?? T cells enhance autoimmunity by restraining regulatory T cell responses via an interleukin-23-dependent mechanism.

Mice that lack interleukin-23 (IL-23) are resistant to T cell-mediated autoimmunity. Although IL-23 is a maturation factor for T helper 17 (Th17) cells, a subset of ?? T cells expresses the IL-23 receptor (IL-23R) constitutively. Using IL-23R reporter mice, we showed that ?? T cells were the first cells to respond to IL-23 during experimental autoimmune encephalomyelitis (EAE). Although ?? T cells produced Th17 cell-associated cytokines in response to IL-23, their major function was to prevent the development of regulatory T (Treg) cell responses. IL-23-activated ?? T cells rendered ?? effector T cells refractory to the suppressive activity of Treg cells and also prevented the conversion of conventional T cells into Foxp3(+) Treg cells in vivo. Thus, IL-23, which by itself has no direct effect on Treg cells, is able to disarm Treg cell responses and promote antigen-specific effector T cell responses via activating ?? T cells.