

Detection of imprinted QTL in the Berkshire x Yorkshire cross

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Introduction

Genome scans have enabled the detection of regions on chromosomes that contain genes that affect economic traits, so-called quantitative trait loci (QTL). An example is the genome scan that was conducted at ISU in an F₂ cross between the Berkshire and Yorkshire breeds (Malek et al. 2001a,b). This study identified many QTL related to growth performance and meat quality. But this analysis only considered QTL with a Mendelian mode of expression. This implies that an effect of the Berkshire allele on the trait was assumed to be the same whether it was inherited from the F₁ sire or from the F₁ dam (see Figure 1). As a result, the two heterozygotes (BY and YB) are assumed to have the same effect (d). There is, however, evidence that the expression of some genes depends on their parental origin. For example, with paternal expression, a Berkshire gene for increased meat quality would only be expressed in the F₂ progeny if it was inherited from the sire (Figure 2). In that case, individuals with QTL genotype BB and BY are expected to have the same genetic value (Figure 2), as do individuals with genotypes YB and YY. The inheritance mechanism for maternal expression is illustrated in Figure 3. In this case, genotype BB has the same value as YB, as do BY and YY.

Figure 1. Mendelian expression.

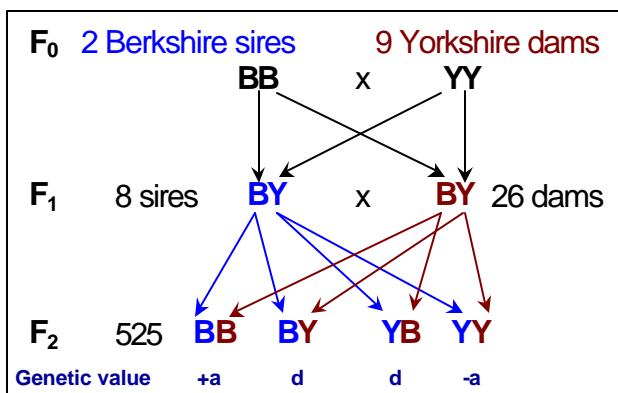
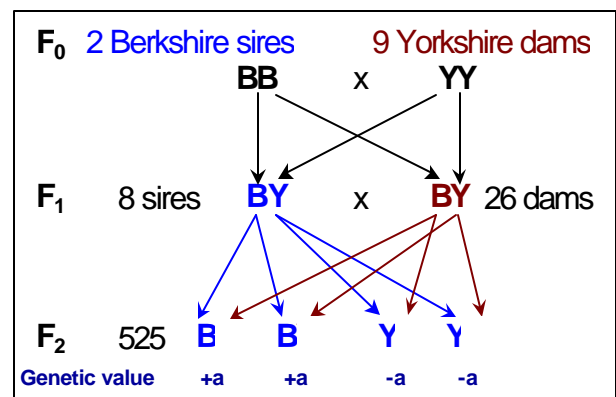
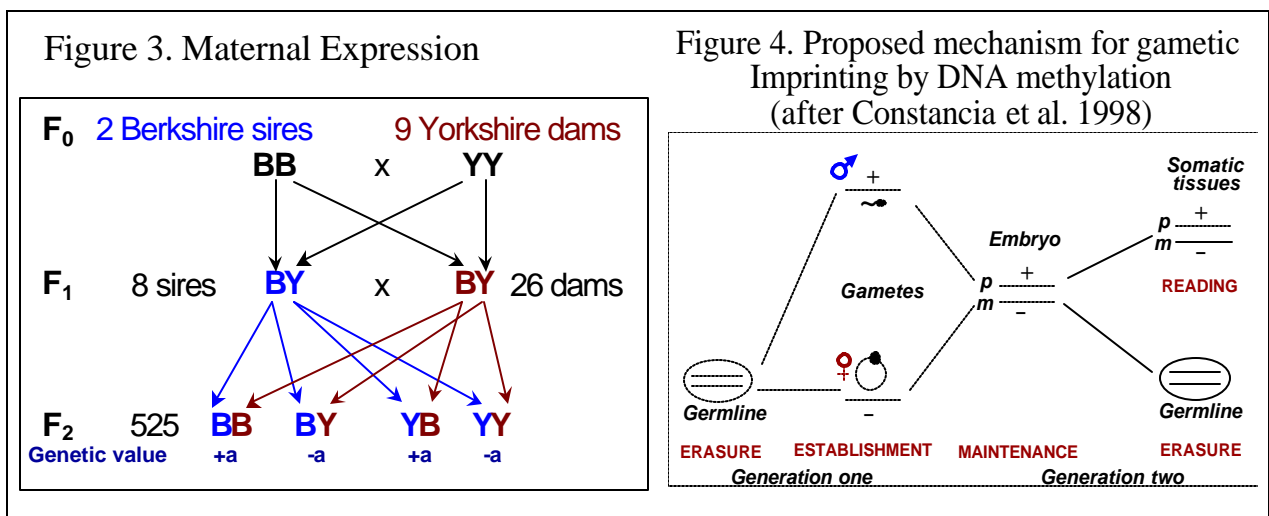


Figure 2. Paternal expression.



The phenomenon of parent-specific expression of genes, and silencing (i.e. non-expression) of alleles received from the other parent, is referred to as genomic imprinting and has been identified in several mammalian species. Methylation of DNA in specific regions of the genome during formation of gametes by either the sire or the dam has been proposed as one of the main mechanisms for gametic imprinting (Constancia et al., 1998). Methylation of a chromosomal region results in silencing of that region in the progeny because of the inability to transcribe the DNA. To illustrate, in Figure 4 is a situation where a chromosomal region is methylated during gamete formation (meiosis) in the sire but not the dam. Methylation patterns are maintained during regular cell division and development in the progeny and results in silencing of alleles inherited from the sire, i.e. maternal-only expression. Methylation patterns are erased when the progeny itself produces gametes and reinstated depending on the sex of the progeny.



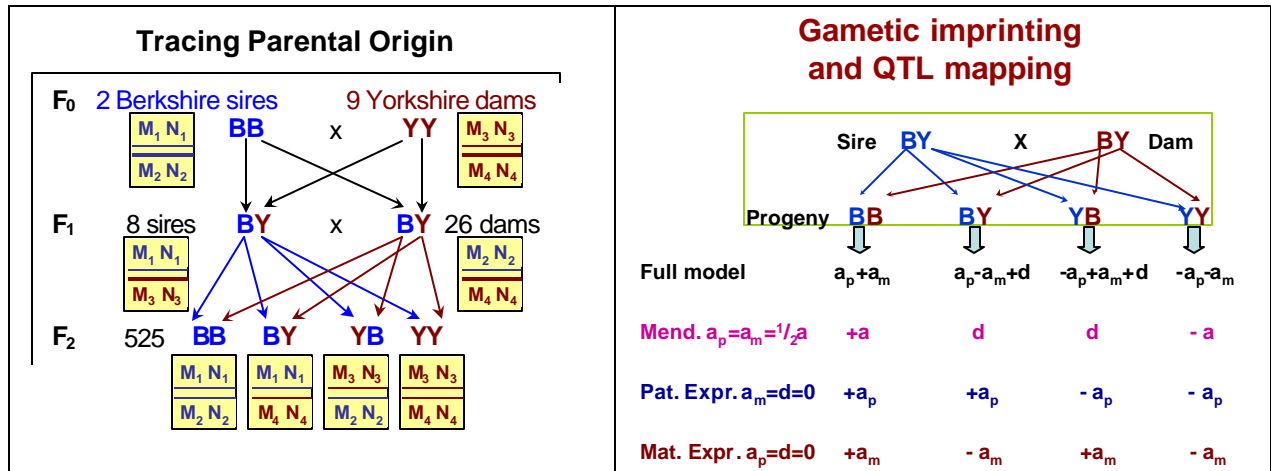
A limited number of examples for gametic imprinting effects in livestock have been described. De Vries et al. (1994) found evidence for population genetic variance associated with gametic imprinting in three pig populations for growth rate and backfat thickness. Knott et al. (1998) were the first to search for imprinted QTL in a genome scan. They inferred imprinting when effects differed significantly from Mendelian expression. Jeon et al. (1999) and Nezer et al. (1999) found paternal expression for muscularity in the *IGF2* region of chromosome 2 in pigs. De Koning et al. (2000, 2001) modified the approach of Knott et al. (1998) and reported a large number of imprinted QTL for growth and meat quality traits in pigs. It should be noted that since imprinting can not be confirmed without further functional tests we will refer to all possible cases of imprinting as parent of origin effects. The purpose of this study was to further analyze the Berkshire-Yorkshire cross data to identify parent of origin effects or imprinted QTL.

Materials and Methods

The data on the Berkshire x Yorkshire F₂ cross, as described by Dekkers et al. (these proceedings), was used. Detection of QTL with gametic imprinting requires the ability to identify the parental origin (i.e. F₁ dam or sire) of chromosomal regions in the F₂, i.e.

QTL genotypes BY and YB must be distinguished. This can be done based on marker data if the F₁ sire and dam have different marker genotypes, as illustrated in Figure 5.

Figure 5. Using markers to trace parental origin. Figure 6. Mendelian and parent-of-origin models.



Thus, using marker data, probabilities of parental and breed origin of alleles were derived for each individual in the F₂ generation at every 1-cM position along the genome based on multi-marker data. These probabilities were then used to fit four alternative gene expression models at each 1-cM position, as illustrated in Figure 6:

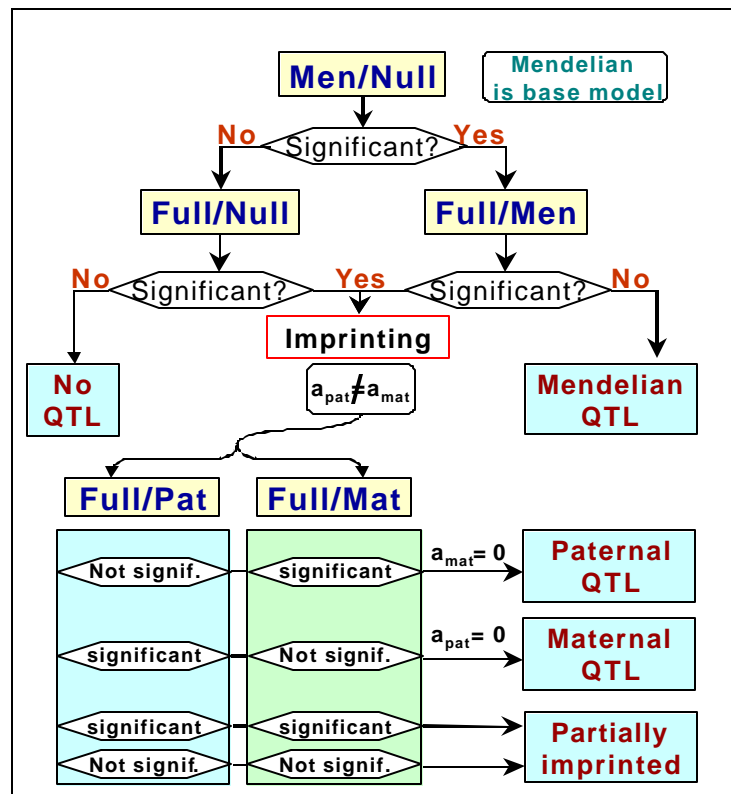
- Full model (Full): both parental alleles are expressed but at different levels.
- Mendelian model (Men): both the parental alleles are expressed and at equal levels.
- Paternal expression model (Pat): only the paternal allele is expressed.
- Maternal expression model (Mat): only the maternal allele is expressed.

To identify QTL and to determine their mode of inheritance, the alternative models were tested against each other in a sequence of tests following the decision tree in Figure 7. Statistical tests were based on an F-statistic that compared the reduced model to the larger model were used at each point in the decision tree. Significance thresholds for each test were derived using specialized permutation tests. The rationale behind the sequence of tests conducted in the decision tree of Figure 7 is that Mendelian expression can be considered the *a priori* model for gene expression and that parent-of-origin effects should be inferred only if the effect of the maternal and paternal alleles are significantly different from each other within the QTL region.

Results

Details on QTL for which parent-of-origin effects were detected are in Table 1. A total of 33 QTL with parent-of-origin effects were detected at the 5% chromosome-wise level, of which 11, 6, and 9 were significant at the 1% chromosome-wise, and at the 5 and 1% genome-wise levels based on their inferred mode of expression. All but twelve of these QTL were not detected by the Mendelian model.

Figure 7. Decision tree to identify QTL and determine their mode of inheritance. Men/Null is a test of the Mendelian expression model against a model with no QTL, and is used to detect QTL. All tests of significance were conducted using 5% chromosome-wise levels.



The central region of SSC1 showed evidence of a paternally expressed, most likely pleiotropic QTL, with effects on backfat traits and on loin eye area (Table 1). Paternally expressed QTL were detected at the proximal end of chromosome 2 for backfat traits and loin eye area. This region is known to contain the *IGF2* gene, which has been shown previously to be paternally expressed (Nezer et al. 1999, Jeon et al. 1999, Georges et al. 2003). Two maternally expressed QTL were detected in the distal part of SSC2 for reflectance and pH in the loin.

Table 1. QTL with evidence of parent-of-origin effects at the 5% chromosome-wise level.

Chr.	Trait	QTL position	Mode of expression	Significance ^a	Effect estimate ^b	
1	Average backfat	43	Paternal	****	-0.23	
1	Last rib backfat	41	Paternal	****	-0.24	
1	Tenth rib backfat	42	Paternal	**	-0.17	
1	Loineye area (cm ²)	39	Paternal	**	0.20	
2	Average backfat	2	Paternal	****	0.23	
2	Tenth rib backfat	5	Paternal	****	0.21	
2	Lumbar backfat	4	Paternal	****	0.22	
2	Last rib backfat	2	Paternal	****	0.19	
2	Loineye area (cm ²)	8	Paternal	****	-0.20	
	2	24-h Loin Hunter	135	Maternal	*	0.18
	2	48-h Loin pH	136	Maternal	***	-0.19
	3	Off flavor score	72	Paternal	**	-0.14
4	Carcass yield	133	Paternal	****	0.22	
	5	Drip loss	29	Paternal	**	0.16
	6	Lipid %	128	Maternal	*	-0.13
	9	Drip loss	93	Maternal	**	-0.17
	9	24-h Loin Hunter	95	Maternal	***	-0.19
	9	48-h Loin Minolta	95	Maternal	**	-0.16
	9	Off flavor score	93	Maternal	***	-0.20
10	Tenth rib backfat	3	Maternal	**	-0.19	
	10	Marbling score	0	Maternal	***	-0.18
10	Loin eye area	87	Paternal	*	0.15	
	10	Cholesterol	119	Maternal	**	0.17
11	Carcass length	3	Maternal	***	-0.18	
12	Tenth rib backfat	96	Maternal	*	0.14	
	14	24-h Ham Hunter	17	Maternal	*	-0.14
	15	Lactate	74	Maternal	**	-0.16
	15	Tenderness score	52	Maternal	****	0.20
	16	24-h Loin Hunter	57	Maternal	*	-0.15
17	ADG early	87	Maternal	*	0.15	
17	16 Day weight	87	Maternal	**	0.17	
	18	Glycogen	24	Paternal	***	-0.18
18	Tenth rib backfat	0	Maternal	**	-0.14	

^a * Significant at 5% chromosome-wise level

** Significant at 1% chromosome-wise level

*** Significant at 5% genome-wise level

**** Significant at 1% genome-wise level

^b Estimated effects for the inferred genetic model. The effect is expressed as effect of the Berkshire allele minus the effect of the Yorkshire allele.

Parent-of-origin effects were also identified on SSC3 for off flavor score (Table 1), one maternally expressed and an adjacent QTL that is paternally expressed. This could also represent a single QTL that is partially expressed. Several QTL with maternal expression were detected in the same marker interval in the central region of SSC9 for traits related to meat quality, including drip loss, light reflectance in the loin, and off flavor score (Table 1). Only the QTL for off flavor score was detected under the Mendelian model. Maternally expressed QTL were also identified for QTL on SSC10 for tenth rib backfat and marbling in the proximal region and for cholesterol in the distal region (Table 1). A paternally expressed QTL was identified for loin eye area in the central region. Only the QTL for marbling was also detected using the Mendelian model.

Another genomic region with multiple QTL with parent-of-origin effects was identified in the distal region of SSC17 (Table 1), where maternally expressed QTL were detected for 16th day weight and average daily gain from birth to weaning (not shown). Chromosome 18 also showed parent-of-origin effects for two traits but in different regions; a paternally expressed QTL for glycogen in the middle range of the chromosome and a maternally expressed QTL for tenth rib backfat in the proximal region. Single parent-of-origin QTL were identified on SSC 4, 5, 6, 11, 12, 14, and 16.

Discussion and implications

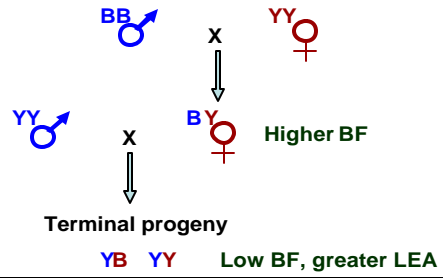
This study has identified several new QTL and identified their mode of inheritance for the Berkshire x Yorkshire breed cross. Characterization of the mode of inheritance of QTL is important to enable proper incorporation of results in selection programs in order to maximize their impact in commercial progeny. For example, as pointed out by De Koning et al. (2000), the mother of piglets has requirements for energy reserves that her offspring do not. Knowing how genes for body fat are inherited and expressed will allow breeders to derive specific crossbreeding and mating combinations to optimise the genetic constitution of animals in relation to their role in the production system (e.g. Figure 8).

Figure 8. Tactical use of QTL with parent-of-origin effects in crossbreeding, using the paternally expressed IGF-2 region as an example.

IGF-2
region

Berkshire allele \Rightarrow higher BF
 \Rightarrow lower LEA
expressed if inherited from sire

Tactical use in cross breeding



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