-3p' 1 120.68 492.51
## - serum.NormFinder.new$'hsa-miR-21-5p' 1 120.83 492.78
## - serum.NormFinder.new$'hsa-miR-27b-3p' 1 121.04 493.12
## <none> 120.08 493.51
## - serum.NormFinder.new$'hsa-let-7b-5p' 1 121.95 494.64
## - serum.NormFinder.new$'hsa-miR-29a-3p' 1 122.07 494.84
## - serum.NormFinder.new$'hsa-miR-1246' 1 122.86 496.15
## - serum.NormFinder.new$'hsa-miR-16-5p' 1 123.34 496.94
## - serum.NormFinder.new$'hsa-miR-130b-3p' 1 124.97 499.61
## - serum.NormFinder.new$'hsa-miR-23a-3p' 1 126.23 501.65
## - serum.NormFinder.new$'hsa-miR-125b-5p' 1 126.77 502.51
##
## Step: AIC=492.51
## serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +
## serum.NormFinder.new$'hsa-miR-16-5p' + serum.NormFinder.new$'hsa-miR-1246' +
## serum.NormFinder.new$'hsa-miR-23a-3p' + serum.NormFinder.new$'hsa-miR-125b-5p' +
## serum.NormFinder.new$'hsa-miR-27b-3p' + serum.NormFinder.new$'hsa-miR-29a-3p' +
## serum.NormFinder.new$'hsa-miR-21-5p' + serum.NormFinder.new$'hsa-miR-130b-3p'
##
##
## Df Deviance AIC
## - serum.NormFinder.new$'hsa-miR-21-5p' 1 121.19 491.37
## <none> 120.68 492.51
## - serum.NormFinder.new$'hsa-miR-27b-3p' 1 122.08 492.85
## - serum.NormFinder.new$'hsa-let-7b-5p' 1 122.38 493.36
## - serum.NormFinder.new$'hsa-miR-29a-3p' 1 122.48 493.53
## - serum.NormFinder.new$'hsa-miR-1246' 1 123.35 494.97
## - serum.NormFinder.new$'hsa-miR-130b-3p' 1 125.30 498.14
## - serum.NormFinder.new$'hsa-miR-16-5p' 1 125.98 499.24
## - serum.NormFinder.new$'hsa-miR-23a-3p' 1 126.85 500.64
## - serum.NormFinder.new$'hsa-miR-125b-5p' 1 127.12 501.08
##
## Step: AIC=491.37
## serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +

```

```
## serum.NormFinder.new$'hsa-miR-16-5p' + serum.NormFinder.new$'hsa-miR-1246' +
## serum.NormFinder.new$'hsa-miR-23a-3p' + serum.NormFinder.new$'hsa-miR-125b-5p' +
## serum.NormFinder.new$'hsa-miR-27b-3p' + serum.NormFinder.new$'hsa-miR-29a-3p' +
## serum.NormFinder.new$'hsa-miR-130b-3p'
```

```
##
##
## Df Deviance AIC
## - serum.NormFinder.new$'hsa-miR-27b-3p' 1 122.35 491.30
## <none> 121.19 491.37
## - serum.NormFinder.new$'hsa-let-7b-5p' 1 122.44 491.46
## - serum.NormFinder.new$'hsa-miR-29a-3p' 1 122.61 491.73
## - serum.NormFinder.new$'hsa-miR-1246' 1 123.59 493.35
## - serum.NormFinder.new$'hsa-miR-16-5p' 1 126.04 497.34
## - serum.NormFinder.new$'hsa-miR-130b-3p' 1 126.15 497.52
## - serum.NormFinder.new$'hsa-miR-23a-3p' 1 126.92 498.75
## - serum.NormFinder.new$'hsa-miR-125b-5p' 1 128.45 501.18
```

```
##
## Step: AIC=491.3
## serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +
## serum.NormFinder.new$'hsa-miR-16-5p' + serum.NormFinder.new$'hsa-miR-1246' +
## serum.NormFinder.new$'hsa-miR-23a-3p' + serum.NormFinder.new$'hsa-miR-125b-5p' +
## serum.NormFinder.new$'hsa-miR-29a-3p' + serum.NormFinder.new$'hsa-miR-130b-3p'
```

```
##
## Df Deviance AIC
## - serum.NormFinder.new$'hsa-miR-29a-3p' 1 123.34 490.94
## <none> 122.35 491.30
## - serum.NormFinder.new$'hsa-let-7b-5p' 1 123.98 491.99
## - serum.NormFinder.new$'hsa-miR-1246' 1 125.03 493.70
## - serum.NormFinder.new$'hsa-miR-130b-3p' 1 126.81 496.57
## - serum.NormFinder.new$'hsa-miR-23a-3p' 1 127.01 496.89
## - serum.NormFinder.new$'hsa-miR-16-5p' 1 128.19 498.77
## - serum.NormFinder.new$'hsa-miR-125b-5p' 1 129.10 500.21
```

```
##
## Step: AIC=490.94
## serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +
## serum.NormFinder.new$'hsa-miR-16-5p' + serum.NormFinder.new$'hsa-miR-1246' +
## serum.NormFinder.new$'hsa-miR-23a-3p' + serum.NormFinder.new$'hsa-miR-125b-5p' +
## serum.NormFinder.new$'hsa-miR-130b-3p'
```

```
##
## Df Deviance AIC
## <none> 123.34 490.94
## - serum.NormFinder.new$'hsa-let-7b-5p' 1 124.92 491.52
## - serum.NormFinder.new$'hsa-miR-1246' 1 126.42 493.94
## - serum.NormFinder.new$'hsa-miR-23a-3p' 1 127.35 495.44
## - serum.NormFinder.new$'hsa-miR-130b-3p' 1 127.80 496.15
## - serum.NormFinder.new$'hsa-miR-125b-5p' 1 129.44 498.74
## - serum.NormFinder.new$'hsa-miR-16-5p' 1 129.70 499.15
```

```
fullmodel.serum.NormFinder = glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +
summary(fullmodel.serum.NormFinder)
```

```
##
## Call:
## glm(formula = serum.all.original$'Biopsy Grade Group' ~ serum.NormFinder.new$'hsa-let-7b-5p' +
## serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-23a-3p' +
```

```
## serum.NormFinder.new$'hsa-miR-130b-3p' + serum.NormFinder.new$'hsa-miR-125b-5p' +
## serum.NormFinder.new$'hsa-miR-16-5p')
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.5432  -0.4986  -0.1969   0.3546   3.4707
##
## Coefficients:
##                                Estimate Std. Error t value Pr(>|t|)
## (Intercept)                -0.23813     0.52084  -0.457   0.64803
## serum.NormFinder.new$'hsa-let-7b-5p'    0.47834     0.30198   1.584   0.11480
## serum.NormFinder.new$'hsa-miR-1246'    -0.14003     0.06331  -2.212   0.02815 *
## serum.NormFinder.new$'hsa-miR-23a-3p'    0.59750     0.23656   2.526   0.01234 *
## serum.NormFinder.new$'hsa-miR-130b-3p'  -0.28190     0.10592  -2.662   0.00842 **
## serum.NormFinder.new$'hsa-miR-125b-5p'   0.17705     0.05688   3.113   0.00213 **
## serum.NormFinder.new$'hsa-miR-16-5p'    0.69695     0.21923   3.179   0.00172 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.6292777)
##
##      Null deviance: 150.31  on 202  degrees of freedom
## Residual deviance: 123.34  on 196  degrees of freedom
## AIC: 490.94
##
## Number of Fisher Scoring iterations: 2
```

EV overlap

```
fullmodel.EV.overlap = glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-107' +
EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-221-3p' +
EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-30c-5p' +
EV.overlap.new$'hsa-let-7a-5p' + EV.overlap.new$'hsa-miR-26b-5p' +
EV.overlap.new$'hsa-miR-330-3p')
step.EV.grade.overlap = stepAIC(object = fullmodel.EV.overlap, direction = "backward")
```

```
## Start:  AIC=313.31
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-221-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-30c-5p' +
## EV.overlap.new$'hsa-let-7a-5p' + EV.overlap.new$'hsa-miR-26b-5p' +
## EV.overlap.new$'hsa-miR-330-3p'
##
##              Df Deviance    AIC
## - EV.overlap.new$'hsa-miR-221-3p'    1    80.246 311.37
## - EV.overlap.new$'hsa-miR-30c-5p'    1    80.252 311.38
## - EV.overlap.new$'hsa-let-7a-5p'    1    80.312 311.47
## - EV.overlap.new$'hsa-miR-330-3p'    1    80.312 311.47
## - EV.overlap.new$'hsa-miR-107'      1    80.344 311.51
## - EV.overlap.new$'hsa-miR-191-5p'   1    80.496 311.74
## - EV.overlap.new$'hsa-miR-103a-3p'  1    80.517 311.77
## <none>                                80.202 313.31
## - EV.overlap.new$'hsa-miR-26b-5p'   1    81.776 313.60
## - EV.overlap.new$'hsa-miR-335-5p'   1    82.078 314.03
## - EV.overlap.new$'hsa-miR-130b-3p'  1    82.409 314.51
##
## Step:  AIC=311.37
```

```

## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
## EV.overlap.new$'hsa-miR-30c-5p' + EV.overlap.new$'hsa-let-7a-5p' +
## EV.overlap.new$'hsa-miR-26b-5p' + EV.overlap.new$'hsa-miR-330-3p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-30c-5p' 1 80.287 309.43
## - EV.overlap.new$'hsa-miR-330-3p' 1 80.333 309.50
## - EV.overlap.new$'hsa-let-7a-5p' 1 80.335 309.50
## - EV.overlap.new$'hsa-miR-107' 1 80.396 309.59
## - EV.overlap.new$'hsa-miR-191-5p' 1 80.497 309.74
## - EV.overlap.new$'hsa-miR-103a-3p' 1 80.557 309.83
## <none> 80.246 311.37
## - EV.overlap.new$'hsa-miR-26b-5p' 1 82.139 312.12
## - EV.overlap.new$'hsa-miR-335-5p' 1 82.209 312.22
## - EV.overlap.new$'hsa-miR-130b-3p' 1 82.547 312.71
##
## Step: AIC=309.43
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
## EV.overlap.new$'hsa-let-7a-5p' + EV.overlap.new$'hsa-miR-26b-5p' +
## EV.overlap.new$'hsa-miR-330-3p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-330-3p' 1 80.378 307.56
## - EV.overlap.new$'hsa-miR-107' 1 80.439 307.65
## - EV.overlap.new$'hsa-let-7a-5p' 1 80.486 307.72
## - EV.overlap.new$'hsa-miR-103a-3p' 1 80.606 307.90
## - EV.overlap.new$'hsa-miR-191-5p' 1 80.798 308.18
## <none> 80.287 309.43
## - EV.overlap.new$'hsa-miR-26b-5p' 1 82.238 310.26
## - EV.overlap.new$'hsa-miR-335-5p' 1 82.249 310.28
## - EV.overlap.new$'hsa-miR-130b-3p' 1 82.569 310.74
##
## Step: AIC=307.56
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
## EV.overlap.new$'hsa-let-7a-5p' + EV.overlap.new$'hsa-miR-26b-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-107' 1 80.485 305.72
## - EV.overlap.new$'hsa-let-7a-5p' 1 80.570 305.85
## - EV.overlap.new$'hsa-miR-103a-3p' 1 80.643 305.95
## - EV.overlap.new$'hsa-miR-191-5p' 1 81.040 306.53
## <none> 80.378 307.56
## - EV.overlap.new$'hsa-miR-26b-5p' 1 82.332 308.40
## - EV.overlap.new$'hsa-miR-130b-3p' 1 82.865 309.16
## - EV.overlap.new$'hsa-miR-335-5p' 1 83.027 309.39
##
## Step: AIC=305.72
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +

```

```

## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-130b-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-let-7a-5p' +
## EV.overlap.new$'hsa-miR-26b-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-let-7a-5p' 1 80.668 303.99
## - EV.overlap.new$'hsa-miR-103a-3p' 1 80.723 304.07
## - EV.overlap.new$'hsa-miR-191-5p' 1 81.150 304.69
## <none> 80.485 305.72
## - EV.overlap.new$'hsa-miR-26b-5p' 1 82.691 306.91
## - EV.overlap.new$'hsa-miR-335-5p' 1 83.089 307.48
## - EV.overlap.new$'hsa-miR-130b-3p' 1 83.461 308.01
##
## Step: AIC=303.99
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-130b-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-26b-5p'
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-103a-3p' 1 80.736 302.09
## - EV.overlap.new$'hsa-miR-191-5p' 1 81.239 302.82
## <none> 80.668 303.99
## - EV.overlap.new$'hsa-miR-26b-5p' 1 83.052 305.43
## - EV.overlap.new$'hsa-miR-130b-3p' 1 83.462 306.01
## - EV.overlap.new$'hsa-miR-335-5p' 1 83.555 306.14
##
## Step: AIC=302.09
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-191-5p' +
## EV.overlap.new$'hsa-miR-335-5p' + EV.overlap.new$'hsa-miR-130b-3p' +
## EV.overlap.new$'hsa-miR-26b-5p'
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-191-5p' 1 81.260 300.85
## <none> 80.736 302.09
## - EV.overlap.new$'hsa-miR-130b-3p' 1 83.478 304.03
## - EV.overlap.new$'hsa-miR-335-5p' 1 83.671 304.30
## - EV.overlap.new$'hsa-miR-26b-5p' 1 84.088 304.89
##
## Step: AIC=300.85
## EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-335-5p' +
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-26b-5p'
##
## Df Deviance AIC
## <none> 81.260 300.85
## - EV.overlap.new$'hsa-miR-335-5p' 1 85.013 304.18
## - EV.overlap.new$'hsa-miR-130b-3p' 1 85.084 304.28
## - EV.overlap.new$'hsa-miR-26b-5p' 1 87.276 307.28

final.model.EV.grade.overlap = glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-335-5p' +
EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-26b-5p', data = EV.all.data, family = binomial)
summary(final.model.EV.grade.overlap)

##
## Call:
## glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.overlap.new$'hsa-miR-335-5p' +

```



```
## EV.overlap.new$'hsa-miR-130b-3p' + EV.overlap.new$'hsa-miR-26b-5p')
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.3500  -0.5704  -0.2492   0.3620   3.1692
##
## Coefficients:
##                                Estimate Std. Error t value Pr(>|t|)
## (Intercept)                2.85879    0.31762   9.001 5.86e-15 ***
## EV.overlap.new$'hsa-miR-335-5p' -0.20787    0.09058  -2.295  0.02358 *
## EV.overlap.new$'hsa-miR-130b-3p' -0.47255    0.20403  -2.316  0.02234 *
## EV.overlap.new$'hsa-miR-26b-5p' -0.56922    0.19594  -2.905  0.00441 **
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.712805)
##
## Null deviance: 96.475  on 117  degrees of freedom
## Residual deviance: 81.260  on 114  degrees of freedom
## AIC: 300.85
##
## Number of Fisher Scoring iterations: 2
```

```
# EV geNorm
```

```
fullmodel.EV.geNorm = glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p'
```

```
step.EV.grade.geNorm = stepAIC(object = fullmodel.EV.geNorm, direction = "backward")
```

```
## Start: AIC=319.68
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-107' + EV.geNorm.new$'hsa-miR-103a-3p' +
## EV.geNorm.new$'hsa-miR-221-3p' + EV.geNorm.new$'hsa-miR-26b-5p' +
## EV.geNorm.new$'hsa-miR-30c-5p' + EV.geNorm.new$'hsa-let-7a-5p' +
## EV.geNorm.new$'hsa-miR-330-3p' + EV.geNorm.new$'hsa-miR-199a-3p' +
## EV.geNorm.new$'hsa-miR-199a-5p' + EV.geNorm.new$'hsa-miR-24-3p'
##
##                                Df Deviance    AIC
## - EV.geNorm.new$'hsa-let-7a-5p' 1  80.462 317.69
## - EV.geNorm.new$'hsa-miR-107'    1  80.474 317.71
## - EV.geNorm.new$'hsa-miR-30c-5p' 1  80.514 317.76
## - EV.geNorm.new$'hsa-miR-330-3p' 1  80.545 317.81
## - EV.geNorm.new$'hsa-miR-103a-3p' 1  80.547 317.81
## - EV.geNorm.new$'hsa-miR-199a-5p' 1  80.620 317.92
## - EV.geNorm.new$'hsa-miR-221-3p' 1  80.638 317.95
## - EV.geNorm.new$'hsa-miR-199a-3p' 1  80.800 318.18
## - EV.geNorm.new$'hsa-miR-191-5p' 1  80.820 318.21
## - EV.geNorm.new$'hsa-miR-24-3p'  1  81.322 318.94
## - EV.geNorm.new$'hsa-miR-26b-5p' 1  81.588 319.33
## <none>                          80.460 319.68
## - EV.geNorm.new$'hsa-miR-335-5p' 1  82.709 320.94
## - EV.geNorm.new$'hsa-miR-130b-3p' 1  82.751 321.00
##
## Step: AIC=317.69
```

```

## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-107' + EV.geNorm.new$'hsa-miR-103a-3p' +
## EV.geNorm.new$'hsa-miR-221-3p' + EV.geNorm.new$'hsa-miR-26b-5p' +
## EV.geNorm.new$'hsa-miR-30c-5p' + EV.geNorm.new$'hsa-miR-330-3p' +
## EV.geNorm.new$'hsa-miR-199a-3p' + EV.geNorm.new$'hsa-miR-199a-5p' +
## EV.geNorm.new$'hsa-miR-24-3p'
##
##
## Df Deviance AIC
## - EV.geNorm.new$'hsa-miR-107' 1 80.476 315.71
## - EV.geNorm.new$'hsa-miR-30c-5p' 1 80.544 315.81
## - EV.geNorm.new$'hsa-miR-330-3p' 1 80.546 315.81
## - EV.geNorm.new$'hsa-miR-103a-3p' 1 80.549 315.81
## - EV.geNorm.new$'hsa-miR-199a-5p' 1 80.624 315.92
## - EV.geNorm.new$'hsa-miR-221-3p' 1 80.656 315.97
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 80.802 316.19
## - EV.geNorm.new$'hsa-miR-191-5p' 1 80.855 316.26
## - EV.geNorm.new$'hsa-miR-24-3p' 1 81.350 316.98
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 81.765 317.58
## <none> 80.462 317.69
## - EV.geNorm.new$'hsa-miR-335-5p' 1 82.745 318.99
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 82.826 319.10
##
## Step: AIC=315.71
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-103a-3p' + EV.geNorm.new$'hsa-miR-221-3p' +
## EV.geNorm.new$'hsa-miR-26b-5p' + EV.geNorm.new$'hsa-miR-30c-5p' +
## EV.geNorm.new$'hsa-miR-330-3p' + EV.geNorm.new$'hsa-miR-199a-3p' +
## EV.geNorm.new$'hsa-miR-199a-5p' + EV.geNorm.new$'hsa-miR-24-3p'
##
##
## Df Deviance AIC
## - EV.geNorm.new$'hsa-miR-330-3p' 1 80.549 313.82
## - EV.geNorm.new$'hsa-miR-30c-5p' 1 80.560 313.83
## - EV.geNorm.new$'hsa-miR-199a-5p' 1 80.635 313.94
## - EV.geNorm.new$'hsa-miR-221-3p' 1 80.675 314.00
## - EV.geNorm.new$'hsa-miR-103a-3p' 1 80.724 314.07
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 80.837 314.24
## - EV.geNorm.new$'hsa-miR-191-5p' 1 80.889 314.31
## - EV.geNorm.new$'hsa-miR-24-3p' 1 81.393 315.04
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 81.837 315.69
## <none> 80.476 315.71
## - EV.geNorm.new$'hsa-miR-335-5p' 1 82.829 317.11
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 83.246 317.70
##
## Step: AIC=313.82
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-103a-3p' + EV.geNorm.new$'hsa-miR-221-3p' +
## EV.geNorm.new$'hsa-miR-26b-5p' + EV.geNorm.new$'hsa-miR-30c-5p' +
## EV.geNorm.new$'hsa-miR-199a-3p' + EV.geNorm.new$'hsa-miR-199a-5p' +
## EV.geNorm.new$'hsa-miR-24-3p'
##
##
## Df Deviance AIC

```

```

## - EV.geNorm.new$`hsa-miR-30c-5p` 1 80.633 311.94
## - EV.geNorm.new$`hsa-miR-199a-5p` 1 80.680 312.01
## - EV.geNorm.new$`hsa-miR-221-3p` 1 80.785 312.16
## - EV.geNorm.new$`hsa-miR-103a-3p` 1 80.821 312.21
## - EV.geNorm.new$`hsa-miR-199a-3p` 1 80.922 312.36
## - EV.geNorm.new$`hsa-miR-191-5p` 1 80.988 312.46
## - EV.geNorm.new$`hsa-miR-24-3p` 1 81.454 313.13
## <none> 80.549 313.81
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 81.932 313.82
## - EV.geNorm.new$`hsa-miR-335-5p` 1 83.276 315.74
## - EV.geNorm.new$`hsa-miR-130b-3p` 1 83.298 315.77
##
## Step: AIC=311.94
## EV.all.original$`Biopsy Grade Group` ~ EV.geNorm.new$`hsa-miR-191-5p` +
## EV.geNorm.new$`hsa-miR-130b-3p` + EV.geNorm.new$`hsa-miR-335-5p` +
## EV.geNorm.new$`hsa-miR-103a-3p` + EV.geNorm.new$`hsa-miR-221-3p` +
## EV.geNorm.new$`hsa-miR-26b-5p` + EV.geNorm.new$`hsa-miR-199a-3p` +
## EV.geNorm.new$`hsa-miR-199a-5p` + EV.geNorm.new$`hsa-miR-24-3p`
##
##
## Df Deviance AIC
## - EV.geNorm.new$`hsa-miR-199a-5p` 1 80.753 310.11
## - EV.geNorm.new$`hsa-miR-103a-3p` 1 80.831 310.23
## - EV.geNorm.new$`hsa-miR-221-3p` 1 80.870 310.29
## - EV.geNorm.new$`hsa-miR-199a-3p` 1 80.975 310.44
## - EV.geNorm.new$`hsa-miR-191-5p` 1 81.205 310.77
## - EV.geNorm.new$`hsa-miR-24-3p` 1 81.461 311.14
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 81.963 311.87
## <none> 80.633 311.94
## - EV.geNorm.new$`hsa-miR-335-5p` 1 83.297 313.77
## - EV.geNorm.new$`hsa-miR-130b-3p` 1 83.299 313.78
##
## Step: AIC=310.11
## EV.all.original$`Biopsy Grade Group` ~ EV.geNorm.new$`hsa-miR-191-5p` +
## EV.geNorm.new$`hsa-miR-130b-3p` + EV.geNorm.new$`hsa-miR-335-5p` +
## EV.geNorm.new$`hsa-miR-103a-3p` + EV.geNorm.new$`hsa-miR-221-3p` +
## EV.geNorm.new$`hsa-miR-26b-5p` + EV.geNorm.new$`hsa-miR-199a-3p` +
## EV.geNorm.new$`hsa-miR-24-3p`
##
##
## Df Deviance AIC
## - EV.geNorm.new$`hsa-miR-103a-3p` 1 80.922 308.36
## - EV.geNorm.new$`hsa-miR-221-3p` 1 80.942 308.39
## - EV.geNorm.new$`hsa-miR-191-5p` 1 81.242 308.83
## - EV.geNorm.new$`hsa-miR-199a-3p` 1 81.445 309.12
## - EV.geNorm.new$`hsa-miR-24-3p` 1 81.472 309.16
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 82.030 309.96
## <none> 80.753 310.11
## - EV.geNorm.new$`hsa-miR-130b-3p` 1 83.304 311.78
## - EV.geNorm.new$`hsa-miR-335-5p` 1 83.542 312.12
##
## Step: AIC=308.36
## EV.all.original$`Biopsy Grade Group` ~ EV.geNorm.new$`hsa-miR-191-5p` +
## EV.geNorm.new$`hsa-miR-130b-3p` + EV.geNorm.new$`hsa-miR-335-5p` +
## EV.geNorm.new$`hsa-miR-221-3p` + EV.geNorm.new$`hsa-miR-26b-5p` +
## EV.geNorm.new$`hsa-miR-199a-3p` + EV.geNorm.new$`hsa-miR-24-3p`

```

```

##
##
##      Df Deviance    AIC
## - EV.geNorm.new$'hsa-miR-221-3p' 1 81.080 306.59
## - EV.geNorm.new$'hsa-miR-191-5p' 1 81.260 306.85
## - EV.geNorm.new$'hsa-miR-24-3p' 1 81.536 307.25
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 81.672 307.45
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 82.113 308.08
## <none> 80.922 308.36
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 83.309 309.79
## - EV.geNorm.new$'hsa-miR-335-5p' 1 83.794 310.48
##
## Step: AIC=306.59
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-26b-5p' + EV.geNorm.new$'hsa-miR-199a-3p' +
## EV.geNorm.new$'hsa-miR-24-3p'
##
##      Df Deviance    AIC
## - EV.geNorm.new$'hsa-miR-24-3p' 1 81.558 305.28
## - EV.geNorm.new$'hsa-miR-191-5p' 1 81.622 305.38
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 81.673 305.45
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 82.155 306.14
## <none> 81.080 306.59
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 84.104 308.91
## - EV.geNorm.new$'hsa-miR-335-5p' 1 84.525 309.50
##
## Step: AIC=305.28
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-191-5p' +
## EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-335-5p' +
## EV.geNorm.new$'hsa-miR-26b-5p' + EV.geNorm.new$'hsa-miR-199a-3p'
##
##      Df Deviance    AIC
## - EV.geNorm.new$'hsa-miR-191-5p' 1 81.717 303.51
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 82.639 304.84
## <none> 81.558 305.28
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 84.213 307.06
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 84.406 307.33
## - EV.geNorm.new$'hsa-miR-335-5p' 1 84.541 307.52
##
## Step: AIC=303.51
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-130b-3p' +
## EV.geNorm.new$'hsa-miR-335-5p' + EV.geNorm.new$'hsa-miR-26b-5p' +
## EV.geNorm.new$'hsa-miR-199a-3p'
##
##      Df Deviance    AIC
## - EV.geNorm.new$'hsa-miR-199a-3p' 1 82.641 302.84
## <none> 81.717 303.51
## - EV.geNorm.new$'hsa-miR-335-5p' 1 84.847 305.95
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 85.034 306.21
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 86.873 308.73
##
## Step: AIC=302.84
## EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-130b-3p' +
## EV.geNorm.new$'hsa-miR-335-5p' + EV.geNorm.new$'hsa-miR-26b-5p'

```

```

##
##
##           Df Deviance    AIC
## <none>                82.641 302.84
## - EV.geNorm.new$'hsa-miR-335-5p' 1 84.916 304.05
## - EV.geNorm.new$'hsa-miR-130b-3p' 1 85.052 304.23
## - EV.geNorm.new$'hsa-miR-26b-5p' 1 86.972 306.87

final.model.EV.grade.geNorm= glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-335-5p' +
summary(final.model.EV.grade.geNorm)

##
## Call:
## glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.geNorm.new$'hsa-miR-335-5p' +
##      EV.geNorm.new$'hsa-miR-130b-3p' + EV.geNorm.new$'hsa-miR-26b-5p')
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.1911  -0.6182  -0.2453   0.3199   3.1756
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)      2.54426    0.25662   9.914  <2e-16 ***
## EV.geNorm.new$'hsa-miR-335-5p' -0.14921    0.08422  -1.772   0.0791 .
## EV.geNorm.new$'hsa-miR-130b-3p' -0.32258    0.17687  -1.824   0.0708 .
## EV.geNorm.new$'hsa-miR-26b-5p' -0.44250    0.18102  -2.444   0.0160 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for gaussian family taken to be 0.7249172)
##
##      Null deviance: 96.475  on 117  degrees of freedom
## Residual deviance: 82.641  on 114  degrees of freedom
## AIC: 302.84
##
## Number of Fisher Scoring iterations: 2

# EV NormFinder
fullmodel.EV.NormFinder = glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-221-3p' +
EV.NormFinder.new$'hsa-miR-143-3p' + EV.NormFinder.new$'hsa-miR-107' +
EV.NormFinder.new$'hsa-miR-130b-3p' + EV.NormFinder.new$'hsa-miR-30a-5p' +
EV.NormFinder.new$'hsa-miR-103a-3p' + EV.NormFinder.new$'hsa-miR-222-3p'
##
##
##           Df Deviance    AIC
## - EV.NormFinder.new$'hsa-miR-221-3p' 1 80.329 309.49
## - EV.NormFinder.new$'hsa-miR-222-3p' 1 80.331 309.50
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 80.432 309.64
## - EV.NormFinder.new$'hsa-miR-30a-5p' 1 80.471 309.70

```

```

## - EV.NormFinder.new$'hsa-miR-107'      1    80.594 309.88
## <none>                                80.319 311.48
## - EV.NormFinder.new$'hsa-miR-143-3p'    1    81.706 311.50
## - EV.NormFinder.new$'hsa-miR-130b-3p'    1    81.784 311.61
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    81.883 311.75
## - EV.NormFinder.new$'hsa-miR-335-5p'    1    83.150 313.56
##
## Step: AIC=309.49
## EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
##     EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-143-3p' +
##     EV.NormFinder.new$'hsa-miR-107' + EV.NormFinder.new$'hsa-miR-130b-3p' +
##     EV.NormFinder.new$'hsa-miR-30a-5p' + EV.NormFinder.new$'hsa-miR-103a-3p' +
##     EV.NormFinder.new$'hsa-miR-222-3p'
##
##                                     Df Deviance    AIC
## - EV.NormFinder.new$'hsa-miR-222-3p'    1    80.340 307.51
## - EV.NormFinder.new$'hsa-miR-103a-3p'    1    80.447 307.67
## - EV.NormFinder.new$'hsa-miR-30a-5p'    1    80.482 307.72
## - EV.NormFinder.new$'hsa-miR-107'      1    80.633 307.94
## <none>                                80.329 309.49
## - EV.NormFinder.new$'hsa-miR-143-3p'    1    81.741 309.55
## - EV.NormFinder.new$'hsa-miR-130b-3p'    1    81.897 309.77
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    82.055 310.00
## - EV.NormFinder.new$'hsa-miR-335-5p'    1    83.593 312.19
##
## Step: AIC=307.51
## EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
##     EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-143-3p' +
##     EV.NormFinder.new$'hsa-miR-107' + EV.NormFinder.new$'hsa-miR-130b-3p' +
##     EV.NormFinder.new$'hsa-miR-30a-5p' + EV.NormFinder.new$'hsa-miR-103a-3p'
##
##                                     Df Deviance    AIC
## - EV.NormFinder.new$'hsa-miR-103a-3p'    1    80.454 305.68
## - EV.NormFinder.new$'hsa-miR-30a-5p'    1    80.482 305.72
## - EV.NormFinder.new$'hsa-miR-107'      1    80.647 305.96
## <none>                                80.340 307.51
## - EV.NormFinder.new$'hsa-miR-143-3p'    1    81.742 307.55
## - EV.NormFinder.new$'hsa-miR-130b-3p'    1    81.916 307.80
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    82.104 308.07
## - EV.NormFinder.new$'hsa-miR-335-5p'    1    83.733 310.39
##
## Step: AIC=305.68
## EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
##     EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-143-3p' +
##     EV.NormFinder.new$'hsa-miR-107' + EV.NormFinder.new$'hsa-miR-130b-3p' +
##     EV.NormFinder.new$'hsa-miR-30a-5p'
##
##                                     Df Deviance    AIC
## - EV.NormFinder.new$'hsa-miR-30a-5p'    1    80.610 303.90
## - EV.NormFinder.new$'hsa-miR-107'      1    81.161 304.71
## - EV.NormFinder.new$'hsa-miR-143-3p'    1    81.799 305.63
## <none>                                80.454 305.68
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    82.140 306.12
## - EV.NormFinder.new$'hsa-miR-130b-3p'    1    82.328 306.39

```

```
## - EV.NormFinder.new$'hsa-miR-335-5p' 1 83.809 308.50
##
## Step: AIC=303.9
## EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
## EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-143-3p' +
## EV.NormFinder.new$'hsa-miR-107' + EV.NormFinder.new$'hsa-miR-130b-3p'
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-107' 1 81.257 302.85
## - EV.NormFinder.new$'hsa-miR-143-3p' 1 81.905 303.78
## <none> 80.610 303.90
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 82.247 304.28
## - EV.NormFinder.new$'hsa-miR-130b-3p' 1 82.373 304.46
## - EV.NormFinder.new$'hsa-miR-335-5p' 1 83.817 306.51
##
## Step: AIC=302.85
## EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$'hsa-miR-335-5p' +
## EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-143-3p' +
## EV.NormFinder.new$'hsa-miR-130b-3p'
##
## Df Deviance AIC
## <none> 81.257 302.85
## - EV.NormFinder.new$'hsa-miR-130b-3p' 1 83.114 303.51
## - EV.NormFinder.new$'hsa-miR-143-3p' 1 83.234 303.69
## - EV.NormFinder.new$'hsa-miR-335-5p' 1 84.039 304.82
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 85.224 306.47
```

```
final.model.EV.grade.NormFinder = glm(formula = EV.all.original$'Biopsy Grade Group' ~ EV.NormFinder.new$
```

Outcome: Adverse pathology

```
# serum overlap
fullmodel.serum.overlap.ap = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ serum.overlap
step.EV.adverse.overlap.final = stepAIC(object = fullmodel.serum.overlap.ap, direction = "backward")
```

```
## Start: AIC=120.26
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-21-5p' +
## serum.overlap.new$'hsa-miR-199a-3p' + serum.overlap.new$'hsa-miR-25-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-107' +
## serum.overlap.new$'hsa-miR-26b-5p' + serum.overlap.new$'hsa-miR-1246' +
## serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-103a-3p' +
## serum.overlap.new$'hsa-miR-16-5p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-122-5p'
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-25-3p' 1 88.337 118.34
## - serum.overlap.new$'hsa-miR-103a-3p' 1 88.427 118.43
## - serum.overlap.new$'hsa-miR-21-5p' 1 88.595 118.59
## - serum.overlap.new$'hsa-miR-199a-3p' 1 88.600 118.60
## - serum.overlap.new$'hsa-miR-19b-3p' 1 88.713 118.71
```

```

## - serum.overlap.new$'hsa-miR-26b-5p' 1 88.736 118.74
## - serum.overlap.new$'hsa-miR-125b-5p' 1 89.325 119.33
## - serum.overlap.new$'hsa-miR-107' 1 89.439 119.44
## - serum.overlap.new$'hsa-miR-330-3p' 1 89.594 119.59
## - serum.overlap.new$'hsa-miR-93-5p' 1 89.634 119.63
## - serum.overlap.new$'hsa-miR-16-5p' 1 89.746 119.75
## - serum.overlap.new$'hsa-miR-23a-3p' 1 89.874 119.87
## <none> 88.259 120.26
## - serum.overlap.new$'hsa-miR-122-5p' 1 90.499 120.50
## - serum.overlap.new$'hsa-miR-1246' 1 91.384 121.38
## - serum.overlap.new$'hsa-miR-375' 1 92.123 122.12
##
## Step: AIC=118.34
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-21-5p' +
## serum.overlap.new$'hsa-miR-199a-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-26b-5p' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-330-3p' +
## serum.overlap.new$'hsa-miR-103a-3p' + serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-375' +
## serum.overlap.new$'hsa-miR-19b-3p' + serum.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-103a-3p' 1 88.541 116.54
## - serum.overlap.new$'hsa-miR-21-5p' 1 88.609 116.61
## - serum.overlap.new$'hsa-miR-19b-3p' 1 88.715 116.72
## - serum.overlap.new$'hsa-miR-199a-3p' 1 88.879 116.88
## - serum.overlap.new$'hsa-miR-26b-5p' 1 89.062 117.06
## - serum.overlap.new$'hsa-miR-125b-5p' 1 89.360 117.36
## - serum.overlap.new$'hsa-miR-16-5p' 1 89.758 117.76
## - serum.overlap.new$'hsa-miR-93-5p' 1 89.903 117.90
## - serum.overlap.new$'hsa-miR-330-3p' 1 89.942 117.94
## - serum.overlap.new$'hsa-miR-107' 1 89.984 117.98
## - serum.overlap.new$'hsa-miR-23a-3p' 1 90.225 118.22
## <none> 88.337 118.34
## - serum.overlap.new$'hsa-miR-122-5p' 1 90.533 118.53
## - serum.overlap.new$'hsa-miR-1246' 1 92.013 120.01
## - serum.overlap.new$'hsa-miR-375' 1 92.141 120.14
##
## Step: AIC=116.54
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-21-5p' +
## serum.overlap.new$'hsa-miR-199a-3p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-26b-5p' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-330-3p' +
## serum.overlap.new$'hsa-miR-16-5p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-21-5p' 1 88.723 114.72
## - serum.overlap.new$'hsa-miR-199a-3p' 1 88.959 114.96
## - serum.overlap.new$'hsa-miR-19b-3p' 1 89.040 115.04
## - serum.overlap.new$'hsa-miR-26b-5p' 1 89.153 115.15
## - serum.overlap.new$'hsa-miR-125b-5p' 1 89.407 115.41
## - serum.overlap.new$'hsa-miR-93-5p' 1 89.903 115.90

```



```

## - serum.overlap.new$'hsa-miR-330-3p' 1 90.087 116.09
## - serum.overlap.new$'hsa-miR-16-5p' 1 90.088 116.09
## - serum.overlap.new$'hsa-miR-107' 1 90.311 116.31
## - serum.overlap.new$'hsa-miR-23a-3p' 1 90.314 116.31
## <none> 88.541 116.54
## - serum.overlap.new$'hsa-miR-122-5p' 1 90.677 116.68
## - serum.overlap.new$'hsa-miR-1246' 1 92.025 118.03
## - serum.overlap.new$'hsa-miR-375' 1 92.153 118.15
##
## Step: AIC=114.72
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-199a-3p' +
## serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-107' +
## serum.overlap.new$'hsa-miR-26b-5p' + serum.overlap.new$'hsa-miR-1246' +
## serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-16-5p' +
## serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-375' +
## serum.overlap.new$'hsa-miR-19b-3p' + serum.overlap.new$'hsa-miR-122-5p'
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-199a-3p' 1 89.057 113.06
## - serum.overlap.new$'hsa-miR-19b-3p' 1 89.075 113.08
## - serum.overlap.new$'hsa-miR-26b-5p' 1 89.321 113.32
## - serum.overlap.new$'hsa-miR-125b-5p' 1 89.818 113.82
## - serum.overlap.new$'hsa-miR-93-5p' 1 89.923 113.92
## - serum.overlap.new$'hsa-miR-16-5p' 1 90.116 114.12
## - serum.overlap.new$'hsa-miR-330-3p' 1 90.132 114.13
## - serum.overlap.new$'hsa-miR-107' 1 90.386 114.39
## - serum.overlap.new$'hsa-miR-23a-3p' 1 90.498 114.50
## <none> 88.723 114.72
## - serum.overlap.new$'hsa-miR-122-5p' 1 91.037 115.04
## - serum.overlap.new$'hsa-miR-1246' 1 92.026 116.03
## - serum.overlap.new$'hsa-miR-375' 1 92.655 116.66
##
## Step: AIC=113.06
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-23a-3p' +
## serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-26b-5p' +
## serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-330-3p' +
## serum.overlap.new$'hsa-miR-16-5p' + serum.overlap.new$'hsa-miR-93-5p' +
## serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-19b-3p' +
## serum.overlap.new$'hsa-miR-122-5p'
##
## Df Deviance AIC
## - serum.overlap.new$'hsa-miR-19b-3p' 1 89.616 111.62
## - serum.overlap.new$'hsa-miR-26b-5p' 1 89.814 111.81
## - serum.overlap.new$'hsa-miR-125b-5p' 1 90.203 112.20
## - serum.overlap.new$'hsa-miR-330-3p' 1 90.310 112.31
## - serum.overlap.new$'hsa-miR-23a-3p' 1 90.501 112.50
## - serum.overlap.new$'hsa-miR-16-5p' 1 90.613 112.61
## - serum.overlap.new$'hsa-miR-93-5p' 1 90.998 113.00
## <none> 89.057 113.06
## - serum.overlap.new$'hsa-miR-122-5p' 1 91.220 113.22
## - serum.overlap.new$'hsa-miR-107' 1 91.402 113.40
## - serum.overlap.new$'hsa-miR-1246' 1 92.223 114.22
## - serum.overlap.new$'hsa-miR-375' 1 93.251 115.25
##

```

```

## Step: AIC=111.62
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-23a-3p' +
##   serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-26b-5p' +
##   serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-330-3p' +
##   serum.overlap.new$'hsa-miR-16-5p' + serum.overlap.new$'hsa-miR-93-5p' +
##   serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-122-5p'
##
##
##           Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-26b-5p' 1 90.441 110.44
## - serum.overlap.new$'hsa-miR-125b-5p' 1 90.695 110.69
## - serum.overlap.new$'hsa-miR-16-5p' 1 90.853 110.85
## - serum.overlap.new$'hsa-miR-330-3p' 1 90.871 110.87
## - serum.overlap.new$'hsa-miR-93-5p' 1 91.188 111.19
## - serum.overlap.new$'hsa-miR-107' 1 91.466 111.47
## - serum.overlap.new$'hsa-miR-23a-3p' 1 91.530 111.53
## - serum.overlap.new$'hsa-miR-122-5p' 1 91.542 111.54
## <none> 89.616 111.62
## - serum.overlap.new$'hsa-miR-1246' 1 92.644 112.64
## - serum.overlap.new$'hsa-miR-375' 1 93.786 113.79
##
## Step: AIC=110.44
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-23a-3p' +
##   serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-1246' +
##   serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-16-5p' +
##   serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-375' +
##   serum.overlap.new$'hsa-miR-122-5p'
##
##
##           Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-16-5p' 1 91.408 109.41
## - serum.overlap.new$'hsa-miR-125b-5p' 1 91.554 109.55
## - serum.overlap.new$'hsa-miR-330-3p' 1 91.652 109.65
## - serum.overlap.new$'hsa-miR-23a-3p' 1 91.946 109.95
## <none> 90.441 110.44
## - serum.overlap.new$'hsa-miR-93-5p' 1 92.741 110.74
## - serum.overlap.new$'hsa-miR-1246' 1 93.127 111.13
## - serum.overlap.new$'hsa-miR-107' 1 93.361 111.36
## - serum.overlap.new$'hsa-miR-122-5p' 1 93.607 111.61
## - serum.overlap.new$'hsa-miR-375' 1 93.808 111.81
##
## Step: AIC=109.41
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-125b-5p' + serum.overlap.new$'hsa-miR-23a-3p' +
##   serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-1246' +
##   serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-93-5p' +
##   serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-122-5p'
##
##
##           Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-125b-5p' 1 92.040 108.04
## - serum.overlap.new$'hsa-miR-23a-3p' 1 92.141 108.14
## - serum.overlap.new$'hsa-miR-330-3p' 1 92.769 108.77
## <none> 91.408 109.41
## - serum.overlap.new$'hsa-miR-375' 1 94.094 110.09
## - serum.overlap.new$'hsa-miR-122-5p' 1 94.550 110.55
## - serum.overlap.new$'hsa-miR-93-5p' 1 95.162 111.16
## - serum.overlap.new$'hsa-miR-1246' 1 95.419 111.42

```

```

## - serum.overlap.new$'hsa-miR-107'      1    98.572 114.57
##
## Step: AIC=108.04
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-23a-3p' + serum.overlap.new$'hsa-miR-107' +
##   serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-330-3p' +
##   serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-375' +
##   serum.overlap.new$'hsa-miR-122-5p'
##
##               Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-23a-3p'  1    93.024 107.02
## - serum.overlap.new$'hsa-miR-330-3p'  1    93.690 107.69
## <none>                                92.040 108.04
## - serum.overlap.new$'hsa-miR-375'    1    94.480 108.48
## - serum.overlap.new$'hsa-miR-122-5p'  1    94.583 108.58
## - serum.overlap.new$'hsa-miR-1246'   1    96.194 110.19
## - serum.overlap.new$'hsa-miR-93-5p'   1    96.442 110.44
## - serum.overlap.new$'hsa-miR-107'    1    99.801 113.80
##
## Step: AIC=107.02
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-1246' +
##   serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-93-5p' +
##   serum.overlap.new$'hsa-miR-375' + serum.overlap.new$'hsa-miR-122-5p'
##
##               Df Deviance    AIC
## - serum.overlap.new$'hsa-miR-375'    1    94.839 106.84
## <none>                                93.024 107.02
## - serum.overlap.new$'hsa-miR-330-3p'  1    95.377 107.38
## - serum.overlap.new$'hsa-miR-122-5p'  1    95.724 107.72
## - serum.overlap.new$'hsa-miR-1246'   1    96.290 108.29
## - serum.overlap.new$'hsa-miR-93-5p'   1    96.806 108.81
## - serum.overlap.new$'hsa-miR-107'    1   100.008 112.01
##
## Step: AIC=106.84
## 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-107' + serum.overlap.new$'hsa-miR-1246' +
##   serum.overlap.new$'hsa-miR-330-3p' + serum.overlap.new$'hsa-miR-93-5p' +
##   serum.overlap.new$'hsa-miR-122-5p'
##
##               Df Deviance    AIC
## <none>                                94.839 106.84
## - serum.overlap.new$'hsa-miR-330-3p'  1    97.037 107.04
## - serum.overlap.new$'hsa-miR-1246'   1    97.834 107.83
## - serum.overlap.new$'hsa-miR-122-5p'  1    98.289 108.29
## - serum.overlap.new$'hsa-miR-93-5p'   1    99.224 109.22
## - serum.overlap.new$'hsa-miR-107'    1   101.835 111.83

final.model.serum.adverse.overlap = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ serum
summary(final.model.serum.adverse.overlap)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ serum.overlap.new$'hsa-miR-330-3p' +
##   serum.overlap.new$'hsa-miR-1246' + serum.overlap.new$'hsa-miR-122-5p' +
##   serum.overlap.new$'hsa-miR-93-5p' + serum.overlap.new$'hsa-miR-107',
##   family = "binomial", data = serum.all.original)

```

```

##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.9995  -0.9916   0.6208   0.9581   1.9048
##
## Coefficients:
##                                Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   1.9989     1.0759   1.858  0.0632 .
## serum.overlap.new$'hsa-miR-330-3p'  0.7436     0.5233   1.421  0.1553
## serum.overlap.new$'hsa-miR-1246' -0.4849     0.2999  -1.617  0.1059
## serum.overlap.new$'hsa-miR-122-5p' -0.2763     0.1558  -1.774  0.0761 .
## serum.overlap.new$'hsa-miR-93-5p'  1.2388     0.6057   2.045  0.0408 *
## serum.overlap.new$'hsa-miR-107' -2.3132     0.9352  -2.473  0.0134 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##    Null deviance: 111.684  on 80  degrees of freedom
## Residual deviance:  94.839  on 75  degrees of freedom
## (122 observations deleted due to missingness)
## AIC: 106.84
##
## Number of Fisher Scoring iterations: 4

# serum geNorm
fullmodel.serum.geNorm.ap = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ serum.geNorm.
step.EV.adverse.final = stepAIC(object = fullmodel.serum.geNorm.ap, direction = "backward")

## Start:  AIC=113.37
## 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-25-3p' + serum.geNorm.new$'hsa-miR-30c-5p' +
##   serum.geNorm.new$'hsa-miR-16-5p' + serum.geNorm.new$'hsa-let-7a-5p' +
##   serum.geNorm.new$'hsa-miR-1246' + serum.geNorm.new$'hsa-miR-24-3p'
##
##                                Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-16-5p'  1  99.425 111.42
## - serum.geNorm.new$'hsa-miR-25-3p'  1  99.702 111.70
## - serum.geNorm.new$'hsa-miR-24-3p'  1  99.705 111.70
## - serum.geNorm.new$'hsa-let-7a-5p'  1  99.978 111.98
## - serum.geNorm.new$'hsa-miR-30c-5p'  1 100.134 112.13
## - serum.geNorm.new$'hsa-miR-1246'  1 101.016 113.02
## <none>                                99.374 113.37
##
## Step:  AIC=111.42
## 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-25-3p' + serum.geNorm.new$'hsa-miR-30c-5p' +
##   serum.geNorm.new$'hsa-let-7a-5p' + serum.geNorm.new$'hsa-miR-1246' +
##   serum.geNorm.new$'hsa-miR-24-3p'
##
##                                Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-24-3p'  1  99.705 109.70
## - serum.geNorm.new$'hsa-miR-25-3p'  1  99.766 109.77
## - serum.geNorm.new$'hsa-let-7a-5p'  1  99.978 109.98
## - serum.geNorm.new$'hsa-miR-30c-5p'  1 100.134 110.13
## - serum.geNorm.new$'hsa-miR-1246'  1 101.110 111.11

```

```

## <none>                                99.425 111.42
##
## Step: AIC=109.71
## 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-25-3p' + serum.geNorm.new$'hsa-miR-30c-5p' +
##   serum.geNorm.new$'hsa-let-7a-5p' + serum.geNorm.new$'hsa-miR-1246'
##
##               Df Deviance    AIC
## - serum.geNorm.new$'hsa-let-7a-5p'  1  100.083 108.08
## - serum.geNorm.new$'hsa-miR-25-3p'  1  100.705 108.70
## - serum.geNorm.new$'hsa-miR-30c-5p'  1  100.755 108.75
## - serum.geNorm.new$'hsa-miR-1246'   1  101.629 109.63
## <none>                                99.705 109.70
##
## Step: AIC=108.08
## 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-25-3p' + serum.geNorm.new$'hsa-miR-30c-5p' +
##   serum.geNorm.new$'hsa-miR-1246'
##
##               Df Deviance    AIC
## - serum.geNorm.new$'hsa-miR-30c-5p'  1  101.66 107.66
## - serum.geNorm.new$'hsa-miR-1246'   1  101.82 107.82
## <none>                                100.08 108.08
## - serum.geNorm.new$'hsa-miR-25-3p'  1  103.03 109.03
##
## Step: AIC=107.66
## 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-25-3p' + serum.geNorm.new$'hsa-miR-1246'
##
##               Df Deviance    AIC
## <none>                                101.66 107.66
## - serum.geNorm.new$'hsa-miR-1246'   1  104.73 108.73
## - serum.geNorm.new$'hsa-miR-25-3p'  1  106.12 110.12

final.model.serum.adverse.geNorm = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ serum.
summary(final.model.serum.adverse.geNorm)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ serum.geNorm.new$'hsa-miR-1246' +
##   serum.geNorm.new$'hsa-miR-25-3p', family = "binomial", data = serum.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.9688  -1.0628   0.6944   1.0474   1.9968
##
## Coefficients:
##               Estimate Std. Error z value Pr(>|z|)
## (Intercept)      -1.0865     1.0384  -1.046   0.2954
## serum.geNorm.new$'hsa-miR-1246' -0.5127     0.3114  -1.647   0.0997 .
## serum.geNorm.new$'hsa-miR-25-3p'  1.6918     0.8446   2.003   0.0452 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 111.68  on 80  degrees of freedom

```

```
## Residual deviance: 101.66 on 78 degrees of freedom
## (122 observations deleted due to missingness)
## AIC: 107.66
##
## Number of Fisher Scoring iterations: 4
```

```
# serum NormFinder
```

```
fullmodel.serum.NormFinder.ap = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ serum.NormFinder.ap,
step.EV.adverse.final = stepAIC(object = fullmodel.serum.NormFinder.ap, direction = "backward")
```

```
## Start: AIC=114.78
## 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-let-7a-5p' +
## serum.NormFinder.new$'hsa-miR-24-3p' + serum.NormFinder.new$'hsa-miR-30c-5p' +
## serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-16-5p' +
## serum.NormFinder.new$'hsa-miR-25-3p'
```

	Df	Deviance	AIC
## - serum.NormFinder.new\$'hsa-miR-16-5p'	1	100.83	112.83
## - serum.NormFinder.new\$'hsa-miR-24-3p'	1	101.10	113.10
## - serum.NormFinder.new\$'hsa-miR-30c-5p'	1	101.18	113.18
## - serum.NormFinder.new\$'hsa-let-7a-5p'	1	101.31	113.31
## - serum.NormFinder.new\$'hsa-miR-25-3p'	1	101.46	113.46
## - serum.NormFinder.new\$'hsa-miR-1246'	1	102.41	114.41
## <none>		100.78	114.78

```
##
## Step: AIC=112.83
## 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-let-7a-5p' +
## serum.NormFinder.new$'hsa-miR-24-3p' + serum.NormFinder.new$'hsa-miR-30c-5p' +
## serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-25-3p'
```

	Df	Deviance	AIC
## - serum.NormFinder.new\$'hsa-miR-24-3p'	1	101.10	111.10
## - serum.NormFinder.new\$'hsa-miR-30c-5p'	1	101.19	111.19
## - serum.NormFinder.new\$'hsa-let-7a-5p'	1	101.37	111.37
## - serum.NormFinder.new\$'hsa-miR-25-3p'	1	101.46	111.46
## - serum.NormFinder.new\$'hsa-miR-1246'	1	102.44	112.44
## <none>		100.83	112.83

```
##
## Step: AIC=111.1
## 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-let-7a-5p' +
## serum.NormFinder.new$'hsa-miR-30c-5p' + serum.NormFinder.new$'hsa-miR-1246' +
## serum.NormFinder.new$'hsa-miR-25-3p'
```

	Df	Deviance	AIC
## - serum.NormFinder.new\$'hsa-let-7a-5p'	1	101.50	109.50
## - serum.NormFinder.new\$'hsa-miR-30c-5p'	1	101.69	109.69
## - serum.NormFinder.new\$'hsa-miR-25-3p'	1	102.67	110.67
## - serum.NormFinder.new\$'hsa-miR-1246'	1	102.97	110.97
## <none>		101.10	111.10

```
##
## Step: AIC=109.5
## 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-miR-30c-5p' +
## serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-25-3p'
```

```

##                                Df Deviance    AIC
## - serum.NormFinder.new$'hsa-miR-30c-5p'  1   102.86 108.86
## - serum.NormFinder.new$'hsa-miR-1246'    1   103.17 109.17
## <none>                                101.50 109.50
## - serum.NormFinder.new$'hsa-miR-25-3p'   1   104.35 110.35
##
## Step:  AIC=108.86
## 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-miR-1246' + serum.NormFinder.new$'hsa-miR-25-3p'
##
##                                Df Deviance    AIC
## <none>                                102.86 108.86
## - serum.NormFinder.new$'hsa-miR-1246'    1   106.01 110.01
## - serum.NormFinder.new$'hsa-miR-25-3p'   1   106.39 110.39

final.model.serum.adverse.NormFinder = glm(data = serum.all.original, formula = 'Adverse Pathology' ~ se
summary(final.model.serum.adverse.NormFinder)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ serum.NormFinder.new$'hsa-miR-1246' +
##      serum.NormFinder.new$'hsa-miR-25-3p', family = "binomial",
##      data = serum.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -2.0802  -1.0629   0.7293   1.0454   1.9682
##
## Coefficients:
##                                Estimate Std. Error z value Pr(>|z|)
## (Intercept)                   -0.8010     0.9745  -0.822   0.4111
## serum.NormFinder.new$'hsa-miR-1246' -0.5037     0.3028  -1.664   0.0962 .
## serum.NormFinder.new$'hsa-miR-25-3p'  1.4152     0.7845   1.804   0.0712 .
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 111.68  on 80  degrees of freedom
## Residual deviance: 102.86  on 78  degrees of freedom
##      (122 observations deleted due to missingness)
## AIC: 108.86
##
## Number of Fisher Scoring iterations: 4

# EV geneglobe
fullmodel.EV.geneglobe.ap = glm(data = EV.all.original, formula = 'Adverse Pathology' ~ 'hsa-miR-31-5p',
step.EV.adverse.final = stepAIC(object = fullmodel.EV.geneglobe.ap, direction = "backward")

## Start:  AIC=67.08
## 'Adverse Pathology' ~ 'hsa-miR-31-5p'
##
##                                Df Deviance    AIC
## - 'hsa-miR-31-5p'  1   64.443 66.443

```

```

## <none>                63.082 67.082
##
## Step:  AIC=66.44
## 'Adverse Pathology' ~ 1

final.model.EV.adverse = glm(data = EV.all.original, formula = 'Adverse Pathology'~'hsa-let-7a-5p', fa
summary(final.model.EV.adverse)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ 'hsa-let-7a-5p', family = "binomial",
##      data = EV.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -1.6862  -1.1163   0.7398   0.8497   2.0737
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)      1.4624     0.5106   2.864  0.00419 **
## 'hsa-let-7a-5p'  -0.8817     0.3645  -2.419  0.01557 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 64.443  on 47  degrees of freedom
## Residual deviance: 55.941  on 46  degrees of freedom
##      (70 observations deleted due to missingness)
## AIC: 59.941
##
## Number of Fisher Scoring iterations: 4

## EV overlap
fullmodel.EV.overlap.AP = glm(data = EV.all.original, formula = 'Adverse Pathology'~ EV.overlap.new$'hsa
step.EV.adverse.overlap = stepAIC(object = fullmodel.EV.overlap.AP, direction = "backward")

## Start:  AIC=63.94
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-21-5p' +
##      EV.overlap.new$'hsa-miR-199a-3p' + EV.overlap.new$'hsa-miR-25-3p' +
##      EV.overlap.new$'hsa-miR-23a-3p' + EV.overlap.new$'hsa-miR-107' +
##      EV.overlap.new$'hsa-miR-26b-5p' + EV.overlap.new$'hsa-miR-1246' +
##      EV.overlap.new$'hsa-miR-330-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
##      EV.overlap.new$'hsa-miR-16-5p' + EV.overlap.new$'hsa-miR-93-5p' +
##      EV.overlap.new$'hsa-miR-375' + EV.overlap.new$'hsa-miR-19b-3p' +
##      EV.overlap.new$'hsa-miR-122-5p'
##
##              Df Deviance    AIC
## - EV.overlap.new$'hsa-miR-21-5p'      1   31.996 61.996
## - EV.overlap.new$'hsa-miR-26b-5p'      1   32.113 62.113
## - EV.overlap.new$'hsa-miR-23a-3p'      1   32.421 62.421
## - EV.overlap.new$'hsa-miR-19b-3p'      1   32.757 62.757
## - EV.overlap.new$'hsa-miR-16-5p'      1   32.995 62.995

```



```

## - EV.overlap.new$'hsa-miR-107'      1    33.433 63.433
## <none>                                31.937 63.937
## - EV.overlap.new$'hsa-miR-103a-3p'  1    34.699 64.699
## - EV.overlap.new$'hsa-miR-330-3p'   1    34.850 64.850
## - EV.overlap.new$'hsa-miR-93-5p'    1    34.910 64.910
## - EV.overlap.new$'hsa-miR-199a-3p'  1    35.011 65.011
## - EV.overlap.new$'hsa-miR-1246'     1    35.225 65.225
## - EV.overlap.new$'hsa-miR-125b-5p'  1    35.824 65.824
## - EV.overlap.new$'hsa-miR-122-5p'   1    35.970 65.970
## - EV.overlap.new$'hsa-miR-375'      1    36.034 66.034
## - EV.overlap.new$'hsa-miR-25-3p'    1    42.284 72.284
##
## Step: AIC=62
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-23a-3p' +
## EV.overlap.new$'hsa-miR-107' + EV.overlap.new$'hsa-miR-26b-5p' +
## EV.overlap.new$'hsa-miR-1246' + EV.overlap.new$'hsa-miR-330-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-16-5p' +
## EV.overlap.new$'hsa-miR-93-5p' + EV.overlap.new$'hsa-miR-375' +
## EV.overlap.new$'hsa-miR-19b-3p' + EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance    AIC
## - EV.overlap.new$'hsa-miR-26b-5p'  1    32.273 60.273
## - EV.overlap.new$'hsa-miR-23a-3p'   1    32.627 60.627
## - EV.overlap.new$'hsa-miR-19b-3p'   1    32.895 60.895
## - EV.overlap.new$'hsa-miR-16-5p'    1    33.028 61.028
## - EV.overlap.new$'hsa-miR-107'      1    33.589 61.589
## <none>                                31.996 61.996
## - EV.overlap.new$'hsa-miR-103a-3p'  1    34.981 62.981
## - EV.overlap.new$'hsa-miR-330-3p'   1    35.002 63.002
## - EV.overlap.new$'hsa-miR-199a-3p'  1    35.161 63.161
## - EV.overlap.new$'hsa-miR-1246'     1    35.871 63.871
## - EV.overlap.new$'hsa-miR-122-5p'   1    35.973 63.973
## - EV.overlap.new$'hsa-miR-375'      1    36.274 64.274
## - EV.overlap.new$'hsa-miR-125b-5p'  1    36.286 64.286
## - EV.overlap.new$'hsa-miR-93-5p'    1    37.764 65.764
## - EV.overlap.new$'hsa-miR-25-3p'    1    42.653 70.653
##
## Step: AIC=60.27
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-23a-3p' +
## EV.overlap.new$'hsa-miR-107' + EV.overlap.new$'hsa-miR-1246' +
## EV.overlap.new$'hsa-miR-330-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
## EV.overlap.new$'hsa-miR-16-5p' + EV.overlap.new$'hsa-miR-93-5p' +
## EV.overlap.new$'hsa-miR-375' + EV.overlap.new$'hsa-miR-19b-3p' +
## EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance    AIC
## - EV.overlap.new$'hsa-miR-23a-3p'  1    32.645 58.645
## - EV.overlap.new$'hsa-miR-16-5p'    1    33.320 59.320
## - EV.overlap.new$'hsa-miR-19b-3p'   1    33.430 59.430
## - EV.overlap.new$'hsa-miR-107'      1    33.943 59.943
## <none>                                32.273 60.273
## - EV.overlap.new$'hsa-miR-330-3p'   1    35.003 61.003

```

```

## - EV.overlap.new$'hsa-miR-199a-3p' 1 35.293 61.293
## - EV.overlap.new$'hsa-miR-103a-3p' 1 35.584 61.584
## - EV.overlap.new$'hsa-miR-122-5p' 1 36.014 62.014
## - EV.overlap.new$'hsa-miR-1246' 1 36.032 62.032
## - EV.overlap.new$'hsa-miR-375' 1 36.291 62.291
## - EV.overlap.new$'hsa-miR-125b-5p' 1 36.312 62.312
## - EV.overlap.new$'hsa-miR-93-5p' 1 37.816 63.816
## - EV.overlap.new$'hsa-miR-25-3p' 1 43.713 69.713
##
## Step: AIC=58.64
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-1246' + EV.overlap.new$'hsa-miR-330-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-16-5p' +
## EV.overlap.new$'hsa-miR-93-5p' + EV.overlap.new$'hsa-miR-375' +
## EV.overlap.new$'hsa-miR-19b-3p' + EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-19b-3p' 1 33.770 57.770
## - EV.overlap.new$'hsa-miR-107' 1 34.520 58.520
## <none> 32.645 58.645
## - EV.overlap.new$'hsa-miR-16-5p' 1 34.846 58.846
## - EV.overlap.new$'hsa-miR-330-3p' 1 35.046 59.046
## - EV.overlap.new$'hsa-miR-199a-3p' 1 36.006 60.006
## - EV.overlap.new$'hsa-miR-103a-3p' 1 36.092 60.092
## - EV.overlap.new$'hsa-miR-122-5p' 1 36.097 60.097
## - EV.overlap.new$'hsa-miR-1246' 1 36.417 60.417
## - EV.overlap.new$'hsa-miR-375' 1 36.557 60.557
## - EV.overlap.new$'hsa-miR-125b-5p' 1 36.992 60.992
## - EV.overlap.new$'hsa-miR-93-5p' 1 38.790 62.790
## - EV.overlap.new$'hsa-miR-25-3p' 1 44.484 68.484
##
## Step: AIC=57.77
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-1246' + EV.overlap.new$'hsa-miR-330-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-16-5p' +
## EV.overlap.new$'hsa-miR-93-5p' + EV.overlap.new$'hsa-miR-375' +
## EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-16-5p' 1 34.856 56.856
## - EV.overlap.new$'hsa-miR-107' 1 35.116 57.116
## <none> 33.770 57.770
## - EV.overlap.new$'hsa-miR-103a-3p' 1 36.469 58.469
## - EV.overlap.new$'hsa-miR-330-3p' 1 36.702 58.702
## - EV.overlap.new$'hsa-miR-375' 1 37.780 59.780
## - EV.overlap.new$'hsa-miR-199a-3p' 1 37.849 59.849
## - EV.overlap.new$'hsa-miR-122-5p' 1 38.283 60.283
## - EV.overlap.new$'hsa-miR-1246' 1 38.656 60.656
## - EV.overlap.new$'hsa-miR-125b-5p' 1 39.835 61.835
## - EV.overlap.new$'hsa-miR-93-5p' 1 39.972 61.972
## - EV.overlap.new$'hsa-miR-25-3p' 1 46.057 68.057
##

```

```

## Step: AIC=56.86
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-107' +
## EV.overlap.new$'hsa-miR-1246' + EV.overlap.new$'hsa-miR-330-3p' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-93-5p' +
## EV.overlap.new$'hsa-miR-375' + EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-107' 1 36.394 56.394
## <none> 34.856 56.856
## - EV.overlap.new$'hsa-miR-330-3p' 1 36.912 56.912
## - EV.overlap.new$'hsa-miR-103a-3p' 1 37.640 57.640
## - EV.overlap.new$'hsa-miR-375' 1 37.943 57.943
## - EV.overlap.new$'hsa-miR-122-5p' 1 38.478 58.478
## - EV.overlap.new$'hsa-miR-199a-3p' 1 38.688 58.688
## - EV.overlap.new$'hsa-miR-1246' 1 39.349 59.349
## - EV.overlap.new$'hsa-miR-125b-5p' 1 39.883 59.883
## - EV.overlap.new$'hsa-miR-93-5p' 1 40.130 60.130
## - EV.overlap.new$'hsa-miR-25-3p' 1 47.101 67.101
##
## Step: AIC=56.39
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-1246' +
## EV.overlap.new$'hsa-miR-330-3p' + EV.overlap.new$'hsa-miR-103a-3p' +
## EV.overlap.new$'hsa-miR-93-5p' + EV.overlap.new$'hsa-miR-375' +
## EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## - EV.overlap.new$'hsa-miR-330-3p' 1 37.681 55.681
## <none> 36.394 56.394
## - EV.overlap.new$'hsa-miR-375' 1 39.901 57.901
## - EV.overlap.new$'hsa-miR-103a-3p' 1 40.159 58.159
## - EV.overlap.new$'hsa-miR-199a-3p' 1 40.187 58.187
## - EV.overlap.new$'hsa-miR-1246' 1 40.905 58.905
## - EV.overlap.new$'hsa-miR-93-5p' 1 41.304 59.304
## - EV.overlap.new$'hsa-miR-125b-5p' 1 41.702 59.702
## - EV.overlap.new$'hsa-miR-122-5p' 1 42.800 60.800
## - EV.overlap.new$'hsa-miR-25-3p' 1 49.912 67.912
##
## Step: AIC=55.68
## 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-125b-5p' + EV.overlap.new$'hsa-miR-199a-3p' +
## EV.overlap.new$'hsa-miR-25-3p' + EV.overlap.new$'hsa-miR-1246' +
## EV.overlap.new$'hsa-miR-103a-3p' + EV.overlap.new$'hsa-miR-93-5p' +
## EV.overlap.new$'hsa-miR-375' + EV.overlap.new$'hsa-miR-122-5p'
##
##
## Df Deviance AIC
## <none> 37.681 55.681
## - EV.overlap.new$'hsa-miR-199a-3p' 1 40.468 56.468
## - EV.overlap.new$'hsa-miR-375' 1 40.511 56.511
## - EV.overlap.new$'hsa-miR-103a-3p' 1 41.080 57.080
## - EV.overlap.new$'hsa-miR-1246' 1 41.531 57.531
## - EV.overlap.new$'hsa-miR-125b-5p' 1 42.038 58.038
## - EV.overlap.new$'hsa-miR-93-5p' 1 42.131 58.131
## - EV.overlap.new$'hsa-miR-122-5p' 1 43.280 59.280

```

```
## - EV.overlap.new$'hsa-miR-25-3p'      1    50.177 66.177

final.model.EV.adverse.overlap = glm(data = EV.all.original, formula = 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-199a-3p' +
summary(final.model.EV.adverse.overlap)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ EV.overlap.new$'hsa-miR-199a-3p' +
##      EV.overlap.new$'hsa-miR-375' + EV.overlap.new$'hsa-miR-103a-3p' +
##      EV.overlap.new$'hsa-miR-1246' + EV.overlap.new$'hsa-miR-125b-5p' +
##      EV.overlap.new$'hsa-miR-93-5p' + EV.overlap.new$'hsa-miR-122-5p' +
##      EV.overlap.new$'hsa-miR-25-3p', family = "binomial", data = EV.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -2.15953  -0.59818   0.05808   0.63206   2.10914
##
## Coefficients:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept)      -12.2755     6.3038  -1.947   0.0515 .
## EV.overlap.new$'hsa-miR-199a-3p'    3.1527     2.0279   1.555   0.1200
## EV.overlap.new$'hsa-miR-375'       -0.6917     0.4384  -1.578   0.1146
## EV.overlap.new$'hsa-miR-103a-3p'    3.4941     2.1377   1.635   0.1021
## EV.overlap.new$'hsa-miR-1246'       1.7427     0.9454   1.843   0.0653 .
## EV.overlap.new$'hsa-miR-125b-5p'   -2.3091     1.2189  -1.894   0.0582 .
## EV.overlap.new$'hsa-miR-93-5p'    -10.9829     6.1679  -1.781   0.0750 .
## EV.overlap.new$'hsa-miR-122-5p'     0.8800     0.4380   2.009   0.0445 *
## EV.overlap.new$'hsa-miR-25-3p'    16.7059     6.6895   2.497   0.0125 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 64.443  on 47  degrees of freedom
## Residual deviance: 37.681  on 39  degrees of freedom
##      (70 observations deleted due to missingness)
## AIC: 55.681
##
## Number of Fisher Scoring iterations: 6

# EV geNorm
fullmodel.EV.geNorm.AP = glm(data = EV.all.original, formula = 'Adverse Pathology' ~ EV.geNorm.new$'hsa-miR-363-3p' +
step.EV.adverse.geNorm = stepAIC(object = fullmodel.EV.geNorm.AP, direction = "backward")

## Start:  AIC=53.72
## 'Adverse Pathology' ~ EV.geNorm.new$'hsa-miR-363-3p' + EV.geNorm.new$'hsa-miR-19b-3p' +
##      EV.geNorm.new$'hsa-miR-16-5p' + EV.geNorm.new$'hsa-let-7a-5p' +
##      EV.geNorm.new$'hsa-miR-451a' + EV.geNorm.new$'hsa-miR-30c-5p' +
##      EV.geNorm.new$'hsa-miR-301a-3p' + EV.geNorm.new$'hsa-miR-199a-5p' +
##      EV.geNorm.new$'hsa-miR-26b-5p' + EV.geNorm.new$'hsa-miR-107' +
##      EV.geNorm.new$'hsa-miR-103a-3p' + EV.geNorm.new$'hsa-miR-191-5p' +
##      EV.geNorm.new$'hsa-miR-27b-3p'
```

```

##
##
## - EV.geNorm.new$`hsa-miR-191-5p` 1 25.854 51.854
## - EV.geNorm.new$`hsa-miR-16-5p` 1 25.960 51.960
## - EV.geNorm.new$`hsa-miR-30c-5p` 1 26.083 52.083
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 26.946 52.946
## - EV.geNorm.new$`hsa-miR-451a` 1 27.441 53.441
## <none> 25.722 53.722
## - EV.geNorm.new$`hsa-miR-199a-5p` 1 28.030 54.030
## - EV.geNorm.new$`hsa-miR-27b-3p` 1 28.483 54.483
## - EV.geNorm.new$`hsa-miR-363-3p` 1 28.788 54.788
## - EV.geNorm.new$`hsa-miR-107` 1 29.959 55.959
## - EV.geNorm.new$`hsa-miR-19b-3p` 1 32.280 58.280
## - EV.geNorm.new$`hsa-let-7a-5p` 1 32.642 58.642
## - EV.geNorm.new$`hsa-miR-301a-3p` 1 35.904 61.904
## - EV.geNorm.new$`hsa-miR-103a-3p` 1 36.552 62.552
##
## Step: AIC=51.85
## `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-363-3p` + EV.geNorm.new$`hsa-miR-19b-3p` +
## EV.geNorm.new$`hsa-miR-16-5p` + EV.geNorm.new$`hsa-let-7a-5p` +
## EV.geNorm.new$`hsa-miR-451a` + EV.geNorm.new$`hsa-miR-30c-5p` +
## EV.geNorm.new$`hsa-miR-301a-3p` + EV.geNorm.new$`hsa-miR-199a-5p` +
## EV.geNorm.new$`hsa-miR-26b-5p` + EV.geNorm.new$`hsa-miR-107` +
## EV.geNorm.new$`hsa-miR-103a-3p` + EV.geNorm.new$`hsa-miR-27b-3p`
##
##
## - EV.geNorm.new$`hsa-miR-16-5p` 1 26.036 50.036
## - EV.geNorm.new$`hsa-miR-30c-5p` 1 26.331 50.331
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 27.192 51.192
## - EV.geNorm.new$`hsa-miR-451a` 1 27.574 51.574
## <none> 25.854 51.854
## - EV.geNorm.new$`hsa-miR-199a-5p` 1 28.080 52.080
## - EV.geNorm.new$`hsa-miR-363-3p` 1 28.788 52.788
## - EV.geNorm.new$`hsa-miR-27b-3p` 1 28.924 52.924
## - EV.geNorm.new$`hsa-miR-107` 1 30.042 54.042
## - EV.geNorm.new$`hsa-miR-19b-3p` 1 32.463 56.463
## - EV.geNorm.new$`hsa-let-7a-5p` 1 35.557 59.557
## - EV.geNorm.new$`hsa-miR-301a-3p` 1 36.235 60.235
## - EV.geNorm.new$`hsa-miR-103a-3p` 1 36.945 60.945
##
## Step: AIC=50.04
## `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-363-3p` + EV.geNorm.new$`hsa-miR-19b-3p` +
## EV.geNorm.new$`hsa-let-7a-5p` + EV.geNorm.new$`hsa-miR-451a` +
## EV.geNorm.new$`hsa-miR-30c-5p` + EV.geNorm.new$`hsa-miR-301a-3p` +
## EV.geNorm.new$`hsa-miR-199a-5p` + EV.geNorm.new$`hsa-miR-26b-5p` +
## EV.geNorm.new$`hsa-miR-107` + EV.geNorm.new$`hsa-miR-103a-3p` +
## EV.geNorm.new$`hsa-miR-27b-3p`
##
##
## - EV.geNorm.new$`hsa-miR-30c-5p` 1 26.371 48.371
## - EV.geNorm.new$`hsa-miR-26b-5p` 1 27.205 49.205
## <none> 26.036 50.036
## - EV.geNorm.new$`hsa-miR-199a-5p` 1 28.151 50.151
## - EV.geNorm.new$`hsa-miR-363-3p` 1 28.838 50.838

```

```

## - EV.geNorm.new$`hsa-miR-451a`      1  28.958 50.958
## - EV.geNorm.new$`hsa-miR-27b-3p`    1  29.368 51.368
## - EV.geNorm.new$`hsa-miR-107`      1  30.566 52.566
## - EV.geNorm.new$`hsa-miR-19b-3p`    1  33.474 55.474
## - EV.geNorm.new$`hsa-let-7a-5p`    1  35.557 57.557
## - EV.geNorm.new$`hsa-miR-301a-3p`   1  36.405 58.405
## - EV.geNorm.new$`hsa-miR-103a-3p`   1  37.270 59.270
##
## Step: AIC=48.37
## `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-363-3p` + EV.geNorm.new$`hsa-miR-19b-3p` +
##   EV.geNorm.new$`hsa-let-7a-5p` + EV.geNorm.new$`hsa-miR-451a` +
##   EV.geNorm.new$`hsa-miR-301a-3p` + EV.geNorm.new$`hsa-miR-199a-5p` +
##   EV.geNorm.new$`hsa-miR-26b-5p` + EV.geNorm.new$`hsa-miR-107` +
##   EV.geNorm.new$`hsa-miR-103a-3p` + EV.geNorm.new$`hsa-miR-27b-3p`
##
##                                     Df Deviance   AIC
## - EV.geNorm.new$`hsa-miR-26b-5p`    1  27.218 47.218
## - EV.geNorm.new$`hsa-miR-199a-5p`    1  28.152 48.152
## <none>                                26.371 48.371
## - EV.geNorm.new$`hsa-miR-27b-3p`    1  29.577 49.577
## - EV.geNorm.new$`hsa-miR-451a`      1  29.712 49.712
## - EV.geNorm.new$`hsa-miR-363-3p`    1  30.239 50.239
## - EV.geNorm.new$`hsa-miR-107`      1  30.676 50.676
## - EV.geNorm.new$`hsa-miR-19b-3p`    1  33.595 53.595
## - EV.geNorm.new$`hsa-miR-301a-3p`   1  36.662 56.662
## - EV.geNorm.new$`hsa-let-7a-5p`    1  37.320 57.320
## - EV.geNorm.new$`hsa-miR-103a-3p`   1  37.450 57.450
##
## Step: AIC=47.22
## `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-363-3p` + EV.geNorm.new$`hsa-miR-19b-3p` +
##   EV.geNorm.new$`hsa-let-7a-5p` + EV.geNorm.new$`hsa-miR-451a` +
##   EV.geNorm.new$`hsa-miR-301a-3p` + EV.geNorm.new$`hsa-miR-199a-5p` +
##   EV.geNorm.new$`hsa-miR-107` + EV.geNorm.new$`hsa-miR-103a-3p` +
##   EV.geNorm.new$`hsa-miR-27b-3p`
##
##                                     Df Deviance   AIC
## <none>                                27.218 47.218
## - EV.geNorm.new$`hsa-miR-199a-5p`    1  29.680 47.680
## - EV.geNorm.new$`hsa-miR-27b-3p`    1  29.781 47.781
## - EV.geNorm.new$`hsa-miR-451a`      1  30.287 48.287
## - EV.geNorm.new$`hsa-miR-363-3p`    1  30.362 48.362
## - EV.geNorm.new$`hsa-miR-107`      1  31.105 49.105
## - EV.geNorm.new$`hsa-miR-19b-3p`    1  34.262 52.262
## - EV.geNorm.new$`hsa-miR-301a-3p`   1  36.823 54.823
## - EV.geNorm.new$`hsa-let-7a-5p`    1  37.361 55.361
## - EV.geNorm.new$`hsa-miR-103a-3p`   1  37.743 55.743

final.model.EV.adverse.geNorm = glm(data = EV.all.original, formula = `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-451a` + EV.geNorm.new$`hsa-miR-363-3p` + EV.geNorm.new$`hsa-miR-107` + EV.geNorm.new$`hsa-miR-19b-3p` + EV.geNorm.new$`hsa-miR-103a-3p`, data = EV.all.original)
summary(final.model.EV.adverse.geNorm)

##
## Call:
## glm(formula = `Adverse Pathology` ~ EV.geNorm.new$`hsa-miR-199a-5p` +

```

```
## EV.geNorm.new$'hsa-miR-27b-3p' + EV.geNorm.new$'hsa-miR-451a' +
## EV.geNorm.new$'hsa-miR-363-3p' + EV.geNorm.new$'hsa-miR-107' +
## EV.geNorm.new$'hsa-miR-19b-3p' + EV.geNorm.new$'hsa-miR-301a-3p' +
## EV.geNorm.new$'hsa-let-7a-5p' + EV.geNorm.new$'hsa-miR-103a-3p',
## family = "binomial", data = EV.all.original)
##
## Deviance Residuals:
##      Min       1Q   Median       3Q      Max
## -2.02986  -0.16077   0.08362   0.35147   1.45166
##
## Coefficients:
##                  Estimate Std. Error z value Pr(>|z|)
## (Intercept)         -9.538      5.124  -1.862   0.0627 .
## EV.geNorm.new$'hsa-miR-199a-5p'    -2.165      1.554  -1.393   0.1636
## EV.geNorm.new$'hsa-miR-27b-3p'     4.667      3.140   1.486   0.1372
## EV.geNorm.new$'hsa-miR-451a'     -3.500      2.500  -1.400   0.1615
## EV.geNorm.new$'hsa-miR-363-3p'     4.952      3.989   1.241   0.2145
## EV.geNorm.new$'hsa-miR-107'    -22.091     13.422  -1.646   0.0998 .
## EV.geNorm.new$'hsa-miR-19b-3p'     6.449      2.936   2.196   0.0281 *
## EV.geNorm.new$'hsa-miR-301a-3p'    -7.741      3.596  -2.153   0.0313 *
## EV.geNorm.new$'hsa-let-7a-5p'    -13.629      7.146  -1.907   0.0565 .
## EV.geNorm.new$'hsa-miR-103a-3p'   40.854     19.658   2.078   0.0377 *
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
##      Null deviance: 64.443  on 47  degrees of freedom
## Residual deviance: 27.218  on 38  degrees of freedom
##      (70 observations deleted due to missingness)
## AIC: 47.218
##
## Number of Fisher Scoring iterations: 7
```

EV NormFinder

```
fullmodel.EV.NormFinder.AP = glm(data = EV.all.original, formula = 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' +
EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
EV.NormFinder.new$'hsa-miR-222-3p' + EV.NormFinder.new$'hsa-miR-93-5p' +
EV.NormFinder.new$'hsa-miR-320a' + EV.NormFinder.new$'hsa-miR-199a-5p' +
EV.NormFinder.new$'hsa-miR-301a-3p' + EV.NormFinder.new$'hsa-miR-107' +
EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-345-5p' +
EV.NormFinder.new$'hsa-miR-103a-3p'
step.EV.adverse.NormFinder = stepAIC(object = fullmodel.EV.NormFinder.AP, direction = "backward")
```

```
## Start: AIC=61.99
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-222-3p' + EV.NormFinder.new$'hsa-miR-93-5p' +
## EV.NormFinder.new$'hsa-miR-320a' + EV.NormFinder.new$'hsa-miR-199a-5p' +
## EV.NormFinder.new$'hsa-miR-301a-3p' + EV.NormFinder.new$'hsa-miR-107' +
## EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-345-5p' +
## EV.NormFinder.new$'hsa-miR-103a-3p'
##
##              Df Deviance    AIC
## - EV.NormFinder.new$'hsa-miR-222-3p'    1    30.011 60.011
## - EV.NormFinder.new$'hsa-miR-320a'      1    30.127 60.127
## - EV.NormFinder.new$'hsa-miR-107'       1    30.131 60.131
## - EV.NormFinder.new$'hsa-miR-199a-5p'   1    30.145 60.145
```

```

## - EV.NormFinder.new$'hsa-miR-345-5p' 1 30.358 60.358
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 30.408 60.408
## - EV.NormFinder.new$'hsa-miR-301a-3p' 1 30.451 60.451
## - EV.NormFinder.new$'hsa-miR-451a' 1 30.963 60.963
## - EV.NormFinder.new$'hsa-miR-16-5p' 1 31.287 61.287
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 31.889 61.889
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 31.981 61.981
## <none> 29.994 61.994
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 34.215 64.215
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 35.669 65.669
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 35.848 65.848
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 37.385 67.385
##
## Step: AIC=60.01
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-320a' +
## EV.NormFinder.new$'hsa-miR-199a-5p' + EV.NormFinder.new$'hsa-miR-301a-3p' +
## EV.NormFinder.new$'hsa-miR-107' + EV.NormFinder.new$'hsa-miR-191-5p' +
## EV.NormFinder.new$'hsa-miR-345-5p' + EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-107' 1 30.191 58.191
## - EV.NormFinder.new$'hsa-miR-320a' 1 30.230 58.230
## - EV.NormFinder.new$'hsa-miR-199a-5p' 1 30.245 58.245
## - EV.NormFinder.new$'hsa-miR-345-5p' 1 30.365 58.365
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 30.500 58.500
## - EV.NormFinder.new$'hsa-miR-451a' 1 30.963 58.963
## - EV.NormFinder.new$'hsa-miR-301a-3p' 1 30.968 58.968
## - EV.NormFinder.new$'hsa-miR-16-5p' 1 31.357 59.357
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 31.980 59.980
## <none> 30.011 60.011
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 32.078 60.078
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 34.288 62.288
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 35.672 63.672
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 35.883 63.883
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 37.477 65.477
##
## Step: AIC=58.19
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-320a' +
## EV.NormFinder.new$'hsa-miR-199a-5p' + EV.NormFinder.new$'hsa-miR-301a-3p' +
## EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-345-5p' +
## EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-320a' 1 30.449 56.449
## - EV.NormFinder.new$'hsa-miR-345-5p' 1 30.480 56.480
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 30.548 56.548
## - EV.NormFinder.new$'hsa-miR-199a-5p' 1 30.564 56.564
## - EV.NormFinder.new$'hsa-miR-301a-3p' 1 31.162 57.162

```



```

## - EV.NormFinder.new$'hsa-miR-16-5p'      1    31.558 57.558
## <none>                                     30.191 58.191
## - EV.NormFinder.new$'hsa-miR-451a'      1    32.421 58.421
## - EV.NormFinder.new$'hsa-miR-363-3p'    1    32.448 58.448
## - EV.NormFinder.new$'hsa-miR-19b-3p'    1    34.406 60.406
## - EV.NormFinder.new$'hsa-miR-93-5p'     1    36.132 62.132
## - EV.NormFinder.new$'hsa-miR-103a-3p'   1    36.791 62.791
## - EV.NormFinder.new$'hsa-miR-30c-5p'    1    36.979 62.979
## - EV.NormFinder.new$'hsa-miR-25-3p'     1    39.046 65.046
##
## Step: AIC=56.45
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-199a-5p' +
## EV.NormFinder.new$'hsa-miR-301a-3p' + EV.NormFinder.new$'hsa-miR-191-5p' +
## EV.NormFinder.new$'hsa-miR-345-5p' + EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-345-5p'    1    30.585 54.585
## - EV.NormFinder.new$'hsa-miR-199a-5p'    1    31.001 55.001
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    31.005 55.005
## - EV.NormFinder.new$'hsa-miR-16-5p'     1    31.914 55.914
## - EV.NormFinder.new$'hsa-miR-301a-3p'    1    32.293 56.293
## <none>                                     30.449 56.449
## - EV.NormFinder.new$'hsa-miR-451a'      1    33.922 57.922
## - EV.NormFinder.new$'hsa-miR-363-3p'    1    34.883 58.883
## - EV.NormFinder.new$'hsa-miR-19b-3p'    1    35.330 59.330
## - EV.NormFinder.new$'hsa-miR-93-5p'     1    36.391 60.391
## - EV.NormFinder.new$'hsa-miR-103a-3p'   1    36.957 60.957
## - EV.NormFinder.new$'hsa-miR-30c-5p'    1    37.089 61.089
## - EV.NormFinder.new$'hsa-miR-25-3p'     1    40.395 64.395
##
## Step: AIC=54.58
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-199a-5p' +
## EV.NormFinder.new$'hsa-miR-301a-3p' + EV.NormFinder.new$'hsa-miR-191-5p' +
## EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-199a-5p'    1    31.132 53.132
## - EV.NormFinder.new$'hsa-miR-191-5p'    1    31.294 53.294
## <none>                                     30.585 54.585
## - EV.NormFinder.new$'hsa-miR-301a-3p'    1    32.659 54.659
## - EV.NormFinder.new$'hsa-miR-16-5p'     1    33.138 55.138
## - EV.NormFinder.new$'hsa-miR-451a'      1    34.462 56.462
## - EV.NormFinder.new$'hsa-miR-363-3p'    1    36.019 58.019
## - EV.NormFinder.new$'hsa-miR-19b-3p'    1    36.268 58.268
## - EV.NormFinder.new$'hsa-miR-93-5p'     1    36.541 58.541
## - EV.NormFinder.new$'hsa-miR-103a-3p'   1    37.249 59.249
## - EV.NormFinder.new$'hsa-miR-30c-5p'    1    37.323 59.323
## - EV.NormFinder.new$'hsa-miR-25-3p'     1    42.393 64.393

```

```

##
## Step: AIC=53.13
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-301a-3p' +
## EV.NormFinder.new$'hsa-miR-191-5p' + EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-191-5p' 1 31.491 51.491
## - EV.NormFinder.new$'hsa-miR-301a-3p' 1 33.024 53.024
## <none> 31.132 53.132
## - EV.NormFinder.new$'hsa-miR-16-5p' 1 33.230 53.230
## - EV.NormFinder.new$'hsa-miR-451a' 1 34.952 54.952
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 36.220 56.220
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 36.589 56.589
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 36.779 56.779
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 37.674 57.674
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 38.215 58.215
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 42.400 62.400
##
## Step: AIC=51.49
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-301a-3p' +
## EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-301a-3p' 1 33.203 51.203
## <none> 31.491 51.491
## - EV.NormFinder.new$'hsa-miR-16-5p' 1 33.547 51.547
## - EV.NormFinder.new$'hsa-miR-451a' 1 36.104 54.104
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 36.620 54.620
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 36.707 54.707
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 36.787 54.787
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 37.924 55.924
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 39.227 57.227
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 43.583 61.583
##
## Step: AIC=51.2
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-16-5p' +
## EV.NormFinder.new$'hsa-miR-30c-5p' + EV.NormFinder.new$'hsa-miR-451a' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## - EV.NormFinder.new$'hsa-miR-16-5p' 1 34.799 50.799
## <none> 33.203 51.203
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 37.742 53.742
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 37.872 53.872
## - EV.NormFinder.new$'hsa-miR-451a' 1 37.917 53.917
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 38.433 54.433
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 38.743 54.743

```

```

## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 39.272 55.272
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 46.019 62.019
##
## Step: AIC=50.8
## 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-25-3p' + EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-30c-5p' +
## EV.NormFinder.new$'hsa-miR-451a' + EV.NormFinder.new$'hsa-miR-93-5p' +
## EV.NormFinder.new$'hsa-miR-103a-3p'
##
##
## Df Deviance AIC
## <none> 34.799 50.799
## - EV.NormFinder.new$'hsa-miR-363-3p' 1 37.772 51.772
## - EV.NormFinder.new$'hsa-miR-19b-3p' 1 38.030 52.030
## - EV.NormFinder.new$'hsa-miR-103a-3p' 1 39.749 53.749
## - EV.NormFinder.new$'hsa-miR-93-5p' 1 40.106 54.106
## - EV.NormFinder.new$'hsa-miR-30c-5p' 1 40.158 54.158
## - EV.NormFinder.new$'hsa-miR-451a' 1 41.728 55.728
## - EV.NormFinder.new$'hsa-miR-25-3p' 1 46.020 60.020

final.model.EV.adverse.NormFinder = glm(data = EV.all.original, formula = 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-363-3p' +
EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-103a-3p' +
EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-30c-5p' +
EV.NormFinder.new$'hsa-miR-451a' + EV.NormFinder.new$'hsa-miR-25-3p',
family = "binomial", data = EV.all.original)

##
## Call:
## glm(formula = 'Adverse Pathology' ~ EV.NormFinder.new$'hsa-miR-363-3p' +
## EV.NormFinder.new$'hsa-miR-19b-3p' + EV.NormFinder.new$'hsa-miR-103a-3p' +
## EV.NormFinder.new$'hsa-miR-93-5p' + EV.NormFinder.new$'hsa-miR-30c-5p' +
## EV.NormFinder.new$'hsa-miR-451a' + EV.NormFinder.new$'hsa-miR-25-3p',
## family = "binomial", data = EV.all.original)
##
## Deviance Residuals:
## Min 1Q Median 3Q Max
## -2.3347 -0.4919 0.1162 0.5955 1.7535
##
## Coefficients:
## Estimate Std. Error z value Pr(>|z|)
## (Intercept) -1.302 3.886 -0.335 0.7376
## EV.NormFinder.new$'hsa-miR-363-3p' 2.787 1.832 1.521 0.1281
## EV.NormFinder.new$'hsa-miR-19b-3p' 3.119 1.937 1.610 0.1073
## EV.NormFinder.new$'hsa-miR-103a-3p' 5.127 2.571 1.994 0.0461 *
## EV.NormFinder.new$'hsa-miR-93-5p' -10.895 5.459 -1.996 0.0460 *
## EV.NormFinder.new$'hsa-miR-30c-5p' -7.057 3.468 -2.035 0.0419 *
## EV.NormFinder.new$'hsa-miR-451a' -5.361 2.389 -2.244 0.0248 *
## EV.NormFinder.new$'hsa-miR-25-3p' 13.995 5.752 2.433 0.0150 *
## ---
## Signif. codes: 0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## (Dispersion parameter for binomial family taken to be 1)
##
## Null deviance: 64.443 on 47 degrees of freedom
## Residual deviance: 34.799 on 40 degrees of freedom
## (70 observations deleted due to missingness)
## AIC: 50.799
##

```

```
## Number of Fisher Scoring iterations: 6
```

hsa-let-7a-5p was removed from the GLM fitting in EV NormFinder due to errors. hsa-miR-25-3p was removed from the GLM fitting in EV geNorm due to errors.

Regression models

Combine grade 1-2 as low-grade and grade 3-5 as high-grade.

```
biopsy.grade$grades = ifelse(biopsy.grade$'Biopsy Grade Group' <= 2, "low", "high") %>% as.factor()
biopsy.grade = biopsy.grade[, -2]
```

Read in data files for covariates.

```
# Import covariate
covariates = readxl::read_excel(path = "./data/3-1 data/Clinical Covariates_Updated.xlsx", sheet = "Covariates")
covariates = covariates[, -2]

# Combine datasets for biopsy grade group
serum.grade.covariates.geneglobe = left_join(serum.geneglobe.new, biopsy.grade, by = "Patient ID")
serum.grade.covariates.geneglobe = left_join(serum.grade.covariates.geneglobe, covariates, by = "Patient ID")

serum.grade.covariates.geNorm = left_join(serum.geNorm.new, biopsy.grade, by = "Patient ID")
serum.grade.covariates.geNorm = left_join(serum.grade.covariates.geNorm, covariates, by = "Patient ID")

serum.grade.covariates.NormFinder = left_join(serum.NormFinder.new, biopsy.grade, by = "Patient ID")
serum.grade.covariates.NormFinder = left_join(serum.grade.covariates.NormFinder, covariates, by = "Patient ID")

serum.grade.covariates.overlap = left_join(serum.overlap.new, biopsy.grade, by = "Patient ID")
serum.grade.covariates.overlap = left_join(serum.grade.covariates.overlap, covariates, by = "Patient ID")

EV.grade.covariates.geneglobe = left_join(EV.geneglobe.new, biopsy.grade, by = "Patient ID")
EV.grade.covariates.geneglobe = left_join(EV.grade.covariates.geneglobe, covariates, by = "Patient ID")

EV.grade.covariates.geNorm = left_join(EV.geNorm.new, biopsy.grade, by = "Patient ID")
EV.grade.covariates.geNorm = left_join(EV.grade.covariates.geNorm, covariates, by = "Patient ID")

EV.grade.covariates.NormFinder = left_join(EV.NormFinder.new, biopsy.grade, by = "Patient ID")
EV.grade.covariates.NormFinder = left_join(EV.grade.covariates.NormFinder, covariates, by = "Patient ID")

EV.grade.covariates.overlap = left_join(EV.overlap.new, biopsy.grade, by = "Patient ID")
EV.grade.covariates.overlap = left_join(EV.grade.covariates.overlap, covariates, by = "Patient ID")

# Combine datasets for adverse pathology
serum.adverse.covariates.geneglobe = left_join(serum.geneglobe.new, adverse.pathology, by = "Patient ID")
serum.adverse.covariates.geneglobe = left_join(serum.adverse.covariates.geneglobe, covariates, by = "Patient ID")

serum.adverse.covariates.geNorm = left_join(serum.geNorm.new, adverse.pathology, by = "Patient ID")
serum.adverse.covariates.geNorm = left_join(serum.adverse.covariates.geNorm, covariates, by = "Patient ID")

serum.adverse.covariates.NormFinder = left_join(serum.NormFinder.new, adverse.pathology, by = "Patient ID")
serum.adverse.covariates.NormFinder = left_join(serum.adverse.covariates.NormFinder, covariates, by = "Patient ID")
```

```

serum.adverse.covariates.overlap = left_join(serum.overlap.new, adverse.pathology, by = "Patient ID")
serum.adverse.covariates.overlap = left_join(serum.adverse.covariates.overlap, covariates, by = "Patient ID")

EV.adverse.covariates.geneglobe = left_join(EV.geneglobe.new, adverse.pathology, by = "Patient ID")
EV.adverse.covariates.geneglobe = left_join(EV.adverse.covariates.geneglobe, covariates, by = "Patient ID")

EV.adverse.covariates.geNorm = left_join(EV.geNorm.new, adverse.pathology, by = "Patient ID")
EV.adverse.covariates.geNorm = left_join(EV.adverse.covariates.geNorm, covariates, by = "Patient ID")

EV.adverse.covariates.NormFinder = left_join(EV.NormFinder.new, adverse.pathology, by = "Patient ID")
EV.adverse.covariates.NormFinder = left_join(EV.adverse.covariates.NormFinder, covariates, by = "Patient ID")

EV.adverse.covariates.overlap = left_join(EV.overlap.new, biopsy.grade, by = "Patient ID")
EV.adverse.covariates.overlap = left_join(EV.adverse.covariates.overlap, covariates, by = "Patient ID")

```

Logistic regression for classification

We firstly want to build logistic regression model using caret package. Since we have 203 observations for serum miRs and 118 observations for EV miRs. We want to subset the training set as 80% of the original data.

Outcome: biopsy grade groups

```
library(caret)
```

```
## Loading required package: lattice
```

```
##
```

```
## Attaching package: 'caret'
```

```
## The following object is masked from 'package:purrr':
```

```
##
```

```
## lift
```

```
library(pROC)
```

```
## Type 'citation("pROC")' for a citation.
```

```
##
```

```
## Attaching package: 'pROC'
```

```
## The following objects are masked from 'package:stats':
```

```
##
```

```
## cov, smooth, var
```

```

set.seed(1029)
rowTrain = createDataPartition(y = serum.grade.covariates.geneglobe$grades,
                                p = 0.75,
                                list = FALSE)

ctrl = trainControl(method = "repeatedcv",
                    repeats = 5,
                    summaryFunction = twoClassSummary,
                    classProbs = TRUE)

# Serum geneglobe
glm.serum.grade.geneglobe = train(x = serum.grade.covariates.geneglobe[rowTrain, -c(1, 59)],
                                   y = serum.grade.covariates.geneglobe$grades[rowTrain],
                                   method = "glm",
                                   metric = "ROC",
                                   trControl = ctrl)

rf.grid = expand.grid(mtry = 1:20,
                     splitrule = "gini",
                     min.node.size = 1:20)

rf.serum.grade.geneglobe = train(x = serum.grade.covariates.geneglobe[rowTrain, -c(1, 59)],
                                   y = serum.grade.covariates.geneglobe$grades[rowTrain],
                                   method = "ranger",
                                   tuneGrid = rf.grid,
                                   metric = "ROC",
                                   trControl = ctrl)

glm.predict.serum.grade.geneglobe = predict(glm.serum.grade.geneglobe, newdata = serum.grade.covariates.geneglobe[-rowTrain, -c(1, 59)],
                                             type = "prob")
rf.predict.serum.grade.geneglobe = predict(rf.serum.grade.geneglobe, newdata = serum.grade.covariates.geneglobe[-rowTrain, -c(1, 59)],
                                             type = "prob")
roc.glm.serum.grade.geneglobe = roc(serum.grade.covariates.geneglobe$grades[-rowTrain], glm.predict.serum.grade.geneglobe)
roc.rf.serum.grade.geneglobe = roc(serum.grade.covariates.geneglobe$grades[-rowTrain], rf.predict.serum.grade.geneglobe)

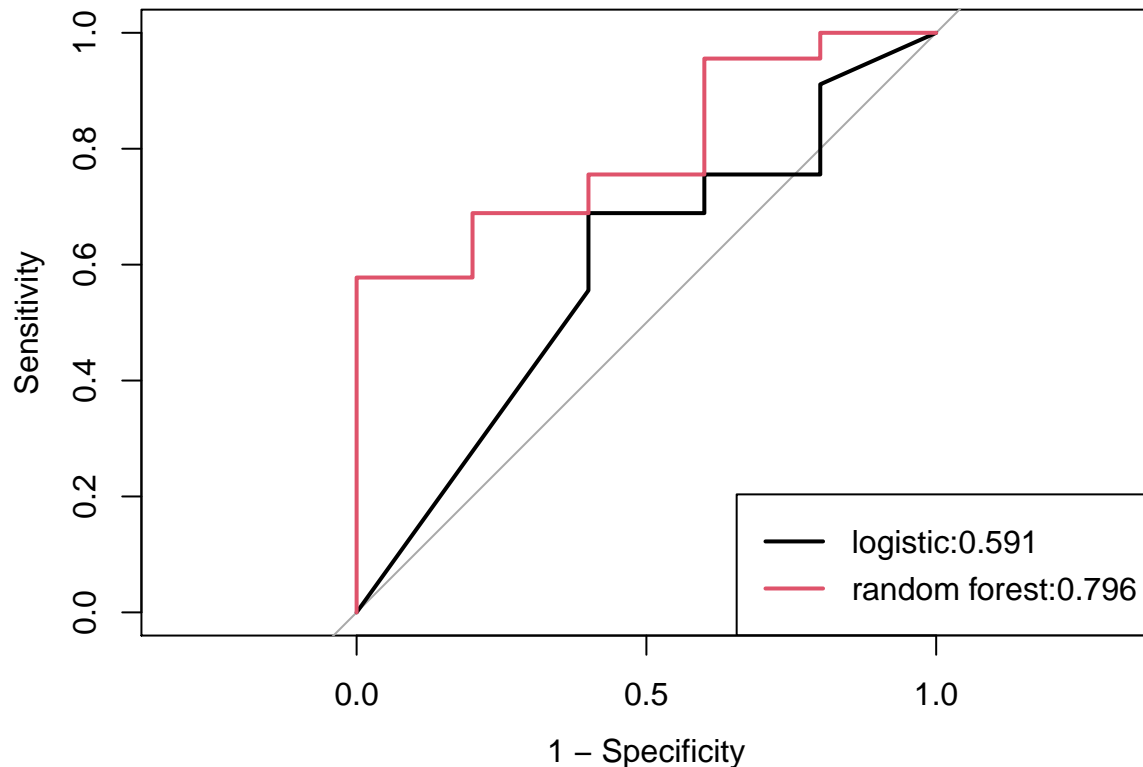
## Setting levels: control = high, case = low
## Setting direction: controls < cases

roc.glm.serum.grade.geneglobe = roc(serum.grade.covariates.geneglobe$grades[-rowTrain], glm.predict.serum.grade.geneglobe,
                                     direction = "less")
roc.rf.serum.grade.geneglobe = roc(serum.grade.covariates.geneglobe$grades[-rowTrain], rf.predict.serum.grade.geneglobe,
                                    direction = "less")

## Setting levels: control = high, case = low
## Setting direction: controls < cases

auc = c(roc.glm.serum.grade.geneglobe$auc[1], roc.rf.serum.grade.geneglobe$auc[1])
plot(roc.glm.serum.grade.geneglobe, legacy.axes = T)
plot(roc.rf.serum.grade.geneglobe, add = T, col = 2)
modelNames = c("logistic", "random forest")
legend("bottomright", legend = paste0(modelNames, ":", round(auc,3)), col = 1:2, lwd = 2)

```



```
# serum grade geNorm
glm.serum.grade.geNorm = train(x = serum.grade.covariates.geNorm[rowTrain, -c(1, 59)],
                               y = serum.grade.covariates.geNorm$grades[rowTrain],
                               method = "glm",
                               metric = "ROC",
                               trControl = ctrl)

rf.grid = expand.grid(mtry = 1:20,
                     splitrule = "gini",
                     min.node.size = 1:20)

rf.serum.grade.geNorm = train(x = serum.grade.covariates.geNorm[rowTrain, -c(1, 59)],
                              y = serum.grade.covariates.geNorm$grades[rowTrain],
                              method = "ranger",
                              tuneGrid = rf.grid,
                              metric = "ROC",
                              trControl = ctrl)

glm.predict.serum.grade.geNorm = predict(glm.serum.grade.geNorm, newdata = serum.grade.covariates.geNorm[, rowTrain])
rf.predict.serum.grade.geNorm = predict(rf.serum.grade.geNorm, newdata = serum.grade.covariates.geNorm[, rowTrain])
roc.glm.serum.grade.geNorm = roc(serum.grade.covariates.geNorm$grades[-rowTrain], glm.predict.serum.grade.geNorm[-rowTrain])
roc.rf.serum.grade.geNorm = roc(serum.grade.covariates.geNorm$grades[-rowTrain], rf.predict.serum.grade.geNorm[-rowTrain])

## Setting levels: control = high, case = low
## Setting direction: controls < cases
```

```
roc.rf.serum.grade.geNorm = roc(serum.grade.covariates.geNorm$grades[-rowTrain], rf.predict.serum.grade
```

```
## Setting levels: control = high, case = low
```

```
## Setting direction: controls < cases
```

```
auc = c(roc.glm.serum.grade.geNorm$auc[1], roc.rf.serum.grade.geNorm$auc[1])
```

```
plot(roc.glm.serum.grade.geNorm, legacy.axes = T)
```

```
plot(roc.rf.serum.grade.geNorm, add = T, col = 2)
```

```
modelNameNames = c("logistic", "random forest")
```

```
legend("bottomright", legend = paste0(modelNames, ":", round(auc,3)), col = 1:2, lwd = 2)
```

