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Role of gut commensal microflora in the development of experimental autoimmune encephalomyelitis.

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Abstract

Mucosal tolerance has been considered a potentially important pathway for the treatment of autoimmune disease, including human multiple sclerosis and experimental conditions such as experimental autoimmune encephalomyelitis (EAE). There is limited information on the capacity of commensal gut bacteria to induce and maintain peripheral immune tolerance. Inbred SJL and C57BL/6 mice were treated orally with a broad spectrum of antibiotics to reduce gut microflora. Reduction of gut commensal bacteria impaired the development of EAE. Intraperitoneal antibiotic-treated mice showed no significant decline in the gut microflora and developed EAE similar to untreated mice, suggesting that reduction in disease activity was related to alterations in the gut bacterial population. Protection was associated with a reduction of proinflammatory cytokines and increases in IL-10 and IL-13. Adoptive transfer of low numbers of IL-10-producing CD25(+)CD4(+) T cells (>75% FoxP3(+)) purified from cervical lymph nodes of commensal bacteria reduced mice and in vivo neutralization of CD25(+) cells suggested the role of regulatory T cells maintaining peripheral immune homeostasis. Our data demonstrate that antibiotic modification of gut commensal bacteria can modulate peripheral immune tolerance that can protect against EAE. This approach may offer a new therapeutic paradigm in the treatment of multiple sclerosis and perhaps other autoimmune conditions.

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