Spontaneous Prion Disease in Transgenic Mice and Implications for Sporadic CJD

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Currently, there are no animal models of sporadic Creutzfeldt-Jakob disease (CJD), and attempts to generate mouse models of familial CJD have been largely unsuccessful. Such models are urgently needed in order to understand how prions replicate in the brain and for testing candidate anti-prion therapeutics. Serendipitously, we have discovered that transgenic (Tg) mice expressing wild-type bank vole prion protein (BvPrP) develop a spontaneous neurological disease that is reminiscent of sporadic CJD. Tg(BvPrP) mice recapitulate numerous neuropathological hallmarks of CJD including spongiform degeneration, elevated levels of activated astrocytes, and PrP deposition. Moreover, this disease could be transmitted to young Tg(BvPrP) mice and to transgenic mice over-expressing mouse PrP, confirming the presence of prions in the brains of spontaneously sick Tg(BvPrP) mice. This is the first demonstration that a wild-type PrP sequence can lead to the spontaneous generation of prions *in vivo*. Thus, Tg(BvPrP) mice may be useful for studying the spontaneous formation of prions, which may provide insight into the etiology of sporadic CJD.