The role of immune cells in repair of the central nervous system (CNS) has been a subject of controversy for decades. We recognized that innate immune cells (macrophages/microglia) play an essential part in CNS recovery from axotomy. Subsequently, we found that T cells recognizing CNS-specific antigens are needed for CNS maintenance and repair. We formulated the concept of "protective autoimmunity," and showed that the role of autoimmune T cells, via their cytokines, is to "shape" resident microglia, produce growth factors, and recruit activated dendritic-like cells from the bone marrow to the damaged CNS, where they promote neuronal survival and renewal. Using several animal models of acute and chronic CNS degeneration, we demonstrated that well-controlled boosting/modulation of the immune response can serve as immune-based therapies for arresting degeneration and inducing repair. While investigating the functions of immune cells in pathological conditions we made the surprising discovery that they also play a vital role in the healthy CNS, where they help to maintain cognitive and mental activities as well as neurogenesis. Our results point to a novel mechanism by which systemic factors affect healthy CNS plasticity including neurogenesis. They also suggest a link between a decline in cognitive ability and age-related changes in immune activity.