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Comparative genomic structure of the human and bovine PRNP locus

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Prion diseases comprise a group of fatal neurodegenerative pathologies such as Creutzfeldt Jakobs disease (CJD) in humans, bovine spongiform encephalopathy (BSE) in cattle, and scrapie in sheep and goat. The PRNP genemay play an important role to BSE, which is known to code for the prion protein. The bovine PRNP locus has been studied previously, but the genomic structure has not yet been defined. In this study, to confirm the genomic structure of bovine (Koran cattle) PRNP locus, we screened the Korean cattle BAC libraries including the PRNP by PCR amplifications using the human STS markers. Selected three BAC clones were sequenced 402 kb: 207,929 bp, 136,365 bp, 98,632 bp, respectively. BAC clones were contained repeat sequences of 42.83% (172,405 bp); G+C content of 42.27%, LINE of 25.55%, SINE of 10.36%, LTR element of 3.92%, DNA element of 2.88%. We compared the genomic structure with the human genomic sequences using the PipMaker, Repeatmasker, GeneScan, TwinScan and FGENESH programs. As a result, we determined the precise breakpoint between the two syntenic genomes, located on the 5' UTR of the PRNP gene. Further analysis demonstrated that the genomic structure of four genes, PRNP, PRND, RASSF2 and SLC23A2, within the syntenic region of the bovine genome is highly conserved in order and orientation. PRNT gene was not found in bovine but is conserved in several primates (chimpanzee, gorilla, orangutan, monkey), including human. Our findings may provide useful clues for understanding the evolutional process in the PRNP locus and also the mechanism that allows TSE from cattle to infect human.