Th17 lymphocytes traffic to the central nervous system independently of \( \alpha_4 \) integrin expression during EAE.

Abstract:

The integrin \( \alpha_4 \beta_1 \) (VLA-4) is used by encephalitogenic T cells to enter the central nervous system (CNS). However, both Th1 and Th17 cells are capable of inducing experimental autoimmune encephalomyelitis (EAE), and the molecular cues mediating the infiltration of Th1 versus Th17 cells into the CNS have not yet been defined. We investigated how blocking of \( \alpha_4 \) integrins affected trafficking of Th1 and Th17 cells into the CNS during EAE. Although antibody-mediated inhibition of \( \alpha_4 \) integrins prevented EAE when MOG(35-55)-specific Th1 cells were adoptively transferred, Th17 cells entered the brain, but not the spinal cord parenchyma, irrespective of \( \alpha_4 \) blockade. Accordingly, T cell-conditional \( \alpha_4 \)-deficient mice were not resistant to actively induced EAE but showed an ataxic syndrome with predominantly supraspinal infiltrates of IL-23R(+)CCR6(+)CD4(+) T cells. The entry of \( \alpha_4 \)-deficient Th17 cells into the CNS was abolished by blockade of LFA-1 (\( \alpha_L \beta_2 \) integrin). Thus, Th1 cells preferentially infiltrate the spinal cord via an \( \alpha_4 \) integrin-mediated mechanism, whereas the entry of Th17 cells into the brain parenchyma occurs in the absence of \( \alpha_4 \) integrins but is dependent on the expression of \( \alpha_L \beta_2 \). These observations have implications for the understanding of lesion localization, immunosurveillance, and drug design in multiple sclerosis.