Abstract:
Transmissible spongiform encephalopathies (TSEs) are fatal neurodegenerative diseases that include Creutzfeldt-Jakob disease, bovine spongiform encephalopathy and sheep scrapie. Although one of the earliest events during TSE infection is the cellular uptake of protease resistant prion protein (PrP-res), this process is poorly understood due to the difficulty of clearly distinguishing input PrP-res from either PrP-res or protease-sensitive PrP (PrP-sen) made by the cell. Using PrP-res tagged with a unique antibody epitope, we examined PrP-res uptake in neuronal and fibroblast cells exposed to three different mouse scrapie strains. PrP-res uptake was rapid and independent of scrapie strain, cell type, or cellular PrP expression, but occurred in only a subset of cells and was influenced by PrP-res preparation and aggregate size. Our results suggest that PrP-res aggregate size, the PrP-res microenvironment, and/or host cell-specific factors can all influence whether or not a cell takes up PrP-res following exposure to TSE infectivity.