

学位論文の要旨

三 重 大 学

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<p>主論文の題名</p> <p>Interleukin-17 Induces an Atypical M2-Like Macrophage Subpopulation That Regulates Intestinal Inflammation</p> <p>主論文の要旨</p> <p>Interleukin 17 (IL-17) is a pleiotropic cytokine that acts on both immune and non-immune cells and is generally implicated in inflammatory and autoimmune diseases. Although IL-17 as well as their source, mainly but not limited to Th17 cells, is also abundant in the inflamed intestine, the role of IL-17 in inflammatory bowel disease remains controversial. In the present study, by using IL-17 knockout (KO) mice, we investigated the role of IL-17 in colitis, with special focus on the macrophage subpopulations. Here we show that IL-17KO mice had increased susceptibility to DSS-induced colitis which was associated with decrease in expression of mRNAs implicated in M2 and/or wound healing macrophages, such as IL-10, IL-1 receptor antagonist, arginase 1, cyclooxygenase 2, and indoleamine 2,3-dioxygenase. Lamina propria leukocytes from inflamed colon of IL-17KO mice contained fewer CD11b+Ly6C+MHC Class II+ macrophages, which were derived, at least partly, from blood monocytes, as compared to those of WT mice. FACS-purified CD11b+ cells from WT mice, which were more abundant in Ly6C+MHC Class II+ cells, expressed increased levels of genes associated M2/wound healing macrophages and also M1/proinflammatory macrophages. Depletion of this population by topical administration of clodronate-liposome in the colon of WT mice resulted in the exacerbation of colitis. These results demonstrate that IL-17 confers protection against the development of severe colitis through the induction of an atypical M2-like macrophage subpopulation. Our findings reveal a previously unappreciated mechanism by which IL-17 exerts a protective function in colitis.</p>			