

## **Genetic Polymorphism of Milk Proteins**

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UDK: 637.045

### **1 Introduction**

The original discovery of the genetic polymorphism of  $\beta$ -Lg by Aschaffenburg & Drewry in 1955 has initiated considerable research activities on milk protein variants. In view of the immense literature dealing with these subjects, reference should be made here to some comprehensive reviews recently published (29, 37, 49, 55, 71). In many studies, possible relationships between milk protein polymorphism and milk production traits, milk composition and technological properties of milk have been shown. Consequently, the genetic variants have received great interest within the dairy industry, in particular to their well confirmed relationship with cheesemaking properties of milk. The question whether cows should be selected for desirable milk protein types, is a matter of controversy today.

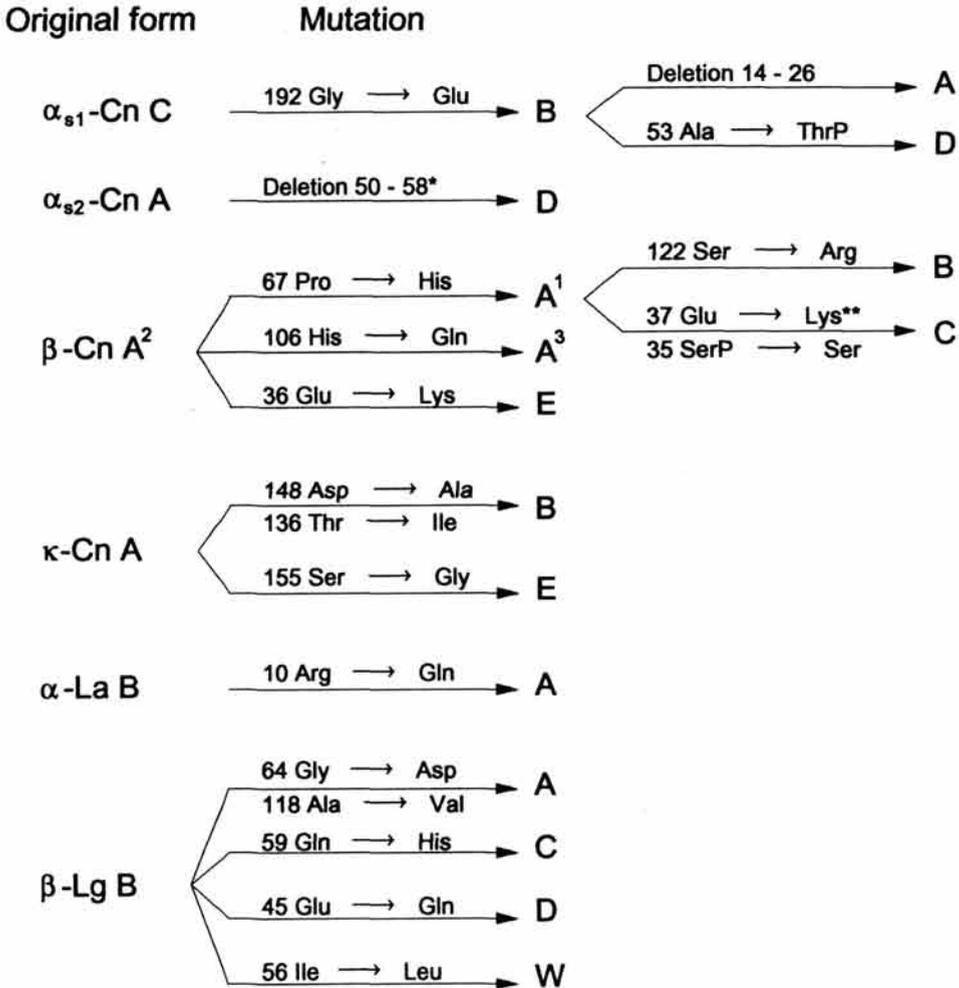
A previous review (Jakob and Puhán, 1992) has concentrated on the literature dealing with relationships between protein variants and technological properties of milk, e.g. the heat stability of milk and evaporated milk, and the rennet coagulation and cheesemaking properties of milk. This report is mainly focused on the effects of genetic variants of milk proteins in milk composition. In addition, some of the most recent findings regarding the technological properties are reviewed.

### **2 Effect of milk protein polymorphism on milk composition**

Genetic polymorphism arises because of the existence of two or more alleles at a gene locus. As an additional condition, in the simple case of biallelism, the rarer allele should occur with a frequency higher than 1% (Grosclaude, 1988). Different types of the protein produced by a polymorphic gene are the »genetic variants«. They differ in their amino acid sequence and have to be distinguished from polymorphs resulting from post translational modifications of the chemical structure of the protein as shown in Fig. 1. The genetic variants are usually identified by electrophoretic separation of proteins. However, it has to be stressed that only variants differing in size or charge can be identified by these separation techniques. Moreover, the phenotypic polymorphism of a protein represents only one etype of the polymorphism existing at the gene level. So far, practically all investigations dealing with the effects of polymorphism of milk protein on any property of cow's milk are based on electrophoretic identification of protein genetic variants. (Fig. 2).

The properties of milk and dairy products are influenced to a large extent by the amounts and relative proportion of each of the milk constituents. Due to its

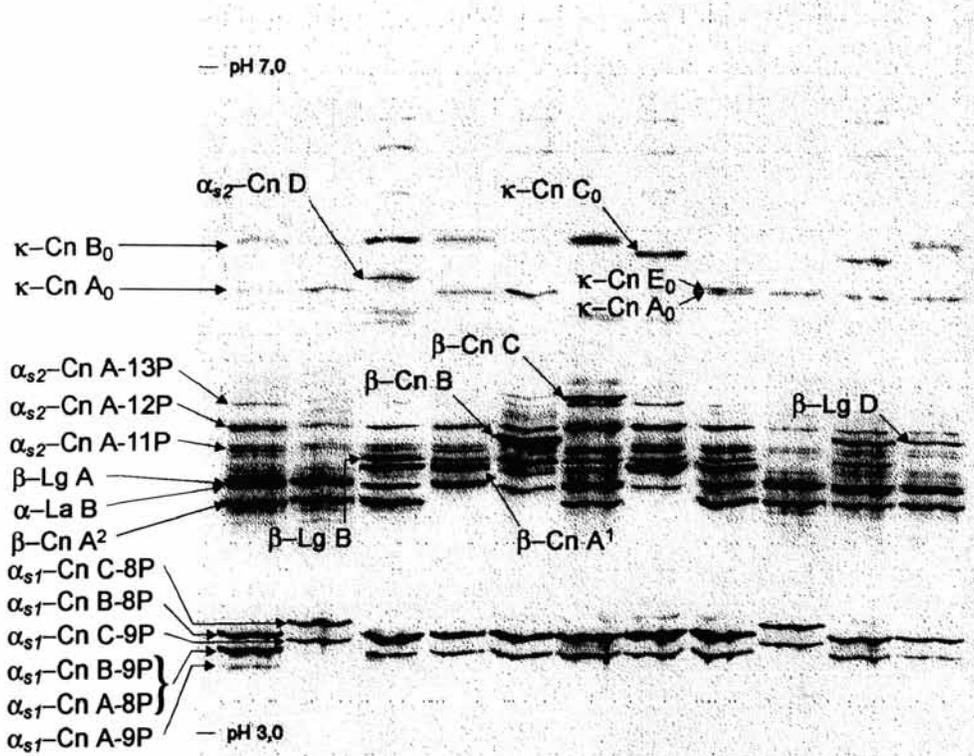
diversity in concentration and type the protein fraction significantly contributes in this regard. There are many reports that relate genetic polymorphism of milk proteins to milk content of fat and protein.



\* This deletion is not exactly located. (Grosclaude, 1988)

\*\* As a consequence of this substitution, Ser<sub>35</sub> is not phosphorylated.

Fig. 1: Differences and phylogenetic relations between the most important genetic variants of milk proteins (29, 23, 89)



	1	2	3	4	5	6	7	8	9	10	11
$\alpha_{s1}$ -casein	AB	CC	BB	BB	BB	BB	BB	BB	CC	BB	BB
$\alpha_{s2}$ -casein	AA	AA	AD	AA	AA	AA	AA	AA	AA	AA	AA
$\beta$ -casein	A <sup>2</sup> A <sup>2</sup>	A <sup>2</sup> A <sup>2</sup>	A <sup>1</sup> A <sup>2</sup>	A <sup>1</sup> A <sup>1</sup>	BB	A <sup>2</sup> C	A <sup>1</sup> A <sup>1</sup>	A <sup>1</sup> A <sup>2</sup>	A <sup>2</sup> A <sup>2</sup>	A <sup>2</sup> B	A <sup>1</sup> A <sup>2</sup>
$\kappa$ -casein	AB	AA	BB	AB	AA	BB	CC	AE	AA	AC	AB
$\beta$ -lactoglobulin	AA	AA	BB	AB	BB	AB	BB	AB	AA	AB	AD

Fig. 2: Isoelectric focusing of milk proteins (Jakob, 1993)  
 ( $\kappa$ -Cn A<sub>0</sub> – E<sub>0</sub> are the carbohydrate free fractions of  $\kappa$ -Cn A – E)

## 2.1. Milk protein content

### $\alpha_{s1}$ -Casein

Since the B variant of  $\alpha_{s1}$ -Cn is occurring with frequencies of about 95 % or higher in most dairy breeds, most studies have been limited to a comparison of the  $\alpha_{s1}$ -Cn BB and BC phenotypes. The investigations undertaken in different cattle breeds have shown that  $\alpha_{s1}$ -Cn C is associated with a higher milk protein content. It was found that type  $\alpha_{s1}$ -Cn BC cows have between 0.05 and 1.1 g/L higher amounts of protein than BB type cows. However, only every second study, demonstrated that the difference was statistically significant (2, 16, 26, 31, 50, 65, 69, 73). Other reports (9, 24, 72), especially those based on mixed populations (6, 8, 18, 20, 59, 62, 86), are indicating no or only a slight superiority of  $\alpha_{s1}$ -Cn C. In the study of Roth (1982) including a total of 1431 daughters of three bulls, a significant effect of  $\alpha_{s1}$ -Cn C was observed within the family of only one of these bulls. The A variant of  $\alpha_{s1}$ -Cn may have become extremely rare because of its detrimental effect on both, the protein and the fat content of milk, as shown by Ng-Kwai-Hang et al. (1986). The effect of the  $\alpha_{s1}$ -Cn locus on the protein percentage in milk is probably due to amount of casein which was reported to be positively associated with  $\alpha_{s1}$ -Cn C (8, 9, 20, 26, 59, 73, 76). However, only Ng-Kwai-Hang demonstrated this correlation as significant. The amount of whey proteins in milk is apparently not related with the  $\alpha_{s1}$ -Cn variants. Accordingly, comparisons of  $\alpha_{s1}$ -Cn BB with BC type milk indicated a higher casein number in the presence of  $\alpha_{s1}$ -Cn C (73, 59).

### $\beta$ -Casein

It is a difficult task to give a summary of the effects of the  $\beta$ -casein polymorphs. The large number of alleles existing for that locus, resulting in many different genotypes (15 if the variants A<sup>1</sup>, A<sup>2</sup>, A<sup>3</sup>, B and C would occur simultaneously), is only one reason for the often conflicting findings. As the different A variants are not resolved with electrophoresis at alkaline pH, in the studies where milk protein phenotypes were identified by means of this technique, only  $\beta$ -Cn A, B and C have been considered, as for example in most of the investigations carried out on Brown cattle and Simmental populations.

Nearly all studies, where the subtypes of  $\beta$ -Cn A were distinguished, were carried out in the Holstein breed or related populations. Only in a few cases, a significant correlation between the  $\beta$ -Cn variants and the protein (Gonyon et al., 1987) and casein content of milk (73, 83) was demonstrated. It was shown that both, the amount of protein and that of casein decreased in the order  $\beta$ -Cn A<sup>1</sup>A<sup>1</sup> > A<sup>1</sup>A<sup>2</sup> > A<sup>2</sup>A<sup>2</sup> (-0.4 g/L from A<sup>1</sup>A<sup>1</sup> to A<sup>2</sup>A<sup>2</sup>). Other studies (2, 62, 72) also tended to indicate a detrimental effect of  $\beta$ -Cn A<sup>2</sup>. It has to be mentioned, however, that among the most comprehensive investigations, Haenlein et al. (1987) with

Guernsey, Ng-Kwai-Hang et al. (1990) with Holstein cattle and Eenennaam & Medrano (1991 b) with a mixed population (80 % Holstein) no significant effect of  $\beta$ -Cn variants on the protein content of milk could be shown. The same is partly true for the investigation of Bovenhuis et al. (1992) where it depended on the statistical model used, whether the effect of the  $\beta$ -Cn locus was significant or not.

In the studies carried out with breeds, where  $\beta$ -Cn B is more frequent (Brown cattle, Simmental, Pinzgauer, Russian Black Pied), the different  $\beta$ -Cn A variants were not distinguished. Although only one of these studies (Graml, et al., 1985) observed a significant effect, they mostly showed that cows bearing the B allele, especially those homozygous for  $\beta$ -Cn B, had about 0.1–1.8 g/L higher amounts of protein as well as, where tested, higher amounts of casein (8, 9, 20, 26, 50, 70, 78). However, Marini et al. (1992) associated the lower casein content rather with  $\beta$ -Cn BB than with  $\beta$ -Cn AA. Similar to  $\beta$ -Cn AB, the milk  $\beta$ -Cn AC was attributed with 0.6 – 1.2 g/L higher protein content (9, 26, 70) and by the same order of magnitude also a higher casein content (Graml et al., 1985). With Holstein cattle,  $\beta$ -Cn A<sup>x</sup>B milk had a similar or higher protein (2, 6, 18, 24, 72, 73, 80, 83) and casein content (72, 80, 83) than  $\beta$ -Cn A<sup>1</sup>A<sup>1</sup> and  $\beta$ -Cn A<sup>2</sup>A<sup>2</sup> type milks. Only McLean et al. (1984) reported a negative effect of  $\beta$ -Cn B on the protein content and a positive effect on the casein content in individual milks from a mixed population (Holstein and Jersey). The differences, however, were not significant. In two studies (73, 83) a significantly higher casein number for milks containing  $\beta$ -Cn B was reported. Regarding the whey protein content of milk, the present findings (8, 9, 20, 26, 62, 73, 80) do not show a clear trend.

### $\kappa$ -Casein

Most of the publications dealing with the effect of  $\kappa$ -Cn alleles on the protein content of milk are summarised in table 1. With the Holstein breed and related populations, milk from  $\kappa$ -Cn BB cows consistently showed the highest protein and casein content. For heterozygous cows ( $\kappa$ -Cn AB) generally intermediate values were reported (BB > AB > AA). With Brown and Simmental cattle, the  $\kappa$ -Cn B allele seems to be associated with lower protein and casein contents. From the few data, however, one cannot yet conclude that the effect of the  $\kappa$ -Cn locus in these breeds is opposed to that in the Holstein breed, even though this would be in line with the observations of Li (1970) who found a significant effect of the  $\kappa$ -Cn locus for the Holstein population, but not with Brown Swiss, Ayrshire and Guernsey.

For all breeds studied, the whey protein content of  $\kappa$ -Cn AB and BB milk is clearly lower than that of  $\kappa$ -Cn AA milk. Moreover, a casein number up to 2 % (absolute) higher than for  $\kappa$ -Cn AA can be expected if  $\kappa$ -Cn B is present (15, 58, 73, 82, 83, 88, 93).

Table 1: Content of protein fractions in milk in relation to  $\kappa$ -casein variants

Breed <sup>1)</sup>	N	total protein [%]				casein [%]				whey protein [%]				ref.
		$\kappa$ -Cn				$\kappa$ -Cn				$\kappa$ -Cn				
		AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	
AY	94	3.31	+0.05	+0.07										33
B	2057	0	-0.01	-0.02	ns	0	-0.0	-0.	ns	0	+0.005	+0.006	ns	26
BSV	135	3.24	+0.18			2.	+0		ns	0.78	-0.01			40
CA	263	3.84	-0.08											33
HF	512	3.17	-0.01	+0.01										33
HF	30	3.50	+0.07											63
HF	44	3.00		+0.28		2.		+0.						56 <sup>5)</sup>
HF	44	3.19	(+0.20) <sup>7)</sup>			2.	(+0.13) <sup>7)</sup>							56 <sup>5)</sup>
HF	16+16	3.24		+0.07		2.		+0.		0.775		-0.043		58 <sup>6)</sup>
HF	1687	0	+0.10	+0.13*										72
HF	74					2.	(+0.11) <sup>7)</sup>	**						87 <sup>5)</sup>
HF	2*11	3.34	-0.05		ns	2.	-0.		ns					88 <sup>5)</sup>
HF	2045	3.37	0.00	+0.07**		2.	+0.	+0.	**	0.71	-0.01	-0.02	**	73
HF	286	3.00	+0.08											92
HF	3111	0	+0.02	+0.04*										24
HF	32	3.16	+0.15	+0.11***		2.	+0	+0.	**					83
HF	3941	0	+0.01	+0.01***										85
HF	2005	9	+0.02	+0.08**										2
HF	384	3.43	+0.11	+0.20										93 <sup>4)</sup>
HF	376	3.74	+0.07	+0.15										93 <sup>4)</sup>
HF	3224	3.13	+0.03	+0.08**										75 <sup>4)</sup>
HF	2885	3.16	+0.02	+0.06**										75 <sup>4)</sup>
HF	2166	3.13	+0.03	+0.04*										75 <sup>4)</sup>
HF	1165	3.58	+0.02	+0.06 #										18
HF	230	3.08	+0.04	+0.13*		2.	+0.	+0.	**	0.71	-0.02	-0.01	ns	82
HF	371	3.11	+0.01	+0.15*										86
HF	371	3.15	-0.03	+0.13*										86
HF	6803	0	+0.03	+0.08***										6
JY	128	4.01	-0.06	+0.14*										33
MB	74	3.50		+0.04		2.		+0.						15
NO	89	3.51		+0.03		2.		+0.						15
RBP	169	3.21	-0.05	+0.11										78
SI	154	3.48	-0.08	-0.05 #										16
SI	45					2.	+0.	-0.3						52
SI	2208	0	+0.01	-0.01	ns	0	+0.	-0.	ns	0	0	-0.01	ns	26
SI	366	0	-0.09	-0.14***		0.	-0.	-0.	**	0	-0.03	-0.03	*	9
TA	60	3.00	+0.11	+0.37		2.	+0.	+0.						15
X	2006	3.26	0	+0.01	ns	2.	0	0	ns	0.68	-0.003	-0.001	ns	20
X	501	3.63	0	-0.01	ns	2.	+0.	+0.	ns	0.83	-0.03	-0.05	ns	62
X	587	0	-0.04	-0.01	ns	0	-0.	-0.	ns	0	-0.01	+0.003*		8
X	135	3.37	+0.02	-0.07	ns	2.	+0.	+0.	ns					1

## **$\beta$ -Laktoglobulin**

Although the  $\beta$ -Lg locus is the most intensively studied within milk composition, its effect on the protein content of milk is still controversial, as shown in table 2. In quite few studies, a significant effect on the protein could be ascribed to the  $\beta$ -Lg variants. Judging by these studies, the allele  $\beta$ -Lg A seems to be slightly superior to the B variant regarding total protein. This is also in line with the findings of other studies that are not tabulated here (31, 48, 46, 81, 76). Many authors, however, could not find any relationship between the  $\beta$ -Lg variants and the protein content (6, 30, 66, 84), or, found slightly higher amounts of protein in the presence of  $\beta$ -Lg B (62, 63, 65, 78, 80, 91).

It is generally agreed upon that  $\beta$ -Lg B is associated with higher amounts of casein in milk. As first reported by Moustgaard et al. (1960),  $\beta$ -Lg BB milk was shown to have between 0.4 and 2 g/L higher casein contents than  $\beta$ -Lg AA milk ( $\beta$ -Lg AA < AB < BB). Only Cerbulis & Farrel (1975) observed an adverse trend. Probably the best known effect of milk protein polymorphisms is that of the  $\beta$ -Lg alleles on the whey protein content as shown by many authors (10, 35, 54, 57, 63, 67, 73, 80, 82, 83, 88, 93). In most cases  $\beta$ -Lg BB type milk was found to contain between 9.5 and 14 % less whey protein than  $\beta$ -Lg AA milk. Consequently, this, along with the higher casein percentage, is resulting in a casein number 2 to 3 % (absolute) higher for  $\beta$ -Lg BB milk than for  $\beta$ -Lg AA milk (1, 10, 20, 35, 40, 54, 57, 62, 63, 67, 73, 80, 82, 83, 88).

Among the rare alleles of  $\beta$ -Lg, only  $\beta$ -Lg C, which occurs in the Jersey and Angler breeds, and  $\beta$ -Lg D, which is present in the European mountain breeds (Swiss Brown, Simmental, Eringer), were studied. As shown by McLean et al. (1984) and Graml et al. (1985), for both variants the effect on the whey protein content of milk is similar to that of  $\beta$ -Lg B. However, the total protein content was reported to be lower when  $\beta$ -Lg C was present in the milk from Jersey cows (McLean et al., 1984), whereas the situation was reversed in case of Angler cattle (Oloffs. et al., 1992).  $\beta$ -Lg D was demonstrated to increase the casein and total protein significantly (Graml et al., 1985)

## **2.2 Content of individual milk proteins**

As mutations of proteins in question are located in the coding section of its gene, this could alter its rate of biosynthesis (Grosclaude, 1988). Therefore, the effect of genetic variant on the protein composition of milk is more likely to be a direct one, as opposed to the effect on the fat content.

In fact, the content of  $\beta$ -lactoglobulin in milk, as well as the amount of individual caseins, depends on the genetic variants of the protein in question. The original discovery by Aschaffenburg and Drewry (1957), that  $\beta$ -Lg AA milk contains more  $\beta$ -Lg than AB or BB milk, was confirmed by many other

Table 2: Content of protein fractions in milk in relation to  $\beta$ -lactoglobulin variants

Breed <sup>1)</sup>	N	total protein [%]				casein [%]				whey protein [%]				ref.
		$\beta$ -Lg				$\beta$ -Lg				$\beta$ -Lg				
		AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>	
AY	100	-	3.45	0.19										33
B	2057	0	-0.01	-0.02	*	0	+0.02	+0.04	***	0	-0.03	-0.06	***	26
BZV	72	3.26	-0.04	-0.06	ns	2.45	+0.01	+0.07	ns	0.81	-0.04	-0.14	**	40
CA	339	3.90	-0.19	0.14										33
HF	680	3.28	-0.003	-0.05	*									12
HF	546	3.20	-0.09	-0.04										33
HF	30	3.58	-0.04	-0.11										63
HF	15+15	3.15		+0.10	ns	2.36		+0.18	*	0.61		-0.077	***	57 <sup>6)</sup>
HF		3.13		+0.03		2.38		+0.10		0.52		-0.05		67
HF		3.37		-0.10		2.62		-0.04		0.56		-0.08		67
HF	2906	0	-0.01	-0.05	**									72
HF	118	3.22	-0.06	+0.03	ns	2.43	0	+0.12	**	0.79	-0.06	-0.09	***	54
HF	3*9	3.12	+0.01	+0.04	ns	2.32	+0.09	+0.19	***					88 <sup>5)</sup>
HF	286	3.05	-0.03	0										92
HF	32	3.28	-0.11	+0.01	*	2.59	-0.05	+0.20	***					83
HF	3941	0	-0.003	-0.006	**									85
HF	2005	0	-0.01	+0.02	ns									2
HF	384	3.52	0	+0.04										93 <sup>4)</sup>
HF	376	3.84	-0.06	-0.01										93 <sup>4)</sup>
HF	1165	3.62	-0.02	-0.03	ns									18
HF	230	3.15	-0.05	-0.01	ns	2.58	+0.05	+0.12	*	0.75	-0.07	-0.09	***	1
HF	116	3.35	-0.06	-0.06		2.56	-0.07	-0.07						37
HF	349	3.13		+0.03	ns	2.49		+0.27	**	0.64		-0.14	***	32
HF	371	3.20	-0.08	-0.04	*									86
HF	371	3.24	-0.11	-0.07	**									86
HF	6803	0	-0.00	+0.01	ns									6
JY	241	4.20	-0.02	0.00										33
RBP	169	3.14	+0.11	+0.14										78
RBP	235	0	+0.16	0.21										65
SI	154	3.43	-0.02	+0.02	ns									16
SI	203	3.19	+0.02	+0.20										91
SI	203	3.12	+0.14	+0.14										91
SI	42					2.85	-0.17	-0.19						52
SI	2208	0	-0.02	-0.03	ns	0	+0.03	+0.08	***	0	-0.05	-0.11	***	26
SI	366	0	-0.01	-0.05	ns	0	+0.04	+0.07	ns	0	-0.01	-0.05	***	9
SI	599	3.71	-0.10	-0.09	*									50
X	151	3.67	-0.07	-0.21	ns	2.98	-0.07	-0.13	ns	0.68	-0.03	-0.09		10
X	2006	3.26	+0.01	0	ns	2.43	+0.05	+0.08	**	0.73	-0.04	-0.07	**	20
X	500	3.59	+0.07	+0.05	ns	2.74	+0.11	+0.12	*	0.85	-0.04	-0.08	*	62
X	587	0	0.02	0.02	ns	0	-0.05	+0.07	***	0	-0.03	-0.05	***	8
X	135	3.36	-0.02	+0.03	ns	2.58	+0.05	+0.15	ns					1

researchers (Table 3). On the average, the differences found are about 13 % and 26 % less  $\beta$ -Lg for  $\beta$ -Lg AB and BB milk, respectively. Only Golikova & Panin (1972) and Khaertdinov (1985), reported a higher proportion of  $\beta$ -Lg B than of  $\beta$ -Lg A in  $\beta$ -Lg AB milk. In the presence of  $\beta$ -Lg C even lower  $\beta$ -Lg contents than those with  $\beta$ -Lg B were found (McLean et al., 1984). Since  $\beta$ -Lg makes up about 50 % of the amount of whey proteins in milk, the effect of the  $\beta$ -Lg variants on the whey protein content mentioned above can largely be explained by altered rate of synthesis of  $\beta$ -Lg.

Table 3:  $\beta$ -Lg content of milk in relation to  $\beta$ -Lg variants

Breed <sup>1)</sup>	N		$\beta$ -Lg phenotype			S <sup>3)</sup>	Ref.
			AA <sup>2)</sup>	AB	BB		
?	24	g/L	6.0	-1.1	-2.5		4 <sup>11)</sup>
?		g/L	4.0	-0.9		*	19
B	1809	g/L	5.93	-0.40	-0.98	*	28
BZV	72	g/L	3.67	-0.42	-0.96	**	40
HF	2650	g/L	5.19	-0.64	-1.37		74
HF	349	g/L	4.48		-1.20	***	32
SI	2059	g/L	7.16	-0.78	-1.48	*	28
X	151	g/L	2.6	-0.4	-0.9	**	10
X	145	g/L	5.07	-0.70	-1.73	**	42
X	537	g/L	4.08	-0.52	-1.14	***	62
?		% rel <sup>8)</sup>	50.4		-5.1	**	67
?		% rel	48.6		-3.6	***	67
HF	15+15	% rel	52.8		-11.7	***	57 <sup>6)</sup>
HF	(17086) <sup>10)</sup>	% rel	0	-4	-10		44
HF	376	% rel	80	-4	-9		93 <sup>9)</sup>
X	135	% rel	80	-5.1	-8.4	***	1 <sub>9)</sub>

Likewise, the casein variants, which have been reported to be associated with a higher casein percentage in milk, were correlated also with higher amounts of the corresponding casein fraction (Table 4).  $\alpha_{s1}$ -Cn C was superior to the B variant regarding the amount of  $\alpha_{s1}$ -casein.  $\beta$ -Cn B generally surpassed the A variants and  $\beta$ -Cn A<sup>1</sup> the variant  $\beta$ -Cn A<sup>2</sup> regarding the amount or relative proportion of  $\beta$ -casein. Many reports have consistently shown, that the B variant of  $\beta$ -Cn increases the level of  $\kappa$ -casein in milk by about 10 % in its heterozygous form (AB) and by about 20 % in its homozygous form (Table 5). In agreement with these findings, about 10-20 % more  $\kappa$ -Cn B was found (17, 39) in  $\kappa$ -Cn AB milk than in  $\kappa$ -Cn A.

There are several studies indicating relationships between the genetic polymorphism of a specific milk protein and the amount of other proteins in milk, for example relationship between the  $\beta$ -Lg polymorphism and the contents of  $\alpha_{s1}$ -casein,  $\alpha$ -lactalbumin and serum albumin. However, most studies have considered relative proportions of the individual caseins or whey proteins rather than their

absolute amounts in milk. Since an alteration in the relative proportion of a single casein is directly affecting the proportion of complementary casein fractions, such changes cannot be interpreted simply as an effect of a specific locus on the expression of the genes encoding complementary fractions. Relatively few investigation, relating to absolute concentrations (1, 74), do not allow to draw final conclusions in this regard.

Table 4: Effect of polymorphism of  $\alpha_{s1}$  – and  $\beta$ -caseins on the amount of the corresponding casein fraction in milk

Breed <sup>1)</sup>	N	$\alpha_{s1}$ -casein				$\beta$ -casein							Ref.
		BB <sup>2)</sup>	BC	CC	S <sup>3)</sup>	A <sup>1</sup> A <sup>1</sup>	A <sup>1</sup> A <sup>2</sup>	A <sup>2</sup> A <sup>2</sup>	A <sup>1</sup> B	A <sup>2</sup> B	BB	S <sup>3)</sup>	
AY		g/L					(0) <sup>7)</sup>		(+0.66) <sup>7)</sup>	+0.52*			64
BSV	135	g/L	9.48	0.5	*		(7.80) <sup>7)</sup>		(+0.12) <sup>7)</sup>			*	40
BV	1809	g/L	8.07	+1.34	+1.84*								28
FV	2059	g/L	8.7	+0.96	+1.48*								28
HF	2650	g/L	16.4 <sup>12)</sup>	+0.21	**	8.6	-0.27	-0.56	+0.39	+0.36		**	74
RSB		g/L					(0) <sup>7)</sup>		(-0.07) <sup>7)</sup>				64
X	538	g/L	8.9	+0.9	+0.3	**	9.6	0	+0.1	+1.3	+1.5	+0.1	62
BV		% rel <sup>8)</sup>	39.5	+1.1	+2.1			(51.1) <sup>7)</sup>		(+1.5) <sup>7)</sup>		+4.8	25
HF	(10013) <sup>10)</sup>	% rel				0	-1.0	-2.0	+2.0	+1.0			45
HF	32	% rel				36.4	-0.2	-1.9	-0.4	+3.1		***	83

Table 5: Effect of  $\kappa$ -casein variants on the  $\kappa$ -casein content of milk

Breed <sup>1)</sup>	N	$\kappa$ -Casein					Ref.
		AA <sup>2)</sup>	AB	BB	S <sup>3)</sup>		
AY		g/L	0	+0.30	0.89		64
BSV	135	g/L	2.07	0.32		*	40
HF	2650	g/L	2.29	+0.09	+0.20	**	74
HF		g/L	0	+1.1	0	*	64
X	538	g/L	3.0	+0.6	+0.7	***	62
AY	42	% rel <sup>8)</sup>	11.8	+1.0	+2.3		13
HF	(10013) <sup>10)</sup>	% rel	0	+0.24	0.47	*	45
HF	32	% rel	5.54	+0.39	+1.10	*	83
HF	28	% rel	5.5	+0.4	+1.1	*	14
HF	376	% rel	11.5	+1.0	+2.5		93
HF	15+15	% rel	6.9		+0.8	*	55 <sup>6)</sup>
HF	2*22	% rel	9.1		+0.7		56 <sup>5)</sup>
MB	74	% rel	11.8		+2.5		15
NO	89	% rel	9.9		+5.1		15
SI		% rel	5.92		+0.43		27
SI	32	% rel	7.5	+0.8	+2.1	*	36
TA	60	% rel	7.0	+1.8	+3.2		15
X	135	% rel	8.5	+2.1	+3.2	***	1

**Legend to Table 1-5**

Values taken from graphs are written in italics.

## 1) Abbreviations used for breeds

AY = Ayrshire

B = Brown cattle

BSV = Bestuzhev

CA = Canadian

HF = Holstein Friesian incl. Black pied

JY = Jersey

MB = Monbéliarde

NO = Normande

RBP = Russian Black Pied cattle

SI = Simmental and related Red and White Spotted cattle, incl. Pinzgauer

TA = Tarentaise

X = Mixed populations

? = Breed not specified

## 2) Phenotype it was referred to. If no absolute concentration was given for this phenotype, it was set to 0.

## 3) Statistical significance

ns = not significant; # =  $P < 0,1$ ; \* =  $P < 0,05$ ; \*\* =  $P < 0,01$ ; \*\*\* =  $P = 0,001$

## 4) Values for different lactations of seasons

## 5) Bulk milk

## 6) Pairwise comparison

7) Milk from different phenotypes, e.g. including milk from  $\alpha$ -Cn BB and  $\alpha$ -Cn AB cows or, in case of  $\beta$ -Cn, no distinction was made between  $\beta$ -Cn A<sup>1</sup>, A<sup>2</sup> and A<sup>3</sup>.8) Relative percentage when total whey protein (in case of  $\beta$ -Lg) or total casein is 100% (in case of individual caseins)9) Relative proportion of  $\beta$ -Lg when amounts of sum of  $\beta$ -Lg and  $\alpha$ -La is 100%

## 10) Number of milk samples

## 11) Values estimated from linear regressions given by the authors

12) Content of  $\alpha_s$ -casein**2.3 Milk fat content** **$\alpha_{s1}$ -Casein**

Although many investigations on different breeds indicated that  $\alpha_{s1}$ -Cn C is superior to the B variant regarding the fat content of milk (9, 22, 26, 50, 51, 62, 69, 72, 73, 76, 79, 96), only a few authors (26, 69, 73) have been able to demonstrate a significant effect of the  $\alpha_{s1}$ -Cn locus. Based on the recordings of about 20'000 Russian Black Pied cows, Zhebrovskii et al. (1977) found no difference between the  $\alpha_{s1}$ -Cn alleles, except 0.02 % less fat in milk produced by  $\alpha_{s1}$ -Cn AB type cows. With Holstein Friesian cattle, Aleandri et al. (1990) as well as Bovenhuis et al. (1992) and Eenennaam & Medrano (1991b) reported a slightly lower fat percentage when  $\alpha_{s1}$ -Cn C was present in the milk. With Angler cattle ( $n = 1507$ ), Oloffs et al. (1992) observed a lower fat content of 4.05% in  $\alpha_{s1}$ -Cn BC milk compared to 4.72 % in  $\alpha_{s1}$ -Cn BB milk.

### $\beta$ -Casein

An often neglected distinction between different A variants of  $\beta$ -casein is again the major problem when the effect of  $\beta$ -casein polymorphism on the fat content of milk is considered. With Braunvieh  $\times$  Brown Swiss (8, 26, 96), Simmental (26, 50) and Pinzgauer cattle (Buchberger et al., 1986b) between 0.04 and 0.14 % higher fat contents for  $\beta$ -Cn BB milk compared to that of  $\beta$ -Cn AA milk, were reported. Several studies with Russian Black Pied cattle, (5, 65, 70, 78) also related  $\beta$ -Cn B with higher milk fat. However, only in the Simmental population (Graml et al., 1985.) was the effect of the  $\beta$ -Cn variants (A, B, C) significant. In contrast to the above findings, from the studies differentiating  $\beta$ -Cn A1, A2, A3 no clear conclusions can be drawn concerning the effect of  $\beta$ -Cn B, neither from studies with Holstein cattle (2, 6, 24, 22, 72, 73, 75, 76, 83, 86) nor with Guernsey (Haenlein et al., 1987) or Simmental (Foissy and Winterer, 1975), or Angler (Oloffs et al., 1992), or mixed populations (18, 62). The problems encountered here, are arising from the often disagreeing results obtained in different studies as well as from the fact, that in the comparisons of phenotype A<sup>1</sup>B with A<sup>1</sup>A<sup>1</sup> and of  $\beta$ -Cn A<sup>2</sup>B with  $\beta$ -Cn A<sup>2</sup>A<sup>2</sup>,  $\beta$ -Cn B is often exhibiting a different effect. With the exception of few reports (22, 24, 41), a general agreement, however, exists that in Holstein cattle  $\beta$ -Cn A<sup>2</sup>A<sup>2</sup> is associated with lower milk fat content than the  $\beta$ -Cn A<sup>1</sup>A<sup>2</sup> and A<sup>1</sup>A<sup>1</sup> types. Differences in the range from -0.04 % to -0.27 % fat between  $\beta$ -Cn A<sup>1</sup>A<sup>1</sup> and  $\beta$ -Cn A<sup>2</sup>A<sup>2</sup> were reported (2, 18, 72, 73, 75, 76, 83).

### $\kappa$ -Casein

Among the numerous reports dealing with the effect of  $\kappa$ -Cn polymorphism on the fat content of milk, only in a few cases have significant correlations been demonstrated. From a comprehensive study of Ng-Kwai-Hang et al (1986), that was confirmed later by Piironen et al., (1992), clearly higher fat content was reported for  $\kappa$ -Cn BB compared to  $\kappa$ -Cn AA milk from Holstein Friesian cows. A later investigation on a four times larger population ( $n \approx 8000$ ) of the same breed, however, (Ng-Kwai-Hang et al., 1990) indicated a negative effect of  $\kappa$ -Cn B on milk fat. The same was observed by Buchberger et al. (1986b) with Pinzgauer cattle. Taking into consideration all the reports for Ayrshire (33, 80), Brown cattle (26, 96), Guernsey (Haenlein et al., 1987), Holstein Friesian (2, 6, 24, 33, 72, 76, 82, 83, 85, 92), Simmental (26, 51), Russian Black Pied (78, 94) the Tartenaise breed (Macheboeuf, et al., 1993.) and for mixed populations (18, 62),  $\kappa$ -Cn A and B have virtually no effect on the fat content of milk. The large investigation of Oloffs et al., (1992) with Angler and Black Pied populations indicate that there might be differences among the breeds in the effect of  $\kappa$ -Cn on the fat content of milk.

At present, only a few studies included  $\kappa$ -Cn C or E. Vlasenko & Vys-hnyakova (1986), as well as Macheboeuf et al. (1993), associated  $\kappa$ -Cn C with higher fat content. No consistent trend, however, could be shown for  $\kappa$ -Cn E (76, 80)

### **$\beta$ -Laktoglobulin**

The findings regarding the effect of  $\beta$ -Lg polymorphism on the fat content generally agree more than the ones on the influence of the casein loci. Although some studies indicate no significant correlation between genetic variants of  $\beta$ -Lg and the fat content of milk (1, 7, 9, 10, 12, 18, 24, 26, 31, 33, 47, 50, 51, 72, 78, 91, 95, 96), others show the contrary (2, 6, 11, 22, 26, 32, 33, 38, 62, 72, 73, 84, 82, 83, 85, 86). In most cases,  $\beta$ -Lg B, either in the homozygous, BB, or heterozygous form, AB, favours a higher fat percentage in the milk. Differences between  $\beta$ -Lg AA and BB within the range from +0.02 (Rozzi et al., 1989) to +0.40 (Hill, 1993) were reported.  $\beta$ -Lg C was correlated to higher fat in Jerseys (McLean et al., 1984) and in Angler (Oloffs et al., 1992) whereas  $\beta$ -Lg D was found to reduce the fat content of milk from Brown cattle (Graml et al., 1988) by 0.09 % and 0.12 % for  $\beta$ -Lg AD and BD, respectively, when compared with  $\beta$ -Lg AA and BB milk.

The positive effect of the  $\beta$ -Lg B allele on the amount of fat and casein in milk, is of special economic interest for the cheese industry. Due to the fact that the total protein in milk is virtually unaffected by the  $\beta$ -lactoglobulins, it is most likely that  $\beta$ -Lg B increases the fat-protein ratio in favour of fat. In view of the increasing market for low-fat food, this would, however, hardly be a desired effect. In this context, it may be of interest that in an investigation on Guernsey cattle, Haenlein et al. (1987) observed a reduction of the fat-protein ratio by  $\beta$ -Lg B when  $\kappa$ -Cn B was present, while in the case of  $\kappa$ -Cn A the opposite was true. In a parallel study with Holstein cattle (Gonyon et al., 1987) this could, however, not be confirmed.

## **3. Technological properties**

### **3.1. Cheesemaking properties**

The favourable effect of  $\kappa$ -Cn B on the renneting properties of milk, e.g. shorter coagulation time and higher curd firmness, has been confirmed in several recent studies (15, 35, 53, 61, 76, 93). Moreover, the influence of  $\kappa$ -Cn C and E on milk coagulation, unknown up to now, has been investigated (15, 35, 53, 61, 76). In a large study with 4853 Friesian and Angler cows, Oloffs et al. (1992) demonstrated the effect of  $\kappa$ -Cn E to be at least as unfavourable as that of  $\kappa$ -Cn A. Compared to  $\kappa$ -Cn AA milk  $\kappa$ -Cn AE took about 3 % longer coagulation time and 10 % lower curd firmness.  $\kappa$ -Cn C has been associated with much longer renneting times than the A or B variant (15, 35, 53). For example, compared to  $\kappa$ -Cn AA milk, between 20 and 30 % longer clotting times have been observed with  $\kappa$ -Cn AC milk. Enzyme kinetic experiments with isolated  $\kappa$ -caseins have shown that  $\kappa$ -Cn C is hydrolysed by chymosin much slower than the variants A

and B (Jakob, 1993). The difference in renneting time between  $\kappa$ -Cn AA and BB milk, however, could not be explained by the substrate properties of the purified  $\kappa$ -caseins. According to this observation, Horn *et al.* (1993) also reported equal rate constants for the proteolysis of  $\kappa$ -Cn AA and BB by chymosin.

According to with earlier studies (Jakob and Puhán, 1992),  $\alpha_{s1}$  C was associated with good rennet coagulation properties (Oloffs *et al.*, 1992). As regards the effect of the  $\beta$ -Cn variants, it was suggested that the influence of the B variant on the renneting properties of milk is similar to that of  $\kappa$ -Cn B. However, this has not been fully confirmed, although more recent studies (35, 60, 76) consistently reported  $\beta$ -Cn B to be related to clearly shorter coagulation time. Compared to  $\beta$ -Cn A<sup>x</sup>A<sup>x</sup>,  $\beta$ -Cn A<sup>x</sup>B was shown to have between 10 and 15 % and  $\beta$ -Cn BB milk about 30 % shorter clotting time. Moreover,  $\beta_{s1}$ -Cn BB/ $\beta$ -Cn BB/ $\kappa$ -Cn BB milk is coagulating in half the time observed for  $\alpha_{s1}$ -Cn BB/ $\beta$ -Cn A<sup>x</sup>A<sup>x</sup>/ $\kappa$ -Cn AA milk (Jakob, 1993). The assessment of curd properties is virtually depending on the parameter considered. In cases where curd firmness was measured 10 min after coagulation had occurred ( $A_{10}$ ),  $\beta$ -Cn B was associated with better coagulum properties (35, 60, 76), similar to the influence of  $\kappa$ -Cn B. If, however, curd firmness was assessed at twice the clotting time after rennet addition ( $A_R$ ), this is no longer true (35, 60). In the latter case,  $\beta$ -Cn A<sup>x</sup> and B are practically equal, while on the other hand,  $\kappa$ -Cn B milk is exhibiting clearly superior curd firmness no matter which parameter ( $A_{10}$  or  $A_R$ ) is taken (Jakob, 1993). Hence,  $\beta$ -Cn B is obviously less important for the rheological properties of renneted milk than  $\kappa$ -Cn B. It is also worth mentioning that using  $\kappa$ -casein phenotype (Oloffs *et al.* 1992) could explain at most 7 % and 16 % of the total genetic variance for rennet clotting time and for curd firmness, respectively. The corresponding values for the whole milk protein phenotype were 9 % and 19 %. It is well known that the rheological properties of curd are to a great extent determined by the casein content of milk. Since the differences in the effect of  $\kappa$ -Cn A/E and B are largely the same at all levels of casein concentrations (15, 35), the absence of  $\kappa$ -Cn B in milk, in combination with low casein contents, will result in very weak curd. Such combinations are related to problems in cheese manufacture, and it was concluded that  $\kappa$ -Cn AA type milk is unsuitable for cheesemaking, when the casein content is 2.4 % ( $\approx$  3.15 % total protein) or lower (Jakob, 1993).

Reports on cheesemaking experiments mostly confirmed earlier investigation, relating  $\kappa$ -Cn B to higher cheese yield. Pabst *et al.* (1991) reported a 2.7% higher recovery of milk protein in Edam cheese manufactured from  $\kappa$ -Cn BB milk when compared to  $\kappa$ -Cn AA. Similar results were reported by Van den Berg *et al.* (1992) for Gouda cheese. Moreover, in the whey obtained from  $\kappa$ -Cn AA milk the same authors observed significantly higher amounts of fat and, even more striking, about 30 % more cheese fines than with  $\kappa$ -Cn AB milk. For the  $\beta$ -Lg phenotypes, however, no significant effects were detected, except the differences in the protein recovery which paralleled the differences in casein number ( $\beta$ -Lg AA < AB < BB). Although the moisture content in  $\kappa$ -Cn AB type cheese was slightly lower, indicating a better syneresis, the degree of proteolysis in cheese

during a ripening period of 6 months was the same as for  $\kappa$ -Cn AA. In an experimental production of Danbo cheese using milk from six different phenotypes ( $\beta$ -Cn/ $\kappa$ -Cn/ $\beta$ -Lg), apparent effects of  $\kappa$ -Cn and  $\beta$ -Lg on the protein recovery disappeared when milk protein content was corrected (Kristiansen, 1991).

### **3.2. Heat stability of milk**

In a large experiment including 4853 Angler and Friesian cows, Schulte-Coerne et al. (1992) confirmed earlier studies associating  $\kappa$ -Cn B with better heat stability. For  $\kappa$ -Cn BB milk, the heat coagulation times at 140° C was between 40 % and 90 % longer than for  $\kappa$ -Cn AA. Similar differences were found for  $\beta$ -Lg phenotypes (HCT:  $\beta$ -Lg BB > AB > AA). Earlier reports (Jakob and Puhán, 1992.) did hardly demonstrate such a clear effect of  $\beta$ -Lg variants on the heat stability of raw milk. Assays of reconstituted milk carried out by the same authors (Schulte – Coerne et al., 1992) indicated only a slight superiority of  $\kappa$ -Cn B.

The effect of  $\kappa$ -Cn variants on the fouling of heat exchangers was studied by Schulte-Coerne et al. (1992). With  $\kappa$ -Cn BB milk higher amounts of deposits were observed than for  $\kappa$ -Cn AB and AA ( $\kappa$ -Cn BB > AB > AA) milk. However, after cleaning with NaOH, less milk residues remained on the surface when  $\kappa$ -Cn BB or AB milk were processed. In view of the small differences, the authors concluded that these findings need further confirmation.

## **4 Conclusions**

Some of the findings emerging from the study of genetic polymorphism of milk may have practical applications in improving the efficiency in different sectors of the dairy industry. As genetic variants of the major milk proteins are inherited in accordance with the Mendelian rules, selection of cows for a specific milk protein type is feasible. This could, however, be a venturesome undertaking.

- We still do not understand very much of the physiological and biochemical mechanisms by which a specific milk protein allele affects the levels of certain milk components and the technological properties of milk.
- Among the numerous possible relationships between genetic polymorphisms of proteins and the composition and technological properties of milk, some of them have been well confirmed, e.g. the effect of  $\beta$ -Lg variants on the casein number or the relationship between the  $\kappa$ -Cn alleles and the renneting properties of milk. Many other relationships, however, are still controversial, and several findings are suggesting correlations might be different among the breeds.
- The detection of  $\kappa$ -Cn E demonstrated that there are probably more alleles existing, which cannot be detected by the analytical techniques commonly used. Since some of these unknown alleles might be relatively frequent in certain populations, as for example  $\kappa$ -Cn E in the Holstein breed, »mistyping« of genetic variants could be one reason for some of the discrepancies occurring when comparing the results from different studies.

- In many studies, the effect of single casein loci rather than the whole set of linked casein genes was considered. Different interrelationships could also explain some of the different effects of genotypes observed up-to-date.
- Because of the close linkage of the casein genes, selection for a specific single variant always means a selection for the set of haplotypes bearing this variant. Therefore, altering the allele frequencies at a specific locus will also alter the gene frequencies at the linked loci. These concomitant changes may be completely different from one breed to another. For example, a rigorous selection for  $\kappa$ -Cn B would lead to a steep regression of  $\beta$ -Cn A<sup>1</sup> in the Swiss Brown cattle population, but possibly to an increase in other breeds. Consequently, such a selection could produce unexpected and undesired results.
- The low frequency of some 'desired' variants in a breed may not have occurred by chance and may have unrecognised undesirable traits.
- A regression of  $\kappa$ -Cn B will impair cheesemaking properties of milk and therefore, should be prevented. Milk quality must, however, satisfy the demands of all kinds of milk utilisation. Consequently, breeding for a specific variant should not be envisaged as long as the effects on milk products other than cheese are not well established.

Despite these uncertainties, breeding for  $\kappa$ -Cn B is already being performed in several countries, e.g. in Austria, Italy and Switzerland. This fact emphasises the need for intensified activities in this field.

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**Received:**

1.6.1994.