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Somatic cell mutations in cerebral tissue of cattle affected by bovine spongiform encephalopathy

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ABSTRACT

In animals the prion disease includes sheep and goat scrapie and the bovine spongiform encephalopathy (BSE). While several polymorphisms of the prion (PRNP) gene have been identified in sheep and some of them have been associated with susceptibility to scrapie, few mutations are reported in cattle and no correlation with BSE have been demonstrated. Genetic screening for mutants in the PRNP gene of 21 BSE positive animals by direct sequencing of the amplified gene, using DNA extracted from brain as template, confirmed that only few polymorphisms are present. However DNA molecules cloned and sequenced from the population of fragments considering a total of 90 clones from 9 BSE positive and 70 clones from 7 BSE negative animals, gave a highly significant differences in the frequency of mutations ($p = 0.01$). The high frequency and type of variants found cannot be explained only with misincorporation error of the Taq polymerase. Interestingly one of the mutations found in the BSE positive animals (F209S) corresponds to a mutant that causes a familiar form of prion disease in humans (F198S). These data can be explained with the presence of somatic mutations modifying the PRNP gene in single brain cells.

KEYWORDS

BSE; Prion; Somatic Mutations

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