

A novel approach in the molecular differentiation of prion strains

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A team from the French Food Safety Agency, Lyon, France, has identified a prion protein characteristic that is unique to some natural but unusual sheep scrapie cases. This finding, reported August 29th in the open-access journal *PLoS Pathogens*, may provide a novel method by which to study prion diversity and their possible changes during cross-species transmission.

Mystery still surrounds the origin of the transmissible agent involved in the food-borne epidemic of bovine spongiform encephalopathy (BSE). Classical BSE, more commonly known as mad cow disease, is a known cause of a variant form of the incurable, degenerative neurological disorder Creutzfeldt-Jakob disease in humans. It has recently been proposed that this could have been the result of the recycling of an atypical, more probably sporadic form of BSE (called bovine amyloidotic spongiform encephalopathy, or L-type BSE) in an intermediate host, such as sheep.

The team, led by Thierry Baron, analyzed the molecular features of the disease-associated protease-resistant prion protein (PrPres) to determine any differences which might discriminate between scrapie and BSE cases. The researchers sampled PrPres from the brains of transgenic mice overexpressing the ovine prion protein after experimental infection with prions from bovine classical BSE, L-type BSE, and ovine scrapie. Scrapie cases were found to include rare "CH1641-like" isolates, which share some PrPres molecular features with classical BSE and L-type BSE.

The molecular features of the prion protein in the "CH1641-like" sheep scrapie cases more closely resemble those found in L-type BSE compared to classical BSE. However, from a series of four "CH1641-like" scrapie cases, the researchers found a pathological C-terminal prion protein product that was undetectable from both L-type and classical BSE transmitted to such mice, clearly suggesting that such scrapie isolates are not linked to these BSE forms.

Further studies to confirm this discriminating factor are needed in sheep, especially from sheep experimentally infected with L-type BSE, which were not available for this study. These findings, however, add a novel approach in the molecular differentiation of prion strains and may help to better understand their possible changes during cross-species transmissions.

Citation: Baron T, Bencsik A, Vulin J, Biacabe A-G, Morignat E, et al. (2008) A C-Terminal Protease-Resistant Prion Fragment Distinguishes Ovine "CH1641-Like" Scrapie from Bovine Classical and L-Type BSE in Ovine Transgenic Mice. PLoS Pathog 4(8): e1000137.

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