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Truncated prion protein fragments in healthy and BSE affected cattle: interference with laboratory diagnosis and implications for disease control

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Key words
BSE, prion, atypical BSE, surveillance, cattle, disease control, prion protein

Aim of the study
In 2011 we identified cases of BSE in Switzerland with a molecular prion protein phenotype different from those in known types of BSE by active disease surveillance. The aims of this project were to: (i) investigate the biochemical and biophysical characteristics of this aberrant prion protein (PrP), (ii) assess the influence of tissue autolysis on the molecular prion protein phenotype and (iii) determine whether these cases involve a transmissible prion agent.

Material and methods
Biochemical and immunochemical characterization of the aberrant PrP fragments was done by epitope mapping, high speed centrifugation, sucrose gradient assay and NaPTA precipitation. The effect of PK activity and autolysis on the generation of the truncated PrP was investigated by PK titration and PK inhibitor assays. In vivo transmission studies were conducted in cattle and bovine PrP-transgenic mice and brain samples derived from these transmissions were analyzed using routine diagnostic tests, RT-QuIC and sucrose gradient assay.

Results and significance
The truncated PrP fragment in the 2011 cases corresponded to the physiological PrP C1-fragment, but with increased aggregation and PK resistance, reminiscent of the PrP in BSE. Results suggest that tissue autolysis was not involved in the generation of this PrP. In the bioassays, clinical disease, brain lesions as well as PrPres were absent. However medium-sized PrP aggregates with mild PK resistance and seeding activity in RT-QuIC were recovered in the brains of inoculated cattle.
Upon experimental inoculation, the truncated 2011 PrP observed in brain samples of two cows in Switzerland did not cause a transmissible spongiform encephalopathy, despite some biochemical similarities with the PrP in BSE affected cattle. These results point out to the need of further investigating the role of PrP aggregation and misfolding in health and disease.

Publications, posters and presentations
Serra, F. et al. (2014) Full-Length PrP but not PrP-C1 is depleted in autolytic brainstem samples of cattle. Abstract published in Prion, Volume 8, Supplement 1, 2014. Poster at the Prion conference Triest, 2014.
Serra, F. et al. (2014) Truncated prion protein fragments in healthy and Bovine Spongiform Encephalopathy (BSE) affected cattle: interference with laboratory diagnosis and implications for disease control. Project presentation at the Neurocenter-Vetsuisse Faculty, May 2014.
Serra, F. et al (2015) Investigation on a particular PrPres fragment in bovine autolytic brain samples. Presentation at the TSE-EURL workshop 2015, June 2015, Weybridge, UK.

Serra, F. et al. (2016) Unusual PrP in Swiss cows shows biochemical similarities with BSE-associated PrP but does not induce a transmissible spongiform encephalopathy. Scheduled talk for the 4th Conference of European Association of Veterinary Laboratory Diagnosticians (EAVLD), Prague 6.-9.11.2016.

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Serra, F. Truncated prion protein fragments in healthy and BSE affected cattle: interference with laboratory diagnosis and implications for disease control. PhD Thesis, Universität Bern, 2017

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