Gut microbiota-derived metabolites shape host physiological homeostasis

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Abstract

The gut microbiota form a highly complex ecological community together with host intestinal cells. The so-called gut ecosystem has a profound influence on human physiology, immunology, and nutrition. It has been reported that imbalance in the structure of gut ecosystem could be a risk factor in human disorders including not only gut-associated disorders such as inflammatory bowel disease and colonic carcinogenesis, but also systemic diseases such as metabolic disorders and allergy [1]. However, the molecular mechanisms of the function of gut microbiota through host-microbial crosstalk remain obscure. To this end, we firstly established a highly integrated omics-based approach involving genome, transcriptome, and metabolome analyses to evaluate gut environmental alterations and to highlight the metabolic pathways of the gut microbiota. Applying this novel method to several mouse models, we found that acetate produced from carbohydrate metabolism by probiotic bifidobacteria largely contributes to the protection of mice from enterohaemorrhagic *E. coli* O157:H7 lethal infection through enhancement of gut epithelial barrier function [2]. In addition, we showed that lactate produced from dietary fiber metabolism by lactic acid bacteria accelerates colonic epithelial cell turnover in starvation-refed mice [3]. Furthermore, we demonstrated that butyrate produced from dietary fiber metabolism by *Clostridia* induces the differentiation of naïve T cells into colonic regulatory T cells by epigenetic changes and they suppress colonic inflammation [4]. Besides, lubiprostone (commonly used for the treatment of constipation) ameliorates the progression of chronic kidney disease and the accumulation of uremic toxins by improving the gut microbiota and intestinal environment [5]. Taken together, gut microbiota-derived metabolites consider to be crucial factors to shape host physiological homeostasis.

Biography

Since June 2012, Dr. Shinji Fukuda has been a project leader of gut environmental systems biology and a project associate professor at the Institute for Advanced Biosciences, Keio University, Japan. Dr. Fukuda has been also a chief executive officer (CEO) of MetaGen, Inc. and special project leader of Precursory Research for Embryonic Science and Technology (PRESTO) program in Japan Science and Technology Agency (JST) concurrently since 2015. He obtained his Ph.D. in 2006 at Meiji University, studying the generation of beneficial probiotics via genetic modification approach. Prior to joining Keio University, Dr. Fukuda worked as research fellow in RIKEN Research Center for Allergy and Immunology, Japan, where he established a novel profiling techniques for understanding host-microbial crosstalk in the gut. His main findings, gut-microbiota derived metabolites shape host physiological homeostasis, were published in two nature papers in 2011 and 2013. He has also published over 40 papers in ISI/SCI/Scopus journals and two book chapters. Dr Fukuda is delivered various keynote and plenary lectures both nationally and internationally. He was the recipient of the Young Scientists' Prize, presented by the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology, Japan in 2013.