

GUT MICROBIOTA

Selecting Clostridia strains that induce T_{REG} cells from gut microbiota

Previous work has shown that a combination of Clostridia strains isolated from mice could induce regulatory T cells (T_{REG}) in the mouse colon, and that oral administration of these strains could protect mice against colitis and allergic responses. “We started the discussion on how to translate those findings to humans,” says Bernat Olle, one of the authors of a study in *Nature*. “We decided that a first critical step would be to identify whether analogous strains exist in humans and whether they could stimulate the immune system in similar ways.”

To that end, the researchers inoculated mice using a stool sample from a healthy human. A series of selection steps was then used to obtain mice colonized with human microbiota that enhanced the production of T_{REG} cells and other anti-inflammatory molecules. 17 bacterial strains were isolated on the basis of their high potency at inducing T_{REG} cells; genome sequencing demonstrated that these strains all belonged to clusters of *Clostridium* species.

The researchers went on to demonstrate that oral administration of these strains attenuated disease in mouse models of colitis and allergic disease. Interestingly, the study also showed that the combination of bacterial strains was much more potent than any strain on its own.

The team believe that their study is one of the first examples of a rationally selected drug candidate—in that the bacterial strains were selected for on the basis of pharmacologically relevant properties. “Ultimately, we want to test our hypothesis in the clinic; that is, that deficits of these bacteria might contribute to disease, and that reconstituting these bacteria to normal levels might help to restore immune tolerance and resolve chronic inflammatory processes,” Olle concludes.

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Original article Atarashi, K. *et al.* T_{reg} induction by a rationally selected mixture of Clostridia strains from the human microbiota. *Nature* doi:10.1038/nature12331