

IGF2 : The Use of a Paternally Expressed QTL influencing Muscle Mass in Marker Assisted Selection in Commercial Pig Populations

Prof. Nadine Buys
Gentec N.V., Lebbeke, Belgium

Recently a Quantitative Trait Locus (QTL) with major effect on muscle mass and fat deposition was mapped to the IGF2 locus on the distal end of Chromosome 2 in pigs (SSC2). This QTL was found in experimental crosses of Pietrain and Large White on the one hand (Nezer et al., 1999) and of Wild boar and Large White on the other (Jeon et. al., 1999) and explained 15 – 30 % of the variation in muscle mass and 10 - 20 % of the variation in back fat thickness. No influence was found on growth, birth weight or pH of meat.

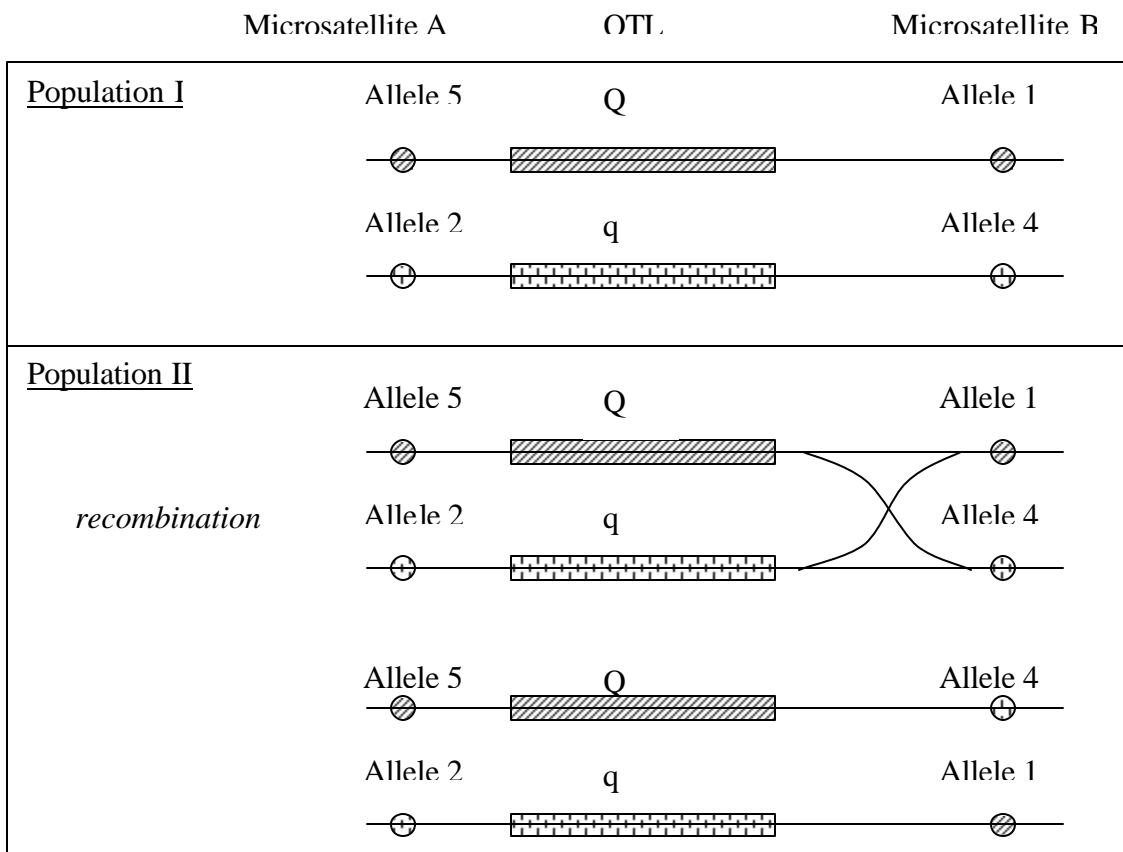


Figure 1. Due to recombination marker alleles linked to the favourable QTL in one population can be linked to the unfavourable one in another population. In Population I haplotype 5/1 is linked to the favourable phenotype (Q) while the haplotype 2/4 is linked to the unfavourable one (q). Due to a recombination that occurred in the ancestors of population II, in this population the haplotype 5/4 is linked to Q while haplotype 2/1 is linked to q.

The large effect of the QTL on lean meat and back fat without influence on growth or meat quality, made this an attractive QTL to use in the breeding programme. Moreover,

the QTL is characterised by paternal expression or maternal imprinting. This means that only the allele inherited from the father will be expressed. The allele coming from the mother is a silent gene and will as a consequence not influence the phenotype. Terminal sires being homozygous for the QTL, will pass the full effect to their offspring. Parent sows do not need to be tested.

The IGF2-QTL is based on linkage between microsatellite markers and an, at that moment, unknown mutation that results in higher muscle mass located at the IGF2 locus.

Application of the QTL in commercial lines

The IGF2-QTL is based on the linkage between markers (microsatellites) at this locus and a mutation causing the QTL effect. This mutation was not known at this moment. In order to be able to use this QTL in a population that is different from the original population, it needs to be tested if the same linkage between the microsatellite markers and the effect exists in this population. Due to a different origin of the new populations recombination might have occurred in between the causative mutation and the marker. This could result in an opposite relationship between the markers and the QTL (Figure 1).

The closer to each other the markers and the causative mutation are situated, the closer the link between both, and the lower the chance on recombination. On the basis of the original linkage analysis, the confidence interval of the IGF2-QTL covered ca. 4 centiMorgans which corresponds to 4% recombination.

In order to be able to select for the IGF2-QTL in a commercial population the following questions have to be answered: 1) Which haplotypes are found in the boars of the commercial population and 2) Does the same relationship exist between these haplotypes and the phenotype corresponding to a higher muscle mass?

In order to answer these questions, segregation analysis was performed in commercial boar lines. Besides the original pedigree, a series of paternal half sib pedigrees based on the commercial lines and counting at least 20 offspring was genotyped for the two microsatellite markers that were linked to the IGF2-QTL in the original populations: SWR2516 and SWC9. The pedigrees of sires that were heterozygous for one or both of these markers were kept for further analysis. In the offspring of these boars lean meat percentages were measured by Piglog.

The QTL genotype of each sire was determined based on the following principle. From all heterozygous boars, the offspring were divided into two groups according to the haplotype they received from their father. Lean meat percentages were compared between both groups. If the difference in lean meat percentage was more than 2.0%, the sire was decided to be Qq, if not the sire was considered to be QQ or qq. This way we could detect the genotype for 14 boars. Seven out of these proved to be heterozygous Qq and the other 7 to be homozygous and thus of either QQ or qq genotype (Nezer et al., 2003).

The original microsatellite markers (SWR2516/SWC9) did not seem to be perfectly linked with the Q chromosome indicating that in these commercial lines recombination had occurred between these markers and the causative mutation. Hence a more detailed mapping of the QTL effect was necessary.

New markers (51 SNP's and 3 microsatellites) were developed in the domain in between the 2 original microsatellites. From all 14 boars genotyped we selected – for each boar - offspring that were homozygous for the alternate paternal SWR2516/SWC9 haplotype. These were genotyped for all new markers available in the region. From these genotypes we manually determined the linkage phase of the boars. This revealed that all Q chromosomes shared a 250 kb common haplotype. At this moment, a test was developed based on SNP's that were different between Q and q chromosomes in the commercial lines. This test was used in the commercial lines involved in order to perform marker assisted selection for lean meat.

Using this test either terminal sires or grand parent animals of sire lines were genotyped for the QTL in order to produce terminal sires homozygous QQ. Boars that are guaranteed homozygous are certified and tagged with a unique ear tag.

Further segregation analysis and fine mapping of the QTL led to the detection of the causative mutation of the QTL (Van Laere et. al., 2003). This is a single nucleotide polymorphism influencing methylation status and hence expression of IGF2 in the muscle. The IGF2 mutation increases meat production at the expense of fat, by 3-4 %.

Currently boars of different breeding programmes, amongst which Newsham Genetics, are tested for the IGF2 mutation. As it is the causative mutation, the link between the mutation and the desired phenotype is 100 %, regardless the origin of the pedigree. The incidence of the mutation is higher in commercial lines that have been selected for leanness as compared to other lines.

Field results

The advantage of the IGF2 QTL is situated at the level of the terminal sire. A number of field experiments were performed in which slaughter pigs sired by homozygous boars were compared to market average. In a trial performed in USA hogs sired by boars homozygous for the IGF2-QTL were compared to previous farm averages (n=1678). The actual advantage of the homozygous boars was 1.98 % lean meat (Table 1). It was also shown that the uniformity of the hogs was increased because the most fat animals were selected out.

Table 1. Actual advantage of using terminal sires homozygous for the IGF2-QTL as compared to previous farm average. Trial performed in USA in 2001 on 1678 hogs.

	Actual advantage of homozygous boars		% improvement
Hot carcass wt.	+ 10.00	lbs.	4.12%
10th rib Back Fat	-.09	inches	9.00%
Loin eye area	+.23	%	9.27%
% Ham	+.31	%	1.03%
% Loin	+.43	%	5.64%
% Belly	+.92	%	10.12%
% Lean	+1.98	%	3.53%
% Yield	+.34	%	
Premium / pig	+ \$ 3.57	Dollars	

References

Jeon, J.-T., Carlborg O, Törnsten A, Giuffra E, Amarger V, Chardon P, Andersson-Eklind L, Andersson K, Hansson I, Lundstrom K, Andersson L, 1999. A paternally expressed QTL affecting skeletal and cardiac muscle mass in pigs maps to the IGF2 locus. *Nature Genetics* 21, 157-158 (1999).

Nezer C, Moreau L, Brouwers ., Coppieters W, Dettleux J, Hanset R, Karim L, Kvasz A, Leroy P, Georges M, 1999. An imprinted QTL with major effect on muscle mass and fat deposition maps to the IGF2 locus in pigs. *Nature Genetics* 21, 155-156

Nezer C, Collette C, Moreau L, Brouwers B, Kim JJ, Giuffra E, Buys N, Andersson L, Georges M., 2003. Haplotype sharing refines the location of an imprinted quantitative trait locus with major effect on muscle mass to a 250-kb chromosome segment containing the porcine IGF2 gene. *Genetics* 165, 277-285.

Van Laere AS, Nguyen M, Braunschweig M, Nezer C, Collette C, Moreau L, Archibald AL, Haley CS, Buys N, Tally M, Andersson G, Georges M, Andersson L., 2003. A regulatory mutation in IGF2 causes a major QTL effect on muscle growth in the pig. *Nature* 425, 832-836.