

# Development of Disease-customized Probiotics for Infection Control and Inflammation Alleviation

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## **Abstract:**

Indigenous microbes inside the host intestine maintain a complex self-regulating community, providing numerous benefits to their host. We aim to develop two commensal microbial species for medical purposes. First, an *Escherichia coli* strain, we named as 'atypical' *E. coli* (atEc) due to its inability to ferment lactose, is extremely resistant to H<sub>2</sub>O<sub>2</sub>, a reactive oxygen species (ROS). Whole genome sequencing analysis revealed that the atEc strain possesses a unique catalase gene, responsible for such a strong H<sub>2</sub>O<sub>2</sub> removal activity. Intestinal inflammation is known to be accompanied with ROS accumulation. When transplanted into the inflamed intestine, atEc alleviated inflammatory symptoms. Expression of *foxp3* gene was elevated, suggesting that atEc can potentially induce the differentiation of colonic T<sub>reg</sub> cells in mouse. Second, we uncovered that *Bacteroides vulgatus*, an abundant member of mouse intestinal microbiota, can suppress infection by *Vibrio cholerae*, an important human pathogen. *B. vulgatus*-depleted mice developed cholera-like symptoms when infected with *V. cholerae*; while germ-free mice monoassociated with cultured *B. vulgatus* is significantly more resistant to the infection. Furthermore, *B. vulgatus* cells killed *V. cholerae* *in vitro*, demonstrating antagonistic relationship between these two species. Together, our results suggest that (i) a commensal microbe with a strong ROS-removing capability has potential to be developed into an inflammation alleviator and (ii) enteric infection is an event that occurs depending on the composition of intestinal microbiota.