Small intestinal microbes act in concert to exacerbate autoimmune inflammation in the central nervous system

Eiji Miyauchi and Hiroshi Ohno
Laboratory for Intestinal Ecosystem, RIKEN Center for Integrative Medical Sciences

Accumulating evidence indicates that gut microbes play a role in pathogenesis of autoimmune diseases including multiple sclerosis (MS). Here, we show that two distinct gut microbial signals coordinately activate myelin oligodendrocyte glycoprotein (MOG)-specific autoreactive T cells in the small intestine (SI). After induction of experimental autoimmune encephalomyelitis (EAE), an animal model for MS, MOG-specific CD4 T cells can be observed in the SI. Germ-free (GF) mice monocolonized with SI microbes demonstrated that a newly isolated Erysipelotrichaceae strain adheres to SI epithelial cells and acted like adjuvant to antigen-nonspecifically enhance Th17 responses, via inducing serum amyloid A and IL-23, that were associated with an increased susceptibility to EAE. Shotgun sequencing of SI contents revealed that a *Lactobacillus* strain possesses potential mimicry peptides to MOG. While monocolonization of GF mice with the *Lactobacillus* strain did not enhance EAE development or severity, co-colonized mice with Erysipelotrichaceae and *Lactobacillus* strains resulted in more severe EAE than Erysipelotrichaceae-monocolonization. These data suggest that the several SI microbes with a different role in the pathogenesis of MS might be therapeutic targets or provide preventive strategies for the disease, and we need to consider the synergistic effects on the pathogenesis by these microbes.