Epilepsy is a neurological disorder characterized by unprovoked seizures that affects 50 million people worldwide. Epilepsy can be genetic, or acquired subsequent to a single episode of a prolonged continuous seizure (>5min), also known as status epilepticus (SE). SE provokes modifications in the vulnerable hippocampal circuitry associated with neuronal and spine loss along with excitatory-inhibitory imbalances that result in seizures and temporal lobe epilepsy. We are interested in defining the role of microglia, the brain’s immune cells and professional phagocytes, in the synaptodendritic pathology associated with the construction of epileptic networks. Specifically, we focus on the role of phagocytic signaling molecules such as those from the immune classical complement cascade C1q-C3 along with the microglial phagocytic receptor Triggering Receptor Expressed On Myeloid Cells 2 (Trem2). We recently found significant alterations of C1q, C3b and Trem2 phagocytosis-signaling molecules in cortical brain tissues surgically resected from patients with drug-resistant epilepsy and in an experimental model of SE and acquired epilepsy. In parallel, we found pronounced microglia-dendritic interactions in association with some of phagocytic complement proteins. Our findings also demonstrated a significant correlation between complement activation and seizure progression suggesting the possibility that aberrant microglial phagocytic mechanisms contribute to epileptogenesis.