High pressure effects on the infectious prion protein

***P. Heindl*[a], *A. Fernández*[a], *M. Büttner*[b], *P. Butz*[a], *B. Tauscher*[a], *E. Pfaff*[b]**

[a] *Federal Research Centre for Nutrition and Food, Institute of Chemistry and Biology, Haid-und-Neu-Str.9, 76131 Karlsruhe, Germany,* philipp.heindl@bfe.uni-karlsruhe.de

[b] *Friedrich-Loeffler-Institute Federal Research Institute for Animal Health, Institute for Immunology, Paul-Ehrlich-Str. 28, 72076 Tübingen, Germany*

Prion diseases are associated with the accumulation of a misfolded form (PrP^{Sc}) of the cellular prion protein (PrP^{C}). This misfolded beta-sheet rich aggregated pathogenic multimer seems to be the main component of the transmissible form. Suitable inactivation procedures are aggressive, with a consequent loss in quality and texture in the treated tissues. Therefore, our interest in assessing the effects of unconventional milder technologies on prion stability and prion infectivity arises from the necessity of providing alternative sterilisation procedures at risk materials.

Crude brain homogenates infected with the 263K strain of scrapie (PrP^{Sc}) and isolated prion proteins were heated and/or pressurised at 800 MPa at 60 °C for different holding times in different buffers and in water. Prion proteins were analysed on immunoblots for their proteinase K (PK) resistance, and in bioassays for their infectivity. Samples pressurised at initial neutral conditions and containing native PrP^{Sc} or the N-truncated PrP 27-30 were negative on immunoblots [1], a 6-7 $\log_{10}$ reduction of infectious units per gram was reported in PBS buffer after a two hour treatment [2]. A pressure induced change in the protein conformation of native PrP^{Sc} leading to less PK resistant and infectious prions was confirmed in all buffers tested at initial neutral conditions and in water.

However, opposite results were found after pressurising isolated prions at neutral conditions and after pressure treatment of native infectious prions at slightly acidic pH, arguing for the existence of pressure sensitive β-structures ($PrP^{Sc}_{\Delta Psen}$), and extremely pressure resistant β-structures ($PrP^{Sc}_{\Delta Pres}$).The distinct behaviour of native and isolated prions indicate differences in the protein structure that have not been taken into consideration before.

References:

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