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Review

Genetic variation in meat quality induced by genomic technologies

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Meat quality is one of the most important economic traits in farm animals. The goal of genomics technologies is to provide genetic map and other resources to identify loci responsible for genetic variation in quantitative traits such as meat quality. Candidate gene and genome scanning are two main techniques for this purpose. In the past decade, advances in molecular genetics led to identify these genes and markers linked to them. Sequencing of animal genome is important to distinguish gene function and molecular basis of meat quality determinants. Candidate gene considers relationship between the traits of interest and known genes, while genome scanning studies relationship between traits and pre-mapped markers. So far, several genes and sequences were detected which affect meat quality, for example quantitative trait loci (QTL) on chromosome 18 in sheep which causes muscle hypertrophy. The aim of this review is introduce and applications of genomic technologies to the improvement of meat quality.

Key words: Genomics technologies, meat quality, candidate gene, genome scanning.

INTRODUCTION

Meat quality is one of the most important economic traits in farm animals. Meat quality trait has a multifactorial background and is controlled by an unknown number of quantitative trait loci (QTL). Genome research in farm animals progressed rapidly in recent years, moving from linkage maps to genome sequence. The work on farm animal genome sequencing began in the early 1990s, and assists in the understanding of genomics function in various organisms (Fadiel et al., 2005). Genomic technologies are combination of different branches of genetics molecular genetics, quantitative genetics, Mendelian genetics and bioinformatics science. This approach can be useful for improvement of meat quality in animal breeding (Kharrati et al., 2009). In the past decade, advances of genomic technologies using linkage mapping and DNA sequencing are manifold. The information of the meat quality trait loci can be applied in breeding programs by using marker-assisted selection (MAS) (Gao et al., 2007).

The goal of genomic technologies is the characterization and mapping of the loci that affected these traits. The main outcome of genomics technologies is the determination of physical effect gene on phenotype, physiology and biochemistry of them.

Generally, meat quality depended on color, water keeping, tenderness and resistance against oxidation. It is influenced by several factors, such as breed, genotype, feeding, fasting, pre slaughter handling, stunning, slaughter methods, chilling and storage conditions (Rosenvold and Andersen, 2003).Improvements of meat quality traits with traditional breeding programs are very difficult, because heritability of them is very low. A lot of work has been carried out in this field to find potential

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genes or chromosome regions associated with the meat quality trait in different farm animals, such as pig, cattle, sheep and chicken (Gao et al., 2007).

GENOMICS TECHNOLOGIES

Candidate gene approach

The candidate gene approach studies the relationship between the traits and known genes that may be associated with the physiological pathways underlying the trait (Liu et al., 2008). In other words, this approach assumes that a gene involved in the physiology of the trait could harbor a mutation causing variation in the trait. The gene or part of gene, are sequenced in a number of different animals, and any variation found in the DNA sequences, is tested for association with variation in the phenotypic trait. This approach has had some success. For example a mutation was discovered in the estrogen receptor locus (ESR) which results increased litter size in pig. There are 2 problems with the candidate gene approach.

Firstly, there are usually a large number of candidate genes affecting the trait, so many genes must be sequenced in several animals and many association studies carried out in a large sample of animals.

Secondly, the causative mutation may lie in a gene that would not have been regarded prior as an obvious candidate for this particular trait. Candidate gene approach is performed in 5 steps: 1) collection of resource population. 2) Phenotyping of the traits. 3) Selection of gene or functional polymorphism that potentially could affect the traits. 4) Genotyping of the resource population for genes or functional polymorphism.

Lastly, one is statistical analysis of phenotypic and genotypic data (Da, 2003). This is an effective way to find the genes associated with the trait. So far a number of genes have been investigated. Candidate gene approach has been ubiquitously applied for gene disease research, genetic association studies, biomarker and drug target selection in many organisms from animals (Tabor et al., 2002).

The traditional candidate gene approach is largely limited by its reliance on existing knowledge about the known or presumed biology of the phenotype under investigation, unfortunately the detailed molecular anatomy of most biological traits remain unknown (Zhu and Zhao, 2007).

Recently, a new developing method on candidate gene approach [digital candidate gene (DigiCGA) has emerged and is primarily applied to identify potential candidate gene in some studies. DigiCGA, which also named in silico candidate gene approach or computer facilitated candidate gene approach, is a novel web resource based candidate gene identification approach. DigiCGA approach is included to ontology–based identification approach, computation-based identification approach and integrated identification approach (including literature-based meta-analysis).

The ontology-based identification approach is mainly involved in the bioinformatics analyses for in silico identification of candidate gene for specific interest in case of the semi structured, structured and controlled vocabularies for systematic annotation of gene function information from biological ontology source available through internet. A typical example of this approach is the prioritization of positional candidate gene by using gene ontology (Harhay and Keele, 2003).

The computation-based identification includes those computational candidate gene identification methods that describe computational framework to prioritize the most likely candidate gene through a variety of web resource-based data sets. There are many statistical algorithms or computational methods, and of which some included data mining analysis (Perez et al., 2002), hidden Markov analysis (Pellegrini-Calace et al., 2006), cluster analysis (Freudenberg and Propping, 2002) and kernel-based data fusion analysis (De Bie et al., 2007). There have been reported many candidate gene prioritized by the integrated identification approach such as pathway and gene ontology combined analysis (Tiffin et al., 2005).

Genome scan approach

The genome scan approach studies the relationship between a trait and markers selected across the genome to identify chromosomal locations associated with the trait (Andersson, 2001). The genome scan will find out the map location of a trait locus with major effect, It involves the following steps: 1) design and construction of resource population, 2) phenotyping traits of resource population, 3) selection of genetic markers, 4) genotyping of the population for selected markers, 5) construction of linkage maps, and 6) statistical analysis of the phenotypic and genotypic data derived from the resource population (Da. 2003).

Using the genome scan, a large amount of QTL can be obtained in farm animals that can provide a useful bridge to link genome information with phenotype. There is an animal QTL data base, which contains all publicly available QTL data on farm animal species for the past decade (Hu et al., 2007). Several groups have worked on the identification of QTL controlling meat quality and most of them are about meat pork quality. QTL are located on almost every porcine chromosome, for instance in pig,

there are 12 types of meat quality and total 1405 QTL for meat quality, such as 595 QTL for anatomy, 25 QTL for conductivity, 64 QTL for fat composition, 18 QTL for chemical, 1 QTL for enzyme activity, 439 QTL for fatness, 5 QTL for odor, 79 QTL for meat color, 26 QTL for flavor, 3 QTL for stiffening, 66 QTL for PH and 84 QTL for texture (http.www.animal genome.org/QTLdb/pig html).

In other studies, quantitative trait locus genome scans was performed for porcine muscle fiber traits. In this research, it was reported that a complete QTL scan of muscle fiber trait in 160 animal from a F_2 cross between Iberian and Landrace pigs using 139 markers and identified 20 genomes regions distributed along 15 porcine chromosome (1, 2, 3, 4, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 and X) with direct and epistatic effect. Epistatic was frequent and some interactions were highly significant. Chromosome 10 and 11 seemed to behave as hubs; they harbored 2 individual QTL, but also 6 epistatic regions. Numerous individual QTL effects had cryptic alleles, with positive effects to phenotypic pure breed difference (Estelle et al., 2002).

Genome scans for QTL affecting carcass trait is another application for this approach for improvement of meat quality in farm animals. For instance, genome wide scans were performed for QTL affecting carcass traits in Hereford x composite double backcross populations. Genome wide scan for chromosomal regions influencing carcass traits was conducted spanning 2.413 morgans on 29 bovine autosomes using 229 microsatellite markers.

Phenotypes measured at harvest were: carcass weight, fat depth, marbling, percentage kidney, pelvic and heart fat and rib eye area. The result indicated promising location for QTL affecting live weight on BTA 17 and marbling on BTA 2 that segregate in *Bos taurus* (MacNeil and Grosz, 2002). Much research was performed to map QTL for carcass composition and meat quality in sheep. For instance, a partial genome scan to map QTL was performed for carcass composition by X-ray computer tomography, and meat quality traits in Scottish Blackface sheep. The population studied was a double backcross between lines of sheep divergently selected for carcass lean content (LEAN and FAT lines), comprising nine half-sib families.

Carcass composition (600 lambs) was assessed nondestructively using computerized tomography (CT) scanning, while meat quality measurements (initial and final pH of semi-membraneous, color, shear force value, carcass weight, lamb flavor, juiciness, tenderness and overall liking) were taken on 300 male lambs. Lambs and their sires were genotyped across candidate regions on chromosomes 1, 2, 3, 5, 14, 18, 20 and 21. QTL analyses were performed using regression interval mapping techniques. In total, nine genome-wise was significant and 11 chromosome-wise and suggestive QTL were detected in seven out of eight chromosomes. Genome-wise significant QTL were mapped for lamb flavor on sheep chromosome 1 (OAR1); for muscle densities (OAR 2 and OAR3); for color (redness) (OAR3); for bone density (OAR 1); for slaughter live weight (OAR 1 and OAR 2) and for the weights of cold and hot carcass (OAR 5). The QTL with the strongest statistical evidence affected the lamb flavor of meat and was on OAR 1, in a region homologous with a porcine chromosome 13 (SSC13) QTL identified for pork flavor. This QTL was segregated in four of the nine families.

This study provides new information on QTL affecting meat quality and carcass composition traits in sheep, which may lead to novel opportunities for genetically improving these traits (Karamichou et al., 2006). Although, a genome scan can give full genome coverage for a trait, it will fail to detect trait loci with smaller effects if they do not reach the stringent significance of the threshold (Gao et al., 2007).

Fine mapping

Fine mapping involves the identification of markers that are very tightly linked to a targeted gene. A genetic fine map of a specific locus will usually give us its goal by the identification and location of marker that flank the targeted gene within one or fewer cent Morgan (cM) with a fine map, and assisted selection precise. Several problems are associated with the generation of fine map around any animal gene.

First, mapping marker to a resolution of one cM requires the investigation of a few hundred sexual progeny. Second, marker polymorphism can be low in mapping population and third, recombination rate per chromosome arm in sexual generation. The ultimate goal of genome scan approach is to identify the genes that underlie polygenic trait and gain better understanding of their physiological and biochemical functions. In fact a region of QTL often spans 5 to 30 cM and it is too large to find the target genes, so fine mapping needs to be done. It is a step towards restricting the region of interest and the number of potential candidate genes. The goal of fine mapping is mapping QTL to a narrow chromosome region so that the physical QTL affecting the phenotype can be identified and cloned (Gao et al., 2007).

Finally fine mapping a gene is usually an essential step in map-based gene isolation. For example, fine mapping quantitative trait loci for body weight and abdominal fat trait in chicken was performed. Highly significant QTL for body weight and abdominal fat trait on chicken chromosome 1 were reported. This research genotyped 9 more microsatellite markers, including 6 novel ones. Linkage analyses were performed. The result of the

linkage analyses showed that the confidence intervals for body weight and abdominal fat percentage were narrowed sharply to a small interval spanning 5.5 and 3.7 Mb, respectively (Harhay and Keele, 2003).

IMPORTANT GENES AFFECTING MEAT QUALITY IN FARM ANIMALS

Cattle

DGAT1 gene

The possible association between the activity of diacylglycerol acyltransferase (DGAT) and muscle fat content was examined by Sorensen et al. (2006) in samples of longissimus dorsi (LD) and semitendinosus (ST) muscles from Holstein and Charolais bulls. The Holstein bulls exhibited higher fat content in both muscles and higher marbling score. In Holstein, DGAT activity was enhanced in the LD muscle, and there was tentative positive relationship between DGAT activity and the fat content in ST muscle. When muscle DGAT activity was examined as a function of DGAT genotype for all animals, regardless of breed, the DGAT activity of LD muscle of the K/K genotype was about five-fold greater than either the K/A or A/A genotypes (Sorensen et al., 2006).

Calpastatin gene

Corva et al. (2007) showed that the activity of the calpastatin proteolytic system is closely related to the postmortem tenderization of meat. The association between beef tenderness and single nucleotide polymorphism (SNP) markers on the CAST gene 3' untranslated region (SNP2870, alleles A/G) was investigated. Samples were provided from nine slaughter groups comprising 313 which had been reared in beef production systems in Argentina between 2002 and 2004 from crosses between Angus, Hereford and Limousine cattle. The results indicated no detectable effects were demonstrated for meat shear in the CAST marker. Body weight, carcass weight and rib eye area were not affected by any of the markers (Corva et al., 2007).

Calpain gene

Single nucleotide polymorphism (SNP) in exon 9 of calpain (CAPN1) is related to tenderness of longissimus dorsi (LD) and semitendinousus (ST) muscles in *Bos taursus*. The SNP causes amino acid substitution of alanine for glycine in the $\propto$ - calpain enzyme. Results demonstrated that the exon 9 SNP is significantly associated with the tenderness of both ST and LD muscles (Esmailizadeh et al., 2005).

Myostatin gene

Effects of the myostatin F94L substitution was studied by Esmailizadeh et al. (2008a) on beef traits. The experiment used crosses between the Jersey and Limousine, with the design being a backcross using first cross bulls of Jersey×Limousine or Limousine×Jersey breeding, mated to Jersey and Limousine cows. The progeny was genotyped for the myostatin SNP and phenotyped. The SNP is a cytosine to adenine transversion in exon 1, causing an amino acid substitution of leucine for phenylalanine (F94L). They reported that the F94L allele in Limousine backcross calves was associated with an increase in meat weight and reduction in fat depth on live calves (600 days) and carcasses. Meat tenderness, pH and cooking loss of the longissimus dorsi (LD) were not affected by the F94L variant.

The results provided strong evidence that this myostatin F94L variant provides an intermediate and more useful phenotype than the severe double-muscling phenotype caused by knockout mutation in the myostatin gene (Esmailizadeh et al., 2008a).

Other genes

In a research by Esmailizadeh et al. (2005), QTL were detected for meat color and pH in *Bos Taurus* cattle. An experimental cattle backcross between the Jersey and Limousine breeds was per- formed in Australia and New Zealand to QTL for diverse production traits. Six crossbreed sires and their progeny were genotyped for 253 informative microsatellite markers covering the 29 bovine autosomes. Results of the genome scan using regression interval mapping revealed evidence for QTL on BTA 10,18,19 and 27 for meat color and BTA2,3,5,6,11,12,13,16,24 and 27 for meat pH. A number of detected QTL were mapped to genomic regions likely to contain the RN or RYR1 genes, which are know to affect meat quality traits in pigs (Esmailizadeh et al., 2005).

In other research by Esmailizadeh, et al. (2008b), 2 QTL were detected affecting beef tenderness, one of them located on the Bovine chromosome 2 and other on Bovine chromosome 29 close to the map position of the growth differentiation factor 8(GDF8) and calpain genes, respectively. They showed molecular dissection of these

QTL and indicated significant association between meat tenderness and SNP 316 in the CAPN1 gene and SNP 433 in the GDF 8 gene.

In this study, three parental half-sib families comprising 357 animals were genotyped for 189 microsatellite DNA marker. Meat tenderness was measured as Warner-Bratzler shear force (Esmailizadeh et al., 2008).

Chicken

In chicken, many investigations focused on fat deposition, such as the percentage of hypodermal fat, abdominal fat, and intramuscular fat in breast and legs (Gao et al., 2007). The intramuscular- fat (IMF) was in positive correlation with meat flavor and succulence, especially tenderness of meat. Increasing IMF and controlling fatty deposition is an increased interest in improving - meat quality.

Extracellular fatty acid binding protein (EX-FABP) gene

Fattiness is an important parameter to estimate meat quality, which has high heritability. Wang et al. (2001) showed, EX-FABP gene could be a candidate locus or linked to a major gene to significantly affect abdominal fat traits in chicken. In this experiment, F2 chickens derived from Broilers crossing to Silky were used to study the effect of EX-FABP gene on abdominal fat accumulation. Then, single nucleotide polymorphisms (SNPs) were detected by the technique of single strand conformation polymorphism (SSCP) and confirmed by sequencing. The results of least square analysis suggested that the birds with BB genotype have a higher abdominal fat weight and abdominal fat percentage than the birds with the other genotypes (AA and AB) (Wang et al., 2001).

Liver fatty acid-binding protein (L-FABP) gene

Wang et al. (2006) studied association between L-FABP gene and abdominal fat weight and percentage of abdominal fat. Fatty acid-binding proteins belong to a super family of lipid-binding proteins that exhibit a high affinity for long-chain fatty acids and appear to function in metabolism and intracellular transportation of lipids. In this research, study was designed to investigate expression characterization and association with growth and composition traits of the L-FABP gene in the chicken.

The results indicated that the L-FABP gene polymorphisms were associated with abdominal fat weight and percentage of abdominal fat, and the L-FABP gene could be a candidate locus or linked to a major gene(s) that affects fatness traits in the chicken. The results of the current study provided basic molecular information for studying the role of the L-FABP gene in the regulation of lipid metabolism in avian species (Wang et al., 2006).

Sheep

Callipyge (CLPG1) gene

Frenking et al. (2002) reported that a small genetic region near the telomere of ovine chromosome 18 was previously shown to carry the mutation causing the callipyge muscle hypertrophy phenotype in sheep. Expression of this phenotype is the only known case in mammals of paternal polar overdominance gene action. A region surrounding two positional candidate genes was sequenced in animals of known genotype. Mutation detection focused on an inbred ram of callipyge phenotype postulated to have inherited chromosome segments identical-by-descent with exception of the mutated position. Initial functional analysis indicated sequence encompassing the mutation is part of a novel transcript expressed in sheep fetal muscle (Frenking et al., 2002).

Pig

Calpastatin (CAST) gene

Suggestive QTL affecting raw firmness scores and average tenderness, juiciness, and chewiness on cooked meat were mapped to pig chromosome 2 using a three-generation intercross between Berkshire and Yorkshire pigs. Based on its function and location, the calpastatin (CAST) gene was considered to be a good candidate for the observed effects. Several misses and silent mutations identified in CAST and haplotypes covering most of the coding region were constructed and used for association analyses with meat quality traits. Results demonstrated that one CAST haplotype was significantly associated with lower Instron force and cooking loss and higher juiciness and therefore, this haplotype is associated with higher eating quality (Ciobanu et al., 2004).

Heart fatty acid-binding protein (H-FABP) gene

Gerbens et al. (1999) studied the relationship between variation in the heart fatty acid-binding protein (H-FABP)

gene and (IMF) content. To estimate the effect of H-FABP, pigs from two Duroc populations were selectively mated in such a way that at least two genotypes were present in each litter. In total, data from 983 pigs and pedigree information from three preceding generations were analyzed. Offspring were tested for IMF content as well as back-fat thickness (BFT), body weight (BW) and drip loss of the meat (DRIP). All pigs were assigned to H-FABP Restriction fragment length polymorphism (RFLP) genotype classes either by the assessed genotype (75%) or based on a probability score determined according to genotypic information of their relatives (25%). Contrasts were detected between homozygous H-FABP RFLP genotype classes for IMF content (0.4%, $P < 0.05$), BFT (0.6 mm, $P < 0.01$), and BW (2.4 kg, $P < 0.01$). No significant contrasts were detected for DRIP.

Results for IMF content, BFT, and BW were confirmed when only genotyped animals were analyzed. H-FABP RFLP can be used as markers to select for increased IMF content and growth in breeding programs (Gerben et al., 1999).

Adipocyte fatty acid-binding protein: A-FABP gene (FABP4)

In the first intron of the porcine A-FABP gene, a microsatellite sequence was detected by Gerbens et al. (1998) that was polymorphic for all six pig breeds tested. This genetic variation within the A-FABP gene was associated with differences in IMF content and possibly growth in a Duroc population, whereas no effect on back-fat thickness and drip loss of the meat was detected. A considerable and significant contrast of approximately 1% IMF was observed between certain genotype classes. It was concluded that the A-FABP locus is involved in the regulation of intramuscular fat accretion in Duroc pigs (Garbsen et al., 1998).

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