

P-004: Structural characterization of ex vivo mammalian prions isolated from multiple strains.

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Until now, the 3-dimensional structure of infectious mammalian prions and how this differs from non-infectious amyloid fibrils remained unknown. Mammalian prions are hypothesized to be fibrillar or amyloid forms of prion protein (PrP), but structures observed to date have not been definitively correlated with infectivity. One of the major challenges has been the production of highly homogeneous material of demonstrable high specific infectivity to allow direct correlation of particle structure with infectivity. We have recently developed novel methods to obtain exceptionally pure preparations of prions from prion-infected murine brain and have shown that pathogenic PrP in these hightiter preparations is assembled into rod-like assemblies (Wenborn et al. 2015. Sci. Rep. 10062). Our preparations contain very high titres of infectious prions which faithfully transmit prion strain-specific phenotypes when inoculated into mice making them eminently suitable for detailed structural analysis. We are now undertaking structural characterization of prion assemblies and comparing these to the structure of non-infectious PrP fibrils generated from recombinant PrP.