

QTL Analysis Report for Baseline White Blood Cell Count Study

The Jackson Laboratory

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Chapter 1. Experiment Design

The overall goal for this experiment is to detect and localize QTL that is responsible for variation of baseline white blood cell count between two mouse inbred strains. An intercross experiment (C57BLKS/J x SM/J) was conducted. White blood cell counts were recorded for 186 F2 progeny that included 91 females and 95 males. Body weight was also recorded for each animal.

Chapter 2. Statistical Methods

2.1 Genome-wide one-dimensional scan

Pseudo-markers were generated at 2-cM spacing for each chromosome, and a whole genome scan was performed using 128 imputations (Sen and Churchill, 2001). One thousand permutations were performed to determine the thresholds for QTL detection (Doerge and Churchill, 1996). Four thresholds 1%, 5%, 10% and 63% were calculated from the permutation results. QTL with LOD score above the 1% threshold were strong QTL, while those above 63% were suggestive QTL (Lander and Kruglyak, 1995). Additive models including QTL and covariates (sex, body weight) effects were employed.

2.2 Statistical software

R/QTL version 1.08-56 was used (Broman et al, 2003).

Chapter 3. Distributions of Data and Quality Control Diagnostics

3.1 Phenotype distribution

As shown in Figure 1, histogram plots were generated for WBC. The original data were left-skewed, and logarithm transformation of raw data was used to reduce the skewness.

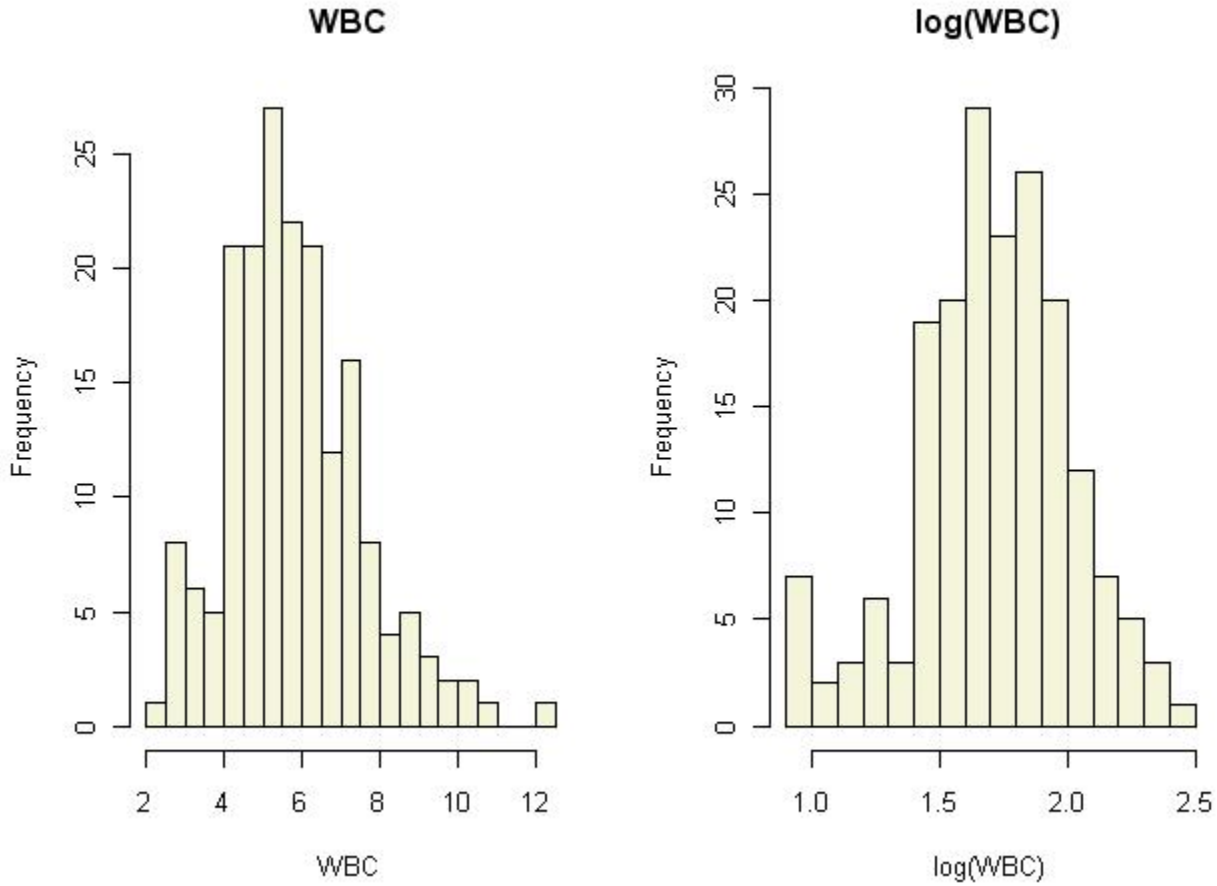


Figure 1. Histogram plots of WBC and logarithm transformed WBC.

3.2 Genotyping quality assessment

3.2.1 Recombination fraction

Recombination fraction (RF) plots are shown in Figure 2. Markers that are physically closer to each other are strongly linked (red color); Markers that are far away from each other on the same chromosome or markers on the different chromosomes are more independent from each other (blue). The left panel in Figure 2 suggests that the last marker on chromosome 16 may have a quality issue. RF plot (right panel) appears in good quality after excluding the last marker on chromosome 16.

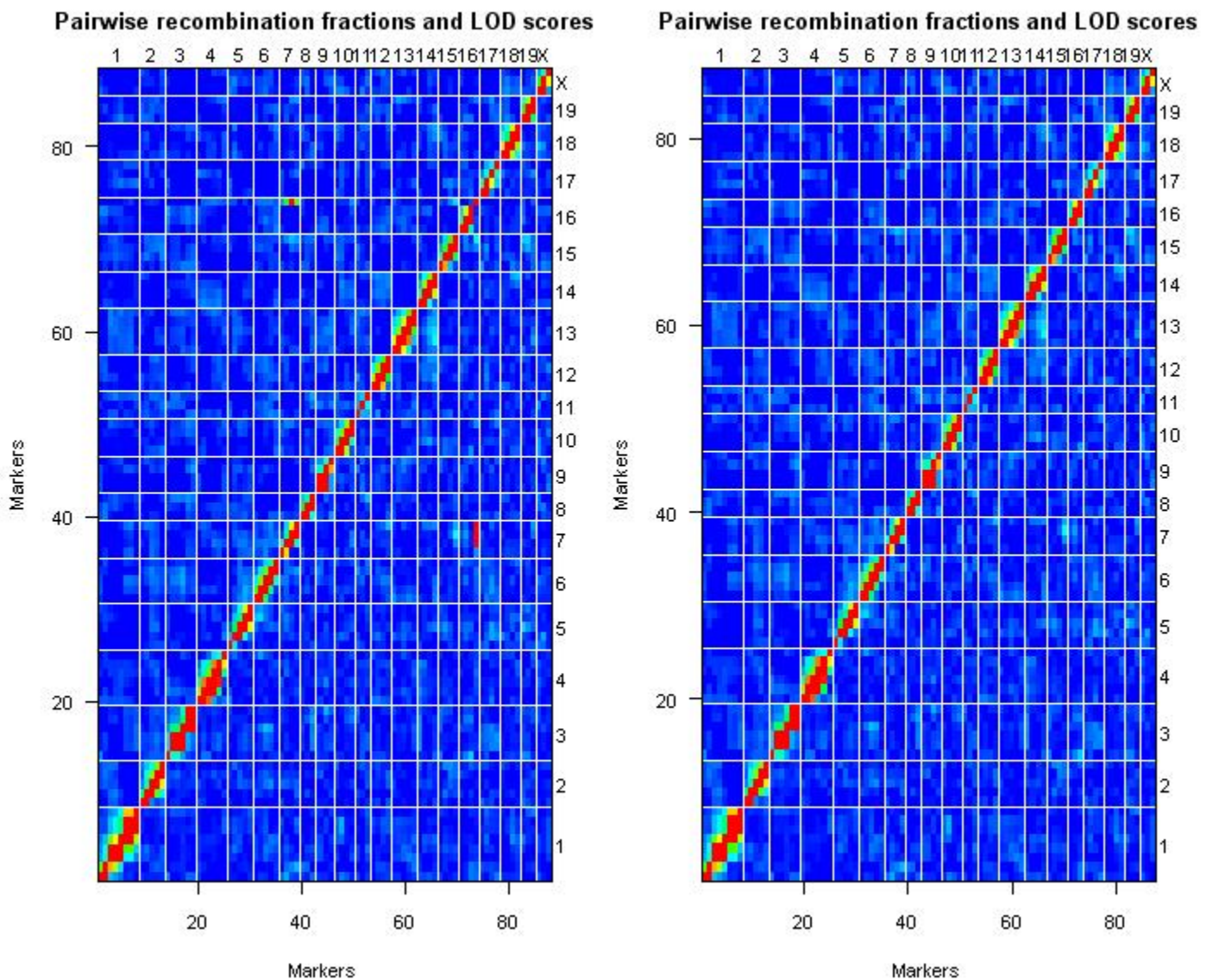


Figure 2. Recombination plots.

3.2.2 Genetic map estimates

Genetic map was re-estimated using the data from this experiment and presented in Figure 3. Figure 3 shows the length of chromosome 16 was too long. Removing the last marker on chromosome 16 fixed the problem.

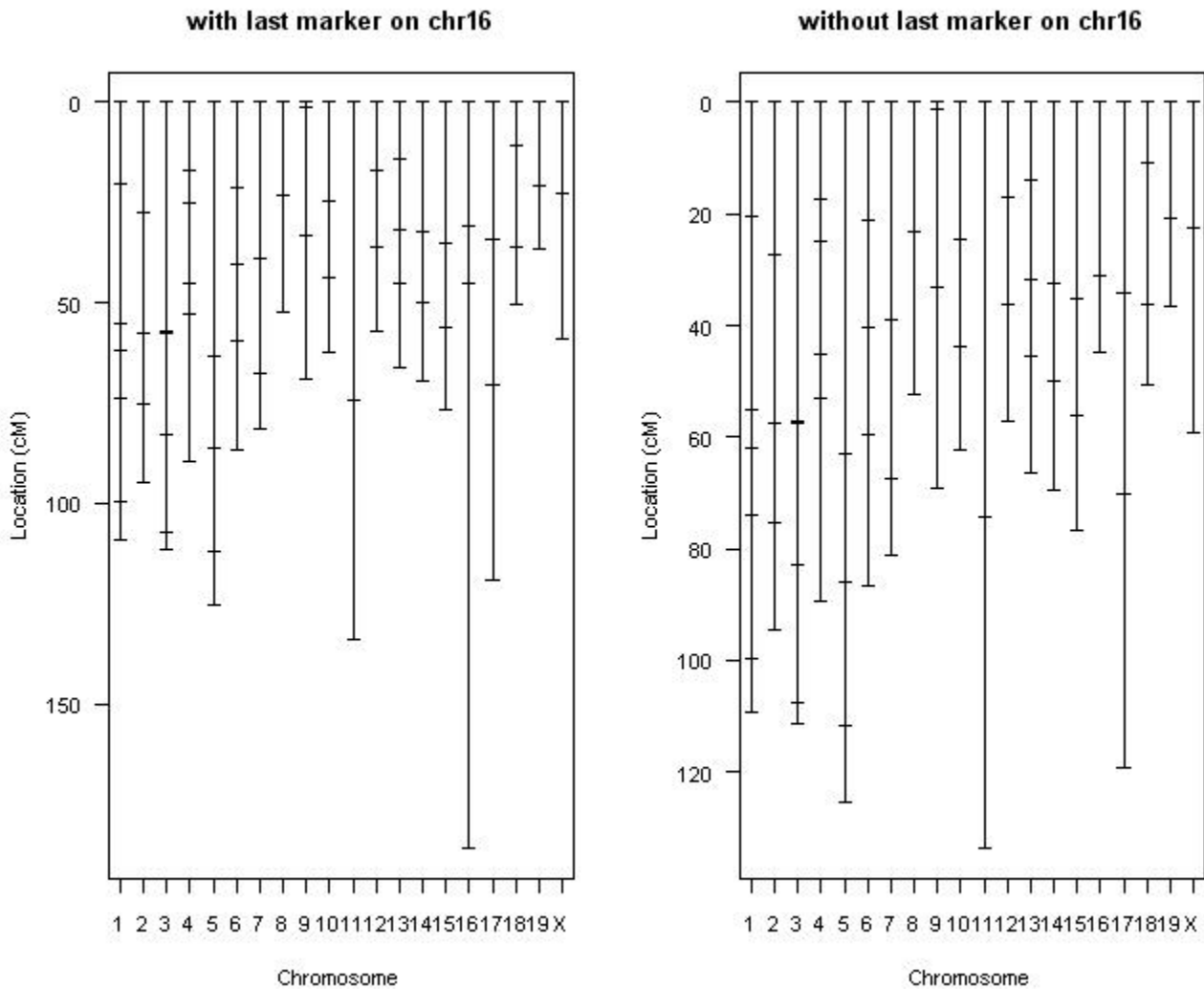


Figure 3. Re-estimated genetic maps.

Chapter 4. Results

4.1 Genome-wide one-dimensional scan

Figure 4 presents the results from a genome-wide one-dimensional QTL scan. The lines bottom-up represent significant thresholds of 63%, 10%, 5% and 1%, respectively. One QTL on chromosome 1 was found significant at 1% level. The other two on chromosome 3 and 15 appear significant at about 10% level.

Model: $\text{Log}(\text{WBC}) = \text{Sex} + \text{Body Weight} + \text{QTL}$

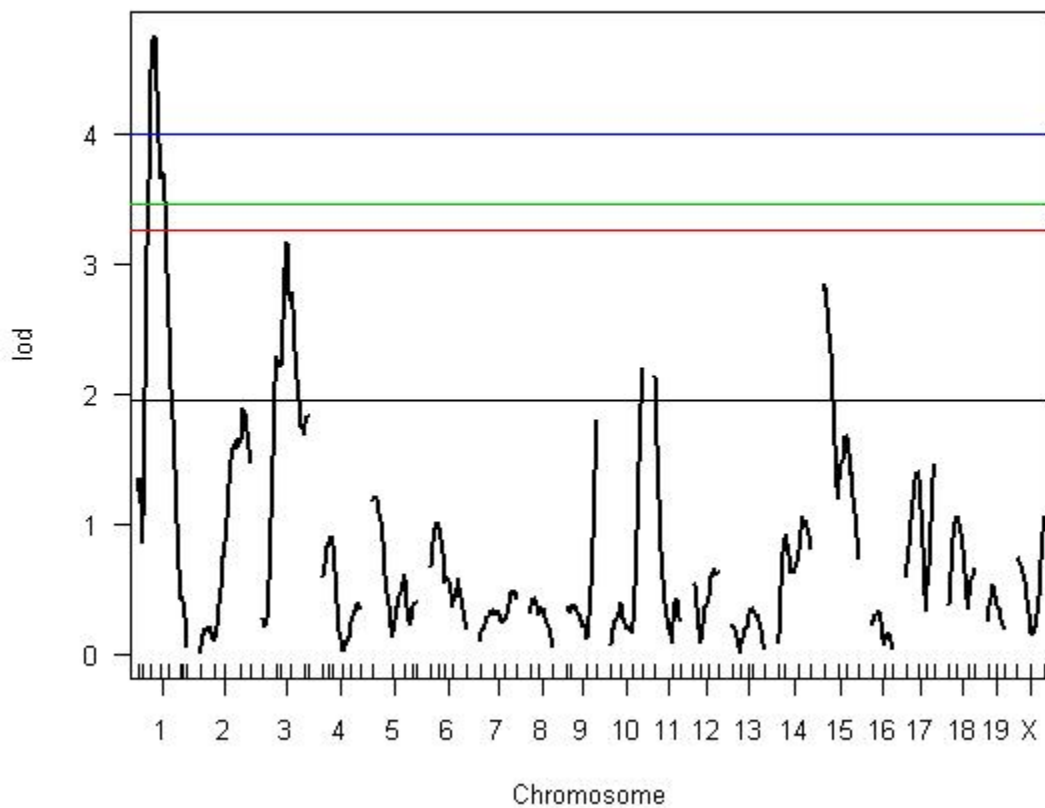


Figure 4. One-dimensional QTL scan plot.

Chapter 5. Conclusions

Based on the additive model from one-dimensional QTL scan, three QTL were detected for baseline white blood cell count. They are chr1@44cM, chr3@44.2cM and chr15@0cM. The LOD scores for the 3 QTL are 4.74, 3.17 and 2.84, respectively.

Chapter 6. References

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