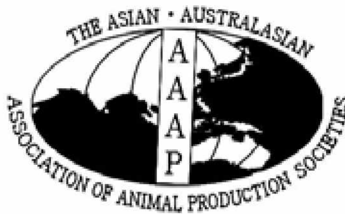

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Genomic Sequence Variability of the Prion Gene (*PRNP*) in Korean Cattle

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ABSTRACT : In this study, we have investigated sequence variants in the *PRNP* gene of 20 individuals belonging to the Korean cattle, and have analyzed and compared genetic features between varieties of other cattle breeds. Of the 73 sequence variants identified in Korean cattle, 27 were identified for the first time in this study, whereas 46 of these polymorphisms had previously been isolated. We discovered a 2.6 kb SNP hot spot region localized on the putative promoter region of the *PRNP* gene. Furthermore, the copy numbers of the octapeptide repeat (24 bp indel) which is detected on the coding sequence (CDS) of the *PRNP* exhibited a completely homozygous 6/6 genotype which is dominant in other cattle breeds. We also characterized a new 19 bp/10 bp allele located on the putative promoter region of the *PRNP* gene, which represented 0.71 in allele frequency. To the best of our knowledge, this report is the first to address polymorphisms of the *PRNP* gene structure in Korean cattle in which BSE has yet to be discovered. Therefore, our findings may prove useful with regard to our current understanding of allelic diversity in bovine species, and may also provide new insights into the genetic factors associated with susceptibility or resistance to BSE. (**Key Words :** *PRNP*, SNP, BSE, Indel, Korean Cattle)

INTRODUCTION

Transmissible spongiform encephalopathies (TSEs), also commonly referred to as prion diseases, are fatal neurodegenerative diseases. Examples of these diseases include scrapie in sheep, Kuru and Creuzfeldt-Jakob disease (CJD) in humans, and bovine spongiform encephalopathy (BSE) in cattle. The pathogenesis of these diseases involves the conversion of the normal- cellular prion protein (PrP^{C}) into a pathological protein (PrP^{sc}), which is infectious (Prusiner 1998). The accumulation of these PrP^{sc} in the brain has been implicated in the development of the diseases themselves. Bovine spongiform encephalopathy (BSE) is generally believed to be caused by the ingestion of scrapie and/or BSE-infected meat or bone meal (Wilesmith 1991). The development of a variant of CJD (vCJD) in humans has also been determined to occur as the result of the ingestion of meat products originating from BSE-infected cattle (Bruce et al., 1997; Scott et al., 1999; Collinge et al., 2001; Asante et al., 2002). Thus, in order to adequately eliminate BSE from the food chain, the determination and identification of genetic factors that confer resistance to BSE would constitute the solution to a fundamental problem.

The *PRNP* gene, which is known to code for the prion protein, has become the focus of increasing attention in the quest to determine the molecular mechanisms underlying the infectious behavior of these prion diseases, as well as the mechanisms relevant to the transmission of prion species between species, most notably transmission between bovines and humans (Bruce et al., 1997; Scott et al., 1999; Collinge et al., 2001; Asante et al., 2002). In studies of the bovine *PRNP* gene, great efforts have been made to identify genetic mutations occurring within the global population, and this gene has been previously examined in such species as Japanese cattle (Takasuga et al., 2003), American beef cattle (Heaton et al., 2003), Holstein-Friesian cattle (Hills et al., 2003), Chinese cattle (Zhang et al., 2004) and German cattle (Sander et al., 2004), as well as 36 other cattle breeds (Seabury et al., 2004b). At present, variations associated with resistance and/or susceptibility to

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the BSE diseases have been fairly regularly reported. Some of these variations include the following: the octapeptide repeat polymorphism in CDS (Goldmann et al., 1991; Hunter et al., 1994; Walawski et al., 2003a; Walawski et al., 2003b; Sander et al. 2004), the large indel polymorphism of 12 bp in the first intron and 23 bp in the putative promoter (Sander et al., 2004; Seabury et al., 2004a), and SNPs (Heaton et al., 2003; Takasuga et al., 2003; Seabury et al., 2004b).

The Hanwoo strain of Korean cattle is one of the few known breeds of cattle in the world in which no individuals have been determined to suffer from or carry BSE. This could be attributable either to adequate control of the food chain in this case, or to a certain specific genetic factor inherent to the Hanwoo lineage. Therefore, the Hanwoo strain may carry important information with which we can more thoroughly understand the genetic features involved with susceptibility to BSE. Nevertheless, the genetic features of this strain of cattle, with regard to BSE, have yet to be determined. It is most that polymorphism research associated with Korean cattle is involved with meat quality and weight (Cheong et al., 2006; Kong et al., 2006; Zhou et al., 2006), and structure of Korean cattle *PRNP* gene was demonstrated by recent study (Choi et al., 2006). In this study, we evaluated *PRNP* polymorphisms in 20 individuals of the Hanwoo breed, which is a well-conserved genetic lineage, maintained carefully by the national breeding system of the Republic of Korea. In this study, we investigated polymorphisms in 31,236 bp region covering putative promoter, three exons and two introns of *PRNP*. Moreover, we discovered several genetically reliable differences between the Hanwoo breed and foreign cattle breeds, which were expected to generate useful information for our understanding of BSE disease in general.

MATERIALS AND METHODS

DNA sample

DNA was isolated from the blood of 20 individual healthy Korean Hanwoo cattle (HW) using the Core-One^{TM} Blood DNA Purification Kit (CoreBioSystem, Seoul, Korea). As was mentioned in the introduction section, these cattle represent a well-conserved genetic lineage, maintained by systematic breeding conducted by the National Livestock Research Institute of Korea.

DNA amplification

In order to generate genomic fragments spanning the *PRNP* gene, 61 different PCR primer sets were designed using the GenBank reference sequence AJ298878, which includes a promoter, three exons, two introns, and a 3'-untranslated region (UTR). These primers were designed to overlap to a length of 100-150 bp between each of the fragments, and to collectively encompass a span of 31,236 bp. Our PCR reactions were conducted using 1 μl (10-20 ng/μl) of genomic DNA, 0.5 μl of 5 pmol primer, 1 μl of 10×buffer, 0.25 μl of dNTP mixture, 6.65 μl of distilled water, and 0.1 μl of *Taq* DNA polymerase (SolGent, Daejeon, Korea), in a total volume of 10 μl. Amplification was conducted using the GeneAmp PCR System 9700 (Applied Biosystems, Foster City, CA), followed by 35 cycles of denaturation at 96°C for 10 s, annealing for 5 s at 50°C, and 4 minutes of extension at 60°C. All of the PCR products were assessed for both yield and purity on agarose gel. The PCR products were purified via ethanol precipitation.

DNA sequencing

The purified PCR products were sequenced directly with a BigDye Terminator (Ver 3.1) Cycle Sequencing Kit (Applied Biosystems, Foster City, CA). The sequencing PCR reactions were conducted using 10 ng of amplified DNA, 0.5 μl of 3 pmol primer, 0.87 μl of 5× buffer, 1.38 μl of distilled water, and 0.25 μl of BigDye, in a total volume of 3 μl. Amplification was conducted with a GeneAmp PCR System 9700 (Applied Biosystems, Foster City, CA), followed by 35 cycles of denaturation at 96°C for 10 s, annealing for 5 s at 50°C, and 4 minutes of extension at 60 °C. The PCR products were purified via ethanol precipitation, and resolved with an ABI 3730XL DNA Analyzer (Applied Biosystems, Foster City, CA). The individual sequences were initially edited and assembled using Sequencher 4.1.4 (Gene Codes Corp., Ann Arbor, USA) software. The complete sequences were generated via a final editing process, which included manual visual confirmation performed using the original chromatograms, with the Sequencher program.

Statistical analysis

Allelic and genotypic distributions were evaluated for significant differences using Fisher's exact test, which was applied using the STAT-SAK program (Dallal GE, freeware).

RESULTS

Sequence variants

We re-sequenced a 31,236 bp genomic region in 20 individual animals. This area encompassed the promoter, three exons, two introns, and the 3'-UTR of the *PRNP* gene. In this region, we were able to identify 73 total polymorphisms, including 65 single nucleotide polymorphisms (SNPs), one polymorphism involving two adjacent nucleotides, four indels (12 bp, 14 bp, 23 bp, and 24 bp), two allelic variants (19/10 bp and 10/3 bp), and one different region containing a 97 bp sequence (Table 1). Comparing with the variants referenced in previous reports

Table 1. i) Allele and genotype frequencies of *PRNP* gene polymorphisms in Korean cattle

PRNP region	Position [a]	Variant	Reference	Allele frequency of the variant
promoter	45752	G/T	this study	0.63
promoter	45957~45975	19 bp/10 bp [b]	this study	0.71
promoter	46327	C/T	this study	0.67
promoter	46795	G/T	Heaton et al., 2003	0.51
promoter	47004	A/G	Heaton et al., 2003	0.50
promoter	47221	C/T	Heaton et al., 2003	0.56
promoter	47238	C/T	Heaton et al., 2003	0.70
promoter	47450	C/T	Sander et al., 2004	0.71
promoter	47836~47837	23 bp indel [c]	Sander et al., 2004	See Table 2
promoter	48584	A/C	Sander et al., 2004	0.86
promoter	48689	C/T	Sander et al., 2004	0.49
promoter	48695	G/T	Sander et al., 2004	0.51
promoter	48732	A/C	Sander et al., 2004	0.57
promoter	48773	A/C	Sander et al., 2004	0.49
promoter	48815	A/C	Sander et al., 2004	0.54
promoter	48890	A/T	Sander et al., 2004	0.51
promoter	48921	C/T	Sander et al., 2004	0.52
promoter	49246	A/G	Hills et al., 2003	0.44
promoter	49345	G/T	Sander et al., 2004	0.61
promoter	49416	C/T	this study	0.56
intron 1	49542	A/G	Hills et al., 2003	0.66
intron 1	49729~49730	12 bp indel [d]	Hills et al., 2003	See Table 2
intron 1	49834	A/G	Sander et al., 2004	0.54
intron 1	50000	A/G	Hills et al., 2003	0.46
intron 1	50121	G/T	this study	0.71
intron 1	50138	A/G	Sander et al., 2004	0.69
intron 1	50297	A/G	Hills et al., 2003	0.75
intron 1	50308	A/G	Sander et al., 2004	0.75
intron 1	50319	A/G	Hills et al., 2003	0.75
intron 1	50352	A/G	Hills et al., 2003	0.75
intron 1	50376	A/G	Sander et al., 2004	0.75
intron 1	50743	G/T	Sander et al., 2004	0.80
intron 1	51199	A/G	Sander et al., 2004	0.73
intron 1	51208	C/T	Sander et al., 2004	0.79
intron 1	51586	A/G	this study	0.86
intron 1	51862	C/T	this study	0.75
intron 1	51879	C/T	this study	0.75
intron 2	52183	A/G	Hills et al., 2003	0.61
intron 2	52445	A/C	Hills et al., 2003	0.58
intron 2	53793	C/T	this study	0.68
intron 2	54420	G/T	this study	0.51

a : Position in reference sequence AJ298878
b : CAGAATCTCTAAGGTGGGC → TTAGGATGGA
c : TCTCAGATGTCTTCCCAACAGCA
d : GGGGGCCGCGGC
e : GAACTTGTTA → CAC
f : GCTGGGGCCAGCCTCATGGAGGTG
g : TTTTTGTAAGGTAC
h : 97bp different region between the Korean cattle and AJ298878
* Number of animals used in this study was 20 individual healthy Korean cattle.

(Heaton et al., 2003; Hills et al., 2003; Sander et al., 2004), 27 of the 73 polymorphisms isolated in Korean cattle were confidently identified to be newly-discovered variants that had never been previously reported, which included 26 SNPs, and one 19 bp/10 bp allelic variant. And also, the remaining 46 polymorphisms matched with that had been previously described. In addition, we also discovered a 97 bp-difference in the 3'-UTR from the Korean cattle, as compared to the previously-used genomic sequence, AJ298878, from *Bos taurus* (Hills et al., 2001).

SNPs of *PRNP* gene in Korean cattle

The SNPs were the most frequently observed form of variation, at 89% (65/73). They were located as follows: on the putative promoter (18), on intron 1 (16), on intron 2 (20), within the 3'-UTR (6), and on exon 3 (5). The positions of SNPs newly identified in this study (27) (Table 1), and those which had been reported previously (46) are

Table 1. ii) Allele and genotype frequencies of *PRNP* gene polymorphisms in Korean cattle

PRNP region	Position [a]	Variant	Reference	Allele frequency of the variant
intron 2	53793	C/T	this study	0.68
intron 2	54420	G/T	this study	0.51
intron 2	54428	C/T	this study	0.65
intron 2	55360	C/T	this study	1.00
intron 2	55903~55905	10 bp/3 bp [e]	Hills et al., 2003	0.04
intron 2	57359	G/T	this study	0.40
intron 2	57904	A/G	Hills et al., 2003	0.66
intron 2	58212	A/T	Hills et al., 2003	0.56
intron 2	58455	C/T	this study	0.82
intron 2	58999	A/G	Hills et al., 2003	0.65
intron 2	59254	G/T	this study	0.64
intron 2	60291	C/T	Hills et al., 2003	0.64
intron 2	60511	A/G	this study	0.70
intron 2	60835	A/G	Hills et al., 2003	0.55
intron 2	61326	A/G	Hills et al., 2003	0.69
intron 2	61426	A/G	this study	0.74
intron 2	64177	A/G	this study	0.81
intron 2	64590	C/T	this study	0.73
intron 2	64611	C/T	this study	0.67
CDS	65754~65825	24 bp indel [f]	Hills et al., 2003	See Table 2
exon 3	66877	C/T	Hills et al., 2003	0.90
exon 3	66948	C/T	Hills et al., 2003	0.94
exon 3	67490~67491	AG del	Sander et al., 2004	0.01
exon 3	67864	A/G	Hills et al., 2003	0.66
exon 3	68019~68046	14 bp indel [g]	Sander et al., 2004	See Table 2
exon 3	69085	A/G	Hills et al., 2003	0.75
exon 3	69359	A/G	this study	0.36
3' utr	69774	A/G	Hills et al., 2003	0.41
3' utr	70637	A/C	this study	0.63
3' utr	73493	C/G	this study	0.36
3' utr	73544~73640	97 bp diff [h]	this study	1.00
3' utr	74256	C/T	this study	0.71
3' utr	74983	A/G	this study	0.58
3' utr	75996	A/G	this study	0.59

a : Position in reference sequence AJ298878
b : CAGAATCTCTAAGGTGGGC → TTAGGATGGA
c : TCTCAGATGTCTTCCCAACAGCA
d : GGGGGCCGCGGC
e : GAACTTGTTA → CAC
f : GCTGGGGCCAGCCTCATGGAGGTG
g : TTTTTGTAAGGTAC
h : 97bp different region between the Korean cattle and AJ298878
* Number of animals used in this study was 20 individual healthy Korean cattle.

summarized and schematically diagrammed in Figure 1. As a result of this, we discovered two remarkable things; the first of these is the existence of a SNP hot spot region, which is located on the putative promoter region, and spans 2.6 kb in length (47,837-50,470). In all of the breeds thus far examined, 1.9 kb (48,584-50,470) of this 2.6 kb region is highly conserved. The second remarkable finding was that the Korean cattle also harbored no SNPs in the CDS region of the *PRNP* gene, although this region contains abundant SNPs in most other breeds of cattle (Heaton et al., 2003; Hills et al., 2003; Takasuga et al., 2003; Sander et al., 2004; Seabury et al., 2004b; Zhang et al., 2004).

Allelic variants and indel polymorphisms

Because indel polymorphisms are more likely to exert regulatory effects than are single nucleotide substitutions or SNPs, indel polymorphisms have frequently been the focus of searches for associations with susceptibility to BSE (Heaton et al., 2003; Hills et al., 2003; Takasuga et al., 2003; Sander et al., 2004; Seabury et al., 2004a; Zhang et al., 2004). Four indels (12 bp, 14 bp, 23 bp and 24 bp) have been reported previously in a variety of other cattle breeds (Goldmann et al., 1991; Hunter et al., 1994; Walawski et al., 2003a; Walawski et al., 2003b; Sander et al., 2004; Seabury et al., 2004a), all of them were confirmed in Korean cattle. Furthermore, we investigated the allelic frequencies of these polymorphic indels using 96 individuals by using PCR amplification method (data not shown), and then compared these frequencies with those found for other breeds of cattle, including both healthy and BSE-affected German cattle

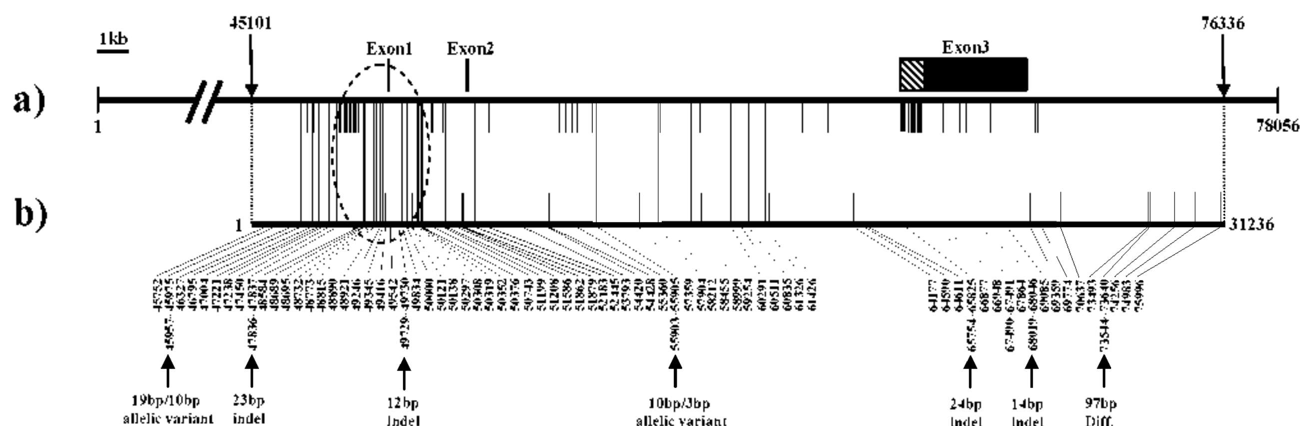

Figure 1. Diagram illustrating the genomic architecture of the bovine *PRNP* gene. All positions of SNPs, allele variants, and indels, whether they are previously described polymorphisms (Heaton et al., 2003; Hills et al., 2003; Sander et al., 2004) or were first detected in this study, are indicated with regard to the *PRNP* reference sequence (Hills et al., 2001; AJ298878). a) Three *PRNP* exons are represented by *black boxes*, and the protein coding region is depicted as a *hatched box* within exon 3. The black vertical lines indicate the positions of the previously reported polymorphisms. b) The positions of the polymorphic sites detected in Korean cattle are also represented with regard to the *PRNP* reference sequence (AJ298878). Long vertical lines represent common polymorphic sites between them, and the short lines represent specific polymorphisms on the respective cattle breeds. The seven large indel polymorphisms are indicated by *arrows*. The particularly highly polymorphic region surrounding the putative promoter is represented by a dotted circle.

Table 2. SNPs distribution of *PRNP* gene in various cattles

Locus			n	Allele frequencies		Genotype frequencies		
				+	-	++	+-	--
Promoter	23 bp indel	Korean cattle	96	0.56	0.44	0.47	0.18	0.35
		Healty[1]	48	0.43	0.57	0.21	0.44	0.35
		BSE-affected[2]	43	0.27	0.73	0.05	0.44	0.51
		U.S sires[3]	132	0.30	0.70	0.14	0.32	0.54
Intron 1	12 bp indel	Korean cattle	96	0.24	0.76	0.00	0.47	0.53
		Healty[1]	48	0.49	0.51	0.21	0.56	0.23
		BSE-affected[2]	43	0.33	0.67	0.09	0.47	0.44
		U.S sires[3]	132	0.49	0.51	0.32	0.35	0.33
				Allele frequencies		Genotype frequencies		
				6	5	6/6	6/5	5/5
CDS	24 bp indel	Korean cattle	96	1.00	0.00	1.00	0.00	0.00
		Healty[1]	48	0.95	0.05	0.90	0.10	0.00
		BSE-affected[2]	43	0.95	0.05	0.91	0.09	0.00
				Allele frequencies		Genotype frequencies		
				2	1	2/2	2/1	1/1
Exon 3	14 bp indel	Korean cattle	96	1.00	0.00	1.00	0.00	0.00
		Healty[1]	48	0.95	0.05	0.90	0.10	0.00
		BSE-affected[2]	43	0.92	0.08	0.86	0.12	0.00
		U.S sires[3]	132	0.94	0.06	0.89	0.11	0.00

[1] Healthy German cattle data from Sander et al. (2004). [2] BSE-affected German cattle data from Sander et al. (2004).
[3] U.S. sires cattle data from Seabury et al. (2004).

breeds, as well as U.S. sires (Table 2). The allele frequencies of the 23 bp indel in Korean cattle were significantly higher than those determined for healthy German cattle breeds, U.S. sires, and BSE-affected German cattle. However, the frequencies of the 12 bp indel were similar to those of BSE-affected German cattle breeds, but differed from above two healthy cattle breeds. Most significant result of the Korean cattle were obtained from the 24 bp indel (octapeptide repeat) and 14 bp indel, which are located on the coding sequence and 3' UTR region respectively. The copy numbers of the octapeptide repeat exhibited a completely homozygous 6/6 genotype, and the allelic frequencies of 14 bp indel were completely fixed into two repeats. In addition, we detected a novel allelic variant, 19 bp/10 bp (CAGAATCTCTAAGGTGGGC→TTAGGATGGA) (Figure 2), which is located on the putative promoter region, upstream from the 23 bp indel and represented 0.71 in allele frequency.

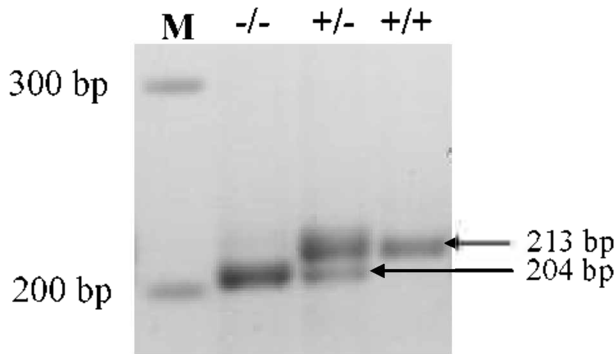

Figure 2. Genotype of 19 bp/10 bp allelic variant. 3% NuSieve agarose gel showing the genotyping of the 19 bp/10 bp variant on the putative promoter of the *PRNP* gene. The genotypes of three different animals are indicated with regard to either the presence (+) or absence (-) of the nine bp sequence. The DNA size marker is represented by the letter M.

Furthermore, we also found 97 bp sequences difference between the Korean cattle and the breeds of *Bos taurus* (AJ298878: Hills et al., 2001, BN000291: Sander et al., 2004) previously reported. the sequences is located 3,884 bp downstream from exon 3 within the 3'-UTR. In order to further evaluate this discrepancy, we amplified the genomic region via PCR, using 10 individual Korean cattle and five individual animals from each of four strains (Simmental, Limousin, Holstein, and Brown Swiss) and determined their sequences. The alignment of these sequences with AJ298878 and BN000291 revealed that all of these sequences, except for two reference sequences, agreed perfectly (data not shown). Our result strongly suggest a possibility that the 97 bp sequence difference between them appears to have been caused by technical errors in AJ298878 and BN000291, although this confirmation is not sufficiently confident so as to completely exclude the possibility of strain specificity, due to the insufficient sample number used in this study.

DISCUSSION

The association of polymorphisms of the *PRNP* and BSE susceptibility has been investigated fairly extensively, in a variety of cattle breeds (Heaton et al., 2003; Hills et al., 2003; Sander et al., 2004; Seabury et al., 2004a). However, the Korean cattle there is not one of the breeds with which such polymorphism studies have been conducted, although the breed is one of the only domestic breeds in which BSE has never been detected. Therefore, in this study, we conducted an analysis of the sequence variability of the Korean cattle in the region including the putative promoter, three exons, two introns, and the 3'-UTR region of the *PRNP* gene locus. Consequently, we identified 73 total polymorphisms, including 65 single nucleotide polymorphisms (SNP), four indel polymorphisms (12 bp, 14 bp, 23 bp, and 24 bp), and four allelic variants exhibiting differences greater than two bp in adjacent nucleotides. A comparison of our findings with database entries and the results of studies performed with other cattle breeds revealed the presence of 27 additional polymorphic sites in Korean cattle, including 25 SNPs, one 19 bp/10 bp allelic variant, and one different region containing a 97 bp sequence.

Polymorphisms in exon 3 within the 3'-UTR region have frequently been the subject of scrutiny in other cattle breeds, as sequence variation in the region has often been believed to exert critical influences with regard to mRNA processing, and this is especially true of the CDS region (Heaton et al., 2003; Hills et al., 2003; Takasuga et al., 2003; Zhang et al., 2004; Sander et al., 2004; Seabury et al., 2004b). We detected eight genetic polymorphic sites in exon 3 of the Korean cattle including six SNPs and two indels (24 bp and 14 bp). However, we were unable to detect any SNPs within the CDS region, which is interesting, as this has not been the case in any other breed of cattle.

The octapeptide repeat is localized on the coding sequence (CDS) of the *PRNP* (Figure 1) and reflected in the occurrence of three alleles: with five, six and seven repeats of the Pro-His/Gln-Gly(Gly)-Gly-Try-Gly-Gln amino-acid sequence. In the previously examined cattle breeds, the 6/6 homozygote genotype showed an extremely higher prevalence than the other genotype, especially in German (Sander et al., 2004), Scottish (Hunter et al., 1994), and Polish Black-and-White cattle breeds (Walawski et al., 2003a). In this study we didn't observe any animals carrying the allele with five or seven octapeptide repeat, all the animals studied here was the 6/6 homozygote genotype.

In the future, other studies will investigate polymorphisms on the putative promoter region spanning exon 1, because mutations in this region may affect the levels of *PRNP* expression, and may also exert some influence on BSE incubation time and susceptibility (Bossers et al., 1996). Thus far, two compelling results have been reported; one involves the noticeably low frequency of repetitive elements in the region ~2.5 kb upstream of exon 1, in which the presence of additional functional elements might be speculated to exist; and the other involves the 23 bp indel located upstream of exon 1, which is generally considered to be an interesting candidate for a hypothetical regulatory mutation, assumed to be associated with mRNA processing.

Analyses of all the genetic variants identified here, as well as those identified in previous studies, indicate the presence of a SNP hot spot region which spans the putative promoter. However, the distribution of the SNPs in Korean cattle differs substantially from that observed in other cattle

breeds. Furthermore, the allelic frequencies of the 23 bp indel in Korean cattle (0.56/0.44) exhibited a higher degree of similarity with those observed in healthy German cattle (0.43/0.57) and U.S. sires (0.30/0.70) than with BSE-affected German cattle (0.27/0.73). This indicates that the genetic resources of the Korean cattle differ significantly from those of other cattle breeds.

An ingestion of meat and bone meal originating from BSE-infected cattle has been implicated as a factor in the spread of BSE between cattle (Wilesmith, 1991). Therefore, the presence of exhaustive controls to avoid and prevent BSE infections might be the actual reason for the total absence of BSE in Korean cattle. And also, genetic factors, especially genetic variants to have found in CDS region of *PRNP* gene, can not rule out as the reason (Sander et al., 2004; Seabury et al., 2004b). Therefore, it is worth speculating that the Korean cattle does not show any SNPs within the CDS region of exon3. These factors may, to some degree, contribute to a genetic resistance to BSE in Korean cattle. Our findings of some reliable genetic differences between foreign and Korean cattle may prove vital to our current understanding of genetic factors associated with susceptibility to BSE.

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