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Journal Club

A METABOLIC BRIDGE BETWEEN MICROBIOTA AND HUMANS

A holistic picture of our intestinal commensal bacteria, now known as the microbiota, has been unveiled in the past decade by the introduction of next-generation sequencing. Subsequently, the microbiota was shown to influence our health; indeed, altered composition of the microbiota, referred to as dysbiosis, has been observed in many diseases. Thus, during the past few years, we have witnessed many notable research endeavours aiming to identify the role of the microbiota in health and disease. These studies raised questions regarding the mechanism by which the microbiota — residing in the intestinal lumen and without invading the tissues — can affect our systemic physical status. Hence, a specific link needed to be elucidated between the microbiota and our physiological processes, and a study by Mackay and colleagues (Maslowski *et al.*, 2009) provided the first evidence that microbial metabolites can directly affect human health.

> “microbiota-derived metabolites have ‘yin and yang’ effects on our health”

The microbiota has long been known to produce nutrients from the dietary compounds that we ingest. These nutrients include short-chain fatty acids (SCFAs), such as acetate, propionate and butyrate. In 2009, Maslowski *et al.* reported that acetate ameliorates several types of inflammatory responses in the gut, lung and joint. Germ-free mice, which are devoid of the microbiota and hence lack SCFAs, were highly sensitive to intestinal inflammation. Acetate administration prevented such inflammation, and this beneficial effect was abrogated in mice deficient for the acetate G protein-coupled receptor 43 (GPR43).

Following this discovery, several studies showed the impact of SCFAs produced by the intestinal microbiota on various aspects of immune and inflammatory responses in both a positive and negative manner. For example, Wang *et al.* discovered in 2011 that microbial metabolites are converted in the liver to harmful products that can cause cardiovascular disease. Thus, microbiota-derived metabolites have ‘yin and yang’ effects on our health.

Microbiota-associated genes, which are thought to far outnumber human genes, presumably encode unique enzymes that produce so-far-unknown metabolites. By studying these microbial enzymes and their microbiota-derived metabolites, we look forward to further elucidation of the mechanisms of mutualism between the microbiota and humans.

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ORIGINAL ARTICLE Maslowski, K. M. *et al.* Regulation of inflammatory responses by gut microbiota and chemoattractant receptor GPR43. *Nature* **461**, 1282–1286 (2009)
FURTHER READING Wang, Z. *et al.* Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* **472**, 57–63 (2011)