Class 12: Genome Informatics

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Section 1: : Identify genetic variants of interest

Downloaded CSV file from Ensemble https://useast.ensembl.org/Homo_sapiens/Variation/Sample?db=core;r=
39895595;v=rs8067378;vdb=variation;vf=959672880#373531_tablePanel

Here we read this CSV file

```
mxl <- read.csv("373531-SampleGenotypes-Homo_sapiens_Variation_Sample_rs8067378.csv")

head(mxl)
```

```
  Sample..Male.Female.Unknown. Genotype..forward.strand. Population.s. Father
1                  NA19648 (F)                       A|A ALL, AMR, MXL      -
2                  NA19649 (M)                       G|G ALL, AMR, MXL      -
3                  NA19651 (F)                       A|A ALL, AMR, MXL      -
4                  NA19652 (M)                       G|G ALL, AMR, MXL      -
5                  NA19654 (F)                       G|G ALL, AMR, MXL      -
6                  NA19655 (M)                       A|G ALL, AMR, MXL      -
  Mother
1      -
2      -
3      -
4      -
5      -
6      -
```

```r
table(mxl$Genotype..forward.strand.)
```

```
A|A A|G G|A G|G 
 22  21  12   9 
```

Find the percentage/proportion for each genotype

```r
round(table(mxl$Genotype..forward.strand.) / nrow(mxl) * 100, 2)
```

```
  A|A   A|G   G|A   G|G 
34.38 32.81 18.75 14.06 
```

Now let's look at a different population. I picked the GBR.

```r
gbr <- read.csv("373522-SampleGenotypes-Homo_sapiens_Variation_Sample_rs8067378.csv")

head(gbr)
```

```
  Sample..Male.Female.Unknown. Genotype..forward.strand. Population.s. Father
1                  HG00096 (M)                       A|A ALL, EUR, GBR      -
2                  HG00097 (F)                       G|A ALL, EUR, GBR      -
3                  HG00099 (F)                       G|G ALL, EUR, GBR      -
4                  HG00100 (F)                       A|A ALL, EUR, GBR      -
5                  HG00101 (M)                       A|A ALL, EUR, GBR      -
6                  HG00102 (F)                       A|A ALL, EUR, GBR      -
  Mother
1      -
2      -
3      -
4      -
5      -
6      -
```

Find the proportion of G|G

```
round(table(gbr$Genotype..forward.strand.) / nrow(gbr) *100, 2)
```

```
  A|A   A|G   G|A   G|G 
25.27 18.68 26.37 29.67 
```

This variant that is associated with childhood asthma is more frequent in the GBR population than the MXL population.

Let's now dig into this further.

Section 4: Population Scale Analysis

One sample is obviously not enough to know what is happening in a population. You are interested in assessing genetic differences on a population scale. So, you processed about ~230 samples and did the normalization on a genome level. Now, you want to find whether there is any association of the 4 asthma-associated SNPs (rs8067378…) on ORMDL3 expression.

> Q13: Read this file into R and determine the sample size for each genotype and their corresponding median expression levels for each of these genotypes.

```
expr <- read.table("rs8067378_ENSG00000172057.6.txt")

head(expr)
```

```
   sample geno      exp
1 HG00367  A/G 28.96038
2 NA20768  A/G 20.24449
3 HG00361  A/A 31.32628
4 HG00135  A/A 34.11169
5 NA18870  G/G 18.25141
6 NA11993  A/A 32.89721
```

```
nrow(expr)
```

```
[1] 462
```

There are 462 samples total.

The sample sizes of each genotype:

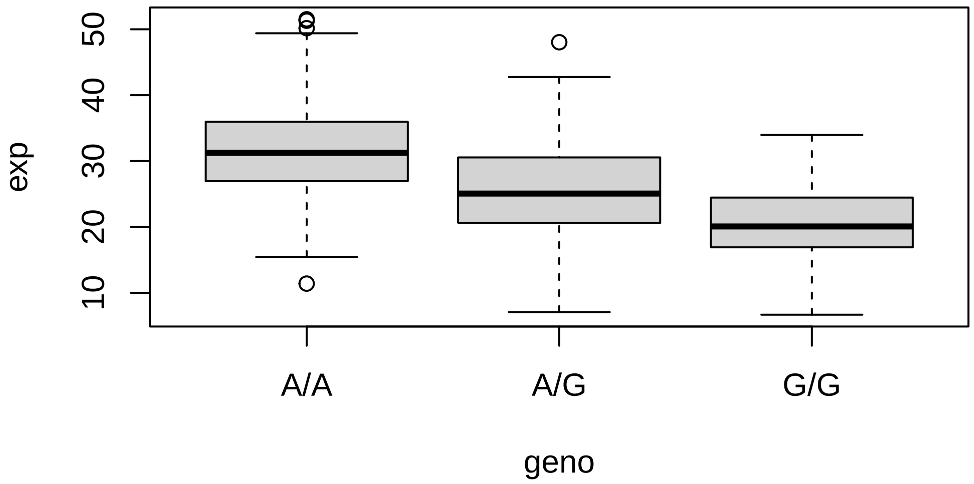
```
table(expr$geno)
```

```

A/A A/G G/G
108 233 121
```

The median expression for each genotype:

```
expr_boxplot <- boxplot(exp ~ geno, expr)
```



```
round(expr_boxplot$stats, 2)
```

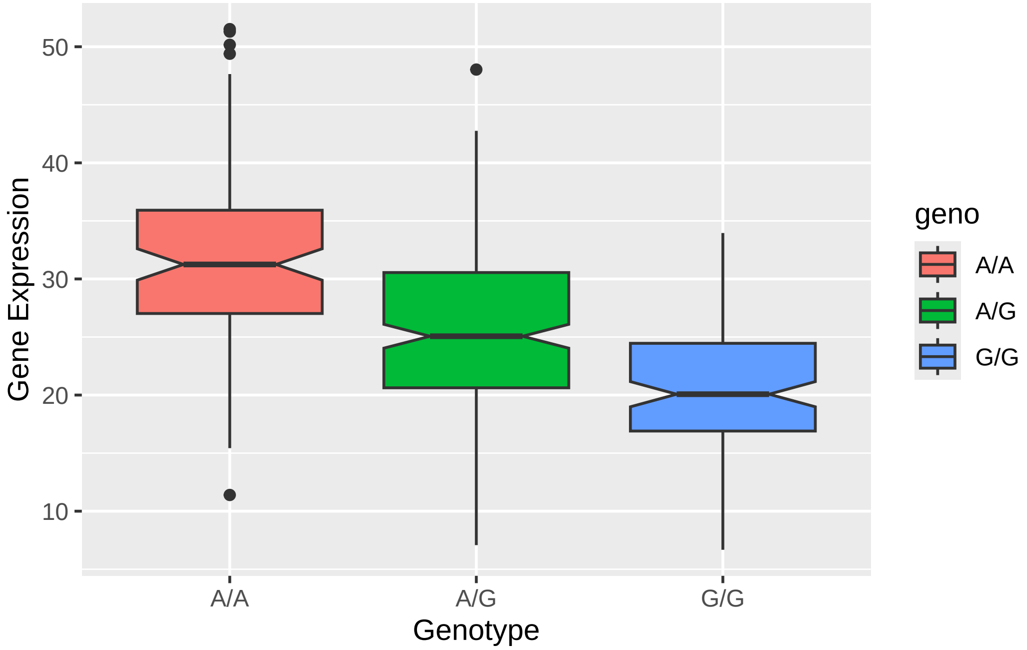
```
      [,1]  [,2]  [,3]
[1,] 15.43  7.08  6.67
[2,] 26.95 20.63 16.90
[3,] 31.25 25.06 20.07
[4,] 35.96 30.55 24.46
[5,] 49.40 42.76 33.96
```

The median for the A|A genotype is 31.25. The median for the A|G genotype is 25.06. The median for the G|G genotype is 20.07.

> Q14: Generate a boxplot with a box per genotype, what could you infer from the relative expression value between A/A and G/G displayed in this plot? Does the SNP effect the expression of ORMDL3?

```
library(ggplot2)

ggplot(expr) +
  aes(x=geno, y=exp, fill=geno) +
  labs(x="Genotype", y="Gene Expression") +
  geom_boxplot(notch=TRUE)
```



The gene expression is higher on average with the A|A genotype than the G|G genotype. Yes, the SNP effects the expression of the ORMDL3 gene. Having a A|G genotype slightly increases the expression and the A|A genotype significantly increases the expression of the ORMDL3 gene. This shows that a SNP with the “G” allele decreases the gene expression.