Prion diseases are caused by protein misfolding in the brain that lead to progressive and fatal symptoms similar to those of Alzheimer's or Parkinson's. At this time there is no effective therapy for prion diseases, but recent studies have found that the endocannabinoid system (ECS) may hold therapeutic potential due to anti-inflammatory, antioxidant and neuro-protective activities. However, no studies have examined the effect of prion disease on the ECS. The goal of this study was to examine the immunohistochemical (IHC) expression of a cannabinoid receptor in the brain, cannabinoid receptor 1 (CBR1) in prion infected mice. Mice infected with scrapie, a prion variant that presents primarily in sheep, were sacrificed and their brain tissues stained using IHC to determine the relative abundance of CBR1 in prion infected tissues compared to a prion negative control. Based on previous ECS studies, we hypothesized that prion infection will result in decreased brain CBR1 expression due to neuronal loss and the detrimental impact of misfolded prions on neurotransmitter release and synaptic plasticity. We found, however, that the CBR1 expression was upregulated in prion-positive animals and hypothesize that this is due to the proposed benefits of such upregulation and a possible ability to help oppose the negative effects of the disease.