# Prion pathogenesis is independent of caspase-12

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 The pathogenic mechanism(s) underlying neurodegenerative diseases associated with protein misfolding is unclear. Several studies have implicated ER stress pathways in neurodegenerative conditions, including prion disease, amyotrophic lateral sclerosis, Alzheimer?s disease and many others. The ER stress response and upregulation of ER stress-responsive chaperones is observed in the brains of patients affected with Creutzfeldt-Jacob disease and in mouse models of prion diseases. In particular, the processing of caspase-12, an ER-localized caspase, correlates with neuronal cell death in prion disease. However, the contribution of caspase-12 to neurodegeneration has not been directly addressed in vivo. We confirm that ER stress is induced and that caspase-12 is proteolytically processed in a murine model of infectious prion disease. To address the causality of caspase-12 in mediating infectious prion pathogenesis, we inoculated mice deficient in caspase-12 with pr