

Methods to detect prion or PrP-Sc protein as an indication of transmissible spongiform encephalopathies (TSEs) are described. In one aspect, the invention is directed to monoclonal antibodies that specifically bind a conserved epitope of prion proteins and use of the antibodies in immunoassays to detect PrP-Sc, in fixed or unfixed tissue, as an indication of the presence of TSE infection. In another aspect, the invention is directed to a monoclonal antibody cocktail having the monoclonal antibody in combination with a second monoclonal antibody which specifically binds to a second conserved epitope of prion proteins. One or both monoclonal antibodies of the cocktail can recognize epitopes found in all mammalian species in which a natural TSE has been reported and in a number of closely related species. Thus, the antibody cocktail provides high sensitivity, defined specificity, and broad reactivity to PrP proteins in spite of interspecies and intraspecies variation of species such as ruminant livestock, cats, mink, humans, and non-human primates.