Preface

Amyotrophic lateral sclerosis (ALS) is an unremitting neurological syndrome affecting motor neurons and is characterized by progressive motor neuron loss in the brain and spinal cord. The most challenging symptom of ALS is respiratory muscle failure, which limits survival time to 2–5 years after disease initiation. To date, only supportive care is available for ALS patients, as no effective treatment or cure has been discovered, and those that have been suggested have a very limited efficacy in either decreasing progression or increasing survival. Therefore, there is a dire need for new therapeutics that will not only stop ALS progression but also provide a cure. The cause of ALS is multifactorial. Recent studies, including ours, have indicated that the immune system plays an active role in ALS progression. Neuroinflammation is the most prominent pathological feature. It is associated with motor neuron loss characterized by monocyte and T cell infiltration, microglial activation, and astrogliosis. CD8+ T cells have been found in the spinal cord of ALS mice and ALS patients, and activated CD8+ T lymphocytes infiltrating the central nervous system of SOD1G93A mutant ALS mice have also been found. Eliminating CD8+ T cells in these mice decreased spinal motor neuron loss. In addition, CD8+ T cells selectively killed motor neurons through peptide–major histocompatibility I complex recognition. Natural killer (NK) cells were also found to be elevated in the peripheral blood of ALS patients and could play a major role in ALS progression. NK-cell-mediated cytotoxicity was also found to be elevated in ALS patients. Although the studies in mice with one dominant mutation are very timely and important, they may not completely represent the disease in humans, for which many gene mutations have been implicated. For these reasons, studies should be conducted to comprehensively establish the function of different immune subsets in ALS patients to determine which main subsets could likely contribute to disease induction and progression and to delineate the interaction between different immune subsets.

In the first of three articles published in this special issue, the authors have not only established the mechanisms by which CD8+ T cells attack motor neurons, but have also proposed the mechanisms underlying the interplay between NK cells and CD8+ T cells that leads to an increase in specific CD8+ T cell activation. In the second article, a therapeutic modality using probiotic bacteria to sway the secretion of anti-inflammatory cytokines to combat the increased pro-inflammatory cytokine interferon-gamma, which is known to be increased in ALS patients, is presented. Finally, in the last article, a longitudinal case study comparing an ALS patient with a genetically identical healthy twin is presented. This study demonstrates some treatment strategies that were used to decrease the function of CD8+ T cells to slow disease progression. The results presented in these three papers provide a road map for future work targeting and taming the function of CD8+ T cells in ALS to achieve therapeutic success.

REFERENCES


