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Characterization and transmission of novel prion protein aggregates in cattle

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Key words
BSE, atypical, prion protein, pathogenesis, risk assessment

Aim of the study
In 2011 two cattle with a distinct prion protein phenoptype, (PrPres/2011) emerged. It remained unknown, whether these findings are related to a transmissible prion disease in cattle. The aims of this study were (i) to investigate the aggregation properties of PrP^{res}/2011 in comparison to the abnormal PrP in H-BSE, L-BSE and C-BSE and to normal PrP in healthy animals and (ii) to gain insights into structural determinants of PrP in the different BSE types by PrP specifc antibodies and conformation stability assay. This part of the project complements an in vivo study in cattle, which is still ongoing in Canada.

Material and methods
We used western immunoblot, ultracentrifugation, detergent solubility assays and antibody binding profiles to characterize the different types of misfolded prion proteins in brain tissues of cattle.

Results and significance
While western blot after proteinase K digestion proved to be of insufficient sensitivity, ultracentrifugation revealed a poor reproducibility. Only detergent treatment in combination with differential antibody binding, the so called conformation stability assay (CSA), was able to show robust differences between normal brain tissues, BSE affected brain tissues and brain tissues of the 2011 cases. First results of inoculation experiments suggested that PrPres/2011 was not transmissible to cattle and transgenic mouse models in the same was as classical BSE. However, due to a relative short experimental period, a second passage (P2) of brain material was conducted in cattle. This method will now serve to investigate samples (brain, body fluids and peripheral organs) of the ongoing in vivo P2-study in Canada, which will deliver valuable information regarding the nature of this putative novel prion protein disorder.

Publications, posters and presentations
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