Insulin-Like Growth Factor 2 Gene for Leanness

Yuefu Liu, CCSI, September, 2003

IGF2 gene and its physiological functions

Insulin-like growth factor 2 (IGF2) gene plays an important role in mammalian growth, influencing foetal cell division and differentiation, and postnatal muscle growth.
It was mapped to the distal tip of chromosome 2p. IGF2 is an imprinting gene, paternally expressed, i.e. only the allele from father can be expressed in progeny. This imprinting inheritance mode of the gene has been reported by several studies.

The beneficial effects of growth hormone (GH) on swine carcass are known for a long time. The GH does not act directly on muscle cells but is instead an intermediate in a series of hormonal signalling events to increase growth (Meadus, 2000). Altering any one of these endocrine genes or their respective receptor genes can modify growth. IGF2 is one of the intermediates in the GH endocrine pathway.

IGF2 gene is a major candidate gene for lean growth and fat composition

Based on its physiological function, IGF2 has been considered as a candidate gene for a quantitative trait locus (QTL) in pigs affecting muscularity. The large effect of IGF2 gene on lean meat content and backfat thickness of swine has been detected by several studies. The evidences from these studies are briefed as follows:

An intercross between wild boar and Large White domestic pigs was used for QTL mapping by Andersson-Eklund et al. (1998). A quantitative trait locus (QTL) on the short arm of chromosome 2 with a moderate effect on muscle mass was detected using conventional Mendelian inheritance model. Jeon et al (1999) reanalyzed the data and tested the presence of an imprinting effect. An imprinted QTL (paternally expressed) was detected at the distal tip of SSC2p that has very large effects on lean meat content in ham and explained 30.6% residual phenotypic variance of F2 population. Large effects on the

area of longissimus dorsi muscle, heart weight and backfat thickness were also detected. This large effect QTL explains 15.4% of F2 phenotypic variance of Longissimus muscle area, 14% of heart weight, 10.4% of backfat depth. The results demonstrated that the paternally expressed QTL maps to the same position as IGF2. This together with the fact that both the gene and the QTL are imprinted makes IGF2 possible candidate gene for the QTL effect. The Large White allele at the IGF2-linked QTL was associated with larger muscle mass and reduced backfat thickness. Notably, this QTL has no effect on abdominal fat.

Nezer et al. (1999) generated an intercross between Large White and Pietrain pig breeds, yielding 1032 F2 progeny. The QTL mapping based on the experiment detected a highly significant QTL at the distal end of the short arm of chromosome 2, influencing muscularity measurement (lean cut %, ham % and loin %) and fat deposition (backfat thickness, backfat % and fat cut %). Sequence analysis (Nezer et al.1999) showed IGF2 gene coincides with the position of the detected large-effect QTL at the distal end of chromosome 2p, and well within the 95% support interval. Nezer (1999) also analyzed the skeletal muscle and liver cDNA from 10-week-old porcine foetuses and found that IGF2 is imprinted in these tissues of pigs as well just as Human and mouse. QTL mapping results of Nezer et al. (1999) based on the F2 data also well confirmed that the QTL at the end of SSC2p is imprinted and paternally expressed. IGF2, therefore, is a positional candidate gene for the QTL at the distal end of SSC2p. Its effects on muscle mass and fat deposition is major and of the same magnitude as those reported for the Halothane gene (Ryanodine receptor 1 gene). Two loci jointly explain 50% of the Pietrain-Large White difference for muscularity and leanness. However, they did not find any evidence for interaction between the QTL at IGF2 gene and Halothane gene locus. In sequence analysis, Nezer et al. (1999) found a single nucleotide mutation, G to A transition in IGF2, which increases lean yield by up to 2.7% (Meadus 2000).

The QTL at IGF2 and FAT1 on chromosome 4 (Andersson et al. 1994) are two QTL with the greatest effect on body composition and fatness, segregating in the wild boar- Large White cross. The QTL at IGF2 controls mainly muscle mass whereas FAT1 has major

effects on fat deposition (Jeon et al. 1999). The two QTL loci explain 33.1% of variance for lean meat content in ham, 31.3% for percentage of lean meat plus bone in back, and 26.2 % for average backfat depth.

According to Kris et al. (2002), IGF2 explains 25% of the phenotypic variation of leanness in experimental crosses. However, it does not influence daily gain and meat PH.

Lee et al. (2001) also tested the existence of the imprinted QTL at IGF2 based a F2 population of 512 pigs from cross between Berkshire and Yorkshire breeds. Their hypothesis tests confirmed that IGF2 gene region is imprinted in pigs and harbours an important QTL for muscularity and fat deposition. The test reached the genome-wide highly significant threshold ($p<0.01$) for average backfat thickness and loin-eye area. The favourable alleles originated from the Yorkshire breed, when transmitted through sires, reduced average backfat by 0.1 cm and increase loin-eye area by 1.0 squared centimetre, compared to Berkshire alleles.

The IGF2 microsatellite was found to be highly polymorphic, with three alleles among the two wild boars founders and another two alleles among eight Large White founders (Jeon et al. 1999). This high polymorphism provides a good potential for improving lean meat content of the swine carcass by selection.

Some important points from briefing the studies above:

- There is a QTL at IGF2 gene or in the IGF2 region located at distal end of SSC 2p, affecting muscularity and fat deposition.
- The IGF2 QTL is imprinted in pigs (paternally expressed).
- The IGF2 QTL has large effects on lean meat content and backfat thickness. It does not influence meat quality and abdominal fat.
- The IGF2 QTL is highly polymorphic. Polymorphism exists between breeds (e.g. between wild boars and Large White, between Large White and Pietrain, and between Berkshire and Yorkshire) and within purebred populations.

Use of IGF2 gene in swine breeding

The gene mapping researches consistently indicated the large effect QTL at IGF2 gene affecting muscle mass and carcass leanness. This QTL have important practical implications for the pig industry because it is imprinted and has large effects on lean meat content.

Use for Uniformity: The QTL at IGF2 gene is paternally expressed only. The genes from boars should show the full effect on progeny, regardless of the sows' genotypes. Besides, this QTL has a large effect on lean meat content of carcass. Use of homozygous terminal sires in producing hogs should be able to increase the lean- meat-content uniformity of hogs because a sire, especially AI sire, can produce a large number of progeny and the Dams' QTL at IGF2 gene will not cause any phenotypic variation in progeny.

Using IGF2 gene to increase the uniformity of pork leanness is not just a theoretical potential. It was confirmed by breeding practices of some company. For example, terminal sires that are homozygous for the favourable allele at the IGF2 QTL were selected in SEGHERSgenetics (Kris et al. 2002) and a field trial with these sires was conducted to investigate whether the QTL can be used in commercial selection program in order to increase uniformity of slaughter pigs without influencing meat quality. The carcass and meat quality of hogs from selected terminal sires were compared with those from unselected boars and with the average of the plant top 25%. All data confirmed that hogs from selected boars were leaner and mores uniform compared to unselected boars. Backfat thickness was reduced with 23mm. Average lean meat percentage, ham percentage and loin percentage were increased by 1.98%, 0.31% and 0.43%, respectively. The variations of these traits are reduced 25% on average. Compared with the average of plant top 25%, hogs from the selected boars were leaner. The increase is 0.64% for lean meat percentage, 0.39% for ham percentage and 0.43% for loin percentage, respectively. The meat quality traits, PH after 24 hours and meat color, were also compared. Hogs from selected boars and those from unselected boars both had the same PH value (5.77 to 5.78 measured after 24 hours) and Minota lightness (44.57 to 43.08) within the optimal

range. The investigation concluded that the selection of homozygous terminal sires with the favourable allele at IGF2 gene increases the uniformity and carcass leanness in market hogs without influencing meat quality.

Improving sow longevity by use of IGF2: Sow durability (or lifetime reproduction) was said to be reducing as a result of the genetic selection for increasing leanness and lowering the fat deposition. Some studies (e.g. Brisbane and Chesnais 1996; Stalder et al. 2001) reported the association between backfat and sow longevity that has been defined as the lifetime number of litters produced by a sow. Besides, body fat deposition is necessary to sustain sow reproduction performance, for example to supply adequate milk production and to limit body weight loss (Ranford et al. 1994).

The selection for leaner carcass demanded by packing industry and consumers may conflict with the sow longevity and lead to increase the replacement costs of sows in swine production. The candidate gene IGF2 provides a possibility to solve the conflictive problem. The imprinting mechanism of this major gene could be used for producing commercial hogs with required leanness from fatter dams since only the favourable alleles from homogenous sires at IGF2 are expressed in progeny. Dams can be fatter.

References

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