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Review article

Bovine kappa-casein (CASK) gene – molecular nature and application in dairy cattle breeding

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Abstract. The bovine kappa-casein (CASK) gene is considered a potential marker for quantitative trait loci (QTL) in dairy cattle. A large amount of research has been performed to explore the nature and variation of the CASK gene and its possible applications in cattle breeding. The purpose of this review is to sum up the knowledge of all known aspects of the CASK gene: molecular structure and function, polymorphism and allele freqeuncy, methods of genotyping and possibilities of the use of CASK polymorphism in dairy cattle breeding.

Key words: cattle, gene frequency, genotyping, kappa-casein, polymorphism, QTL.

CASK gene – structure and function in casein micelle

The gene encoding CASK belongs to the cluster of four bovine casein genes (BONSING, MACKINLAY 1987) located within a 200 kb fragment on chromosome 6 at q 31-33 in the order of alfa S1-, alfa S2-, beta-, kappa-casein. (FERETTI et al. 1990, THREADGILL, WOMACK 1990). The CASK cDNA sequence was published by GORODETSKY et al. (1983).

The complete genomic sequence of the CASK gene has been discovered and characterized by ALEXANDER et al. (1988). According to these authors, the overall length of the CASK gene is close to 13 kb and is devided into five exons. Most of the sequence coding for the mature CASK molecule is contained within a single large exon IV. Characterization of the 5' region as well as possiblities of CASK gene genetic engeneering are a subject of a separate publication.

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Several reports indicate that the kappa-casein gene, although linked to other casein genes, is unrelated to them (BONSING, MACKINLAY 1987, GORODETSKY, KALEDIN 1987). It has been concluded therefore that if three calcium-sensitive casein genes arose as a result of duplication of an ancestral sequence, association the CASK gene with other casein genes is the result of recruiting an unrelated sequence into this linkage group. It has been suggested that CASK may be related to the fibrinogens, especially gamma-fibrinogen (JOLLES et al. 1986). Both proteins display a number of functional parallels, like susceptibility to specific limited proteolysis with subsequent formation of a clot and fibrious characteristics.

Kappa-casein is a phosphoglycoprotein that constitutes approximately 12% of the casein complex of bovine milk (FOX 1989). The major function of the 169 amino acid CASK protein is to prevent other caseins precipitation by calcium through micelle formation. Calcium sensitive caseins (alfa S1, alfa S2 and beta) are phosphorylated and, together with CASK, they are the primary source of amino acids, phosphate and calcium for young suckling animal. Following ingestion, the caseins are immobilized in the stomach as a result of clot formation. This occurs when chymosin (rennin) or pepsin specifically cleaves a single Phe-Met bond (between amino acid residue 105 and 106) to form insoluble para-casein and a soluble macropeptide containing the C-terminal 64 amino acid residues.

Milk caseins have long been considered principally a source of amino acids for young animals. Recently, however, they have been found to have a biological activity, particulary opioid-like activity (CHIBA et al. 1989).

In comparison to other casein genes, the CASK gene expression and regulation are relatively poorly investigated (GROENEN, van der POEL 1994). In this part of the review main attention will be paid to possible associations between the CASK gene variation and the CASK protein behavior and role in the casein micelle.

An interesting study has been published by van EENENNAAM, MEDRANO (1991a) who found that the CASK B allele is expressed in a greater amount of the total CASK present in the milk of cows with CASK AB phenotype. The cause of this greater expression is not understood but may be due to differences in cis-acting sequences involved in the quantitative expression of CASK gene. Examination of the sequence upstream of the bovine kappa-casein gene reveals several consensus sequences of some transcription factors with different extent of homology. Within these consensus sequences point mutation were found (SCHILD et al. 1994, KAMIŃSKI 1995).

LAW (1993) found that the relative amount of CASK in whole casein varied with phenotype in the order CASK BB > AB > AA and, on average, there was about 25% more CASK in the BB phenotype than in the AA phenotype. The relative amount of a minor fraction which contained mainly gamma-caseins (fraction 1, A, B, C), increased with phenotype in the same way as CASK.

NIKI et al. (1994) have investigated the influence of the amount of CASK in casein micelles on the physical properties and the microstructure of rennet gels. It was revealed that smaller micelles contained more CASK than larger ones. Rennet gels of smaller casein micelles contained more elastically active network chains and were more elastic. The overall variation found in the amount of CASK, within and between phenotypes, seems to be sufficiently large to cause a considerable difference in the distribution of micellar size and processing. Differences in the realtive amount of CASK, especially in view of the location of CASK on the surface of the micelle, may be large enough to exert a direct effect on renneting kinetcs and curd properties (DONNELLY et al. 1984, JAKOB, PUHAN 1992). However, DALGLEISH (1986) found no relationships between renneting kinetics and micelle size as well as the rate of the CASK breackdown during renneting.

Polymorphism of the CASK gene

CASK polymorphism has been discovered indepentdetly by NEELIN (1964), SCHMIDT (1964) and WOYCHIK (1964). The inheritance of this polymorphism has been established by GROSCLAUDE et al. (1965).

So far, 35 CASK gene mutations have been detected (Table 1). Most of them are DNA variants located within the CASK 5' flanking region. The best described mutation of CASK gene are those coding genetic variants of CASK protein: A, B, C, E. They are the result of five point mutations within exon 4 (Fig. 1).

Variant A and B differ in amino acid 136 and 148. In position 136, Thr (ACC) is changed for Ile (ATC) and in position 148, Asp (GAT) is changed for Ala (GCT), in the case of the A and B allele, respectively (GROSCLAUDE et al. 1972, GORODETSKY, KALEDIN 1987).

The CASK E allele is determined by the substitution of Ser for Gly in amino acid position 155 and was confirmed by DNA sequencing (ERHARDT 1989, SCHLIEBEN et al. 1991). For the C allele two substitutions for amino acids 81 (Asn to Asp) and 97 (Arg to His) were identified at the protein level (CHIANESE et al. 1991) and confirmed by DNA analysis (SCHLEE, ROTTMANN

Table 1. DNA variants of CASK gene

No.	Position	Nature of mutation	Reference
1	–1029 [5']	C/T	
2	–999 [5']	T/–	
3	–972 [5']	G/C	
4	–957 [5']	C/T	
5	–945 [5']	A/G	
6	–882 [5']	C/T	
7	–684 [5']	A/G	SCHILD et al. 1994, GROENEN, POEL 1994, (EMBL data base accession no. M75887)
8	–670 [5']	A/T	
9	–638-637 [5']	AT/–	
10	–611 [5']	A/G	
11	–515 [5']	G/T	
12	–427 [5']	C/T	
13	–385 [5']	C/T	
14	–251 [5']	C/T	
15	–60 [5']	A/T	
16	9980 - 10012 [in.III]	{(CA) (TA)}13	MOORE et al., 1992
17	"	{(CA) (TA)}14	MOORE et al., 1992
18	"	{(CA) (TA)}15	MOORE et al., 1992,
19	"	{(CA) (TA)}16	MOORE et al. 1992
20	10600 [exon 4]	C/T	SCHLIEBEN et al. 1991
21	10780 [exon 4]	T/C	SCHLIEBEN et al. 1991
22	10787 [exon 4]	C/G	SCHLIEBEN et al. 1991
23	10791 [exon 4]	G/A	SCHLEE, ROTTMANN 1992
24	10885 [exon 4]	C/T	SCHLIEBEN et al. 1991
25	10908 [exon 4]	C/T	GORODESKY, KALEDIN 1987
26	10944 [exon 4]	A/C	GORODESKY, KALEDIN 1987
27	10959 [exon 4]	T/C	SCHLIEBEN et al. 1991
28	10964 [exon 4]	A/G	SCHLIEBEN et al. 1991
29	11002 [exon 4]	T/C	ALEXANDER et al. 1988
30	11006 [exon 4]	G/A	ALEXANDER et al. 1988
31	11014 [intron 4]	T/A	ALEXANDER et al. 1988
32	11047 [intron 4]	G/A	SCHLIEBEN et al. 1991
33	11049 [intron 4]	C/T	SCHLIEBEN et al. 1991
34	11060 [intron 4]	C/T	SCHLIEBEN et al. 1991
35	12981 [exon 5]	C/T	ALEXANDER et al. 1988

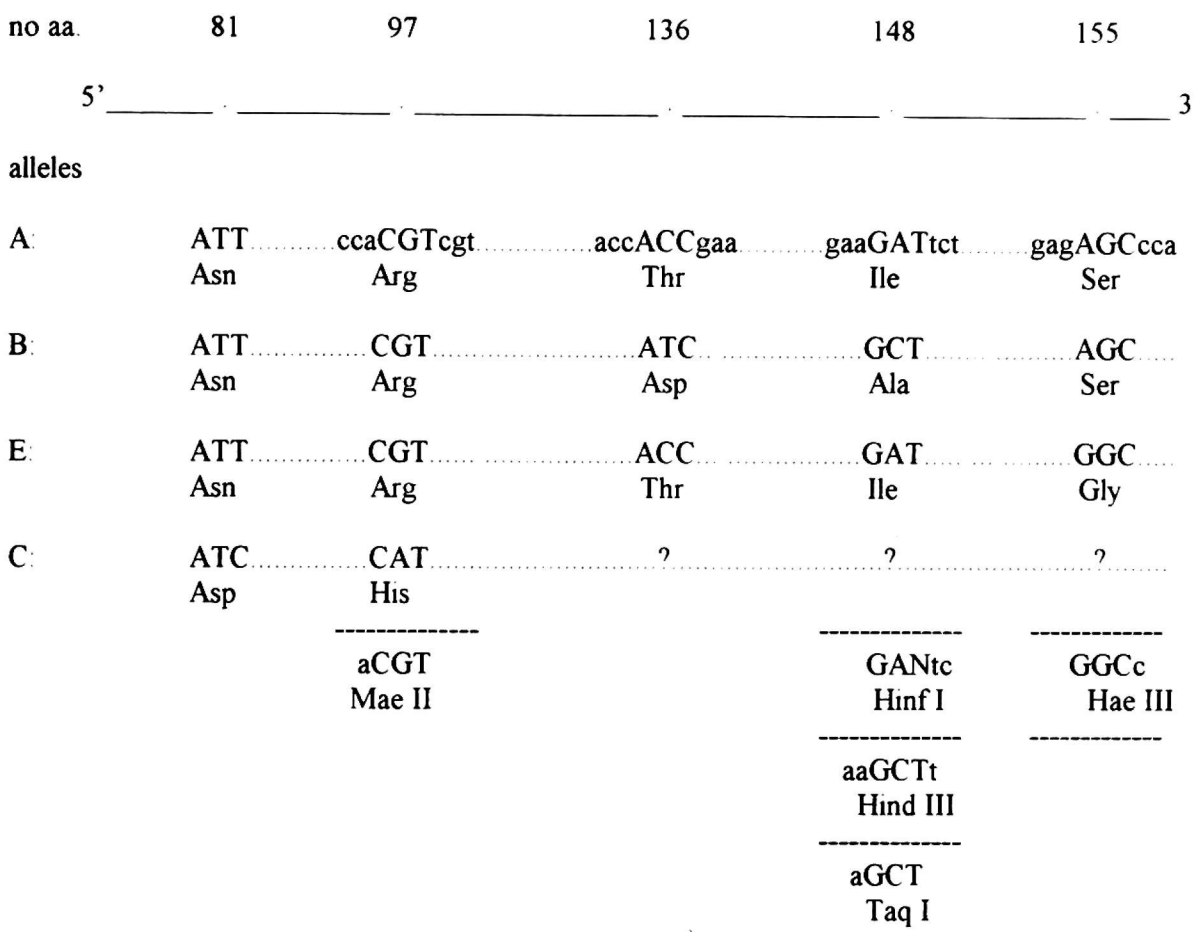

Fig. 1. The molecular determination of CASK protein variants

1992). Futhermore, some silent mutations (NG-KWAI-HANG, CHIN 1992) as well as 5 microsatellites (MOORE et al. 1992) have been detected. Recently, two new alleles in the CASK locus have been found: CASK F in Finnish Ayrshire cattle and CASK G in Pinzgauer cattle (ERHARDT, personal communication).

At present, CASK is considered to be the sole glycosylated component of the casein group and exhibits heterogeneity that can be attributed to genetic variations not only in the protein portion but also in the composition of carbohydrates, particularly in the number of N-acetyloneuroamic acid molecules (OTANI et al. 1995). The genetic backround for the number of CASK protein sites of glycosylation (Thr131, Thr133, Thr135, Ser141, Thr142) is not known.

ROBITAILLE et al. (1991) found that N-acetyloneuraminic acid content of CASK was higher in the milk with CASK AB than in the milk with CASK AA, especially in the later period of lactation, suggesting that the B variant is more efficiently glycosylated than the A variant.

Table 2. The frequency of CASK B allele in different cattle breeds

Breed	Frequency of CASK B allele	Reference
Cows		
Jersey	0.690	Bech, Kristiansen 1990
Brown Cattle	0.560	Mayer et al. 1991
Belgian Red Pied	0.550	De Moor, Huyghebaert 1991
Swiss Brown	0.542	Jakob 1991
Dutch Red and White	0.510	Bovenhuis 1991
Belgian White-Blue	0.500	De Moor, Huyghebaert 1991
Braunvieh	0.479	Erhardt 1989
Simmental	0.475	Jakob 1991
Red Holstein-Fresian (Denmark)	0.467	Bovenhuis 1991
Tyrolian Grey	0.460	Mayer et al. 1991
Deutsche Rotbunte	0.353	Erhardt 1989
Angler	0.350	Gravert et al. 1991
Montbeliarde	0.329	Jakob 1991
Angler	0.332	Erhardt 1989
Belgian Black and White	0.310	De Moor, Huyghebaert 1991
Simmental	0.300	Mayer et al. 1991
Pinzagau	0.260	Mayer et al. 1991
Simmental	0.250	Buchberger et al. 1991
Belgian White and Red	0.250	De Moor, Huyghebaert 1991
Holstein-Friesian (Canada)	0.250	Ng-Kwai-Hang et al. 1991
Swiss Black Pied	0.237	Jakob 1991
Holstein-Friesian	0.230	Mao et al. 1992
Fleckvieh	0.224	Erhardt 1989
Belgian Red	0.180	De Moor, Huyghebaert 1991
Dutch Friesian	0.169	Bovenhuis 1991
Swidish Red and White	0.167	Nilsson 1991
Holstein-Friesian (Denmark)	0.153	Bovenhuis 1991
Holstein-Friesian (Germany)	0.140	Gravert et al. 1991
Deutsche Schwarzbunte	0.135	Erhardt 1989
Swidish Holstein	0.133	Nilsson 1991
Holstein-Friesian	0.090	Mayer et al. 1991
Bulls		
Jersey	0.920	Sabour et al. 1992
Ayrshire	0.220	Sabour et al. 1992
Polish Black and White cross H-F	0.237	Kamiński, Figiel 1993
Holstein-Friesian (Canada)	0.140	Sabour et al. 1992
Holstein-Friesian (USA)	0.130	De Nise et al. 1992
Holstein-Friesian (Canada)	0.130	Ng-Kwai-Hang et al. 1991
Holstein-Friesian (USA)	0.090	De Nise et al. 1992

Table 3. Methods for CASK genotyping

Type of sample	Method of genotyping	Reference
milk	starch electrophoresis	SCHMIDT 1964
	agarose electrophoresis	BECH, MUNK 1988
	isoelectric focusing	SEIBERT et al. 1985
	isoelectric focusing	VAGERUD et al. 1989
DNA	Southern blotting RFLP: Hind III, Taq I	LEVEZIEL et al. 1988
	Southern blotting RFLP: Pst I	RANDO et al. 1988
	Southern Blotting RFLP: Hind III, Hinf I	ROGNE et al. 1989
	PCR, RFLP: Hinf I	MEDRANO, AQUILAR-CORDOVA 1990
	PCR, RFLP: Hind III, Taq I	DENICOURT et al. 1990
	PCR, RFLP: Mbo II, Taq I	ZADWORNY, KUHNLEIN 1990
	PCR, Sanger sequencing	
	RFLP: Hind III, Hinf I, Hae III	SCHLIEBEN et al. 1991
	PCR, RFLP: Mae II	SCHLEE, ROTTMANN 1992
	Allele Discrimination by Primer Length and Automated DNA Sizing Technology	LINDERSSON et al. 1995

Frequency of CASK variants

The frequency of CASK alleles in different cattle breeds has been the subject of many studies. In this review, only studies performed on relatively representative numbers of animals and published within the last six years are presented.

Because of the preference for the B allele and its potential utility in breeding strategies, only its frequency is shown in Table 2. The A allele of CASK is the most dominant in different cattle breeds, particulary in Holstein-Friesians. The frequency of the C and E alleles is relatively low and specific of particular breeds. The frequency of the CASK alleles C and E was observed by JAKOB (1991). Among 4000 cows of 4 breeds, the C variant was found in Swiss Braunvieh and in one single cow in Black Pied and in Red Holstein crossbred. ERHARDT (1989) found the C allele in Fleckvieh and Braunvieh in frequences of 0.017 and 0.015, respectively, and the E allele in Dt. Rotbunte, Dt. Schwarzbunte and Angler, in frequences of 0.023, 0.060 and 0.029, respectively.

The published preliminary preassumptions concern only the frequency of mutations within the 5' region of CASK gene (SCHILD et al. 1994, KAMIŃSKI 1995) and microsatellites located in CASK intron III (KUHN et al. 1994) .

A constant trend of the CASK B allele frequency towards decreasing was observed in Dutch Black-and White (BECH, KRISTIANSEN 1990), Simmental (BUCHBERGER et al. 1991) and in Friesians (BOVENHUIS 1991).

The decreasing frequency of the CASK B allele indicates that selection criteria used to prove bulls discriminate against the B allele. Why this should

be so is not clear since extensive analysis revealed no unequivocal correlations between kappa-casein variants and milk yield (MCLEAN et al. 1984, NG-KWAI-HANG et al. 1984, the author's data are unpublished). An interesting aspect is the frequency of the B allele in proven and unproven bulls. SABOUR et al. (1992) compared the frequency of the B allele between 643 unproven bulls and 125 proven bulls chosen from them. No significant differences in the CASK allele frequencies were found for both groups. This also suggests that no differential survival were observed between these two groups and that selection of bulls is not linked with the CASK locus. Similar results on a smaller bull population were obtained by De NISE et al. (1992).

Methods of CASK genotyping

For over 30 years of CASK research different methods for its genotyping have been applied (Table 3). Identification of CASK phenotype by gel electrophoresis is difficult to interpret and classify because of multiple banding patterns of other milk proteins. It seems that the most effective, fast and reliable method is isoelectric focusing established by SEIBERT et al. (1985) and BECH, MUNK (1988). However, direct milk tests are limited to mature lactating females. Genotyping sires demands an analysis of multiple dam/daughter pairs requiring about six years. The cost and the length of time needed for sire analysis have made it impractical to establish breeding programs aimed at increasing the frequency of the desired CASK B allele.

Among several of the DNA-based methods for CASK genotyping, the most common is the PCR-RFLP technique (Polymerase Chain Reaction – Restriction Fragment Length Polymorphism) using Hind III or Hinf I restrictases. Some modifications have been introduced into this protocol (CHIKINI et al. 1991, PINDER et al. 1991, SULIMOVA et al. 1991, VELMALA et al. 1993, KAMIŃSKI, FIGIEL 1993).

Typing blood DNA can give erroneous results when the animal concerned is a twin; this can be overcome by retesting using milk or semen (PINDER et al. 1991). In some reports CASK genotyping is combined with genotyping of all other casein genes (LIEN et al. 1993), beta-lactoglobulin and beta-casein (BARDIN et al. 1992), sex of bovine embryo (SCHELLANDER et al. 1992), beta-lactoglobulin of bovine embryo (SCHWERIN et al. 1994).

Recently, LINDERSSON et al. (1995) published a method called Primer Length and Automated DNA Sizing Technology which seems to be the method of choice for wide screening programs. But if used for rather small projects,

it needs a relatively expensive equipment. For a small number of genotyped animals, the method described by SCHLIEBEN et al. (1991) is fast, cheap, most effective and realiable. The tendency to run multiplex PCR for several genes simultanously is very desirable from the technical and economical point of view. Simpler and more effective molecular techniques, like LCR, SSCP and DGGE, have not been applied yet for CASK genotyping, although they eliminate the use of restriction enzyme and shorten the time of analysis.

Before incorporating genetic variants into selection program, their genotyping at the DNA level should be coupled with all CASK alleles already described for a given breed. Only if a complete DNA test for all alleles is available the risk of misidentification can be excluded and the test can be included in animal breeding programs (ERHARDT et al. 1992).

Potential application of CASK gene polymorphism into dairy cattle breeding

Animal breeding programs based on quantitative genetics have been successful in increasing genetic progress for economically important traits in farm animals. However, direct information on the underlying genetic variation could significantly contribute to the genetic gain, especially regarding traits controlled by a few major genes. Cattle, lactating or nonlactating, can now be genotyped for the CASK and other mlik protein genes on DNA level. Therefore, the CASK gene has become a convinient candidate in search for major gene or marker gene for quantitative trait loci. The gene becomes known as a major gene when its effect on a bio-economic important quantitative trait can be discriminated over and above polygene effects. In contrast to other milk proteins, the allele B of CASK is rare in the most popular dairy cattle breed, Holstein-Friesian. Therefore, there has been much discussion of selection to increase the frequency of the B variant of CASK for its role, not only in higher protein yield and protein % but in the properties of milk which are favourable for cheesemaking (MAO et al. 1992).

A large number of research has proved that the CASK B allele is favourable for technological properties of milk such as greater proportion of CASK in micelle, better heat stability, shorter clotting time, firmer curd, better recovery of fat from the milk and higher cheese yield (JAKOB, PUHAN 1992) as well as for milk performance traits (GONYON et al. 1987, LIN et al. 1989, NG-KWAI-HANG et al. 1990, COWAN 1992, BOVENHUIS, WELLER 1994). Moreover, VAGERUD et al. (1992) showed that milk from cows with the CASK genotype AB or BB had a better taste of sweet milk stored for 5 days at syneresis of

fermented milk, gave shorter renneting and geletion time and showed stronger gel than milk from cows with CASK AA genotype. SCHULTE-COERNE, PABST (1992) found that consistently between breeds the CASK BB genotypes were superior in HCT (Heat Coagulation Time), more heat resistant and better to produce UHT-milk. PABST (1992) found in the study of 5000 Holstein and Angler cows, that though the protein content in processed milk was lower for the CASK BB (3.70 vs. 3.95 for AA) the protein content in ripe cheese was the same. However, protein transfer into cheese was 2.7% better for the CASK BB. Lately, MAO et al. (1992) in a relatively large population of 11015 Holstein cows have showed that the B allele of CASK was clearly favourable for higher milk and protein yields but may be recessive to the A allele. It was also the favourite and dominated over the A allele for a higher level of protein % in milk. WALAWSKI et al. (1994) in his studies carried out on 123 Black-and-White cows from one herd showed that the CASK AA and AB genotypes were associated with a higher productivity and the CASK AB and CASK BB with a higher protein content as well as higher citric acid and phosphorus contents in the milk of cows with the CASK BB genotype.

HILL et al. (1992) screened 456 000 dairy cows and identified two groups of high breeding index Jersey cows, one group producing milk with a high protein content and a control group giving milk with a lower protein content. These cows were purchased and subjected to identical feeding, reproduction and milking practices. The high protein content group (11 cows) gave 7.05 l/day milk at 4.8% protein average in late season and the group of control cows (10 cows) gave 9.2 l/day milk at 4% protein average in late season. The milk of these cows was typed for milk protein phenotypes and subjected to compositional analysis. In the high protein group cows were exclusively of the CASK BB phenotype with no cows in the control group having this phenotype. The level of protein was, on average, 21% higher in the high protein group than in the control and was accompanied by a higher level of fat, on the average, by 22%.

BOVENHUIS et al. (1992) used maximum likelihood methodology to estimate both the direct and linked QTL effects of casein polymorphisms. CASK genotypes showed a significant direct effect on protein percentage, whereas a significant direct effect of beta-casein (CASB) was found on both fat and protein percentage. Linked QTL effects on fat percentage were found for both CASK and beta-casein (CASB). Since CASB and CASK are closely linked, it is likely that the same linked QTL was detected for these two markers.

JAKOB (1991) and GRAVERT et al. (1991) found that cheesemaking properties of milk from cows with the E allele are similar to those of milk from cows with the A allele.

Contradictory results were published by KUHN et al. (1994) who found no significant associations between the CASK genotype AB and a microsatellite located within intron III of CASK gene used as markers of QTLs and milk performance traits (milk yield, milk fat yield, milk protein yield, milk protein content, milk fat content and relation milk protein/milk fat content). This is probably caused by a small size of samples and defective calculations. For example, positive lod scores for fat yield and the casein complex in all six families were obtained, but in summary the results did not reach significance. Calculation showed that in the available structure about 800 daughters would have been necessary to detect a QTL located in this region (they used only 264 daughters). Whether these effects are technologically relevant is a matter of question. It has to be emphasized that technological processes themselves significantly affect technological properties of milk. Moreover, in all cases bulk milk from a large number of cows is being bioprocessed. Likewise, cold storage as well as heat treatment of milk for cheesemaking, the both techniques being widely applied all over the world, also impair renneting properties in comparison to fresh raw milk (JAKOB, PUHAN 1992).

Most studies examining correlation between CASK polymorphism and quantitative traits have treated the CASK locus individually. However, casein genes are tightly linked, so the associations between milk production traits and a given casein polymorphism could in fact be caused by mutations in other casein genes. Casein haplotype analyses in different breeds were published by JAKOB (1991), NUYTS, DELACROIX-BECHET (1991), van EENENNAAM, MEDRANO (1991b), LIEN et al. (1993) and VELMALA et al. (1995). It is very difficult to compare casein haplotypes in different breeds, because of a different number of animals analysed, and a different way of estimation of casein haplotype frequencies.

The most reliable analysis is that of LIEN et al. (1993) who concluded that casein haplotypes are well suited as genetic markers on bovine chromosome 6. The association between casein haplotypes and milk production traits has been studied in several families of bulls. Casein haplotypes are arranged according to their position on the bovine chromosome 6 in the following order: CASAS1 (B, C), CASB (A1, A2, A5, B), a microsatellite in intron III of CASK (14 and 16 repeats) and CASK (A, B, E).

Two haplotypes, B A1 14 B and B A1 16 B, were associated with a higher protein percentage and haplotype B B 14 B with a significant lower protein percentage when compared to the other haplotype inherited from the sire. Apparently, if the association between protein percentage and the CASK B was caused by a direct effect of mutations diverging the B from the A variant, the difference should be consistent in different haplotypes with the CASK B. Different associations between the CASK B haplotypes and protein percentage,

suggest that the association of the CASK B with protein percentage is caused by mutations linked to the CASK gene. Consequently, the association would not only vary between different breeds but also between bulls with different CASK B haplotypes in the same breed. However, the most promising haplotype is C A5 14 A because it is associated with an increase of 7.4 kg of milk protein in Norwegian Cattle. This haplotype is very rare (8%) and nearly all bulls with this haplotype were descendants of one bull. NUYTS, DELACROIX-BECHET (1991) found that casein haplotypes C A2 B and B B B (CASAS1, CASB, CASK) are associated with a higher coagulating ability of milk, better texture and solid curd, firmer, less elastic and with less breakable Saint-Paulin cheese. Lately, VELMALA et al. (1995) found no associations between nine different casein haplotypes and milk production traits in Finnish Ayrshire dairy breed.

When the economic profit of increasing yield is reduced because of milk quota systems and because of decreasing marginal profits from milk production, the objective of selection may change from the improvement of milk quantity towards the improvement of milk quality. The effects of genetic CASK variants on cheese yield are a kind of challenge for the selection programs. To assess practical effects of introducing CASK genotyping into breeding programs, some computer simulation has been done.

PEDERSEN (1991) analysed theoretical consequences of including the CASK genotype in the selection objective under various assumptions, mainly with respect to the initial frequency of the B gene, the level of production and the economic value of milk production and that of the B gene. Three strategies of selection for CASK genotype were investigated and compared to a strategy without selection for CASK genotype: strategy 0: no selection for genotype, strategy 1: preselection of BB genotype; animals were ranked accorging to the milk yield index, strategy 2: preselection of both AB, BB genotypes; animals were ranked according to the milk yield index, strategy 3: all genotypes were candidates for selection but they were ranked according to an index based on the combined value of milk yield and genotype. The conclusion of this study is that when the additional sales value of CASK BB milk compared to AA milk is below 1%, the results of selection in all strategies to improve the frequency of the CASK B allele did not outweigh the cost of identifying the genotypes. At 1% the additional response was between 0% and 1% and at 3% the response improved by 1% to 7%, if genotypes were included in the selection objective. The improvement was the lowest at high frequencies of the B allele. If the additional value of BB milk was 5%, the response improved by 3% at high frequencies of the B allele and by 20%, if the initial frequency of the B allele was only 0.25. The basic assumption was also that interaction between the milk yield index and the genotype did not exist. It seems to be an interesting

result for the cheese industry: in case of a big cheese production (eg. 20 000 t/year) a lot of money could be earned after investment in breeding costs for increased BB genotype frequency. However, additional payment should be given to farmers delivering this type of milk (PABST 1992).

Presently, dairy farmers are not paid according to the genotype of their cows. The profit of selection for increased frequency at CASK variant B would accrue to the processing industry. Only if the profit can be transferred from the processing industry, dairy farmers will be interested in selection for CASK genotype. HARGROVE et al. (1980) found that effects of milk protein polymorphisms on conception rate, days open and first service period were not significant. This kind of research needs futher investigations before setting up breeding strategies that could modify frequencies of genes important for reproduction.

Conclusions and perspectives

The CASK gene is a good QTL marker for technological properties of milk and milk protein content and may be utilized in some limited dairy cattle population. However, the margin of superiority, although statistically significant, does not appear to warrant a strict breeding scheme in which candidate breeding cattle must have a BB genotype for CASK before they are being considered as potential parents for herd replacements. If selection for milk protein content is concerned, more effective is haplotyping of all caseins. In spite of this, the programs for CASK genotyping in dairy cattle are neccesary and should be applied to strickly determined subpopulation of dairy cattle located near cheese industry. In this region of cheese production a special price system should function to motivate dairy farmers for increasing frequency of the desirable CASK B allele. However, milk composition is dependent not only on different variants but also on the degree of transcription of the milk protein genes. Therefore, both typing of different protein variants and knowledge on the regulation of the expression of milk protein genes are of great importance in dairy cattle breeding.

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