Pathogenic function of bystander T cells in autoimmune encephalomyelitis.

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Abstract

T cells generate antigen-specific immune responses to their cognate antigen as a hallmark of adaptive immunity. Despite the importance of antigen-specific T cells, here we show that antigen non-related, bystander memory-like $CD4^+$ T cells also significantly contribute to autoimmune pathogenesis. Transcriptome analysis demonstrates that interleukin (IL)-1β- and IL-23-prime T cells that express pathogenic T_H17 signature genes such as RORγt, CCR6, and granulocyte macrophage colony-stimulating factor (GM-CSF). Importantly, when co-transferred with myelin-specific 2D2 TCR-transgenic naive T cells, unrelated OT-II TCR-transgenic memory-like T_H17 cells infiltrate the spinal cord and produce IL-17A, interferon (IFN)-γ, and GM-CSF, increasing the susceptibility of the recipients to experimental autoimmune encephalomyelitis in an IL-1 receptor-dependent manner. In humans, IL-1R1^{high} memory $CD4^+$ T cells are major producers of IL-17A and IFN-γ in response to IL-1β and IL-23. Collectively, our findings reveal the innate-like pathogenic function of antigen non-related memory $CD4^+$ T cells, which contributes to the development of autoimmune diseases.