

Figure S1. Representative photomicrographs illustrating a scoring system for astroglial activation in murine scrapie based on glial fibrillary acidic protein (GFAP) immunohistochemistry. (A) Score 1 (*posterior medial cerebral cortex*, parvalbumin (PV)^{-/-}, mock-inoculated); single reactive fibrillary astrocytes within the neuropil (not to be confounded with reactive perivascular astrocytes also found in healthy, not inoculated animals). (B) Score 2 (*hypothalamus*, PV^{-/-}, scrapie-infected); moderate number of reactive fibrillary astrocytes and low background of GFAP positive astrocytic processes in the neuropil. (C) Score 3 (*anterior medial cerebral cortex*, PV^{-/-}, scrapie-inoculated); moderate to high number of reactive fibrillary astrocytes and high background of GFAP positive astrocytic processes in the neuropil. (D) Score 4 (*posterior medial cerebral cortex*, PV^{-/-}, scrapie-infected); high number of reactive astrocytes with transition features towards gemistocytic astrocytes and high background of GFAP positive astrocytic processes in the neuropil. (E) Score 5 (*hippocampus*, PV^{-/-}, scrapie-inoculated); high number of highly reactive gemistocytic astrocytes and high background of GFAP positive astrocytic processes in the neuropil. Score 0 (no reactive fibrillary astrocytes within the neuropil) has been omitted from the figure. Scale bar in (A) indicates 25 μm .

Figure S2. Representative photomicrographs illustrating a scoring system for pathological isoform of the prion protein (PrP^{Sc}) deposition in murine scrapie based on PrP^{Sc} immunohistochemistry. (A) Score 1 (*hypothalamus*, parvalbumin (PV)^{-/-}, scrapie-infected); mild, loosely distributed, granular deposition of PrP^{Sc}. (B) Score 2 (*superior colliculus*, PV^{-/-}, scrapie-infected); moderate deposition of PrP^{Sc}. (C) Score 3 (*posterior medial cerebral cortex*, PV^{-/-}, scrapie-infected); strong, confluent deposition of PrP^{Sc}. Score 0 (no deposition of pathological PrP protein) is not shown. Scale bar in (A) corresponds to 25 μm .



