

# Personalized Probiotics Based on Phenotypes and Dietary Habit: A Critical Evaluation

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## Abstract

It is now established that probiotics are strain-dependent, to further advance the concept of probiotic in the maintenance of health and treatment of dysbiosis, the scope of personalized probiotics need to be defined. Currently, probiotic products are marketed worldwide, with the assumption that probiotics with demonstrated health effects work on all people, irrespective of the genetic (ethnicity), environment (geographical location), dietary habit and life style. The effectiveness of probiotics are determined by 1) interactions with prevailing gastrointestinal (GI) commensal microbes, in promoting the establishment of beneficial microbes and elimination of pathogens, 2) Interaction with the host, in achieving a desirable probiotic effect, 3) Interaction with diet, to survive, proliferate and colonize GI, albeit temporary, and in the production of beneficial bioactive metabolites, such as short-chain-fatty acids (e.g. butyric acid), bile acid derivatives and trimethylamines. The benefits acquired from a probiotic are personal, depending on the health status, dietary habit and prevailing GI microbiota. Personalized probiotics should be established to achieve precision administration of specific probiotic effects for targeted population. Globalization and urbanization of human activities have led to merging of dietary habit, thus effective probiotics should evolve in tandem. Ultimately the probiotics of choice should be directed at specific physiological stage, health condition and targeted diseases.

**Keywords:** Microbe-microbe; Microbe-host; Microbe-diet; Cross-talk

## Introduction-Current Probiotics

The concept of probiotics, which impart beneficial effects to the host when consumed in sufficient quantity [1], has come of age. The effectiveness of probiotics in modulation of gut microbiome is widely demonstrated [2,3]. It is generally accepted scientifically and clinically that probiotics are strain dependent [4-8], and thus food regulations in many countries demand the declaration of probiotic strain on the label, as well as to provide scientific and clinical evidences on efficacy and effective dosage. Currently, probiotic products are marketed worldwide, with the assumption that probiotics with demonstrated health effects work on all people, irrespective of their genetic (ethnicity), environment (geographical location), dietary habit and life style. General properties, such as hydrolysis of lactose in milk for lactose intolerant individual is deemed universal. However, the assumption that probiotics work on all people has not been verified scientifically and clinically. There are examples where a selected probiotic strain was demonstrated clinical effective in the prevention and treatment of specific disease [9-10], but studies conducted in other regions (countries), using the same probiotic strain and protocol were not able to confirm the reported effects [11-14]. Could the difference in the clinical outcome be due to confounding factors, such as ethnicity (gene) dietary habit and living environment on the effects of the probiotic strain? This is a relevant question which needs to be verified, to achieve precision administration of a specific probiotic for targeted population. And more importantly, the verification will avoid disillusion and confusion of the general public on the health promoting effects of probiotics.

## Factors Determine Probiotic Effects

The following are factors, which have been demonstrated to determine probiotic effects:

### Microbe-microbe interaction in Gastrointestinal (GI) environment

In the compact space of the GI tract, there reside more than 1,000 types and number  $10^{10}/\text{cm}^3$  of bacteria, some preferentially adhering on the mucosal surface, others in the lumen. Competition, antagonistic, symbiotic, co-metabolic and other interactions are expected in such community. Indeed, some bacteria have been observed to positively co-exist with other defined groups of bacteria [15], whereas other negatively associated [16]. Thus one would expect that the ability of a probiotic to reside in the GI and to interact (cross talk) with the host are determined by the prevailing commensal GI microbiota, and talk (signalling) above the background level of signals from commensals and dietary components to be heard by the host. GI commensal microbiota profile (enterotype) varied across geographical regions in a continuous matter [17-19]. It is apparent that the GI microenvironment and microbial community among Southeast Asian are not favourable for the establishment and proliferation of *Bifidobacterium* and *Bacteroides*, both of each have been suggested to play major roles in maintenance of health and are probiotics [7,20-23]. It is reasonable to assume that *Bifidobacterium* and *Bacteroides* probiotics may need to be administered together with prebiotics (as synbiotic) for people in the South-East Asian. Prebiotics are nondigestible food ingredients (mostly fermentable complex carbohydrates), that selectively stimulate proliferation and/or activity of probiotics and desirable microbiota (bifidobacteria in particular)

already resident in the GI tract [24]. The persistence of an East Asia originated probiotic strain in the GI system of Southeast Asian has been found temporary, disappearing from their GI tract within a week after termination of consumption [25-27].

Probiotics with demonstrated antagonistic interaction with pathogens [28,29] would benefit people living in unhygienic environment but may impart no obvious benefit to people living in modern hygienic cities. Interestingly, GI *Enterococcus faecalis* which is an opportunistic and nosocomial pathogen [30,31] may serve to modulate inflammatory responses of children in unhygienic condition [32,33]. This illustrates the complexity of microbe-host interaction, and co-evolution may lead to establishment of homeostasis in microbiome, providing survival advantage to the host. As such, dysbiosis could occur through disturbance from drugs (antibiotics), dietary change (globalization of dietary habit), mental and physical stresses (work-life).

### Microbe-host interaction

The profile of GI microbiota is closely associated with allergies [34,35] obesity [36,37] diabetes [38,39], gout [40,41], mental health [42,43] and many other physiological dysfunctions of the human host.

Conversely, host gene may not be the major factor determining the overall GI microbiota profile [44,45]. Nevertheless host genes would determine expression of receptors for adhesion of a bacterium on specific site on the GI surface, and response to signals initiated by the bacterium. Different strains of a probiotic bacterium have been demonstrated to adhere differentially on the same GI cell type and between different GI cell types [46,47]. The abundance and persistence of adhered probiotic cells on a segment of GI tract would presumably determine the extent and duration of microbe-host interaction, and resulted in varied probiotic effects.

Children living in highly hygiene condition and delivered with the assistance of modern medical procedures, such as caesarean birth and use of antibiotics, would benefit from probiotics that modulate development of Th1-regulated immunity and dumping of allergic immune responses [48,49]. Whereas children who were born in underdeveloped regions and constantly exposed to environmental pathogens would benefit from probiotics that enhanced pathogen-resistant immunities [50].

Ironically, most of the commercial probiotics are developed in developed countries and marketed in underdeveloped countries under the general banner of "probiotics", without a demonstrated "defined" probiotic effect that is beneficial to the local consumers.

### Microbe-diet interaction

Food components provide the necessary nutrient for GI microbiota and they also determine adhesion and colonization of microbes on GI surface [51,52]. Animal fats preferentially support growth and establishment of Bacteroides, whereas carbohydrates encourage the Prevotella [18,53]. Slow and non-digestible carbohydrates, termed prebiotics could be utilized by selected lactic acid bacteria [54]. Slow and non-digestible complex carbohydrate (e.g. oligosaccharide) and dietary fibre are in general high in Asian diets (in food sources such as beans, legumes, nuts, seeds, sea weeds), while Southeast Asian diets are particularly high in resistant-starch (Barley, Buckwheat, Indica rice, millet, sorghum). It is therefore not surprising that beneficial effects of complex carbohydrate utilizing probiotics, such as *Bifidobacterium*

spp. are amplified among East Asian [18,22] while meat-fat eating European and American may benefit from Bacteroides probiotics [21,23,55]. Selected strains of the respective bacteria group may serve as potent probiotics, if they are not already present among the commensals, for people of different dietary habit.

Fermentation production of short chain fatty acids, such as butyric acid from fibre and oligosaccharides are assumed beneficial [56,57]. Short-chain-fatty acids and other microbial derived metabolites, such as bile acid derivatives [23] and trimethylamines [58] are also communication signals modulating host physiological functions. Typical Asian diets are high in fibre and carbohydrate as compared with typical Western diet, and presumably lead to high production of short-chain-fatty-acids (SCFAs) in their gut [59]. On the other hand, *Lactobacillus plantarum* is linked to butyrogenic pathway through glutamine metabolism, which is rich in Western meaty diet [60]. The choice of probiotic bacteria should depend on the nature and composition of the habitual diet.

### Dietary Globalization

Globalization and urbanization of human activities have led to Asian and Western cultures merging at many sites across the globe affecting lifestyle and diets. The urban Western and East Asian are well nourished and their gut microbiota (Bacteroides-*Bifidobacterium* type) is metabolically more active with simple sugars, amino acids, and lipids; and they suffer more often from allergic and inflammatory diseases. The rural Southeast Asia Prevotella abundant gut microbiome is more involved in digestion of complex carbohydrates [53,59] and they are experiencing more commonly infectious diseases. The effective probiotics should evolve in tandem with the changing dietary habit in a community, based on their phenotype and dietary preference.

### Biomarkers for Tailored Probiotics

Cross talks between microbe and other microbes in the GI tract, and with the human host maintain health status and disease state of the host. There are ample evidences to suggest that gut microbiota profile is largely determined by the dietary habit.

### Conclusion

It is therefore reasonable to assume that dietary habit could serve as the first criterion for selection of probiotics for a specific group of people. This assumption could be verified by faecal microbiome and biomarkers (such as SCFAs, cytokines) in faecal water. Ultimately the probiotics of choice should be directed at specific physiological stage, health condition and targeted diseases.

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