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The Changing Landscape of the Effect of food/diet on the gut Microbiota in Relation to Health and Disease

Tao Zuo*

Department of Medicine and Therapeutics, Institute of Digestive Disease, State Key Laboratory of Digestive Diseases, LKS Institute of Health Science. The Chinese University of Hong Kong, Hong Kong, China

***Corresponding Author:** Tao Zuo, Department of Medicine and Therapeutics, Institute of Digestive Disease, State Key Laboratory of Digestive Diseases, LKS Institute of Health Science. The Chinese University of Hong Kong, Hong Kong, China.

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Over the past decades, more and more forms of disease, including inflammatory bowel disease, obesity, diabetes mellitus and autism, are unraveled to be associated with alterations in the gut microbiota [1]. As the gastrointestinal (GI) tract is the prominent digestive organ, in intimate and frequent contact with ingested foods, there is a growing perception of the roles of different diets and different functional food components on modulating the configuration and metabolic activities of the human gut microbiota, which in turn influence host health. A primary function of the gut microbiota is to process food ingredients so that the products of their biotransformation, either those derived from the food or the metabolites of gut microorgnisms, can be utilized in salutary ways to support myriad aspects of our human biology [2-4].

Among the well-known food derived components linked to microbiota and human health are short-chain fatty acids (SCFA) generated from fermentation of dietary polysaccharides, modified pharmacologic agents from plant flavonoids, and bioactive indoles resulting from tryptophan metabolism [5-7]. Of note, members of the microbiota garner benefit from the processing of host-derived biomolecules, such as bile acid and mucus glycans, and from the products of one another's metabolisms [8,9]. We believe this is a hot topic of active research. It is timely for the scientists to envision in the next decade how food (and ingredients) can be metabolized and biotransformed by the gut microbiota, in parallel modulating the gut microbiota configuration, and how food influences intra- and inter-kingdom interactions between gut microorganisms, hence providing an avenue to accelerate discovery and development efforts to identify functional food products that promote health. Achieving this goal necessitates elucidating the effects of foods/diets on the microbiota of its consumers. Meanwhile, we propose the concept of "personalized food", which is used to deliberately manipulate a microbiota in a selective manner so as to benefit certain facets of host biology, aiming to improve health status in different individuals. Personalized food can operate through providing beneficial substrates for the host or the microbiota for producing biomolecules necessary for a healthy state, by changing the functional capacity of a consumer's gut microbiota, or by acting through a combination of these mechanisms.

Other rising trends comprise the detailed biochemical characterization of components prevalent and consumed across the world, the effect of food preparation and processing on this component profile, and how these components, in isolation and in combination, alter properties of the gut microbiota in association with human health. Recently, a diet low in fiber has been shown to promote the expansion

and activity of colonic mucus-degrading bacteria and colitis by enteric pathogens [10]. Interestingly, neither purified prebiotic fibers nor time-to-time diet oscillations between fiber-rich and fiber-deprived diet alleviate degradation of the mucus layer [10].

The gut microbiota studies have been dominated by gut bacteria, while the viral and fungal component of the gut microbiota received scant investigation. To date, the importance of the gut virome and fungome have been better understood using high-throughput sequencing technologies [11-13]. The virome, which is composed of both eukaryote viruses and bacteriophages that infect bacterial cells, contains a more diverse genetic entity than the gut bacteria but has been much less extensively studied [14,15]. A recent study has demonstrated that a high-fat, high-sucrose western diet can cause an enrichment of *Caudovirales* bacteriophages, major constituent of the gut virome, in obese mice [16]. High-fat diet is also recently uncovered to change fungome and inter-kingdom relationships in the murine gut [17]. Overall, data regarding the effect of different foods (and food ingredients) on the gut virome and fungome in relation to health are scarce. We expect more observational, functional, and mechanistic insights should be gained in the coming years to reveal this enigma.

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