

Nutritional Metabonomics

Deciphering Nutrition Effects through Metabolic Profiling



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The molecular bases of the interactions between human health and nutrition are being revisited with genomic, transcriptomic, proteomic and metabonomic technologies. These approaches allow the characterization of molecular events at different levels of biological organization. Metabonomics addresses the comprehensive analysis of metabolites in biological matrices. The application of metabonomics in nutrition is promising in defining metabolic health, monitoring nutritional status and identifying biomarkers for early diagnosis of diseases.



Modern nutrition has expanded its mission to providing health and wellness. This positioning has promoted the use of state of the art “omics” techniques providing information on biological processes for the understanding of the interactions between nutrition and health. Metabonomics was defined as “the quantitative measurement of the dynamic multiparametric metabolic response of living systems to pathophysiological stimuli or genetic modifications” [1]. The concept of metabonomics has mainly arisen from applications of nuclear magnetic resonance and mass spectroscopy which allow the acquisition of multicomponent metabolic profiles from biological matrices. Based on the analysis of the “real endpoints” of the physiological regulatory processes, the metabonomic approach is uniquely suited to understand biological functionalities of nutrients and foods.

Nutritional Metabonomics in Practice

We have recently reviewed various applications of metabonomics in nutrition research [2]. Metabonomics is foreseen as a powerful approach for health management through the characterization of metabolic phenotypes or metatypes, which result from the expression of multiple factors being genetic and environmental-dependants. The dietary profile of an individual is itself multifactorial and plays an essential role in the final expression of the metatype. Moreover, metabonomics appears as a well-established approach for risk management providing a holistic analysis of multiple pathways, and the identification of new biomarkers of homeostasis disruption [2].

Metabonomics has already demonstrated its potential for disease diagnosis [3] and toxicity assessment [4]. However, nutritional metabonomics relies on the detection of metabolic changes in healthy populations that are expected to be subtle when compared to those resulting from toxic insults, genetic modifications or a disease state. This challenge appears even more complex when considering that the metabolic response to foods cannot be ascribed to the effect of a single active molecule as for drug metabolism, but to complex mixtures of nutrients. Additional source of complexity is the intra- and inter-individual variability reflected in the metabolism as consequences of genetic polymorphism, metabolic interactions with gut microflora, environmental and lifestyle components, gender, and age for instance. The control of a maximum of these sources of variability with a well designed experimental trial is then crucial to recover relevant metabolic signatures of specific nutritional interventions. This includes a subject selection optimized with pertinent inclusion and exclusion criteria, which is most of the time completed with the collection of data on dietary habits.

Understanding the Complexity of Host-microbiome Interactions

Highly complex animals, such as humans, have a web of interactions with the consortium of gut microorganisms that is the product of a long co-evolution. The symbiotic gut microbiome acts as an extended genome, which represents an important source of metabolic variability in the host. Our gut symbionts exert control on a number of important mammalian metabolic regulatory functions involved in the energy metabolism, biosynthesis and conversion of nutrients [5], and microflora activity can be either associated to metabolic health or various pathophysiological states (fig. 1). It is then of high importance in nutrition to understand and characterize the interactive molecular processes between the host and its microbiome.

The symbiotic relationship that animals have with the microorganisms is well illustrated by Martin *et al.* who describe the effects of different gut flora on the metabolic profiles in a mouse model [6]. It was indeed demonstrated how bile acid changes are correlated with the gut microbial composition and suggest that germfree mice re-colonized with a non-adapted microflora are relatively unable to hydrolyse taurine-conjugated bile acids, with consequent effects on the amount of fat absorbed from diet and its

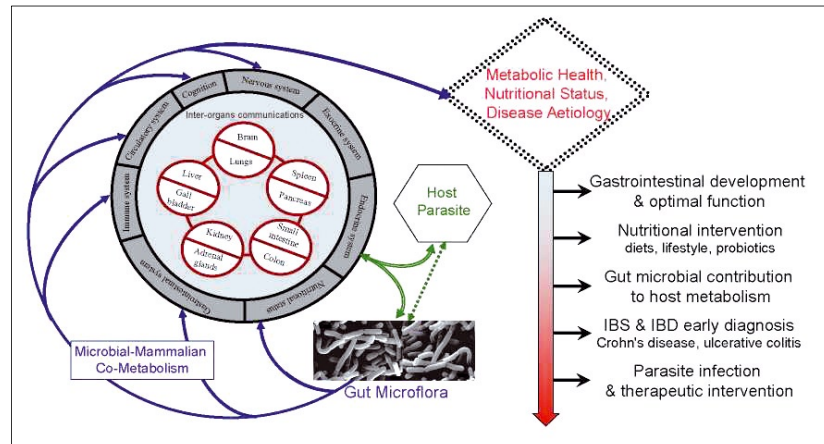


Fig. 1: Schematic representation of host-microbial metabolic interactions and their potential impact on health

distribution within the organisms. Recent publications have also shown that the mammalian-microbe symbiotic relationship may have an implication in the etiology of disorders such as insulin resistance [7], irritable bowel syndrome (IBS) [8] and irritable bowel disease (IBD) [3] and may be contributors to obese phenotypes [5]. In particular, Marchesi *et al.* illustrated the use of metabonomics as a non-invasive technique for the diagnosis and the surveillance of two types of IBD in human subjects [3]. Martin *et al.* have additionally characterized the metabolic phenotypes of mice in a model of *Trichinella spiralis* induced IBS, with which they assessed the effects of a therapeutic intervention with *Lactobacillus paracasei* probiotic on normalizing the metabolic disorders, which was observed at both system and tissue-specific levels [8]. Altogether, these recent metabonomic investigations revealed the considerable potential of the metabonomics approach for monitoring and surveying therapeutic modulation of the mammalian-microbiota interactions.

The Future

Metabonomic-generated data will help understanding the molecular bases of the interactions between nutrition and physiological processes, including the contribution of microbial activity. The holistic feature of the metabonomic analysis opens new opportunities to develop and validate biomarker patterns for the assessment of efficacy and safety aspects of foods at the individual level for maintaining metabolic health. One of the main challenges will be to predict the likelihood of an individual to develop well-defined diseases and to recommend appropriate dietary patterns for delaying the onset of homeostasis disruption. As a strategic approach, the characterization

of metabolotypes could provide a way to define the boundaries of the metabolic health in human populations [2]. The recently developed “pharmaco-metabonomic” concept is based on the ability to predict a post-intervention metabolic profile from a pre-intervention metabolotype [9]. Applied to nutritional interventions, this concept could provide a means to predict dietary responses in individuals as a step towards personalized nutrition.

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