Class 12: Lab Session

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Section 1. Proportion of G/G in a population

Download a CSV file from Ensemble < https://useast.ensembl.org/Homo_sapiens/Variation/Sample?db=core;r 39895595;v=rs8067378;vdb=variation;vf=959672880;sample=HG00109 >

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      -
```

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

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

```
table(mxl$Genotype..forward.strand.) / nrow(mxl) * 100
```

```
    A|A     A|G     G|A     G|G 
34.3750 32.8125 18.7500 14.0625 
```

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

```
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      -
```

```
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	-
7	HG00103 (M)	A|G	ALL, EUR, GBR	-
8	HG00105 (M)	A|A	ALL, EUR, GBR	-
9	HG00106 (F)	G|A	ALL, EUR, GBR	-
10	HG00107 (M)	G|G	ALL, EUR, GBR	-
11	HG00108 (M)	A|A	ALL, EUR, GBR	-
12	HG00109 (M)	G|G	ALL, EUR, GBR	-
13	HG00110 (F)	A|G	ALL, EUR, GBR	-
14	HG00111 (F)	A|A	ALL, EUR, GBR	-
15	HG00112 (M)	G|G	ALL, EUR, GBR	-
16	HG00113 (M)	G|G	ALL, EUR, GBR	-
17	HG00114 (M)	G|A	ALL, EUR, GBR	-
18	HG00115 (M)	A|G	ALL, EUR, GBR	-
19	HG00116 (M)	G|G	ALL, EUR, GBR	-
20	HG00117 (M)	A|A	ALL, EUR, GBR	-
21	HG00118 (F)	G|G	ALL, EUR, GBR	-
22	HG00119 (M)	G|A	ALL, EUR, GBR	-
23	HG00120 (F)	G|G	ALL, EUR, GBR	-
24	HG00121 (F)	A|G	ALL, EUR, GBR	-
25	HG00122 (F)	G|G	ALL, EUR, GBR	-
26	HG00123 (F)	G|A	ALL, EUR, GBR	-
27	HG00125 (F)	A|G	ALL, EUR, GBR	-
28	HG00126 (M)	G|G	ALL, EUR, GBR	-
29	HG00127 (F)	G|A	ALL, EUR, GBR	-
30	HG00128 (F)	A|G	ALL, EUR, GBR	-
31	HG00129 (M)	G|G	ALL, EUR, GBR	-
32	HG00130 (F)	A|G	ALL, EUR, GBR	-
33	HG00131 (M)	G|G	ALL, EUR, GBR	-
34	HG00132 (F)	A|A	ALL, EUR, GBR	-
35	HG00133 (F)	G|A	ALL, EUR, GBR	-
36	HG00136 (M)	G|G	ALL, EUR, GBR	-
37	HG00137 (F)	G|A	ALL, EUR, GBR	-
38	HG00138 (M)	A|A	ALL, EUR, GBR	-
39	HG00139 (M)	G|G	ALL, EUR, GBR	-
40	HG00140 (M)	G|A	ALL, EUR, GBR	-
41	HG00141 (M)	G|G	ALL, EUR, GBR	-
42	HG00142 (M)	G|G	ALL, EUR, GBR	-
43	HG00143 (M)	G|A	ALL, EUR, GBR	-
44	HG00145 (M)	A|A	ALL, EUR, GBR	-
45	HG00146 (F)	A|A	ALL, EUR, GBR	-
46	HG00148 (M)	G|A	ALL, EUR, GBR	-
47	HG00149 (M)	G|A	ALL, EUR, GBR	-

48	HG00150 (F)	G|A ALL, EUR, GBR	-
49	HG00151 (M)	G|A ALL, EUR, GBR	-
50	HG00154 (F)	G|G ALL, EUR, GBR	-
51	HG00155 (M)	A|G ALL, EUR, GBR	-
52	HG00157 (M)	A|A ALL, EUR, GBR	-
53	HG00158 (F)	A|A ALL, EUR, GBR	-
54	HG00159 (M)	A|A ALL, EUR, GBR	-
55	HG00160 (M)	A|A ALL, EUR, GBR	-
56	HG00231 (F)	A|G ALL, EUR, GBR	-
57	HG00232 (F)	G|G ALL, EUR, GBR	-
58	HG00233 (F)	G|G ALL, EUR, GBR	-
59	HG00234 (M)	G|G ALL, EUR, GBR	-
60	HG00235 (F)	A|A ALL, EUR, GBR	-
61	HG00236 (F)	A|A ALL, EUR, GBR	-
62	HG00237 (F)	A|A ALL, EUR, GBR	-
63	HG00238 (F)	G|G ALL, EUR, GBR	-
64	HG00239 (F)	G|A ALL, EUR, GBR	-
65	HG00240 (F)	G|A ALL, EUR, GBR	-
66	HG00242 (M)	G|A ALL, EUR, GBR	-
67	HG00243 (M)	A|G ALL, EUR, GBR	-
68	HG00244 (M)	G|A ALL, EUR, GBR	-
69	HG00245 (F)	A|G ALL, EUR, GBR	-
70	HG00246 (M)	A|G ALL, EUR, GBR	-
71	HG00250 (F)	G|G ALL, EUR, GBR	-
72	HG00251 (M)	G|A ALL, EUR, GBR	-
73	HG00252 (M)	G|A ALL, EUR, GBR	-
74	HG00253 (F)	A|A ALL, EUR, GBR	-
75	HG00254 (F)	A|G ALL, EUR, GBR	-
76	HG00255 (F)	A|G ALL, EUR, GBR	-
77	HG00256 (M)	A|G ALL, EUR, GBR	-
78	HG00257 (F)	G|G ALL, EUR, GBR	-
79	HG00258 (F)	A|A ALL, EUR, GBR	-
80	HG00259 (F)	G|A ALL, EUR, GBR	-
81	HG00260 (M)	G|G ALL, EUR, GBR	-
82	HG00261 (F)	G|G ALL, EUR, GBR	-
83	HG00262 (F)	A|A ALL, EUR, GBR	-
84	HG00263 (F)	G|A ALL, EUR, GBR	-
85	HG00264 (M)	A|G ALL, EUR, GBR	-
86	HG00265 (M)	G|G ALL, EUR, GBR	-
87	HG01334 (M)	A|G ALL, EUR, GBR	-
88	HG01789 (M)	G|A ALL, EUR, GBR	-
89	HG01790 (F)	G|A ALL, EUR, GBR	-
90	HG01791 (M)	A|A ALL, EUR, GBR	-

91	HG02215 (F)	G|G ALL, EUR, GBR	-

	Mother
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3	-
4	-
5	-
6	-
7	-
8	-
9	-
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74	-
75	-
76	-
77	-
78	-
79	-
80	-
81	-
82	-
83	-
84	-

```
85       -
86       -
87       -
88       -
89       -
90       -
91       -
```

Find the proportion of G|G:

```r
table(gbr$Genotype..forward.strand.) / nrow(gbr) * 100
```

```

     A|A      A|G      G|A      G|G 
25.27473 18.68132 26.37363 29.67033 
```

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 [HOMEWORK]

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.

How many samples do we have?

> 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.

First, we need to read the file in.

```r
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
```

I want to see how many total samples there are in the dataset.

```
nrow(expr)
```

```
[1] 462
```

Now I want to see how many of each genotype there are in the dataset.

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

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

Now let's see the corresponding median expression levels for each of these genotypes.

```
medians <- tapply(expr$exp, expr$geno, median)
medians
```

```
     A/A      A/G      G/G 
31.24847 25.06486 20.07363 
```

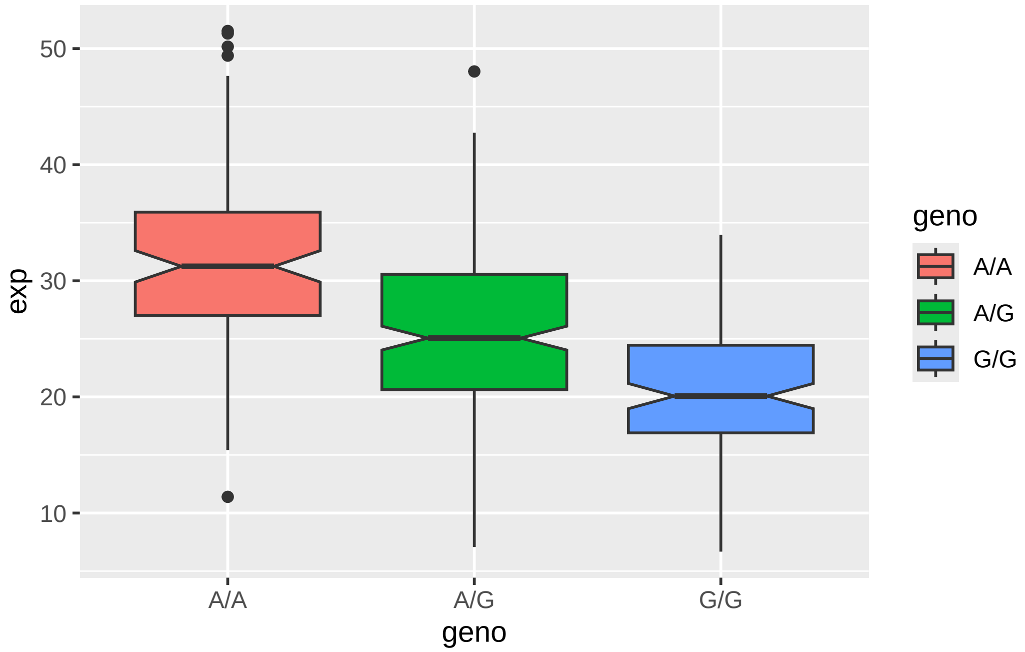
> Q14. Generate a boxplot with a box per genotype, what could you infer from the relative expression value between A/A and G/G displayed in this plot? Does the SNP affect the expression of ORMDL3?

I want to load ggplot so that I can make a boxplot.

```
library(ggplot2)
```

Let's make a boxplot.

```r
ggplot(expr) + aes(x=geno, y=exp, fill=geno) +
  geom_boxplot(notch=TRUE)
```



From the boxplot, we can see that there is a difference between the different genotypes and their respective expression levels. You can see that the expression level of the ORMDL3 gene is lowest when there is a G/G and highest when there is A/A, on average. Based on the boxplot, it seems that the SNP does affect the expression of ORMDL3.