Genetic analysis of meat quality in cattle

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ABSTRACT

Genetic linkage maps enable scientists to identify regions of the genome that influence production related traits. Sufficient number of polymorphic markers (>1800) are available for a genome-wide quantitative trait loci (QTL) search and subsequent use of markers for selection. Selection for carcass traits has been limited because current market systems do not provide carcass information to the cattle producer. Information obtained from mapping studies will allow producers to select for carcass traits and other traits that are difficult and expensive to measure in production settings. Mapping information will also be used to identify the molecular mechanisms controlling the genetic component of carcass traits and other quantitative traits.

Keywords: Quantitative trait loci (QTL), carcass traits, genetic linkage maps.

INTRODUCTION

Livestock producers attempting to improve animal production, use selection to increase the frequency of desirable alleles within a population. The response to selection depends upon the percentage of phenotypic variation that is genetic and gene action. Selection response is very high for simple or qualitative traits because the phenotypic variation associated with the trait can be completely explained by a few genes or loci. Selection for complex or quantitative traits is more difficult because the genetic component is controlled by many loci which may only explain a small portion of the phenotypic variation. Dramatic improvements in quantitative trait selection have been realized with use of performance records for estimating the genetic value of each animal. Estimated breeding values (EBV) are calculated from records of related animals and used to improve the accuracy of selection. Selection for some traits has been limited because they are difficult to measure in a production setting or require a long time to measure. Current technology enables scientists to study genetic material at the molecular level and identify the regions of the genome that cause genetic variation. Characterization of the allelic differences at each locus will enable animal breeders to identify animals containing the most desirable alleles and use them for producing the next generation.

Selection for carcass quality and composition traits has been limited despite the moderate to high heritability estimates for these traits. Genetic evaluations are not routinely conducted because current marketing systems do not provide carcass information to cattle producers. Mapping carcass trait loci will allow characterization of the different alleles at these loci within and across populations. Subsequently, marker assisted selection (MAS) programs can be implemented to identify the genetically superior animals. The cost of collecting carcass data will be reduced or eliminated after the allelic variation has been characterized at each locus depending upon the resolution of the mapped locus.

Status of Bovine Genome Project

Genetic linkage maps have been developed for cattle (Barendse *et al.*, 1994; Bishop *et al.*, 1994; Georges *et al.*, 1995; Ma *et al.*, 1996; Barendse *et al.*, 1997; Kappes *et al.*, 1997) and have been used to identify regions containing genes with major effects (horn development, Georges *et al.*, 1993a; coat color, Klungland *et al.*, 1995; Charlier *et al.*, 1996; Weaver disease, Georges *et al.*, 1993b; muscle hypertrophy, Charlier *et al.*, 1995; and milk production, Georges *et al.*, 1995).

The status of the bovine mapping effort is summarized from four published maps (Georges *et al.*, 1995; Ma *et al.*, 1996; Barendse *et al.*, 1997; Kappes *et al.*, 1997). These maps contain 1774 linked markers with more than 175 of the markers associated with coding sequences. All 30 linkage groups are oriented to the chromosome with 128 physically assigned polymorphic markers. The current number of polymorphic markers could provide sufficient resolution (~2 cM) for a thorough QTL search provided they were mapped in one population. Fortunately, two maps contain the majority of polymorphic markers (Kappes *et al.*, 1997; Barendse *et al.*, 1997). Comparisons of the four maps can be made since the Kappes *et al.* map contains 47% (323/689), 78% (211/269) and 47% (75/159) of the markers reported by Barendse *et al.* (1997), Ma *et al.* (1996), and Georges *et al.*, (1995), respectively.

While bovine maps have improved dramatically they are still dwarfed by the human (5,264 polymorphic markers, Dib *et al.*, 1996; 15,086 loci, Hudson *et al.*, 1995) and mouse mapping efforts (7,377 polymorphic markers, Dietrich *et al.*, 1996). A Human Genome Project objective is to sequence the entire genome by the year 2003. This wealth of information provided by the human and mouse mapping efforts can be used to improve livestock maps.

Comparative mapping information between humans and cattle is very limited (O'Brien *et al.*, 1993). However, two recent papers (Solinas-Toldo *et al.*, 1995, Hayes, 1995) have used human chromosome specific probes to paint bovine metaphase spreads to determine homologous regions between the two species. As the comparative mapping information increases, the chromosomal break points between cattle and humans will be identified and resolution of synteny conservation will be improved. This will greatly enhance the efficiency of identifying genes associated with a quantitative trait.

Comparative mapping between livestock species can also benefit mapping efforts. The genomic organization between cattle and sheep appears to be very similar for genes and noncoding DNA. Bovine markers amplify sheep DNA (54%; 575/1076) with 31% (336) being polymorphic (De Gortari *et al.*,1997). Similar rates are observed with ovine markers on cattle DNA. The MARC bovine (Kappes *et al.*, 1997) and ovine maps (De Gortari *et al.*, in preparation) contain 348 common markers, 26 ovine and 322 bovine. Marker order within linkage groups was consistent between the two species with limited exceptions. The previously reported translocation of the telomeric end of BTA9 to BTA14 in sheep (OOV9) (Crawford *et al.*, 1994) is represented by a 15 cM region containing five common markers. The other exceptions involved five independent markers (1.5% of the 348 common markers) from different linkage groups that did not map to the expected homologue linkage group. This is most likely due to amplification of closely related sequences at a different locus by the heterologous primers rather than actual translocation. The high degree of genomic conservation between sheep and cattle will allow simultaneous use of conserved linkage and physical mapping information while searching for quantitative trait loci in both species.

Use of Genetic Linkage Maps

The primary objective of developing linkage maps is to provide a tool for identifying regions of the genome that are causing the genetic variation associated with a trait. As previously mentioned, linkage maps have already been used to identify a number of loci that have major effects in livestock species. Information obtained from mapping a QTL can be used to improve selection practices in two different manners. Markers closely linked to the locus can be used to select animals containing the desirable QTL alleles (marker assisted selection; MAS) and the closest flanking markers can be used to positionally clone the DNA sequence that is responsible for the genetic variation associated with the QTL. Diagnostic tests detecting the allelic sequence differences can be developed for identifying the genetically superior animals.

The probability of detecting a QTL is dependent on the variation associated with different QTL alleles, the number of informative meioses and the resolution of informative markers near the locus. A QTL mapping population should be designed to maximize QTL allelic differences and marker heterozygosity within each parent. Mapping information is only obtained from parents that are heterozygous for markers and QTL. Marker heterozygosity varies with the degree of genetic diversity found within an animal. Only 47% of the markers tested on purebred Hereford and Angus cows were heterozygous while marker heterozygosity levels were 60 and 75% for F_1 *Bos taurus/Bos taurus* and F_1 *Bos taurus/Bos indicus* cattle, respectively (Kappes *et al.*, 1997). The number of possible informative markers within a F_1 *Bos taurus/Bos taurus* parent will be ~1,000 markers (1,774 polymorphic markers 60%) for QTL mapping and a number of these markers are very difficult to genotype. Marker heterozygosity will also limit the number of markers available for MAS or positional cloning efforts. Continual map development will be required for increasing marker density in specific regions of the genome.

Several mapping populations may be needed to identify a significant number of QTL affecting a quantitative trait. Only a fraction of the QTL may be heterozygous within a population therefore only explaining a small portion of the total genetic variation. Two independent mapping studies (Stuber *et al.*, 1992, Beavis *et al.*, 1994) were designed to identify corn yield QTL with a cross of two inbred lines (B73 and Mo17). A number of unique QTL were detected in the second study and the authors concluded that the most likely explanation was that the sources of the parental lines were different for the two studies. The probability of QTL heterozygosity for a cross between two inbred maize lines is much higher than the probability for most cattle mapping populations.

Current bovine mapping studies at the U.S. Meat Animal Research Center include populations designed to identify QTL with emphasis on meat quality and composition. The populations consists of four paternal half-sib families with the sire breeds of Brahman/Hereford, Brahman/Angus, Belgium Blue/MARCIII (1/4 Angus, 1/4 Hereford, 1/4 Pinzgaur and 1/4 Red Poll) and Piedmontese/Angus. The four sires were mated to crossbred *Bos taurus* cows to produce 1,300 progeny. The phenotypic data collected includes birth weight, growth rate, meat quantity and quality measurements. Meat tenderness (Warner-Bratzler Shear force) is the primary focus for the progeny of the F_1 *Bos indicus* sires and lean retail product and fat content for the progeny of the F_1 Belgium Blue and Piedmontese sires.

Marker Assisted Selection

Marker assisted selection can increase genetic response over traditional selection because it is a more accurate selection procedure and selection can be practiced at an earlier age. Lande and Thompson (1990) have shown that MAS can be 50% more effective than a selection index for traits with a heritability of .1 and markers that explain 20% of the genetic variance and 3.5 times more effective for traits with a heritability of .05 and markers explaining 40% of the genetic variance. Zhang and Smith (1992, 1993) concluded that selection based on markers and phenotypic selection was 10-20% more effective than selection based on Best Linear Unbiased Prediction (BLUP) when markers are linked closely to the QTL. The most

efficient use of MAS will likely be in conjunction with current selection practices.

Mapping studies can also improve selection for previous highly selected traits as milk production (Georges *et al.*, 1995). Data was collected for milk, protein and fat yield and protein and fat percentage and analyzed in a granddaughter design. Four chromosomal regions were identified that explained 11-52% of the total variation of daughter yield deviation within half-sib families. Georges *et al.* (1995) discussed several possibilities to explain why QTL of such large effects were still segregating in a population that has been under long term selection: 1) the effects might represent the joint action of several unlinked QTL, 2) positive and negative effects for some of the detected QTL could balance out to make the locus near neutral during selection programs, 3) positive effects on milk yield may have negative effects on fitness as observed with Weavers disease in Brown Swiss cattle, 4) the QTL represent relatively recent mutations or , 5) any QTL study will be limited in its power to detect QTLs and the estimated effect of those that are detected may be inflated by chance sampling effects.

Selection based upon DNA markers can also improve selection for qualitative traits. Stuber (1995) indicated that simple inherited traits like disease resistance in maize, might be "semi-quantitative" traits because expression may be controlled by a major gene and several modifiers. A similar situation has been reported for red/black coat color in cattle. The melanocyte-stimulating hormone receptor (MSH-R) was identified as the red/black coat color locus and three mutations within the gene were associated with different coat colors (Klungland *et al.*, 1995). Adalsteinsson *et al.* (1995) also reported that a second locus was causing a brown coat color in Icelandic cattle and hypothesized that it was similar to the *Agouti* locus in mice. Identification of modifier genes affecting single-gene traits, like the *Agouti* locus, may be the most important application of QTL mapping (Lander and Schork, 1994).

Before MAS can be implemented the alleles within a parent will need to be characterized relative to the other alleles found in the population. The relationship between marker alleles and QTL alleles is family dependent and will have to be evaluated for every new source of genetics. The linkage distance between the marker and locus and length of time since the QTL mutation occurred will determine if linkage disequilibrium exists between a marker and QTL.

Positional Cloning

Alternatively to MAS, the DNA sequence that is responsible for the genetic variation of the locus can be identified and used for selection decisions. Determining the mutation is labor and time intensive. The amount of effort required to identify the change in DNA sequence is directly related to the interval size containing the QTL. Development of region specific markers will be needed to improve marker resolution near the QTL. Comparative mapping information from human and mouse maps should reduce the effort to identify specific mutations by providing potential candidate genes based upon location and function. At times the QTL mutation may be located in a regulatory element and not in a gene. These particular cases may prove to be more challenging. The benefits of identifying the mutation will be the development of a diagnostic test to determine the allelic sequence of the QTL. These alleles will not have to be characterized in each new genetic source but any new alleles (mutations) at the same locus will need to be identified and characterized.

CONCLUSION

The current status of bovine linkage maps enables scientists to identify loci influencing a large number of production related traits. The information obtained from these mapping studies will improve selection strategies and help elucidate the molecular mechanisms controlling the genetic component of qualitative and quantitative traits.