

International Symposium 2-4A probiotic strain, *Clostridium butyricum*, induces IL-10 from intestinal macrophages in inflammatory condition to suppress gut inflammation

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The intestinal immune homeostasis is balanced by gut microbiota including beneficial and pathogenic microorganisms. It has been shown that the colonization of a mixture of *Clostridium* species suppresses colitis through the induction of IL-10-producing regulatory T (Treg) cells (Atarashi, et al. Nature 2011). However, it has remained largely unknown which specific bacteria influence IL-10-producing macrophage/dendritic cell phenotypes *in vivo*. After this discovery, we recently confirmed that in the physiological conditions monoassociation of *Clostridium butyricum* (CB), which is a distinct strain of *Clostridium* species, induces IL-10-producing Treg cells. In contrast, in colitic conditions, CB induced IL-10 production by intestinal macrophages and prevented acute experimental colitis, while the number of IL-10-producing Treg cells was not altered. IL-10-mediated anti-inflammatory effect of CB was retained in lymphocyte-deficient *Rag2*^{-/-} mice, but abolished in macrophage-specific IL-10^{-/-} mice. CB directly induced IL-10 production by intestinal macrophages via TLR2/MyD88 pathway. Furthermore, administration of heat-killed CB also prevented the development of colitis. Consistent with these data from our animal model, we confirmed that IL-10 was markedly induced from CD14⁺ macrophages obtained from inflamed mucosa of human IBD patients. Collectively, a single strain of *Clostridium* species, CB, indirectly and directly induces IL-10 production in intestine that regulates the gut homeostasis and intestinal inflammation, respectively, and might be a feasible probiotic for inflammatory bowel diseases. We are under way to conduct several human trials to investigate a possibility to apply this probiotic to maintain remission stage of ulcerative colitis.