

Prion Strain Mutation Determined by Prion Protein Conformational Compatibility and Primary Structure

A study of CWD prion conformational changes, performed at the University of Kentucky Medical Center, was published in the last edition of Science. The scientific team included Dr J. Castilla, now at CIC bioGUNE's Prion Laboratory.

The mechanism underlying prion strain mutation in the absence of nucleic acids remains unresolved. Using susceptible transgenic mice, two prevalent chronic wasting disease (CWD) prion strains were identified - with divergent biological properties but composed of PrP^{Sc} with indistinguishable biochemical characteristics. Although CWD transmissions indicated stable, independent strain propagation by elk PrP^C, strain coexistence in the brains of deer and transgenic mice demonstrated unstable strain propagation by deer PrP^C. The primary structures of deer and elk prion proteins differ at residue 226, which, in concert with PrP^{Sc} conformational compatibility, determines prion strain mutation in these cervids.

This discovery supplies new data suggesting a possible mechanism of controlling the stability of prion strains by changing the primary structure of the prion protein.

Link:

<http://www.ncbi.nlm.nih.gov/pubmed/20466881>

Picture:

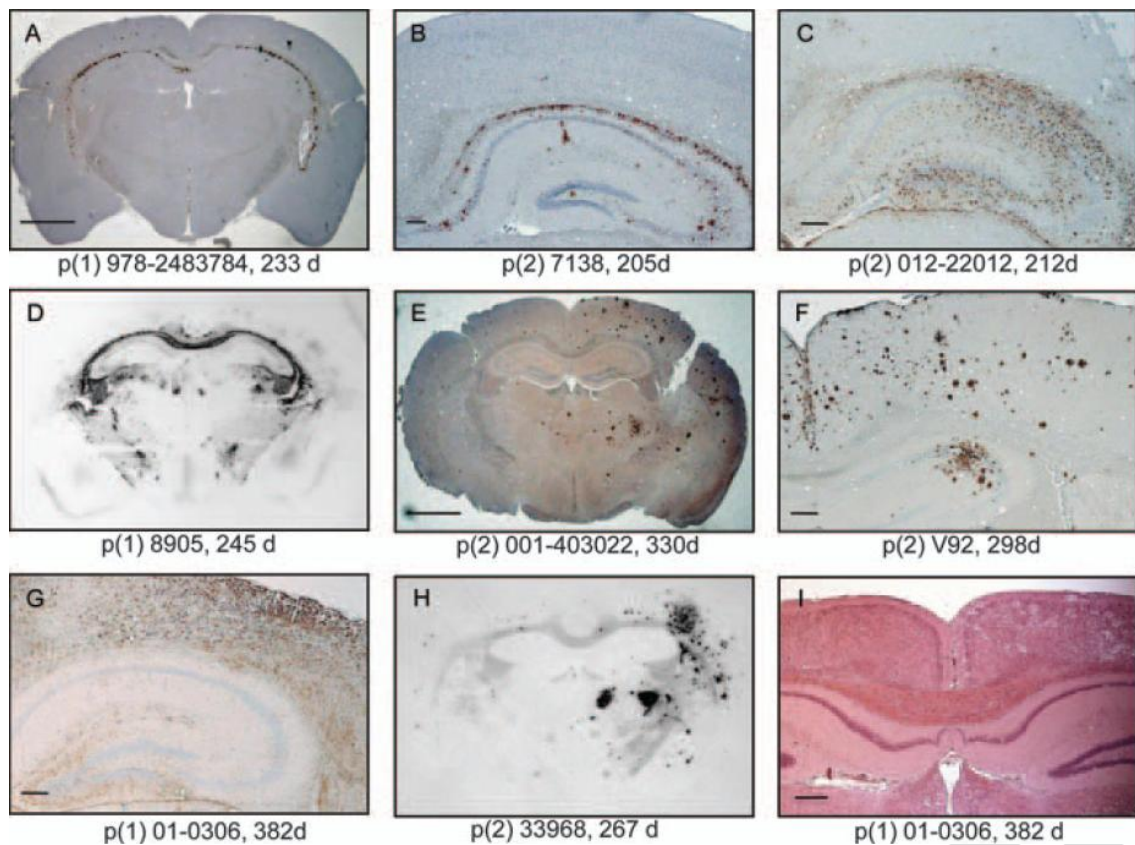


Fig. 3. Representative distributions of CerPrP^{Sc} in the brains of diseased Tg(CerPrP)1536^{+/-} mice. Sections encompassing the hippocampus and cortex were analyzed by IHC using anti-PrP mAb 6H4 (**A**, **B**, **E**, and **F**) or by using antibodies against glial fibrillary acidic protein (**C** and **G**). (**D** and **H**) CerPrP^{Sc} distribution was evaluated by histoblotting of coronal sections of similar regions. (**I**) Asymmetrical distribution of cortical florid plaques and associated neuronal vacuolation in CWD2-infected mice. Scale bars in (**A**) and (**E**), 1 mm; in (**B**), 50 μ m; in (**C**), (**F**), (**G**), and (**I**), 100 μ m. Isolate passage number (p) and incubation times of mice are shown (d, days).