ANTI-IL-16 THERAPY REDUCES CD4+ T CELL INFILTRATION AND IMPROVES PARALYSIS AND HISTOPATHOLOGY OF RELAPSING EAE

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Infiltration of the CNS by CD4+ Th1 cells precedes onset and relapses of experimental autoimmune encephalomyelitis (EAE). We reported that (B6 x SJL) F1 (H-2b/s) mice, with severe relapsing-remitting disease, had extensive infiltration by CD4+ T cells compared to C57BL/6 (B6) (H-2b) mice, which developed mild low-relapsing disease in response to myelin oligodendrocyte peptide 35-55 (MOG35-55). This observation led us to search for mechanisms that specifically regulate trafficking of CD4+ cells in relapsing H-2b/s mice. In this report we show that the CD4+ cell chemoattractant cytokine IL-16, has an important role in regulation of relapsing EAE induced by MOG35-55 in the (B6 x SJL) F1, (H-2b/s) mice. We found production of IL-16 within the CNS of mice with EAE. Levels of IL-16 in the CNS correlated well with the extent of CD4+ T cells and B cells infiltration during acute and relapsing disease. Production of IL-16 was observed by infiltrating CD4+ T cells, CD8+ T cells and B cells. Treatment with neutralizing anti-IL-16 antibody successfully reversed paralysis and ameliorated relapsing disease. In treated mice, diminished infiltration by CD4+ T cells, lesser demyelination and more sparing of axons were observed. Taken together, we show an important role of IL-16 in regulation of relapsing EAE. We describe a novel therapeutic approach to specifically impede CD4+ T cell chemoattraction in EAE, based on IL-16 neutralization. Our findings have high relevance for the development of new therapies for relapsing EAE and potentially MS.