Modulating neural stem cell Fas expression in EAE

Charles Hackett[1], Julia Knight[2], Yang Mao-Draayer MD, PhD[1]
[1]Department of Neurology, University of Vermont College of Medicine, Burlington, VT 05405
[2]Neuroscience Graduate Program, University of Vermont, Burlington, VT 05405

MS is a chronic debilitating disease characterized by multifocal lesions of the white matter and a variable clinical course. MS commonly presents first as a relapsing-remitting disease and later progresses to a state of chronic neurodegeneration with white matter loss and cognitive decline. Neural stem/progenitor cell (NPC) transplantation holds significant promise as a novel treatment strategy for MS. Although studies have shown that NPC transplantation is beneficial in the established animal model of MS (experimental autoimmune encephalomyelitis or EAE); it is unclear whether NPCs have the ability to integrate into the host CNS and replace lost cells or if their main mechanism of action is via bystander support of resident tissue. Using the EAE model and a mutant strain of NPCs (*lpr*), we investigated the effects of altering the Fas system in NPC transplantation therapy. Understanding the mechanisms by which NPCs exert beneficial effects as well as exploring methods of increasing post-transplantation survival and differentiation is critical to advancing this treatment strategy. We show the transplantation of NPCs into EAE mice ameliorates clinical symptoms with greater efficacy than sham treatments regardless of cell type (*wt* or *lpr*). Mice treated with NPC transplantation via retro-orbital injections showed significantly decreased inflammatory infiltrates and clinical scoring (indicative of increased treatment efficacy) at the acute time point with similar findings observed at the chronic time point. As minimal numbers of NPCs enter the CNS and these cells do not express terminal differentiation markers, our results suggest NPCs mainly exert their effects via bystander and peripheral immunomodulation as opposed to direct cell replacement.