

## Mini Review

# From Gut Microbial Ecogroup to Precision Nutrition and Human Health

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Over the past decade, the gut microbiome has emerged as an important regulator of host immunity and energy metabolism, which is associated with multiple diseases, including inflammatory bowel disease, obesity, diabetes mellitus and autism [1]. Modulation of the human gut microbiota through probiotics, prebiotics, dietary fiber and fecal Microbial Transplant (FMT) are recognized as workable strategies to improve health and prevent disease [2,3]. However, the gut microbiome is malleable and varies significantly from host to host, and thus respond differentially to the same treatment in different individuals [4]. In addition, the human gut microbiota included innumerable compositional members, it is formidable to dissect association *versus* causation with disease pathogenesis and therapeutics. Therefore, in many clinical studies, there were a percentage of participants failed to response the microbiome-based medicine treatment [2]. To enhance the efficacy of precision nutrition intervention for human health, can we parse out a fraction of the gut microbes from the large collection of the gut microbiota to distinguish healthy *versus* diseased individuals, treatment responders *versus* non-responders, which can be further developed as biomarker to predict disease and responsiveness to interventions, and as functional consortium to treat disease?

To work toward such a goal, it is crucial to elucidate how members of the gut microbes, in isolation and in combination, respond when exposed to treatment. Scientists are beginning to develop more advanced ecologically relevant methodologies to reduce the dimensionality of microbiome datasets than the conventional taxon-based analysis to facilitate the identification of functionally important members of gut microbiota in human health and disease. Zhao, et al [5] offered a guild-based analysis by which they identified a group of acetate and butyrate-producing bacterial strains that co-occurred when adapting to increased availability of diverse fermentable carbohydrates. The abundance and evenness of the small functional group could correlate with host clinical outcomes and might be a novel target to manage diabetes. Raman, et al [6] developed a statistical approach to identify 15 co-varying bacterial taxa that exhibited consistently over time in healthy Bangladeshi children, and the co-varying consortium of microbes could be used to distinguish

the microbiota of children with different degrees of undernutrition. By targeting these 15 co-varying microbes, they reconfigured the under-nutrition gut microbial communities toward a healthy profile, through diet intervention. They for the first time testified the concept of ecogroup, which is a sparse covarying unit that may reflect the property of whole microbial community. If an ecogroup can better describe a healthy phenotype, it is tangible to target on a specific “optimal” microbial composition to achieve certain goals, by way of diet modulations or even microbial therapies.

Apart for gut bacteria, the importance of the gut virome and fungome have been better understood using high-throughput sequencing technologies [7-9]. High-fat diet is also recently uncovered to change fungome and inter-kingdom relationships in the murine gut [10]. We also recently reported that fungal species *Candida albicans* and bacteriophages influenced FMT efficacy in recurrent *Clostridium difficile* infections, suggesting that modulations of gut viruses and fungi are also important for successful outcomes [11,12]. Hence, it is imperative for the scientific and clinical communities to consider multi-kingdom interactions and identify combined ‘ecogroups’ that incorporates bacteria, fungi, viruses and other biotic dark matters to define a more accurate ‘healthy microbiota’.

In addition, the gut metabolites are an critical linkage between diet, gut microbiome and the host. Many metabolites largely derived from diet components are also influenced or even produced by the gut resident microbiota [13]. Cirulli, et al [14] used non-targeted metabolomics and whole-genome sequencing to identify metabolic and genetic signatures of obesity and found that the metabolome captures clinically relevant phenotypes of obesity and is a better health predictor than genetic risk. Gasparrini, et al [15] built a sparse model trained using only 15 predictors that comprise microbiome and resistome signatures, which turned out to be highly accurate to distinguish preterm and term infants. These studies highlighted the necessity of integration of multi-omics data to pinpoint keystone factors, which provide targets for dietary and/or clinical interventions to improve health.

To date, the interrelationships between the human genome, the microbiome, the metabolome, the proteome, the epigenome, the transcriptome, and other factors in relation to human health are just unfolding. It is urgent to develop more biostatistics, machine learning, and artificial intelligence algorithms to parse out the sparse ecogroup, which are intimately associated with disease and health. That will pave the way towards precision editing of the microbiome by diet or nutrition strategies. We envision more insights to be gained in the coming years in this field.

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