

Abstract

Maternal effects generally refer to the impact that a mother's traits have upon the connection between direct genes of the offspring and the maternal environment provided for the offspring, shaping offspring's growth and development. While direct maternal effects occur through maternal provisioning or behavior, indirect maternal effects occur through the transmission of maternal traits to the offspring via their interaction with the environment. Indirect maternal effects on offspring growth act through a sequence of developmental processes, which are under intrinsic genetic control, influenced by the young animal's own genes, and also strongly influenced by the environment provided by the mother for her developing offspring. Indirect genetic effects build the conceptual framework necessary for considering both the direct effects of the offspring's own genes and the indirect effects of the mother's genes on the offspring's characteristics (Cheverud and Wolf 2009). Interval mapping revealed several significant QTLs, or places where the maternal genome is directly affecting the offspring phenotype, ranging from weeks 1-20, on chromosomes (chrs) 7 and 18 respectively, and other suggestive QTLs on Chrs 1, 3, 4, 6, and 14.

Methods and Research Design

Mouse models of maternal effects on offspring growth allow the discovery of genes and molecular effects due to the environments mothers provide for their offspring. Growth is calculated as the difference in weight from week 1 to 3 (preweaning growth), as well as juvenile growth from weeks 3 to 6, late growth from 6 to 10 weeks, and adult growth from 10 to 20 weeks. Basic statistics, genetic mapping, interpretation of the maps, and genomic imprinting analysis were all performed along with bioinformatic work to assess the genetic architecture of growth in the cross between SM and LG strains. We performed a genome-wide quantitative trait locus (QTL) analysis of body weight from 1 to 20 weeks of age-specific weights in the cross between SM and LG strains. For each marker in the chromosome, the three following models were used:

1. Null-sex+diet+family
2. Reduced-sex+diet+family+ A_0+D_0
3. Full- sex+diet+family+ $A_0+D_0 + A_M+ D_M$

These computer-generated linear models of the various age-specific weights and growth rates along with covariates (sex, diet, generation) and the additive and dominance genotype scores of the offspring and their mothers were used to compare the results of offspring direct and maternal indirect effects for these traits.

Results

Number of QTLs can be defined as the number of different regions wherein the maternal genome is directly affecting offspring phenotype (not passing genotype to generation). All these Manhattan plots were generated using the full comparison (Full x Null) only. The higher the peak, stronger association with specific traits (weeks).

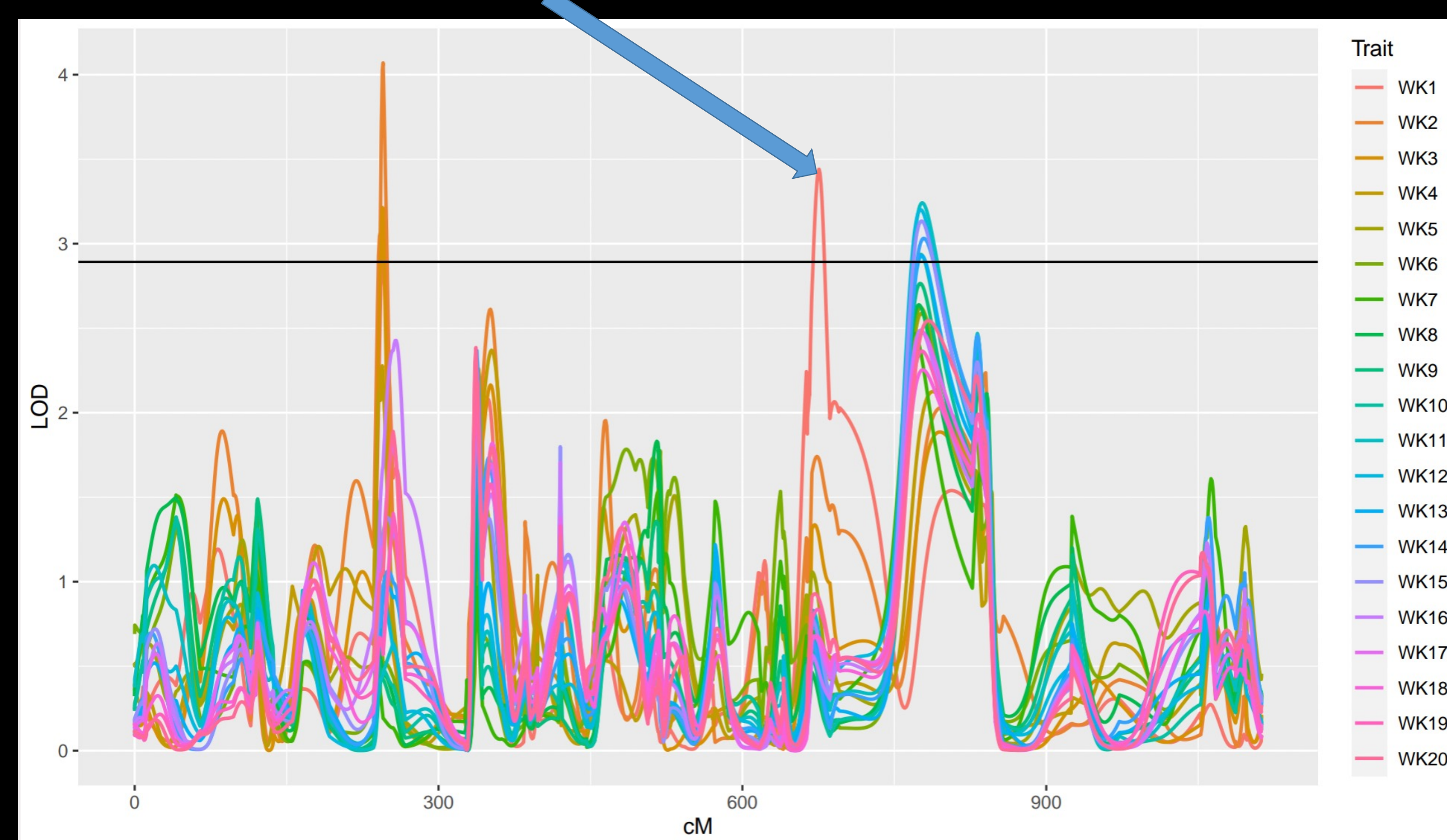


Figure 1:

Chromosome 7

The three specific co-occurrences of early and late growth remain relatively spurious. The three chromosome 3 QTLs have an odd age distribution of effects, with a gap in significant results between 1 or 2 and 3 week body weights overlap and 10-15 week overlap. The early growth effects tend to fall off by 2-3 weeks around 261 cM while the significant association between later growth and maternal effects first appear in the 872-906 cM for 10-15 weeks overlapping interval.

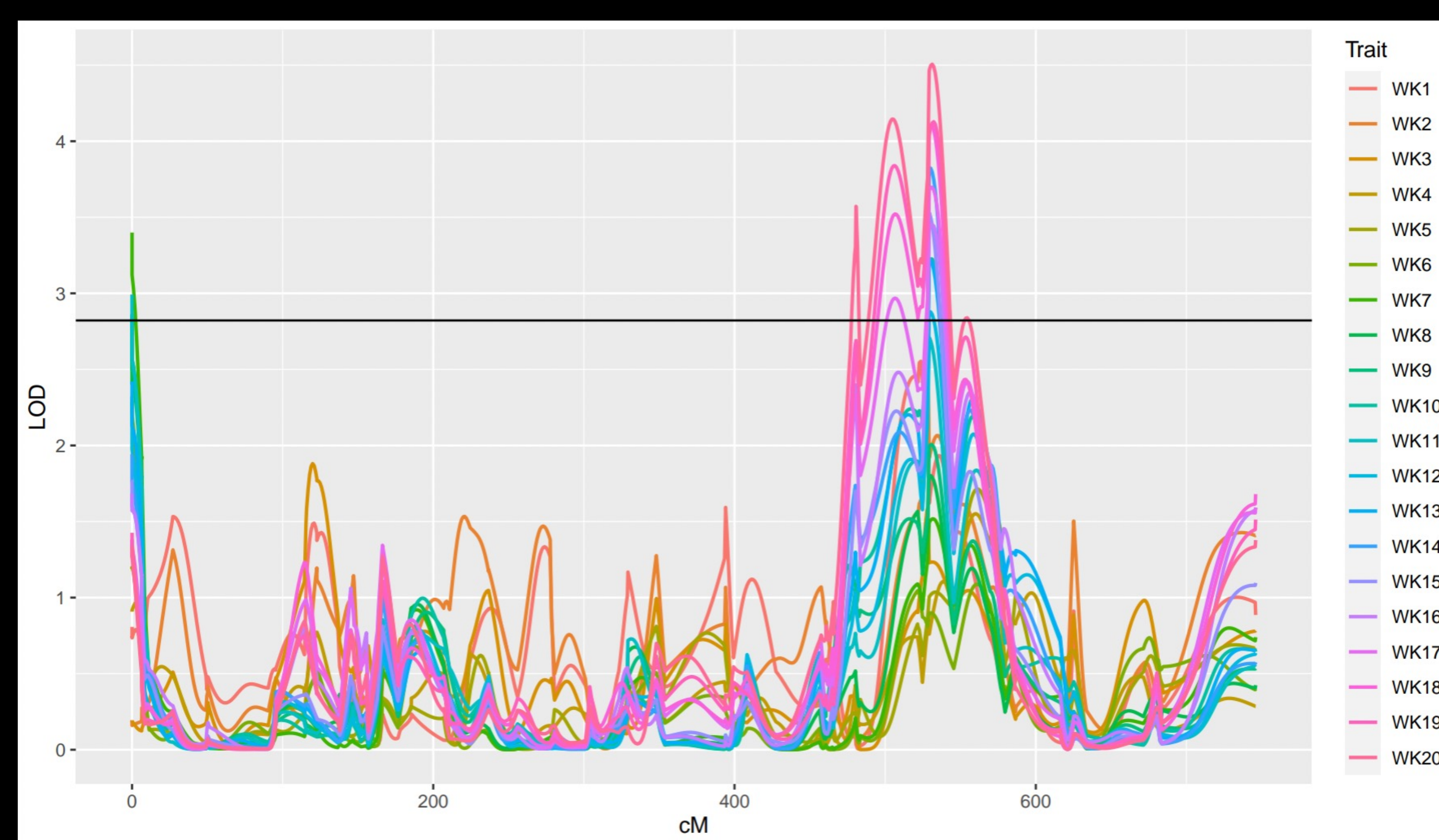


Figure 2:

Chromosome 18

The genetic architecture of late growth and 8-20 week weight at these two loci contrasts with the architecture displayed at the beginning, with strong overdominance of significant association between weeks 13-20 overlapping peaks and maternal effects, arising at around 577-582 and underdominance at the 1-8 locus for week 8 and 11.

Discussion and Conclusions

Mapping of the genomic locations that have indirect genetic maternal effects on offspring growth and comparing the size of these effects relative to other factors revealed how the mother's genome directly affected offspring's phenotype, not through the additive effect passing genome to offspring.

Referring to Figure 2 (chromosome 7), one can see how the maternal effects mapped in weeks 1, 2, 3 remain in same peak: because genetics of early growth remains correlated but genetics of late growth remains different. This further results in many of the QTL retaining significant effects for the early and intermediate growth periods or late and intermediate growth periods but not for the whole postnatal growth. As different parts of growth phenotypes have different correlations, some regions hold multiple associations with different phenotypes (weeks).

In the future, funding permitted, the saved tissues from these generations can be used to further evaluate measures of gene expression and methylation in offspring as a function of maternal care.

References

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