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Induction of Treg cells by commensal bacteria in the human gut

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ABSTRACT

The mammalian intestinal tract is colonized by trillions of commensal bacteria that shape complex and dynamic community, termed the gut microbiota. The gut microbiota plays an important role in modulating immune responses. Imbalances in the structure of the gut microbiota lead to immune disorders and result in inflammatory and allergic states. We previously reported that strains from the murine indigenous gut microbiota can induce CD4⁺Foxp3⁺ regulatory T (Treg) cells. Here we demonstrate that Treg cell-inducing strains rationally isolated from the human indigenous microbiota. Starting from a healthy human fecal sample, a sequence of selection steps were applied to obtain gnotobiotic mice colonized with a human microbiota enriched in Treg-inducing strains. We cultured and selected 17 strains of bacteria, belonging to the order Clostridiales. When the mixture of 17 strains was inoculated into germ-free mice, we observed a strong accumulation of Treg cells in the intestine. And also the expression levels of interleukin (IL)-10, CTLA-4 and ICOS were dramatically increased in Treg cells. Furthermore, oral administration of 17 strains attenuated disease in adult mouse models of colitis and allergic diarrhea. Use of these bacterial mixes could allow for tailored therapeutic manipulation of human immune disorders.